Plus Medicare Part D Formulary Prior Authorization Guidelines

FOREWORD

This document will serve as a reference to assist with administration of clinical and administrative prior authorization (PA) criteria for Part D Standard formulary clients. This document should not be used to determine formulary status or effective date for a PA guideline. To determine formulary status or effective date for a PA guideline, refer to the formulary ASCII and PA ASCII files produced monthly.

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

5HT3 ANTI-NAUSEA AGENT BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ONDANSETRON HCL	ZOFRAN	06055		ROUTE = ORAL
ONDANSETRON	ZOFRAN ODT ZUPLENZ	19058		
GRANISETRON	KYTRIL GRANISOL	07611		ROUTE = ORAL
DOLASETRON	ANZEMET	16576		ROUTE = ORAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding and applies to ORAL forms of these agents only.

GUIDELINES FOR USE

1. Is the prescription written for greater than a 2 days (48 hours) supply?

   If yes, continue to #3.
   If no, continue to #2.

2. Is the prescription written for a full therapeutic replacement for an intravenous anti-emetic drug as part of a cancer chemotherapeutic regimen for use within 48 hours of the patient receiving cancer treatment?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #3. **(CSR: If unknown, ask the caller to submit MRF.)**

3. **Approve for up to 12 months under Part D. (Populate B vs. D field with "D" in the PA override field.)**

RATIONALE
Ensure that any use as a full therapeutic replacement for an intravenous anti-emetic drug as part of a cancer chemotherapeutic regimen within 48 hours of the patient receiving cancer treatment is billed under Part B. The assumption is that any prescription that exceeds a 2 days supply is by default not intended to specifically comply with the Medicare Part B requirement for Part B coverage of antiemetics, and therefore should be covered under Part D, irrespective of the timing relative to chemo (i.e. even if the prescription is filled within 48 hours of chemo).

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5HT3 ANTI-NAUSEA AGENT BVD DETERMINATION (PART D)

FDA APPROVED INDICATIONS

The ORAL FORM OF ZOFRAN and ORAL SOLUBLE FILM ZUPLENZ are indicated for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m^2, with initial and repeat courses of moderately emetogenic cancer chemotherapy, with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen, and prevention of postoperative nausea and/or vomiting.

ORAL KYTRIL is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin, and nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

ORAL ANZEMET is indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses and the prevention of postoperative nausea and vomiting.

REFERENCES

- Glaxo Smith Kline. Zofran® (ondansetron) package insert. Research Triangle Park, NC. September 2009.
- Par Pharmaceuitcals. Zuplenz® (ondansetron) package insert. Woodcliff Lake, NJ. July 2010.
- Roche Laboratories Inc. Kytril® (granisetron) package insert. Nutley, NJ. March 2010.
- Sanofi Aventis U.S. LLC. Anzemet® (dolasetron) package insert. Kansas City, MO. October 2009.
- Antiemesis version 2.2010. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology v 2.2010 [online]. Available at: http://www.nccn.org/professionals/physician_gls/PDF/antiemesis.pdf. [Accessed October 23, 2012].
- American Society of Clinical Oncology Guideline for Antiemetics in Oncology: Update 2006 [online]. Available at: http://jco.ascopubs.org/cgi/content/short/24/18/2932. [Accessed October 23, 2012].
- ACOG (American College Of Obstetrics And Gynecology): Practice Bulletin: Nausea And Vomiting Of Pregnancy. Obstet Gynecol 2004 Apr; 103(4): 803-14.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed October 23, 2012].

Part D Effective: 01/01/13	Created: 09/05	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

ABATACEPT – IV (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ABATACEPT	ORENCIA - IV	33411		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has the treatment been prescribed by or is it being supervised by a rheumatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of rheumatoid arthritis or juvenile idiopathic arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

2. Does the patient have active rheumatoid arthritis?

   If yes, continue to #3.
   If no, continue to #6.

3. Is the patient intolerant to or has the patient tried at least one of the following DMARDS: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

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INITIAL CRITERIA (CONTINUED)

4. Has the patient failed a TNF inhibitor (Enbrel, Humira, Remicade, Simponi, or Cimzia)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

5. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, continue to #10.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

6. Does the patient have juvenile idiopathic arthritis?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of juvenile idiopathic arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

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INITIAL CRITERIA (CONTINUED)

7. Has the patient tried at least one of the following DMARDS: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes continue to #8.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of juvenile idiopathic arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

8. Has the patient failed a TNF inhibitor (Enbrel, Humira or Remicade)?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of juvenile idiopathic arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

9. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, continue to #11.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist for a diagnosis of juvenile idiopathic arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira-which may also require prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

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INITIAL CRITERIA (CONTINUED)

10. For the treatment of RHEUMATOID ARTHRITIS, **approve the initiation of Orencia therapy as follows: (Enter 2 authorizations.)**
    PAC NOTE: For requests for the SQ dosage form of Orencia, please see the Orencia SQ PA Guideline.

    - **Approve maximum #60mL (= 4 vials) per fill for 3 fills with an end date 1 month from today AND,**
    - **Approve maximum #60mL (= 4 vials) per fill for 1 fill per month for 2 months (start date 1 month from today).**
      APPROVAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

11. For the treatment of JUVENILE IDIOPATHIC ARTHRITIS, **approve the initiation of Orencia therapy as follows: (Enter 2 authorizations.)**
    PAC NOTE: For requests for the SQ dosage form of Orencia, please see the Orencia SQ PA Guideline.

    - **Approve maximum #60mL (= 4 vials) per fill for 3 fills with an end date 1 month from today AND,**
    - **Approve maximum #60mL (= 4 vials) per fill for 1 fill per month for 2 months (start date 1 month from today).**
      APPROVAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

RENEWAL CRITERIA

1. Has the patient experienced or maintained a 20% or greater improvement in tender and swollen joint count?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

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RENEWAL CRITERIA (CONTINUED)

2. Is the patient currently on methotrexate or does the patient have a contraindication to methotrexate?

   If yes, **approve for 12 months with a maximum of #60mL (= 4 vials) per month.**
   APPROVAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.
   If no, do not approve.
   DENIAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

RATIONALE
Ensure appropriate diagnostic, utilization and safety criteria are met for the management of requests for abatacept.

FDA APPROVED INDICATIONS
Monotherapy or concomitant use with DMARDs other than TNF antagonists in patients with moderate to severe active rheumatoid arthritis or concomitantly with MTX for moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older.

Adult Rheumatoid Arthritis (RA)
Moderately to severely active RA in adults. ORENCIA may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.

Juvenile Idiopathic Arthritis
Moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older. ORENCIA may be used as monotherapy or concomitantly with MTX.

Important Limitations of Use
Should not be given concomitantly with TNF antagonists.

REFERENCES
- Bristol-Myers Squibb Corp. Orencia package insert. Princeton, NJ. September 2011.
- Orencia. MedImpact P&T Monograph, November 2011.

Part D Effective: 04/01/13 Created: 05/05
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

ABATACEPT – SQ (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ABATACEPT	ORENCIA - SQ	37825		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has the treatment been prescribed by or is it being supervised by a rheumatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is 18 years or older with a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

2. Is the patient 18 years or older?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is 18 years or older with a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

3. Does the patient have active rheumatoid arthritis?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is 18 years or older with a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

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INITIAL CRITERIA (CONTINUED)

4. Is the patient intolerant to or has the patient tried at least one of the following DMARDS: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, that the patient is 18 years or older with a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

5. Has the patient failed a TNF inhibitor (Enbrel, Humira, Remicade, Simponi, or Cimzia)?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, that the patient is 18 years or older with a diagnosis of rheumatoid arthritis; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate.

6. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?
   PAC NOTE: For requests for the IV dosage form of Orencia, please see the Orencia IV PA Guideline.

   If yes, for the treatment of RHEUMATOID ARTHRITIS, **approve the initiation of Orencia therapy for a maximum #4 syringes per month for 3 months (start date today).**
   APPROVAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of rheumatoid arthritis; supervision by a rheumatologist, that the patient is 18 years or older; a trial of one of the following DMARDS (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of a TNF inhibitor (such as Humira or Cimzia-which may also require a prior authorization), and that the patient is currently taking or has a contraindication to methotrexate

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ABATACEPT – SQ (PART D)

RENEWAL CRITERIA

1. Has the patient experienced or maintained a 20% or greater improvement in tender and swollen joint count?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

2. Is the patient currently on methotrexate or does the patient have a contraindication to methotrexate?

   If yes, for the treatment of RHEUMATOID ARTHRITIS, **approve the renewal of Orencia therapy for a maximum #4 syringes per month for 12 months.**
   APPROVAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.
   If no, do not approve:
   DENIAL TEXT: Renewal requires the patient to have experienced or maintained a 20% or greater improvement in tender and swollen joint count or maintained previously documented response and be on methotrexate or has a contraindication to methotrexate.

RATIONALE

Ensure appropriate diagnostic, utilization and safety criteria are met for the management of requests for abatacept. Abatacept subcutaneous administration is only approved for the treatment of adult RA. Abatacept intravenous administration is approved for both treatment of adult RA and juvenile idiopathic arthritis.

FDA APPROVED INDICATIONS

Monotherapy or concomitant use with DMARDs other than TNF antagonists in patients with moderate to severe active rheumatoid arthritis or concomitantly with MTX for moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older.

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ABATACEPT – SQ (PART D)

FDA APPROVED INDICATIONS (CONTINUED)

Adult Rheumatoid Arthritis (RA)
Moderately to severely active RA in adults. ORENCIA may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.

Juvenile Idiopathic Arthritis
Moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older. ORENCIA may be used as monotherapy or concomitantly with MTX.

Important Limitations of Use
Should not be given concomitantly with TNF antagonists.

REFERENCES

- Bristol-Myers Squibb Corp. Orencia package insert. Princeton, NJ. September 2011.
- Orencia. MedImpact P&T Monograph, November 2011.

Part D Effective: 07/01/13 Created: 11/11
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

ABIRATERONE

Generic	Brand	HICL	GCN	Exception/Other
ABIRATERONE ACETATE	ZYTIGA	37571		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic castration-resistant prostate cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic castration-resistant prostate cancer and concurrent prednisone therapy.

2. Will the patient be taking Zytiga in combination with prednisone?

   If yes, **approve for 12 months with a quantity limit of #120 tablets per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic castration-resistant prostate cancer and concurrent prednisone therapy.

RATIONALE
To ensure appropriate use of Zytiga consistent with FDA approved indication.

FDA APPROVED INDICATIONS
Zytiga is indicated for use in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

REFERENCES
- Centocor Ortho Biotech Inc. package insert. Horsham, PA. December 2012.

Part D Effective: 04/01/13 Created: 06/11
Commercial Effective: 04/01/13 Client Approval: 02/13 P&T Approval: 02/13

ADALIMUMAB (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ADALIMUMAB	HUMIRA	24800		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has this drug been prescribed by or is it currently being supervised by a dermatologist, rheumatologist, or gastroenterologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist, rheumatologist, or gastroenterologist and a diagnosis of active rheumatoid arthritis, active psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, chronic plaque psoriasis, moderate to severe Crohn's disease, or moderately to severely active ulcerative colitis.

2. Does the patient have active rheumatoid arthritis?

   If yes, continue to #3.
   If no, continue to #5.

3. Has the patient previously tried or does the patient have a contraindication to at least one of the following DMARDs: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, a diagnosis of active rheumatoid arthritis, a trial of at least one DMARD (disease-modifying antirheumatic drug) such as methotrexate, hydroxychloroquine, leflunomide, or sulfasalazine; and that the patient is currently taking or has a contraindication to methotrexate.

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ADALIMUMAB (PART D)

INITIAL CRITERIA (CONTINUED)

4. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, **approve for one kit (#2 syringes/pens) per month x 3 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, a diagnosis of active rheumatoid arthritis, a trial of at least one DMARD (disease-modifying antirheumatic drug) such as methotrexate, hydroxychloroquine, leflunomide, or sulfasalazine, and that the patient is currently taking or has a contraindication to methotrexate.

5. Does the patient have active psoriatic arthritis?

   If yes, continue to #6.
   If no, continue to #7.

6. Has the patient previously tried or does the patient have a contraindication to at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, **approve for one kit (#2 syringes/pens) per month x 3 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; diagnosis of active psoriatic arthritis and the patient has tried at least one DMARD (disease-modifying antirheumatic drug) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

7. Does the patient have ankylosing spondylitis?

   If yes, **approve for one kit (#2 syringes/pens) per month x 3 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #8.

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INITIAL CRITERIA (CONTINUED)

8. Does the patient have juvenile idiopathic arthritis?

   If yes, continue to #9.
   If no, continue to #11.

9. Has the patient previously tried or does the patient have a contraindication to at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, continue to #10.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of at least one DMARD (disease-modifying antirheumatic drug) such as methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide; and that the patient is currently taking or has a contraindication to methotrexate.

10. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?

    If yes, **approve 1 kit (2 syringes/pens, 20mg/0.4mL if 15-30kg (33-66 lbs) in weight or 40mg/0.8mL if >= 30kg weight) per month x 3 months.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of at least one DMARD (disease-modifying antirheumatic drug) such as methotrexate, hydroxychloroquine, sulfasalazine, or leflunomide; and that the patient is currently taking or has a contraindication to methotrexate.

11. Does the patient have chronic moderate to severe plaque psoriasis?

    If yes, continue to #12.
    If no, continue to #14.

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INITIAL CRITERIA (CONTINUED)

12. Does the plaque psoriasis involve ≥ 10% body surface area (BSA) or do the psoriatic lesions affect the hands, feet, or genital area?

    If yes, continue to #13.
    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a dermatologist; a diagnosis of plaque psoriasis; psoriatic lesions covering greater than 10% of BSA (Body Surface Area) or lesions on the hands, feet, or genital area; and a trial of or contraindication to one or more forms of preferred therapy (e.g., PUVA, UVB, methotrexate or cyclosporine).

13. Has the patient previously tried at least one or more forms of preferred therapy (e.g. PUVA, UVB, acitretin, methotrexate, or cyclosporine)?

    If yes, **approve Psoriasis starter package (contains 4 x 40mg syringes) x 1, then approve 1 kit (#2 syringes/pens) per month x 2 months.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a dermatologist; a diagnosis of plaque psoriasis; psoriatic lesions covering greater than 10% of BSA (Body Surface Area) or lesions on the hands, feet, or genital area; and a trial of or contraindication to one or more forms of preferred therapy (e.g., PUVA, UVB, methotrexate or cyclosporine).

14. Does the patient have a diagnosis of moderate to severe Crohn's disease?

    If yes, continue to #15.
    If no, continue to #16.

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INITIAL CRITERIA (CONTINUED)

15. Has the patient tried one or more conventional therapies for Crohn's disease such as: corticosteroids (i.e. budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine?

    If yes, **approve Crohn's Disease Starter Package (contains 6 x 40mg syringes) x 1, then approve 1 kit (#2 syringes/pens) per month x 2 months.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a gastroenterologist, a diagnosis of moderate to severe Crohn's disease and a trial of one or more conventional therapies for Crohn's disease such as corticosteroids (e.g. methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine.

16. Does the patient have a diagnosis of moderately to severely active ulcerative colitis?

    If yes, **approve for three kits (#6 syringes/pens) x 1, then approve 1 kit (#2 syringes/pens) per month x 2 months.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a dermatologist, rheumatologist, or gastroenterologist and a diagnosis of active rheumatoid arthritis, active psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, chronic plaque psoriasis, moderate to severe Crohn's disease, or moderately to severely active ulcerative colitis.

RENEWAL CRITERIA

1. Does the patient have active rheumatoid arthritis, psoriatic arthritis, or juvenile idiopathic arthritis?

   If yes, continue to #5.
   If no, continue to #2.

2. Does the patient have ankylosing spondylitis?

   If yes, continue to #6.
   If no, continue to #3.

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RENEWAL CRITERIA (CONTINUED)

3. Does the patient have chronic plaque psoriasis?

   If yes, continue to #7.
   If no, continue to #4.

4. Does the patient have Crohn's disease or ulcerative colitis?

   If yes, **approve one kit (#2 syringes/pens) per month x 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, chronic plaque psoriasis, Crohn's disease, or ulcerative colitis.

5. Has the patient experienced or maintained a 20% improvement in tender or swollen joint count while on therapy?

   If yes, process as follows:
   - For rheumatoid arthritis, continue to #8.
   - For psoriatic arthritis, continue to #9.
   - For juvenile idiopathic arthritis, **approve one kit (#2 syringes/pens) per month x 12 months.**
     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   RHEUMATOID ARTHRITIS DENIAL TEXT: Renewal for the diagnosis of rheumatoid arthritis requires that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy and concurrent methotrexate therapy or a contraindication to methotrexate.
   PSORIATIC ARTHRITIS DENIAL TEXT: Renewal for the diagnosis of psoriatic arthritis requires and a 20% improvement in tender or swollen joint count while on therapy.
   JUVENILE IDIOPATHIC ARTHRITIS DENIAL TEXT: Renewal for the diagnosis of juvenile idiopathic arthritis requires that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy.

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RENEWAL CRITERIA (CONTINUED)

6. Has the patient experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Renewal for the diagnosis of ankylosing spondylitis requires at least a 50% improvement or increase of 2 units from baseline on the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index).

7. Has the patient achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more?

   If yes, **approve two kits (#4 syringes/pens) per month x 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Renewal requires that the patient has achieved clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more.

8. Is the patient taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Approval for the diagnosis of rheumatoid arthritis requires a 20% improvement in tender or swollen joint count and concurrent methotrexate therapy or a contraindication to methotrexate.

9. Is the dose of Humira 40mg **every other week**?

   If yes, **approve one kit (#2 syringes/pens) per month x 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #10.

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RENEWAL CRITERIA (CONTINUED)

10. Has the patient tried and failed at least a 3-month trial of Humira 40mg every other week?

    If yes, continue to #11.
    If no, do not approve. **Enter a proactive authorization for 12 months one kit (#2 syringes/pens) per month.**

    DENIAL TEXT: Renewal of Humira at the dose requested requires at least a 3-month trial of Humira 40mg every other week. Consider trial of this agent at once every other week dosing. Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

11. Is the prescribed dose of Humira 40mg **every week**?

    If yes, **approve two kits (#4 syringes/pens) per month x 12 months.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: The dosing schedule requested is not covered for the diagnosis provided.

RATIONALE
Ensure appropriate diagnostic, utilization and safety criteria are used for the management of requests for adalimumab.

FDA APPROVED INDICATIONS
HUMIRA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis and psoriatic arthritis. HUMIRA can be used alone or in combination with methotrexate or other DMARDs.

HUMIRA is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

HUMIRA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adults with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. HUMIRA is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

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ADALIMUMAB (PART D)

FDA APPROVED INDICATIONS (CONTINUED)

HUMIRA is indicated for the treatment of adults with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.

HUMIRA is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical functions in patients with psoriatic arthritis. Humira can be used alone or in combination with DMARDs.

HUMIRA is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older. HUMIRA can be used alone or in combination with methotrexate.

HUMIRA is indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of HUMIRA has not been established in patients who have lost response to or were intolerant to TNF blockers.

Dosing:

Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis
40 mg every other week. Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.

Juvenile Idiopathic Arthritis
15 kg (33 lbs) to <30 kg (66 lbs): 20 mg every other week
≥30 kg (66 lbs): 40 mg every other week

Crohn's Disease and Ulcerative Colitis
Initial dose (Day 1) is 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days), followed by 80 mg two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg every other week.

Plaque Psoriasis
80 mg initial dose followed by 40 mg every other week starting one week after initial dose.

DOSAGE FORMS AND STRENGTHS
40 mg/0.8 mL in a single-use prefilled pen (HUMIRA Pen)
40 mg/0.8 mL in a single-use prefilled glass syringe
20 mg/0.4 mL in a single-use prefilled glass syringe

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REFERENCES

- Abbott Laboratories. Humira product information. North Chicago, IL. September, 2011.
- Bristol-Myers Squibb. Orencia product information. Princeton, NJ. November, 2009.
- Felson D, Anderson J, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum 1995; 38:727-35.
- Mease P, Gladman D, Ritchlin C, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis. Arthritis and Rheumatism 2005; 52:3279-89.
- Braun J, Davis J et al.. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with ankylosing spondylitis. Ann Rheum Dis. 2006; 65(3):316-20.
- Hanauer SB, Sandborn WJ, Rutgeerts P, et al. Human Anti-Tumor Necrosis Factor Monoclonal Antibody (Adalimumab) in Crohn's Disease: the CLASSIC-I Trial. Gastroenterology. 2006; 130: 323-333.
- Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for Maintenance of Clinical Response and Remission in Patients With Crohn's Disease: The CHARM Trial. Gastroenterology. 2007; 132: 53-65.
- Papadakis KA, Shaye OA, Vasiliauskas EA, et al. Safety and Efficacy of Adalimumab (D2E7) in Crohn's Disease Patients with an Attenuated Response to Infliximab. Am J Gastro. 2005; 75-79.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed: June 22, 2010].

Part D Effective: 01/01/13 Created: 05/03
Commercial Effective: N/A Client Approval: 11/12 P&T Approval: 11/12

ADO-TRASTUZUMAB EMTANSINE

Generic	Brand	HICL	GCN	Exception/Other
ADO-TRASTUZUMAB EMTANSINE	KADCYLA	40046		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

2. Is the patient's breast cancer HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

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GUIDELINES FOR USE (CONTINUED)

3. Has the patient received prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or developed disease recurrence during or within six months of completing adjuvant therapy?

   If yes, **approve for 12 months with a fill limit of 12 fills of #2 vials per 21 day supply.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask you doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

RATIONALE
To ensure appropriate use aligned with FDA approved indications and NCCN guidelines.

The recommended dose of Kadcyla is 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. Do not administer Kadcyla at doses greater than 3.6 mg/kg. Do not substitute Kadcyla for or with Herceptin. Administer infusion over 90 minutes for first dose. Patients should be observed during the infusion and for at least 90 minutes following the initial dose for fever, chills, or other infusion related reactions. Subsequent infusions can be administered over 30 minutes if prior infusions were well tolerated. Patients should be observed during the infusion and for at least 30 minutes after infusion.

If a planned dose is delayed or missed, it should be administered as soon as possible; do not wait until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses. The infusion may be administered at the dose and rate the patient tolerated in the most recent infusion. The infusion rate of Kadcyla should be slowed or interrupted if the patient develops an infusion-related reaction. Permanently discontinue Kadcyla for life-threatening infusion related reactions.

Management of increased serum transaminases, hyperbilirubinemia, left ventricular dysfunction, thrombocytopenia, pulmonary toxicity or peripheral neuropathy may require temporary interruption, dose reduction, or treatment discontinuation of Kadcyla. The first dose reduction is to 3mg/kg, followed by a reduction to 2.4mg/kg. Any further reduction should result in discontinuation of treatment.

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RATIONALE (CONTINUED)

A reduction in the dose is recommended in the case of hepatotoxicity signaled by increases in serum transaminases and/or hyperbilirubinemia or in the case of Grade 4 thrombocytopenia (platelets < 25,000/mm^3). Temporary discontinuation is recommended for patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. Permanent discontinuation is advised for patients with serum transaminases > 3 x ULN and concomitant total bilirubin > 2 x ULN; patients diagnosed with nodular regenerative hyperplasia (NRH), interstitial lung disease (ILD), or pneumonitis.

Kadcyla (ado-trastuzumab emtansine) is a HER2-targeted antibody-drug conjugate of Herceptin (trastuzumab) and DM1, a microtubule inhibitor. DM1 is too toxic to deliver directly into a patient's bloodstream, like other chemotherapy drugs. The Herceptin component of Kadcyla targets and delivers DM1 directly into cancer cells, sparing noncancerous cells. Upon binding to sub-domain IV of the HER2 receptor, ado-trastuzumab emtansine undergoes receptor-mediated internalization and subsequent lysosomal degradation, resulting in intracellular release of DM1-containing cytotoxic catabolites. Binding of DM1 to tubulin disrupts microtubule networks in the cell, which results in cell cycle arrest and apoptotic cell death.

Breast cancer is the most common cancer among women and the second leading cause of cancer death. An estimated 232,340 Americans will be diagnosed with breast cancer and another 39,620 will die of it in 2013. The most common risk factors are female gender and increasing age. The five year survival rate for metastatic breast cancer is 15%. In HER2-positive breast cancers, the increased amount of the protein contributes to cancer call growth and survival. Nearly 20% of breast cancers have increased amounts of HER2.

The National Comprehensive Cancer Network (NCCN) guidelines recommend Perjeta (pertuzumab) with Herceptin and a taxane (either docetaxel or paclitaxel) as the preferred first-line therapy for HER2 positive metastatic breast cancer. Other first-line regimens include Herceptin with: paclitaxel ± carboplatin, docetaxel, vinorelbine, or Xeloda (capecitabine). Regimens for Herceptin-exposed HER2-positive disease include:

- Tykerb + Xeloda
- Herceptin + Xeloda
- Herceptin + Tykerb (without cytotoxic therapy)
- Herceptin + other agents

CONTINUED ON NEXT PAGE

RATIONALE (CONTINUED)

Additional phase III studies may expand upon Kadcyla's initial indication. Kadcyla alone or in combination with Perjeta is being evaluated against Herceptin plus taxane (docetaxel or paclitaxel) in patients with HER2-positive progressive or recurrent locally advanced or previously untreated metastatic breast cancer in the MARIANNE study, with initial results expected in the first half 2014. The TH3RESA study will evaluate Kadcyla with treatment of the physician's choice in patients with metastatic or unresectable locally advanced/recurrent HER2-positive breast cancer previously treated with Herceptin, a taxane, and Tykerb and disease progression after at least two regimens of HER2-directed therapy. Additionally Kadcyla is being studied as adjuvant therapy for HER2-positive breast cancer in the KATHERINE study and for advanced gastric cancer in another trial.

Kadcyla's pivotal trial included in the prescribing information was the EMILIA study; a randomized, multicenter, open-label Phase III trial of 991 patients with HER2-positive, unresectable locally advanced or metastatic breast cancer. Prior taxane and trastuzumab-based therapy was required before trial enrollment. Patients with only prior adjuvant therapy were required to have disease recurrence during or within six months of completing adjuvant therapy. Breast tumor samples were required to show HER2 over expression defined as 3+ IHC or FISH amplification ratio ≥ 2.0 determined at a central laboratory. Patients were randomly allocated (1:1) to receive Tykerb plus Xeloda or Kadcyla. Randomization was stratified by world region (United States, Western Europe other), number of prior chemotherapy regimens for unresectable locally advanced or metastatic disease (0–1, >1) and visceral versus non-visceral disease as determined by the investigators.

Kadcyla was given intravenously at 3.6 mg/kg on Day 1 of a 21-day cycle. Tykerb was administered at 1250 mg/day orally once per day of a 21-day cycle and Xeloda was administered at 1000 mg/m^2 orally twice daily on Days 1−14 of a 21-day cycle. Patients were treated with Kadcyla or Tykerb plus Xeloda until progression of disease, withdrawal of consent, or unacceptable toxicity. At the time of the primary analysis, median time on study drug was 5.7 months for Kadcyla, 4.9 months for Tykerb, and 4.8 months for Xeloda.

The co-primary efficacy endpoints of the study were progression-free survival (PFS) based on tumor response assessments by an independent review committee (IRC), and overall survival (OS). Additional endpoints included PFS (based on investigator tumor response assessments), objective response rate (ORR), duration of response and time to symptom progression.

Patient demographics and baseline tumor characteristics were balanced between treatment arms. The median age was approximately 53 years (range 24-84 years and all but 5 patients were women. Tumor prognostic characteristics including hormone receptor status (positive: 55%, negative: 43%), presence of visceral disease (68%) and non-visceral disease only (33%) and the number of metastatic sites (< 3: 61%, ≥ 3: 37%) were similar in the study arms.

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RATIONALE (CONTINUED)

The majority of patients (88%) had received prior systemic treatment in the metastatic setting. All but one patient received Herceptin prior to study entry; approximately 85% of patients received prior Herceptin in the metastatic setting. Over 99% percent of patients had received a taxane, and 61% of patients had received an anthracycline prior to study entry. Overall, patients received a median of 3 systemic agents in the metastatic setting. Among patients with hormone receptor-positive tumors, 44.4% received prior adjuvant hormonal therapy and 44.8% received hormonal therapy for locally advanced/metastatic disease.

Median progression-free survival as assessed by independent review was 9.6 months with Kadcyla versus 6.4 months with Tykerb plus Xeloda (hazard ratio for progression or death from any cause, 0.65; 95% confidence interval [CI], 0.55 to 0.77; P<0.001), and median overall survival at the second interim analysis crossed the stopping boundary for efficacy (30.9 months vs. 25.1 months; hazard ratio for death from any cause, 0.68; 95% CI, 0.55 to 0.85; P<0.001). The objective response rate was higher with Kadcyla (43.6%, vs. 30.8% with Tykerb plus Xeloda; P<0.001); results for all additional secondary end points favored Kadcyla.

A treatment benefit with Kadcyla in terms of PFS and OS was observed in patient subgroups based on stratification factors, key baseline demographic and disease characteristics, and prior treatments. In the subgroup of patients with hormone receptor-negative disease (n=426), the hazard ratios for PFS and OS were 0.56 (95% CI: 0.44, 0.72) and 0.75 (95% CI: 0.54, 1.03), respectively. In the subgroup of patients with hormone receptor-positive disease (n=545), the hazard ratios for PFS and OS were 0.72 (95% CI: 0.58, 0.91) and 0.62 (95% CI: 0.46, 0.85), respectively. In the subgroup of patients with non-measurable disease (n=205), based on IRC assessments, the hazard ratios for PFS and OS were 0.91 (95% CI: 0.59, 1.42) and 0.96 (95% CI: 0.54, 1.68), respectively; in patients with measurable disease the hazard ratios were 0.62 (95% CI: 0.52, 0.75) and 0.65 (95% CI: 0.51, 0.82), respectively. The PFS and OS hazard ratios in patients who were younger than 65 years old (n=853) were 0.62 (95% CI: 0.52, 0.74) and 0.66 (95% CI: 0.52, 0.83), respectively. In patients ≥ 65 years old (n=138), the hazard ratios for PFS and OS were 1.06 (95% CI: 0.68, 1.66) and 1.05 (95% CI: 0.58, 1.91), respectively.

Kadcyla has boxed warnings for hepatotoxicity, cardiac toxicity, and embryo-fetal toxicity. Warnings and precautions include pulmonary toxicity, infusion-related reactions, hypersensitivity reactions, thrombocytopenia, and neurotoxicity. The most common adverse drug reactions (frequency > 25%) with Kadcyla were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation.

Nursing mothers should discontinue nursing or discontinue Kadcyla taking into consideration the importance of the drug to the mother. Females of reproductive potential should be counseled on pregnancy prevention and planning. These patients are encouraged to participate in the MotHER Pregnancy Registry. Kadcyla is pregnancy category D.

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RATIONALE (CONTINUED)

NCCN considers either immunohistochemistry (IHC) or *in situ* hybridization (ISH) tests as an acceptable method for making an initial determination of HER2 tumor status. Breast cancer tumors are classified as HER2 positive if they are scored as 3+ by an IHC method.

FDA APPROVED INDICATIONS

Kadcyla (ado-trastuzumab emtansine) is indicated, as a single agent, for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

REFERENCES

- Kadcyla [Prescribing Information]. South San Francisco, CA: Genentech, Inc.; February 2013.
- Verma S, Miles D, Gianni L, et al. Trastuzumab Emtansine for HER2-Positive Advanced Breast Cancer. N Engl J Med 2012; 367:1783-91.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology : Breast Cancer. Version 1.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf [Accessed March 4, 2013].
- American Cancer Society. Breast Cancer Detailed Guide. Available at: http://www.cancer.org/cancer/breastcancer [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine (T-DM1) Plus Pertuzumab/Pertuzumab Placebo Versus Trastuzumab [Herceptin] Plus a Taxane in Patients With Metastatic Breast Cancer (MARIANNE). Available at: http://clinicaltrials.gov/show/NCT01120184 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine in Comparison With Treatment of Physician's Choice in Patients With HER2-Positive Breast Cancer Who Have Received at Least Two Prior Regimens of HER2-Directed Therapy (TH3RESA). Available at: http://clinicaltrials.gov/show/NCT01419197 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy in Patients With HER2-Positive Breast Cancer Who Have Residual Tumor in the Breast or Axillary Lymph Nodes Following Preoperative Therapy (KATHERINE). Available at: http://clinicaltrials.gov/ct2/show/NCT01772472 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine Versus Taxane in Patients With Advanced Gastric Cancer. Available at: http://clinicaltrials.gov/ct2/show/NCT01641939 [Accessed March 4, 2013].

Part D Effective: 10/01/13 Created: 03/13
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

ALEFACEPT (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ALEFACEPT	AMEVIVE	24899		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This request can only be reviewed by a Prior Authorization Coordinator (PAC). Please request your caller to submit a Medication Request Form (MRF) for review.

GUIDELINES FOR USE

1. Has the treatment been prescribed or is it currently being supervised by a dermatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist.

2. Is this the initial request for treatment with alefacept?

   If yes, continue to #6.
   If no, continue to #3.

3. Has the patient already received two 3-month courses of alefacept treatment?

   If yes, do not approve.
   DENIAL TEXT: Approval is limited to two 3-month courses of alefacept treatment.
   If no, continue to #4.

4. Has there been a 3-month interval since the end of the patient's previous 3-month course of treatment with alefacept?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Renewal requires at least a 3-month interval since the end of patient's previous course of alefacept treatment.

CONTINUED ON NEXT PAGE

ALEFACEPT (PART D)

GUIDELINES FOR USE (CONTINUED)

5. Did the patient receive clinical benefit on alefacept therapy as measured by Psoriasis Area and Severity Index (PASI 50: ≥ 50% improvement in PASI score) or a significant improvement in Quality of Life observed by the physician and patient (i.e. Dermatology Life Quality Index)?

   If yes, continue to #8.
   If no, do not approve.
   DENIAL TEXT: Renewal requires at least a 50% improvement in PASI (Psoriasis Area and Severity Index) score or a significant improvement in Quality of Life observed by the physician and patient (i.e. Dermatology Life Quality Index) with the previous course of Amevive.

6. Does the patient have chronic moderate to severe plaque psoriasis involving ≥ 10% body surface area (BSA)?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic moderate to severe plaque psoriasis involving at least 10% of body surface area (BSA).

7. Has the patient tried or does the patient have a contraindication to one or more forms of preferred therapy (PUVA [Phototherapy Ultraviolet Light A], UVB [Ultraviolet Light B], acitretin, methotrexate, or cyclosporine)?

   If yes, continue to #8.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of at least one form of preferred therapy (e.g., PUVA [Phototherapy Ultraviolet Light A], UVB [Ultraviolet Light B], methotrexate, or cyclosporine).

8. **Approve for 3 months with a quantity limit of #4 vials per month.**

RATIONALE
To ensure appropriate use of Amevive.

FDA APPROVED INDICATIONS
Amevive is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.

CONTINUED ON NEXT PAGE

ALEFACEPT (PART D)

REFERENCES

- Astellas Pharma, Inc. Amevive package insert. Deerfield, IL, May 2010.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed: June 21, 2010].
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 21, 2010].

Part D Effective: 07/01/13 Created: 05/03
Commercial Effective: N/A Client Approval: 05/13 P&T Approval: 11/12

ANAKINRA (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ANAKINRA	KINERET	22953		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS)?

   If yes, **approve for 12 months with a quantity limit of #56 syringes per 28 days.**
   If no, continue to #2.

2. Has the patient tried Humira (adalimumab) or Cimzia (certolizumab)?

   If yes, continue to #3.
   If no, do not approve. (Note: Ask the caller to submit a MRF for Humira or Cimzia.)
   DENIAL TEXT: Approval requires a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS); or a trial of the preferred formulary tumor necrosis factor Humira (adalimumab) or Cimzia (certolizumab) which is supervised by a rheumatologist; or a diagnosis of moderate to severe rheumatoid arthritis for a patient that is 18 or older and had a trial of at least one DMARD (disease modifying antirheumatic drug) such as methotrexate, azathioprine, cyclosporine, hydroxychloroquine, sulfasalazine, or penicillamine.

3. Has the treatment been prescribed, or is it currently being supervised by a rheumatologist?

   If yes, **approve for 3 months with a quantity limit of #28 syringes per 28 days.**
   If no, continue to #4.

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ANAKINRA (PART D)

INITIAL CRITERIA (CONTINUED)

4. Does the patient have diagnosis of moderate to severe rheumatoid arthritis?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS) or a trial of the preferred formulary tumor necrosis factor Humira (adalimumab) or Cimzia (certolizumab); supervision by a rheumatologist; a diagnosis of moderate to severe rheumatoid arthritis; the patient must be age 18 or older and had a trial of at least one DMARD (disease modifying antirheumatic drug) such as methotrexate, azathioprine, cyclosporine, hydroxychloroquine, sulfasalazine, or penicillamine.

5. Is the patient 18 years of age or older?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS) or a trial of the preferred formulary tumor necrosis factor Humira (adalimumab) or Cimzia (certolizumab); supervision by a rheumatologist; a diagnosis of moderate to severe rheumatoid arthritis; the patient must be age 18 or older and had a trial of at least one DMARD (disease modifying antirheumatic drug) such as methotrexate, azathioprine, cyclosporine, hydroxychloroquine, sulfasalazine, or penicillamine.

6. Has the patient previously tried at least one of the following DMARD agents: methotrexate, leflunomide, azathioprine, cyclosporine, hydroxychloroquine, penicillamine, sulfasalazine, gold sodium thiomalate, or auranofin?

   If yes, **approve for 3 months with a quantity limit of #28 syringes per 28 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS) or a trial of the preferred formulary tumor necrosis factor Humira (adalimumab) or Cimzia (certolizumab); supervision by a rheumatologist; a diagnosis of moderate to severe rheumatoid arthritis; the patient must be age 18 or older and had a trial of at least one DMARD (disease modifying antirheumatic drug) such as methotrexate, azathioprine, cyclosporine, hydroxychloroquine, sulfasalazine, or penicillamine.

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ANAKINRA (PART D)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cryopyrin-Associated Periodic Syndromes (CAPS)?

   If yes, **approve for 12 months with a quantity limit of #56 syringes per 28 days.**
   If no, continue to #2.

2. Has the patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count?

   If yes, **approve for 12 months with a quantity limit of #28 syringes per 28 days.**
   If no, do not approve.
   DENIAL TEXT: Renewal requires at least a 20% improvement in tender joint count and swollen joint count.

RATIONALE

Ensure appropriate diagnostic, utilization, and safety criteria.

FDA APPROVED INDICATION

Rheumatoid Arthritis (RA)

- Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs).

Cryopyrin-Associated Periodic Syndromes (CAPS)

- Treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

REFERENCES

- Swedish Orphan Biovitrum. Kineret package insert. Stockholm Sweden, December 2012.
- Cohen S, et al. Treatment of Rheumatoid Arthritis with anakinra, a recombinant human interleukin-1 receptor antagonist, in combination with methotrexate. Arthritis & Rheum 2002; 46(3):614-24.
- Nuki G et al. Long-term safety and maintenance of clinical improvement following treatment with anakinra (recombinant human interleukin-1 receptor antagonist) in patients with Rheumatoid Arthritis. Am College of Rheumatol. 2005; 46(11):2838-46.
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed: June 21, 2010].

Part D Effective: 07/01/13 Created: 02/03
Commercial Effective: N/A Client Approval: 05/13 P&T Approval: 05/13

APREPITANT BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
APREPITANT	EMEND	25058		ROUTE = ORAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the patient undergoing surgery with a high risk of postoperative nausea and vomiting (i.e., intra-abdominal procedures, major gynecologic surgery, orthopedic surgery, ear-nose-throat surgery, laparoscopic surgery, adenotonsillectomy, or strabismus surgery)?

   If yes, **approve one Emend 40mg capsule x 1 fill under Part D. (Populate the B vs. D field with a "D" in the PA override field)**
   If no, continue to #2.

2. Is Emend being prescribed as full therapeutic replacement for an intravenous anti-emetic drug in combination with both a 5-HT3 antagonist (i.e., Kytril, Zofran, Anzemet, and Aloxi) and dexamethasone for use within 48 hours of one or more of the following chemotherapy drugs?

   - Carmustine (BICNU)
   - Cisplatin (Platinol)
   - Cyclophosphamide (Cytoxan)
   - Dacarbazine (DTIC)
   - Mechlorethamine (Mustargen)
   - Streptozocin (Zanosar)
   - Doxorubicin (Adriamycin)
   - Epirubicin (Ellence)
   - Lomustine (CEENU)

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #3. **(CSR: If unknown, ask the caller to submit MRF.)**

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APREPITANT BVD DETERMINATION (PART D)

GUIDELINES FOR USE (CONTINUED)

3. Is the patient receiving any cancer chemotherapy agent?

   If yes, **approve under Part D for up to 6 months or length of therapy, whichever is less, of one of the following (Populate B vs. D field with "D" in the PA override field):**

   a. **one Emend Trifold per chemotherapy cycle, OR**
   b. **one 125mg and two 80mg capsules per chemotherapy cycle, OR**
   c. **one bi-fold per chemotherapy cycle.**

   If no, do not approve.
   DENIAL TEXT: Approval requires this medication is being used for the management of high risk postoperative nausea and vomiting, or chemotherapy-induced nausea and vomiting.

RATIONALE
Ensure Emend is used for patients receiving chemotherapeutic agents likely to cause delayed nausea and vomiting.

FDA APPROVED INDICATIONS
Emend is indicated, in combination with other antiemetic agents, for prevention of both acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin, and for prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer therapy.

Emend is also indicated for the prevention of postoperative nausea and vomiting.

REFERENCES

- Merck & Co. Emend package insert. Whitehouse Station, NJ. March 2011.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 23, 2011].
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Antiemesis. Version 3.2011.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13 Created: 09/05
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

ASPARAGINASE

Generic	Brand	HICL	GCN	Exception/Other
ASPARAGINASE	ELSPAR		38750	
ASPARAGINASE (ERWINIA CHRYSAN)	ERWINAZE		30918	
PEGASPARGASE	ONCASPAR		24231	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of acute lymphoblastic leukemia (ALL)?

   If yes, continue to #2.
   If no, do not approve.
   ERWINAZE DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL) and a hypersensitivity reaction to Elspar or Oncaspar, which may also require prior authorization, or be covered under the medical benefit.

   ELSPAR and ONCASPAR DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL).

2. Is the request for Erwinaze?

   If yes, continue to #3.
   If no, **approve as follows:**
   ELSPAR: **Approve for 3 months up to #60 vials per month.**
   ONCASPAR: **Approve for 3 months up to #2 vials per month.**

3. Has the patient developed a hypersensitivity to *E. coli*-derived asparaginase for example, Elspar or Oncaspar?

   If yes, **approve for 3 months up to #60 vials per month.**
   If no, do not approve.
   ERWINAZE DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL) and a hypersensitivity reaction to Elspar or Oncaspar, which may also require prior authorization, or be covered under the medical benefit.

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ASPARAGINASE

RATIONALE

Promote appropriate utilization and dosing of asparaginase products for their FDA approved indication as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL). Require hypersensitivity to *E. coli*-derived asparaginase prior to Erwinaze therapy as per its FDA approved indication. Both Elspar and Oncaspar are derived from *E. coli*. The dosing approved in this prior authorization guideline allows for appropriate dosing of patients with a body surface area (BSA) of 2.0 m^2 or less. Clinical review is required for patients with a BSA above 2.0 m^2.

Elspar is administered either as a single dose of up to 25,000IU/m^2 once weekly for 2 weeks, 600IU/m^2 every other day for 3 to 4 weeks, or daily doses of 1,000 to 20,000IU/m^2 for 10 to 12 days.

Erwinaze is dosed as follows:

- To substitute for a dose of pegaspargase the recommended dose is 25,000 IU/m^2 three times a week (Monday, Wednesday, Friday) for six doses for each planned dose.
- To substitute for a dose of native *E. coli* asparaginase the recommended dose is 25,000 IU/m^2 for each schedule dose of native *E. coli* asparaginase within a treatment.

Oncaspar is dosed 2,500IU/m^2 no more frequently than every 14 days.

FDA APPROVED INDICATIONS

Elspar is indicated in therapy of patients with acute lymphocytic leukemia. This agent is useful primarily in combination with other chemotherapeutic agents in the induction of remissions of the disease in pediatric patients. Elspar should not be used as the sole induction agent unless combination therapy is deemed inappropriate. Elspar is not recommended for maintenance therapy.

Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to E. coli-derived asparaginase.

Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL and hypersensitivity to native forms of L-asparaginase.

REFERENCES

- EUSA Pharma (USA), Inc. Erwinaze package insert. Langhorne, PA. November 2011.
- Lundbeck Inc. Elspar package insert. Deerfield, IL. April 2010.
- Sigma-Tau Pharmaceuticals, Inc. Oncaspar package insert. Gaithersburg, MD. May 2011.

Part D Effective: 10/01/13 Created: 12/11
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 11/12

AXITINIB

Generic	Brand	HICL	GCN	Exception/Other
AXITINIB	INLYTA	38446		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) and a trial of at least one systemic therapy for the treatment of RCC such as Nexavar (sorafenib), Torisel (temsirolimus), Sutent (sunitinib), Votrient (pazopanib), or Avastin (bevacizumab) in combination with interferon, all of which may require prior authorization. Additionally Avastin may be covered under the medical benefit rather than the pharmacy benefit.

2. Has the patient tried at least one systemic therapy for the treatment of RCC such as Nexavar (sorafenib), Torisel (temsirolimus), Sutent (sunitinib), Votrient (pazopanib), or Avastin (bevacizumab) in combination with interferon?

   If yes, **approve each strength for 12 months by GPID with the following quantity limits:**
   - **Inlyta 1mg: #6 tablets per day**
   - **Inlyta 5mg: #2 tablets per day**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) and a trial of at least one systemic therapy for the treatment of RCC such as Nexavar (sorafenib), Torisel (temsirolimus), Sutent (sunitinib), Votrient (pazopanib), or Avastin (bevacizumab) in combination with interferon, all of which may require prior authorization. Additionally Avastin may be covered under the medical benefit rather than the pharmacy benefit.

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AXITINIB

RATIONALE

Ensure appropriate utilization of Inlyta based on FDA approved indication and NCCN guidelines.

Inlyta (axitinib) is a receptor tyrosine kinase inhibitor shown to have activity against vascular endothelial growth factor receptors 1, 2, and 3. National Comprehensive Cancer Network (NCCN) category 1 options for first line treatment of patients with relapsed or medically unresectable predominantly clear cell stage IV renal carcinoma include sunitinib, bevacizumab with interferon-alfa, pazopanib, and temsirolimus. NCCN lists sorafenib as a category 2A option.

Approval of Inlyta was based on a randomized, open-label, multicenter Phase 3 study comparing progression-free survival (PFS) of patients with advanced RCC whose disease had progressed on or after treatment with 1 prior systemic therapy, including sunitinib, bevacizumab, temsirolimus, or cytokine-containing regimens. Other endpoints included objective response rate (ORR) and overall survival (OS) 99% of study subjects had clear cell histology. Patients were randomized to receive Inlyta or sorafenib. There was a statistically significant advantage for Inlyta over sorafenib for the endpoint of PFS (6.7 vs. 4.7 months, respectively, $P < 0.0001$). There was no statistically significant difference between the arms in OS.

The most common (≥ 20%) adverse reactions are diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, palmar-plantar erythrodysesthesia (hand-foot) syndrome, weight loss, vomiting, asthenia, and constipation. Please reference the prescribing information for a complete list of warnings and precautions.

Dosage: The starting dose is 5 mg orally twice daily. Administer dose approximately 12 hours apart with or without food. Dose may be increased to 7mg twice daily and further increased to 10mg twice daily for patients who tolerate Inlyta for at least two consecutive weeks. In the pivotal trial, the dosage of 10mg twice daily was not associated with an improved outcome over the 5mg twice daily dosage. If a strong CYP3A4/5 inhibitor is required or for patients with moderate hepatic impairment, the dose may be decreased to 3mg twice daily and further reduced to 2mg twice daily.

FDA APPROVED INDICATION

Inlyta is indicated for the treatment of advanced renal cell carcinoma after failure of one prior systemic therapy.

REFERENCES

- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 1.2012).
- Pfizer. Inlyta package insert. New York, NY. January 2012.

Part D Effective: 04/01/13	Created: 02/12	
Commercial Effective: 04/01/13	Client Approval: 03/13	P&T Approval: 11/12

BACILLUS OF CALMETTE AND GUERIN VACCINE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
BCG LIVE	THERACYS BCG VACCINE (TICE STRAIN)	04219		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is this drug to be administered to patients in a physician's office?

   If yes, **submit via Part B (Populate the B vs. D field with "B" in PA override field and approve for one time in 12 months by HICL. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, **approve for one time in 12 months by HICL under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE

Bacillus of Calmette and Guerin requires a Part B vs. Part D determination. The vaccine is Part B only if given within the physician's office. Part D for all outpatient and other preventive uses.

FDA APPROVED INDICATIONS

It is indicated for people not previously infected with *Mycobacterium tuberculosis.* TICE® BCG is indicated for the treatment and prophylaxis of CIS of the urinary bladder and for prophylaxis of primary or recurrent stage Ta and/or T1 papillary tumors following transurethral section (TUR). TICE® BCG is not indicated for papillary tumors of stages higher than T1.

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BACILLUS OF CALMETTE AND GUERIN VACCINE BVD DETERMINATION (PART D)

REFERENCES

- Organon. Tice BCG package insert. Durham, NC. June 2009.
- Sanofi Pasteur. TheraCys package insert. Swiftwater, PA. July 2006.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13	Created: 02/08	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

BARBITURATES (PART D)

Generic	Brand	HICL	GCN	Exception/Other
AMOBARBITAL SODIUM	AMYTAL SODIUM	01564		
BUTABARBITAL SODIUM	BUTISOL SODIUM	01566		
MEPHOBARBITAL	MEBARAL MEPHOBARBITAL	01895		
PHENOBARBITAL SODIUM	LUMINAL SODIUM PHENOBARBITAL	01561 01560		Exclude GCN = 14790, 13980
SECOBARBITAL SODIUM	SECONAL SODIUM	01570		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the request for phenobarbital?

   If yes, continue to #2.
   If no, continue to #3.

2. Does the patient have a diagnosis of epilepsy or seizures?

   If yes, **approve for lifetime under Part D.**
   If no, continue to #3.

3. Is the drug being prescribed for the treatment of insomnia?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval under Part D benefit requires that barbiturates are used for the medical indications of epilepsy or its use for insomnia in relation to cancer or a chronic mental health disorder. Centers for Medicare & Medicaid Services (CMS) consider the requested medication to be of high risk for patients 65 years old or older. Requests for patients 65 years or older for the treatment of insomnia requires a trial of Rozerem or Silenor.

4. Does the patient have a diagnosis of cancer?

   If yes, continue to #6.
   If no, continue to #5.

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BARBITURATES (PART D)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a chronic mental health disorder (a condition affecting cognition, emotion, and behavior)? Examples of a chronic mental health disorder include but are not limited to:
   - Any Anxiety Disorder
   - Simple Phobia
   - Social Phobia
   - Agoraphobia
   - Panic Disorder
   - Obsessive-Compulsive Disorder
   - Any Mood Disorder
   - Major Depressive Episode
   - Unipolar Major Depression
   - Dysthymia
   - Bipolar I
   - Bipolar II
   - Schizophrenia
   - Somatization
   - Antisocial Personality Disorder
   - Anorexia Nervosa
   - Severe Cognitive Impairment

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval under Part D benefit requires that barbiturates are used for the medical indications of epilepsy or its use for insomnia in relation to cancer or a chronic mental health disorder. Centers for Medicare & Medicaid Services (CMS) consider the requested medication to be of high risk for patients 65 years old or older. Requests for patients 65 years or older for the treatment of insomnia requires a trial of Rozerem or Silenor.

6. Is the member 65 years old or older?

   If yes, continue to #7.
   If no, **approve for 6 months under Part D.**

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BARBITURATES (PART D)

GUIDELINES FOR USE (CONTINUED)

7. Has the patient tried or does the patient have a contraindication to Rozerem or Silenor?

   If yes, **approve for 6 months under Part D.**
   If no, do not approve.
   DENIAL TEXT: Approval under Part D benefit requires that barbiturates are used for the medical indications of epilepsy or its use for insomnia in relation to cancer or a chronic mental health disorder. Centers for Medicare & Medicaid Services (CMS) consider the requested medication to be of high risk for patients 65 years old or older. Requests for patients 65 years or older for the treatment of insomnia requires a trial of Rozerem or Silenor.

RATIONALE

Section 175 of the Medicare Improvements for Patients and Providers Act of 2008 (MIPPA), amended section 1860D-2(e)(2)(A) of the Act to include barbiturates, when used for the medical indications of epilepsy, cancer, or a chronic mental health disorder. These amendments apply to prescriptions dispensed on or after January 1, 2013. Like any covered prescription drugs under the Part D benefit program, barbiturates must meet all other conditions as defined in §423.100 of a Part D covered drug such as: FDA approved for safety and effectiveness as a prescription drug under section 505 of the Federal Food, Drug, and Cosmetic Act; used and sold in the United States; not otherwise covered by Medicare Part A or Part B; and used only for medically accepted indications.

CMS does not define what constitutes a chronic mental health disorder. However the CDC definition of mental illness is a condition that affects cognition, emotion, and behavior (e.g., schizophrenia, depression, autism). A Surgeon General report lists common mental health disorder in patients over the age of 55 including:

- Any Anxiety Disorder
- Simple Phobia
- Social Phobia
- Agoraphobia
- Panic Disorder
- Obsessive-Compulsive Disorder
- Any Mood Disorder
- Major Depressive Episode
- Unipolar Major Depression
- Dysthymia
- Bipolar I
- Bipolar II
- Schizophrenia
- Somatization
- Antisocial Personality Disorder
- Anorexia Nervosa
- Severe Cognitive Impairment

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BARBITURATES (PART D)

RATIONALE (CONTINUED)
Barbiturates are also listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS
Phenobarbital is FDA approved for the treatment of epilepsy, sedation, and short-term management of insomnia.

Butabarbital is FDA approved for the treatment of insomnia and sedation.

REFERENCES:

- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [October 23, 2012]
- Manderscheid RW, Ryff CD, Freeman EJ, McKnight-Eily LR, Dhingra S, Strine TW. Evolving definitions of mental illness and wellness. Prev Chronic Dis 2010;7(1):A19. Available at: http://www.cdc.gov/pcd/issues/2010/jan/09_0124.htm. Accessed [October 23, 2012].
- Medicare Program; Proposed Changes to the Medicare Advantage and the Medicare Prescription Drug Benefit Programs for Contract Year 2013 and Other Proposed Changes; Considering Changes to the Conditions of Participation for Long Term Care Facilities Published in the Federal Register on October 11, 2011.
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [October 23, 2012].
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [October 23, 2012].
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- U.S. Public Health Service. Mental Health: A Report of the Surgeon General. Chapter 5 Older Adults and Mental Health. Available at: http://www.surgeongeneral.gov/library/mentalhealth/chapter5/sec1.html. Accessed [October 23, 2012].

Part D Effective: 02/07/13	Created: 03/12	
Commercial Effective: N/A	Client Approval: 02/13	P&T Approval: 11/12

BECAPLERMIN

Generic	Brand	HICL	GCN	Exception/Other
BECAPLERMIN	REGRANEX	17028		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosed neoplasm (i.e. cancer) at the site of application?

   If yes, do not approve.
   DENIAL TEXT: Approval criteria require a diagnosis of lower extremity diabetic neuropathic ulcers caused by diabetes mellitus without known neoplasms at the site of application, and to be overseen by a vascular surgeon, podiatrist, endocrinologist, or a physician practicing in a specialty wound clinic.
   If no, continue to #2.

2. Is the diagnosis of lower extremity diabetic neuropathic ulcers caused by diabetes mellitus?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval criteria require a diagnosis of lower extremity diabetic neuropathic ulcers caused by diabetes mellitus without known neoplasms at the site of application, and to be overseen by a vascular surgeon, podiatrist, endocrinologist, or a physician practicing in a specialty wound clinic.

3. Is the prescription written or is it currently being supervised by a vascular surgeon, podiatrist, endocrinologist, or a physician practicing in a specialty wound clinic?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval criteria require a diagnosis of lower extremity diabetic neuropathic ulcers caused by diabetes mellitus without known neoplasms at the site of application, and to be overseen by a vascular surgeon, podiatrist, endocrinologist, or a physician practicing in a specialty wound clinic.

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GUIDELINES FOR USE (CONTINUED)

4. Is there pressure ulcers, venous stasis ulcers, or ulcers that do not extend through the dermis at the site of application?

   If yes, do not approve.
   DENIAL TEXT: Approval criteria require that this medication is not used for pressure ulcers, venous stasis ulcers, or ulcers that do not extend through the dermis.
   If no, **approve for 3 months for #2 tubes per month maximum.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE
Ensure use consistent with FDA approved indication.

FDA APPROVED INDICATIONS
Becaplermin is indicated for treatment of lower-extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond, and have an adequate blood supply. To be used as an adjunct to, and not a substitute for good ulcer care practices, including initial sharp debridement, pressure relief, and infection control.

REFERENCES
- OMJ Pharmaceutical. Regranex package insert. Raritan, NJ. March 2011.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: www.thomsonhc.com/hcs/librarian/ PFDefaultActionId/pf.LoginAction. [Accessed: June 20, 2011].

Part D Effective: 01/01/13 Created: 11/00
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

BEDAQUILINE FUMARATE

Generic	Brand	HICL	GCN	Exception/Other
BEDAQUILINE FUMARATE	SIRTURO		33934	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient at least 18 years of age?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

2. Does the patient have a diagnosis of latent or extra-pulmonary tuberculosis?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.
   If no, continue to #3.

3. Does the patient have a diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB) or evidence of an isolate of M. tuberculosis that is resistant to at least isoniazid and rifampin, and possibly additional agents?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

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GUIDELINES FOR USE (CONTINUED)

4. Will Sirturo be used in combination with at least 3 other antibiotics?

   If yes, **approve by GPID with a quantity limit of #68 tablets for the first 28 days of treatment and then followed by #24 tablets per 28 days for the next 20 weeks (5 fills).**
   Note: The total duration of treatment with Sirturo is 24 weeks.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

RATIONALE
To ensure appropriate use aligned with FDA approved indication.

The recommended dosage of Sirturo is 400 mg once daily for 2 weeks followed by 200 mg 3 times per week for 22 weeks. Sirturo should be administered by directly observed therapy (DOT). Sirturo should be swallowed whole and administered with food and water. No dosage adjustment is necessary in patients with mild to moderate renal or hepatic impairment.

Sirturo should only be used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible in vitro. If in vitro testing results are not available, treatment may be initiated with Sirturo in combination with at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible.

The term multi-drug resistant tuberculosis (MDR-TB) refers to an isolate of M. tuberculosis that is resistant to at least isoniazid and rifampin, and possibly additional agents. Treatment of suspected MDR-TB should be guided by drug susceptibility testing whenever possible. Susceptibility data is often not available (at least initially), and empiric therapy must be used. Empiric regimens for patients in areas with a known high prevalence of MDR-TB (or for patients with a new diagnosis of TB following contact with an individual known to have MDR-TB) should include first-line agents plus any additional drugs necessary to ensure a combination regimen containing at least four drugs which are active against the most prevalent drug-resistant strains. In general, treatment of MDR-TB should include a fluoroquinolone (levofloxacin 1000mg daily is favored by the WHO MDR-TB treatment guidelines) and an injectable agent (in many countries, kanamycin [dosed at 15mg/kg/daily IV or IM] is the first-choice injectable agent since it is relatively inexpensive and readily available). There is no role for the use of more than one fluoroquinolone or injectable agent. Subsequently, if needed, ethionamide, cycloserine, and aminosalicylic acid may be added to complete the regimen such that it consists of at least four active drugs. Alternative agents should be added only when the preceding drugs are not sufficient.

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RATIONALE (CONTINUED)
Treatment failure refers to failure of cultures to become negative during the course of treatment, or reappearance of positive cultures after the cultures convert to negative during treatment. Treatment failure implies resistance to all of the drugs being administered at the time when failure is diagnosed. The relatively poor response of drug resistant TB to treatment is likely a function of the relatively weak potency of the drugs used rather than the inherent properties of the microbe.

The FDA approval of Sirturo was based on two studies.

Study 1
The placebo-controlled, double-blind, randomized trial enrolled 160 newly diagnosed patients with multi-drug resistant pulmonary Mycobacterium tuberculosis. Subjects were randomized to receive treatment with either Sirturo or placebo, both added to other drugs used to treat MDR-TB. Sirturo was administered as 400 mg once daily for the first 2 weeks and as 200 mg 3 times per week for the following 22 weeks. After the 24-week Sirturo or placebo treatment phase, subjects continued to receive their other drugs used to treat MDR-TB until a total treatment duration of 18 to 24 months. Time to sputum culture conversion was measured as the interval between the first dose of the study drug and the date of the first two consecutive negative sputum cultures collected. The Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 24. Treatment success was reached by 77.6% of the Sirturo arm versus 57.6% of the placebo arm at Week 24 (p=0.014). At Week 72 success was reached by 70.1% and 56.1% of the respective arms. Median time to culture conversion was 83 days for the Sirturo treatment group compared to 125 days for the placebo treatment group.

Study 2
This placebo controlled study was designed similarly to Study 1 except that Sirturo or placebo was given for only 8 weeks instead of 24 weeks. A total of 47 subjects were treated. The Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 8. At Weeks 8 and 24, the differences in culture conversion proportions were 38.9% (p-value: 0.004) and 15.7% (p-value: 0.32) respectively.

Sirturo has two boxed warnings. The first warns of an increased risk of death seen in those treated with Sirturo (9/79, 11.4%) compared to the placebo treatment group (2/81, 2.5%). The imbalance in deaths is unexplained. No discernible pattern between death and sputum culture conversion, relapse, sensitivity to other drugs used to treat TB, HIV status, or severity of disease could be observed. It is recommended that Sirturo only be used when an effective treatment regimen cannot otherwise be provided. The second warning states that QT prolongation can occur with Sirturo. Concomitant use with other drugs that prolong the QT interval is discouraged as this may cause additive QT prolongation. Sirturo should be discontinued if significant ventricular arrhythmia or a QTc interval > 500 ms develops.

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BEDAQUILINE FUMARATE

RATIONALE (CONTINUED)
The most common adverse reactions reported in ≥10% of patients treated with Sirturo are nausea, arthralgia, and headache. Additional adverse events reported in ≥10% of patients treated with Sirturo and with a higher frequency than the placebo treatment group are hemoptysis and chest pain. Hepatic-related adverse drug reactions have also been reported with use of Sirturo. As a result, liver function tests should be monitored.

The major CYP isoenzyme involved in the metabolism of bedaquiline is CYP3A4. Co-administration of Sirturo with strong CYP3A4 inhibitors may increase the systemic exposure to bedaquiline, which could potentially increase the risk of adverse reactions. Therefore, the use of strong CYP3A4 inhibitors used systemically for more than 14 consecutive days should be avoided while on Sirturo, unless the benefit of treatment with the drug combination outweighs the risk. Alcohol should also be avoided throughout the treatment period.

Pregnancy Category B.

FDA APPROVED INDICATIONS
Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adults (≥ 18 years) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Sirturo is reserved for use when an effective treatment regimen cannot otherwise be provided. Sirturo is not indicated for the treatment of latent, extra-pulmonary, or drug-sensitive tuberculosis.

REFERENCES

- Sirturo [Prescribing Information]. Titusville, NJ: Janssen Therapeutics; December 2012.
- UpToDate, Inc. Diagnosis, treatment, and prevention of drug-resistant tuberculosis. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated March 19, 2013. 25, 2013.
- Center Watch Clinical Trials Listing [database online]. Sirturo (bedaquiline fumarate). Available at http://www.centerwatch.com/ Accessed: April 30, 2013.

Part D Effective: 10/01/13	Created: 05/13	
Commercial Effective: 10/01/13	Client Approval: 08/13	P&T Approval: 08/13

BELIMUMAB

Generic	Brand	HICL	GCN	Exception/Other
BELIMUMAB	BENLYSTA	37462		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of severe active lupus nephritis or severe active central nervous system lupus?

   If yes, do not approve.
   DENIAL TEXT: Benlysta is not covered for the treatment of severe active lupus nephritis or severe active central nervous system lupus.
   If no, continue to #2.

2. Is the patient currently taking corticosteroids, antimalarials, NSAIDs or immunosuppressives?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of autoantibody positive systemic lupus erythematosus (SLE) and SELENA-SLEDAI score > or = 6; patient is currently taking standard of care lupus treatment such as corticosteroids, antimalarials, NSAIDs or immunosuppressives and not taking biologics or intravenous cyclophosphamide.

3. Is the patient currently taking biologics or intravenous cyclophosphamide?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of autoantibody positive systemic lupus erythematosus (SLE) and SELENA-SLEDAI score > or = 6; patient is currently taking standard of care lupus treatment such as corticosteroids, antimalarials, NSAIDs or immunosuppressives and not taking biologics or intravenous cyclophosphamide.
   If no, continue to #4.

4. Is the patient currently taking Benlysta?

   If yes, continue to #7.
   If no, continue to #5.

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GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a diagnosis of lupus?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of autoantibody positive systemic lupus erythematosus (SLE) and SELENA-SLEDAI score > or = 6; patient is currently taking standard of care lupus treatment such as corticosteroids, antimalarials, NSAIDs or immunosuppressives and not taking biologics or intravenous cyclophosphamide.

6. Does the patient have a positive autoantibody test and a SELENA-SLEDAI score ≥ 6?

   If yes, **approve. Enter two authorizations as follows:**
   - **Approve for 1 month by HICL for #6 vials, AND**
   - **Approve for 5 fills by HICL for #2 vials per month with a start date 1 week prior to the end date of the 1 month authorization.**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of autoantibody positive systemic lupus erythematosus (SLE) and SELENA-SLEDAI score > or = 6; patient is currently taking standard of care lupus treatment such as corticosteroids, antimalarials, NSAIDs or immunosuppressives and not taking biologics or intravenous cyclophosphamide.

7. Has the patient achieved or maintained at least a 4 point reduction in their SELENA-SLEDAI score from baseline?

   If yes, **approve for 12 months by HICL with a quantity of #2 vials per month.**
   If no, do not approve.
   DENIAL TEXT: Renewal requires that the patient achieved or maintained at least a 4 point reduction in their SELENA-SLEDAI score from baseline.

RATIONALE
Ensure appropriate utilization of Benlysta consistent with its FDA approved indication.

FDA APPROVED INDICATIONS
Benlysta is indicated for the treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy.

Limitations of Use: Not recommended for patient with severe active lupus nephritis or severe active central nervous system lupus or in combination with other biologics or intravenous cyclophosphamide.

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REFERENCES

- Bertsias G, Ioannidis JPA, Boletis J et al. EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. *Ann Rheum Dis* 2008; 67:195-205.
- Human Genome Sciences, Inc. Benlysta package insert. Rockville, MD. March 2011.
- Mosca M, Bombardieri S. Assessing remission in systemic lupus erythematosus. *Clin Exp Rheumatol* 2006; 24 (Suppl. 43): S100-S104.

Part D Effective: 07/01/13 Created: 03/11
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 11/12

BOCEPREVIR (PART D)

Generic	Brand	HICL	GCN	Exception/Other
BOCEPREVIR	VICTRELIS	37609		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

Boceprevir (Victrelis) is part of a three drug regimen for use with ribavirin and peginterferon alfa. Ribavirin and peginterferon alfa are started first in therapy. Boceprevir is added to peginterferon alfa and ribavirin regimen after 4 weeks of treatment (TW4).

GUIDELINES FOR USE

1. Is the requested medication being used with ribavirin and peginterferon alfa?
   Note: The patient must have an active prior authorization for peginterferon alfa before proceeding.

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient has a contraindication/intolerance to telaprevir (Incivek). Approval requires that the patient does not have coinfection with hepatitis B, or have a history of a previous solid organ transplant. Approval requires that the patient has not failed therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.

2. Is the patient currently taking the requested medication as indicated on the MRF, claims history, or prior authorization history?

   If yes, continue to #10.
   If no, continue to #3.

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GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a contraindication to telaprevir or has previously failed a short trial with telaprevir (e.g. rash early in therapy or other intolerance)?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient has a contraindication/intolerance to telaprevir (Incivek). Approval requires that the patient does not have coinfection with hepatitis B or have a history of a previous solid organ transplant. Approval requires that the patient has not failed previous therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.

4. Is the patient at least 18 years old with a diagnosis of chronic hepatitis C, genotype 1?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient has a contraindication/intolerance to telaprevir (Incivek). Approval requires that the patient does not have coinfection with hepatitis B or have a history of a previous solid organ transplant. Approval requires that the patient has not failed previous therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.

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GUIDELINES FOR USE (CONTINUED)

5. Is the patient currently supervised by a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (e.g. hepatologist), or specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient has a contraindication/intolerance to telaprevir (Incivek). Approval requires that the patient does not have coinfection with hepatitis B or have a history of a previous solid organ transplant. Approval requires that the patient has not failed previous therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.

6. Has the patient failed a prior full course of triple therapy (with telaprevir [Incivek] or boceprevir [Victrelis])?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient has not failed a full course of therapy with telaprevir (Incivek) or boceprevir (Victrelis). Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient does not have coinfection with hepatitis B, or have a history of a previous solid organ transplant. Approval requires that the patient has not failed therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.
   If no, continue to #7.

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GUIDELINES FOR USE (CONTINUED)

7. Has the patient previously failed a prior course of peginterferon and ribavirin as a null responder (defined as less than 2 log reduction in HCV RNA at week 12)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient is not a previous null responder to a course of peginterferon/ribavirin and has not failed a full course of therapy with telaprevir (Incivek) or boceprevir (Victrelis). Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.
   If no, continue to #8.

8. Is the patient currently taking carbamazepine, phenobarbital, phenytoin, or rifampin?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient is not currently taking carbamazepine, phenobarbital, phenytoin, or rifampin. Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa.
   If no, continue to #9.

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GUIDELINES FOR USE (CONTINUED)

9. Does the patient have a coinfection with hepatitis B, or have a history of a previous solid organ transplant?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient does not have coinfection with hepatitis B, or have a history of a previous solid organ transplant. Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient has not failed therapy with telaprevir (Incivek) or boceprevir (Victrelis) and is not a previous null responder. Approval requires that the patient is not concurrently taking carbamazepine, phenobarbital, phenytoin, or rifampin.

   If no, **approve the first fill for #12 capsules per day for 12 weeks.**
   PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = #12 capsules and a duration of 84 days (with start date 3 weeks after the start date of peginterferon).
   APPROVAL TEXT: Renewal requires HCV RNA levels at baseline, and then at treatment weeks 4, 8, 12 and 24. Also the request must specify if the patient qualifies for 44 weeks boceprevir treatment (for example one of the following: cirrhosis or poorly interferon responsive at treatment week 4 during current therapy). Drugs that are contraindicated with Victrelis include alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, ergot derivatives, cisapride, St John's Wort, lovastatin, simvastatin, drospirenone, sildenafil or tadalafil (at doses used to treat pulmonary arterial hypertension [PAH]), pimozide, triazolam, or orally administered midazolam.

10. **Renewal criteria for treatment week 16:** If the patient has received one previous boceprevir approval for 12 weeks of boceprevir (now at treatment week 16), continue to #11.

    Renewal criteria for treatment week 28: If the patient has received two previous approvals (now at treatment week 28), continue to #12.

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GUIDELINES FOR USE (CONTINUED)

11. **Renewal criteria for treatment week 16:** Did the patient have an HCV RNA level/viral load of ≥ 100 IU/mL at 8 weeks of boceprevir therapy (treatment week 12)?

    If yes, do not approve.
    CLINICAL SPECIALISTS: Triple therapy will be discontinued at this time. Review the prior authorization history and close peginterferon PA (and ribavirin PA, if applicable).
    DENIAL TEXT: Renewal requires HCV RNA level/viral load of less than 100 IU/mL at 8 weeks of boceprevir therapy (treatment week 12).

    If no, **approve the second fill for #12 capsules per day for 12 weeks.**
    PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = #12 capsules and a duration of 84 days.
    APPROVAL TEXT: Renewal requires HCV RNA level at treatment week 24. Drugs that are contraindicated with Victrelis include alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, ergot derivatives, cisapride, St John's Wort, lovastatin, simvastatin, drospirenone, sildenafil or tadalafil at doses used to treat pulmonary arterial hypertension (PAH), pimozide, triazolam, or orally administered midazolam.

12. **Renewal criteria for treatment week 28:** Did the patient have a detectable HCV RNA level/viral load at treatment week 24?

    If yes, do not approve.
    CLINICAL SPECIALISTS: Triple therapy will be discontinued at this time. Review the prior authorization history and close peginterferon PA (and ribavirin PA, if applicable).
    DENIAL TEXT: Renewal requires an undetectable HCV RNA level/viral load at 20 weeks of boceprevir therapy (treatment week 24).
    If no, continue to #13.

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GUIDELINES FOR USE (CONTINUED)

13. Is the patient one of the following:
    - a patient with cirrhosis
    - a patient that was poorly interferon responsive at treatment week 4 during present therapy (less than 0.5 log HCV RNA decline at treatment week 4)

    If yes, **approve the third fill for #12 capsules per day for 20 weeks.**
    PAC: The days supply is based on benefit structure. Enter the Maximum Daily Dose (MDD) = #12 capsules and a duration of 140 days.
    APPROVAL TEXT: Drugs that are contraindicated with Victrelis include alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, ergot derivatives, cisapride, St John's Wort, lovastatin, simvastatin, drospirenone, sildenafil or tadalafil at doses used to treat pulmonary arterial hypertension (PAH), pimozide, triazolam, or orally administered midazolam.
    If no, continue to #14.

14. Did the patient have an undetectable HCV RNA level at both treatment week 8 and treatment week 24?

    If yes, continue to #16.
    If no, continue to #15.

15. Did patient have a detectable level at treatment week 8 but an undetectable level at treatment week 24?

    If yes, **approve for a third fill for #12 capsules per day for 8 weeks.**
    PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = #12 capsules and a duration of 56 days.
    CLINICAL SPECIALISTS: Continue three medication regimens through treatment week 36 and the patient will receive peginterferon/ribavirin through treatment week 48.
    APPROVAL TEXT: Drugs that are contraindicated with Victrelis include alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, ergot derivatives, cisapride, St John's Wort, lovastatin, simvastatin, drospirenone, sildenafil or tadalafil at doses used to treat pulmonary arterial hypertension (PAH), pimozide, triazolam, or orally administered midazolam.
    If no, do not approve.
    DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. The patient must have an undetectable level at treatment week 24.

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GUIDELINES FOR USE (CONTINUED)

16. Did the patient fail (partial responder or relapser) a prior trial of ribavirin and peginterferon alfa therapy (does not include previous null responders, defined as less than 2 log reduction in HCV RNA at week 12)?

    - *Partial responder* is defined as 2 log or higher reduction in HCV RNA at week 12 but not undetectable HCV RNA at end of treatment;
    - *Relapser* is defined as undetectable HCV RNA at end of therapy but detectable during follow-up.

    If yes, **approve for a third fill for #12 capsules per day for 8 weeks.**
    PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = #12 capsules and a duration of 56 days.
    APPROVAL TEXT: Drugs that are contraindicated with Victrelis include alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, ergot derivatives, cisapride, St John's Wort, lovastatin, simvastatin, drospirenone, sildenafil or tadalafil at doses used to treat pulmonary arterial hypertension (PAH), pimozide, triazolam, or orally administered midazolam.
    If no, continue to #17.

17. Is the patient treatment naïve (previously untreated prior to current regimen)?

    If yes, do not approve.
    CLINICAL SPECIALISTS: Review prior authorization history, complete triple therapy at treatment week 28.
    DENIAL TEXT: Previously untreated patients must complete triple therapy at treatment week 28. Twenty four weeks of boceprevir was previously approved; therefore no further boceprevir is approved after treatment week 28.
    If no, do not approve.
    DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, minimum age of 18, current supervision by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Patient must have an undetectable level at treatment week 24.

RATIONALE
Ensure appropriate utilization of boceprevir based on FDA approved indication.

FDA APPROVED INDICATION
Victrelis is indicated for the treatment of chronic hepatitis C genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients (=18 years of age) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy.

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BOCEPREVIR (PART D)

FDA APPROVED DOSAGE

Victrelis 800mg (four 200mg capsules) orally three times daily is added to peginterferon alfa and ribavirin after 4 weeks of treatment. Duration of treatment is determined based on patient's HCV-RNA levels at treatment week (TW) 8, 12, and 24. Patients with HCV RNA level greater than or equal to 100 IU/mL at TW 12 or any detectable HCV RNA level at treatment week 24 should discontinue the three medication regimen. Patients with compensated cirrhosis, patients with poor interferon response at TW 4 should receive 4 weeks of peginterferon alfa and ribavirin followed by 44 weeks of Victrelis in combination with peginterferon alfa and ribavirin.

OTHER INFORMATION

Currently AASLD treatment guidelines recommend, "Any use of boceprevir in HIV-coinfected or transplant populations infected with HCV should be done with caution and under close clinical monitoring. A clinical trial evaluating use of boceprevir triple therapy in HCV/HIV co-infected patients showed significantly higher rates of SVR than in patients treated with peginterferon/ribavirin alone."

REFERENCE

- Arora S, Thornton K, Murata G, et al. Outcomes of Treatment for Hepatitis C Virus Infection by Primary Care Providers. NEJM 364; 23: 2199-2207.
- Ghany M, Nelson D, Strader D, Thomas D, and Seeff L. An Update on Treatment of Genotype I Chronic Hepatitis C Virus Infection: 2011 Practice Guidelines by the American Association for the Study of Liver Diseases. Hepatology 2011; 54 (4): 1433-1443. Accessed online March 9, 2012 at http://www.aasld.org/practiceguidelines/Documents/2011UpdateGenotype1HCVbyAASLD24641.pdf
- Merck/Schering Corporation. Victrelis package insert. Whitehouse Station, NJ. May 2011.
- Poizant-Martin, I, Bellissant E, et al. Phase IIb trial results (http://clinicaltrials.gov/ct2/show/NCT01335529); presented at the 19th Conference on Retroviruses and Opportunistic Infections (CROI): Presented March 2012.

Part D Effective: 07/01/13	Created: 05/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

BOSUTINIB (PART D)

Generic	Brand	HICL	GCN	Exception/Other
BOSUTINIB	BOSULIF	39590		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) and a trial of Gleevec, Sprycel, or Tasigna.

2. Has the patient previously tried or does the patient have a contraindication to Gleevec, Sprycel, or Tasigna?

   If yes, **approve for 12 months by GPID and enter two authorizations as follows:**

   - **Bosulif 500mg #1 per day and**
   - **Bosulif 100mg #4 per day**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) and a trial of Gleevec, Sprycel, or Tasigna.

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BOSUTINIB (PART D)

RATIONALE

Ensure appropriate utilization of bosutinib based on FDA approved indication and dosage. The recommended dosage is 500mg once daily with food. Dose escalation to 600mg once daily can be considered for patients who do not reach CHR by week 8 or have a complete cytogenetic response by week 12, and do not have grade 3 or higher adverse reactions while taking 500mg daily. If liver transaminases exceed 5x the institutional upper limit of normal (ULN), withhold treatment until recovery of liver transaminases reach a level of no more than 2.5x ULN and resume at 400mg once daily. If recovery takes longer than 4 weeks or transaminase elevations of at least 3x ULN occur with bilirubin elevations of least 2x ULN discontinue treatment. In the presence of grade 3-4 diarrhea, or clinically significant, moderate or severe non-hematological toxicity, withhold treatment and resume at 400mg once daily. Patients with baseline hepatic impairment should reduce dose to 200mg daily. Consider dose reduction by 100mg in the presence of neutropenia or thrombocytopenia. Doses less than 300 mg/day have not been evaluated. Patients should also be monitored for the development of pancreatitis.

Bosulif is a once daily tyrosine kinase inhibitor (TKI) for treatment-resistant CML. CML is a malignant clonal disorder of hematopoietic stem cells arising from a genetic mutation that results in increased myeloid cells, and occasionally in erythroid cells, and platelets in the peripheral blood along with myeloid hyperplasia in the bone marrow. It typically presents in chronic phase but can progress to the more deadly accelerated phase and ultimately blast phase or blast crisis. The National Comprehensive Cancer Network treatment guidelines consider the use of TKIs (Gleevec, Sprycel, and Tasigna) as first line in the treatment of CML. Choice of TKI therapy is dependent on disease phase (chronic, accelerated, or blast crisis) and response to previous therapy. Choice of TKI may be further guided by BCR-ABL KD mutation status. While Bosulif is only approved for treatment-resistant patients, it is currently being studied in a phase III open-label trial versus Gleevec for patients with newly diagnosed CML.

Bosulif 500mg once daily was evaluated in a single-arm phase 1/2 open-label trial in patients (N=546) with Gleevec-resistant or -intolerant CML with separate cohorts for chronic (CP), accelerated (AP), and blast phase (BP) disease previously treated with one prior TKI, Gleevec, or more than one TKI (Gleevec followed by Sprycel and/or Tasigna). The protocol was amended to exclude patients with a known history of the T315I mutation after 396 patients were enrolled in the trial. The primary endpoints varied by cohort:

- Rate of major cytogenetic response (MCyR) by 12 months and duration of MCyR for CP CML previously treated with one prior TKI
- Cumulative rate of MCyR by 12 months and duration of MCyR for CP CML previously treated with both Gleevec and at least 1 additional TKI
- Confirmed complete hematologic response (CHR) and overall hematologic response (OHR) for patients with previously treated AP and BP CML

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RATIONALE (CONTINUED)

The study population consisted of 73% imatinib resistant and 27% imatinib intolerant patients. Among evaluable patients, there were 266 patients with CP CML previously treated with one prior TKI (Gleevec), 108 patients with CP CML previously treated with both Gleevec and at least 1 additional TKI, and 129 patients with advanced phase CML previously treated with at least one TKI.

At 24 weeks 33.8% of patients with prior treatment of Gleevec only and 26.9% of patients with prior treatment of Gleevec and Sprycel or Tasigna achieved MCyR. After a minimum follow-up of 23 months, 53.4% of patients with CP CML treated with one prior TKI (imatinib) achieved a MCyR at any time and the median duration of MCyR was not reached. After a minimum follow-up of 13 months 32.4% of patients with CP CML treated with imatinib and at least one additional TKI achieved a MCyR at any time and the median duration of MCyR was not reached. Of 374 patients with CP CML, 16 progressed to AP or BP while on Bosulif treatment. At 48 weeks 30.4% of AP CML and 15% of BP CML patients achieved CHR. OHR was achieved by 55.1% of AP CML and 28.3% of BP CML patients. With a minimum follow up of 12 months for the 69 patients with AP CML, 4 progressed to BP while on Bosulif treatment.

The most common adverse reactions observed in clinical trials were diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, and fatigue. Warnings include gastrointestinal toxicity, hepatic toxicity, and fluid retention. Avoid the concomitant use of strong or moderate CYP3A and/or P-gp inhibitors (such as ritonavir, indinavir, nelfinavir, saquinavir, ketoconazole, boceprevir, telaprevir, itraconazole, voriconazole, posaconazole, clarithromycin, and telithromycin). Avoid the concomitant use of strong or moderate CYP3A inducers (such as rifampin, phenytoin, carbamazepine, St. John's Wort, rifabutin and phenobarbital). Bosulif is pregnancy category D and may cause fetal harm. Females of reproductive potential should avoid pregnancy while undergoing Bosulif treatment.

FDA APPROVED INDICATIONS

Bosulif is approved for treatment of adult patients with chronic, accelerated, or blast phase Ph+ chronic myelogenous leukemia (CML) with resistance or intolerance to prior therapy.

REFERENCES

- Bosulif [Prescribing Information]. New York, NY: Pfizer; September 2012.
- Compare Bosutinib to Imatinib in Subjects with Newly Diagnosed Chronic Phase Philadelphia Chromosome Positive CML. Available at: http://clinicaltrials.gov/ct2/show/NCT00574873?term=bosutinib&rank=14 [Accessed September 17, 2012].
- National Comprehensive Cancer Network. Chronic Myelogenous Leukemia 2.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf [Accessed September 17, 2012].

Part D Effective: 07/01/13 Created: 09/12
Commercial Effective: N/A Client Approval: 05/13 P&T Approval: 05/13

BEDAQUILINE FUMARATE

Generic	Brand	HICL	GCN	Exception/Other
BEDAQUILINE FUMARATE	SIRTURO		33934	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient at least 18 years of age?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

2. Does the patient have a diagnosis of latent or extra-pulmonary tuberculosis?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.
   If no, continue to #3.

3. Does the patient have a diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB) or evidence of an isolate of M. tuberculosis that is resistant to at least isoniazid and rifampin, and possibly additional agents?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

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GUIDELINES FOR USE (CONTINUED)

4. Will Sirturo be used in combination with at least 3 other antibiotics?

   If yes, **approve by GPID with a quantity limit of #68 tablets for the first 28 days of treatment and then followed by #24 tablets per 28 days for the next 20 weeks (5 fills).**
   Note: The total duration of treatment with Sirturo is 24 weeks.
   If no, do not approve.
   DENIAL TEXT: Approval requires that Sirturo only be used in the treatment of pulmonary multi-drug resistant tuberculosis (MDR-TB), in adults (18 years of age or older), and used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible.

RATIONALE
To ensure appropriate use aligned with FDA approved indication.

The recommended dosage of Sirturo is 400 mg once daily for 2 weeks followed by 200 mg 3 times per week for 22 weeks. Sirturo should be administered by directly observed therapy (DOT). Sirturo should be swallowed whole and administered with food and water. No dosage adjustment is necessary in patients with mild to moderate renal or hepatic impairment.

Sirturo should only be used in combination with at least 3 other antibiotics to which the patient's MDR-TB isolate has been shown to be susceptible in vitro. If in vitro testing results are not available, treatment may be initiated with Sirturo in combination with at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible.

The term multi-drug resistant tuberculosis (MDR-TB) refers to an isolate of M. tuberculosis that is resistant to at least isoniazid and rifampin, and possibly additional agents. Treatment of suspected MDR-TB should be guided by drug susceptibility testing whenever possible. Susceptibility data is often not available (at least initially), and empiric therapy must be used. Empiric regimens for patients in areas with a known high prevalence of MDR-TB (or for patients with a new diagnosis of TB following contact with an individual known to have MDR-TB) should include first-line agents plus any additional drugs necessary to ensure a combination regimen containing at least four drugs which are active against the most prevalent drug-resistant strains. In general, treatment of MDR-TB should include a fluoroquinolone (levofloxacin 1000mg daily is favored by the WHO MDR-TB treatment guidelines) and an injectable agent (in many countries, kanamycin [dosed at 15mg/kg/daily IV or IM] is the first-choice injectable agent since it is relatively inexpensive and readily available). There is no role for the use of more than one fluoroquinolone or injectable agent. Subsequently, if needed, ethionamide, cycloserine, and aminosalicylic acid may be added to complete the regimen such that it consists of at least four active drugs. Alternative agents should be added only when the preceding drugs are not sufficient.

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RATIONALE (CONTINUED)
Treatment failure refers to failure of cultures to become negative during the course of treatment, or reappearance of positive cultures after the cultures convert to negative during treatment. Treatment failure implies resistance to all of the drugs being administered at the time when failure is diagnosed. The relatively poor response of drug resistant TB to treatment is likely a function of the relatively weak potency of the drugs used rather than the inherent properties of the microbe.

The FDA approval of Sirturo was based on two studies.

Study 1
The placebo-controlled, double-blind, randomized trial enrolled 160 newly diagnosed patients with multi-drug resistant pulmonary Mycobacterium tuberculosis. Subjects were randomized to receive treatment with either Sirturo or placebo, both added to other drugs used to treat MDR-TB. Sirturo was administered as 400 mg once daily for the first 2 weeks and as 200 mg 3 times per week for the following 22 weeks. After the 24-week Sirturo or placebo treatment phase, subjects continued to receive their other drugs used to treat MDR-TB until a total treatment duration of 18 to 24 months. Time to sputum culture conversion was measured as the interval between the first dose of the study drug and the date of the first two consecutive negative sputum cultures collected. The Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 24. Treatment success was reached by 77.6% of the Sirturo arm versus 57.6% of the placebo arm at Week 24 (p=0.014). At Week 72 success was reached by 70.1% and 56.1% of the respective arms. Median time to culture conversion was 83 days for the Sirturo treatment group compared to 125 days for the placebo treatment group.

Study 2
This placebo controlled study was designed similarly to Study 1 except that Sirturo or placebo was given for only 8 weeks instead of 24 weeks. A total of 47 subjects were treated. The Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 8. At Weeks 8 and 24, the differences in culture conversion proportions were 38.9% (p-value: 0.004) and 15.7% (p-value: 0.32) respectively.

Sirturo has two boxed warnings. The first warns of an increased risk of death seen in those treated with Sirturo (9/79, 11.4%) compared to the placebo treatment group (2/81, 2.5%). The imbalance in deaths is unexplained. No discernible pattern between death and sputum culture conversion, relapse, sensitivity to other drugs used to treat TB, HIV status, or severity of disease could be observed. It is recommended that Sirturo only be used when an effective treatment regimen cannot otherwise be provided. The second warning states that QT prolongation can occur with Sirturo. Concomitant use with other drugs that prolong the QT interval is discouraged as this may cause additive QT prolongation. Sirturo should be discontinued if significant ventricular arrhythmia or a QTc interval > 500 ms develops.

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BEDAQUILINE FUMARATE

RATIONALE (CONTINUED)
The most common adverse reactions reported in ≥10% of patients treated with Sirturo are nausea, arthralgia, and headache. Additional adverse events reported in ≥10% of patients treated with Sirturo and with a higher frequency than the placebo treatment group are hemoptysis and chest pain. Hepatic-related adverse drug reactions have also been reported with use of Sirturo. As a result, liver function tests should be monitored.

The major CYP isoenzyme involved in the metabolism of bedaquiline is CYP3A4. Co-administration of Sirturo with strong CYP3A4 inhibitors may increase the systemic exposure to bedaquiline, which could potentially increase the risk of adverse reactions. Therefore, the use of strong CYP3A4 inhibitors used systemically for more than 14 consecutive days should be avoided while on Sirturo, unless the benefit of treatment with the drug combination outweighs the risk. Alcohol should also be avoided throughout the treatment period.

Pregnancy Category B.

FDA APPROVED INDICATIONS
Sirturo is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adults (≥ 18 years) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Sirturo is reserved for use when an effective treatment regimen cannot otherwise be provided. Sirturo is not indicated for the treatment of latent, extra-pulmonary, or drug-sensitive tuberculosis.

REFERENCES

- Sirturo [Prescribing Information]. Titusville, NJ: Janssen Therapeutics; December 2012.
- UpToDate, Inc. Diagnosis, treatment, and prevention of drug-resistant tuberculosis. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated March 19, 2013. 25, 2013.
- Center Watch Clinical Trials Listing [database online]. Sirturo (bedaquiline fumarate). Available at http://www.centerwatch.com/ Accessed: April 30, 2013.

Part D Effective: 10/01/13	Created: 05/13	
Commercial Effective: 10/01/13	Client Approval: 08/13	P&T Approval: 08/13

C1 ESTERASE INHIBITOR

Generic	Brand	HICL	GCN	Exception/Other
C1 ESTERASE INHIBITOR	BERINERT CINRYZE	18568		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the requested medication Berinert?

   If yes, continue to #2.
   If no, continue to #3.

2. Does patient have a diagnosis of hereditary angioedema (HAE)?

   If yes, **approve Berinert for a 12 month duration for one fill of up to for #4 vials.**
   If no, do not approve.
   BERINERT DENIAL TEXT: Approval requires a diagnosis of hereditary angioedema (HAE).

3. Is Cinryze being prescribed or overseen by a hematologist or immunologist?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a hematologist or immunologist and a trial of danazol.

4. Has the patient tried or does the patient have a contraindication to danazol?

   If yes, **approve Cinryze for 12 months for up to #20 vials per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a hematologist or immunologist and a trial of danazol.

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C1 ESTERASE INHIBITOR

RATIONALE
To ensure the appropriate use of Berinert and Cinryze in patients with Hereditary Angioedema.

FDA APPROVED INDICATIONS
Berinert is a plasma-derived C1 Esterase Inhibitor (Human) indicated for the treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema in adult and adolescent patients. The safety and efficacy of Berinert for prophylactic therapy have not been established.

Cinryze is a C1 inhibitor indicated for routine prophylaxis against angioedema in adolescent and adult patients with hereditary angioedema.

REFERENCES

- CSL Behring LLC. Berinert package insert. Kankakee, IL. December 2011.
- ViroPharma, Inc. Cinryze product information. Exton, PA. November 2010.
- United States Hereditary Angioedema Association [online]. Available from: www.haea.org [Accessed: June 22, 2010].
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: www.thomsonhc.com/hcs/librarian/ [Accessed: June 30, 2011].

Part D Effective: 01/01/13 Created: 04/09
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

CABOZANTINIB S-MALATE

Generic	Brand	HICL	GCN	Exception/Other
CABOZANTINIB S-MALATE	COMETRIQ	39815		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of recurrent or persistent metastatic medullary thyroid cancer (MTC) or MTC that is symptomatic or structurally progressive?

   If yes, **approve for 12 fills by HICL with a quantity limit of #112 capsules per 28 days.**
   [**Note:** Cometriq is available in three dosage packs each containing 7 days supply:
   - 140mg daily dose pack (seven 80mg capsules and twenty one 20mg capsules
   - 100mg daily dose pack (seven 80mg capsules and seven 20mg capsules)
   - 60mg daily dose pack (twenty one 20mg capsules]

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of symptomatic or progressive medullary thyroid cancer with unresectable locally advanced or metastatic disease.

RATIONALE
Ensure appropriate utilization of Cometriq based on FDA approved indication and NCCN guidelines.

The recommended daily dose of Cometriq is 140 mg (one 80mg and three 20mg capsules). Patients should not to eat for at least 2 hours before and at least 1 hour after taking Cometriq. Capsules should be swallowed whole. Avoid foods (e.g., grapefruit, grapefruit juice) or nutritional supplements that are known to inhibit cytochrome P450.

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RATIONALE (CONTINUED)
Avoid the use of concomitant strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, nefazodone, saquinavir, telithromycin, ritonavir, indinavir, nelfinavir, voriconazole). For patients who require treatment with a strong CYP3A4 inhibitor, reduce the daily Cometriq dose by 40 mg (for example, from 140mg to 100mg daily or from 100mg to 60mg daily). Resume the dose that was used prior to initiating the CYP3A4 inhibitor 2 to 3 days after discontinuation of the strong inhibitor. Avoid the chronic use of concomitant strong CYP3A4 inducers (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital) if alternative therapy is available. For patients who require treatment with a strong CYP3A4 inducer, increase the daily Cometriq dose by 40mg (for example, from 140mg to 180mg daily or from 100mg to 140mg daily) as tolerated. Resume the dose that was used prior to initiating the CYP3A4 inducer 2 to 3 days after discontinuation of the strong inducer. The daily dose of Cometriq should not exceed 180mg.

Dosage reduction recommended to 100mg and then 60mg in the presence of NCI CTCAE Grade 4 hematologic adverse reactions, Grade 3 or greater non-hematologic adverse reactions or intolerable Grade 2 adverse reactions. Continue treatment until disease progression or unacceptable toxicity occurs.

Cometriq joins Caprelsa as the second oral once daily kinase inhibitor for the treatment of MTC. Cometriq inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, -2 and -3, KIT, TRKB, FLT-3, AXL, and TIE-2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment.

The American Cancer Society estimates that 56,460 Americans will be diagnosed with thyroid cancer and 1,780 will die from the disease in 2012. Nearly two thirds of cases occur in patients under the age of 55 years. Medullary thyroid cancer, which is derived from the neuroendocrine parafollicular C cells of the thyroid, accounts for only about 3 to 5 percent of all thyroid cancers. The 5 year survival rate for metastatic MTC is 28 percent.

The National Comprehensive Cancer Network (NCCN) guidelines consider both Cometriq and Caprelsa as category 1 treatments for recurrent or persistent metastatic MTC. They are also considered appropriate for unresectable MTC that is symptomatic or structurally progressive.

Two additional phase III trials are recruiting for Cometriq: COMET-1 and COMET-2 evaluating its use in the castration-resistant prostate cancer (CRPC) setting. Cometriq is available only through a limited distribution network.

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CABOZANTINIB S-MALATE

RATIONALE (CONTINUED)
Cometriq was approved based on the results of EXAM, a randomized phase 3 clinical trial conducted in 330 patients with progressive, metastatic MTC. Patients were randomized to receive Cometriq 140 mg (n =219) or placebo (n=111) orally once daily, without food, until disease progression determined by the treating physician or until intolerable toxicity. The median age of the study population was 55 years, 23% were 65 years or older. Twenty-five percent had two or more prior systemic therapies and 21% had been previously treated with a kinase inhibitor.

EXAM met its primary efficacy endpoint of improving progression-free survival (PFS): 11.2 months in the Cometriq arm compared to 4.0 months in the placebo arm. Partial responses were observed only among patients in the Cometriq arm (27 vs. 0 percent). There was no statistically significant difference in overall survival between the treatment arms at the planned interim analysis.

Cometriq has a boxed warning for increased occurrence of gastrointestinal perforations, fistula formation, and severe hemorrhage. Warnings and precautions include; thrombotic events, wound complications, hypertension, osteonecrosis of the jaw, palmar-plantar erythrodysesthesia syndrome (PPES), proteinuria, and reversible posterior leukoencephalopathy syndrome (RPLS).

The most commonly reported adverse drug reactions (≥25%) are diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, and constipation. The most common laboratory abnormalities (≥25%) are increased AST, increased ALT, lymphopenia, increased alkaline phosphatase, hypocalcemia, neutropenia, thrombocytopenia, hypophosphatemia, and hyperbilirubinemia.

Cometriq is not recommended for use in patients with moderate and severe hepatic impairment. Cometriq caused fetal harm in animal models and is pregnancy category D.

FDA APPROVED INDICATION
Cometriq is a kinase inhibitor indicated for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).

REFERENCES

- Cometriq [Prescribing Information]. South San Francisco, CA: Exelixis, Inc.; November 2012.
- Thyroid Cancer. American Cancer Society. Available at: http://www.cancer.org/cancer/thyroidcancer/index [Accessed January 22, 2013].
- Summary Review Application Number: 203756Orig1s000. Center for Drug Evaluation and Research. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203756Orig1s000SumR.pdf [Accessed January 22, 2013].

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REFERENCES (CONTINUED)

- NCCN Clinical Practice Guideline in Oncology: Thyroid Carcinoma Version 1.2013. National Comprehensive Cancer Network. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf [Accessed January 22, 2013].

Part D Effective: 04/01/13 Created: 01/13
Commercial Effective: 04/01/13 Client Approval: 02/13 P&T Approval: 02/13

CALCINEURIN INHIBITORS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
PIMECROLIMUS	ELIDEL	23167		
TACROLIMUS	PROTOPIC	20974		ROUTE = TOPICAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient at least 2 years old?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 2 years of age, a diagnosis of atopic dermatitis, and a trial of topical corticosteroids.

2. Does patient have a diagnosis of atopic dermatitis?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 2 years of age, a diagnosis of atopic dermatitis, and a trial of topical corticosteroids.

3. Has the patient had a therapeutic trial of topical corticosteroids without clinical improvement in the signs and symptoms of atopic dermatitis (i.e., itchy skin, erythema, edema/induration/papulation, excoriation, oozing/weeping/crusting, scaling and lichenification), OR was patient unable to tolerate topical corticosteroids or had adverse effects (i.e., thinning of the skin or telangiectasias (small dilated blood vessels near the surface of the skin or mucous membranes))?

   If yes, **approve as follows:**
   - **ELIDEL 1%: Approve for 12 months for patients 2 years old or older.**
   - **PROTOPIC 0.03%: Approve for 12 months for patients 2 years old or older.**
   - **PROTOPIC 0.1%: Approve for 12 months for patients older than 15 years old.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 2 years of age, a diagnosis of atopic dermatitis, and a trial of topical corticosteroids.

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CALCINEURIN INHIBITORS (PART D)

RATIONALE
Ensure appropriate use of Elidel and Protopic.

FDA APPROVED INDICATIONS
Atopic dermatitis (mild to moderate) as second-line therapy for short term and non-continuous chronic treatment in non-immunocompromised adults and children (2 years of age or older) failing other topical treatments or when those treatments are not advisable.

REFERENCES

- Novartis Pharmaceuticals Corp. Elidel package insert. East Hanover, NJ. August 2010.
- Astellas Pharma US, Inc. Protopic package insert. Deerfield, IL. June 2009.
- FDA Alert for Healthcare Professionals, June 2006.
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare; Available at: http://www.thomsonhc.com/micromedex2/librarian. [Accessed: June 20, 2011].

Part D Effective: 01/01/13 Created: 08/02
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

CERTOLIZUMAB PEGOL (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CERTOLIZUMAB PEGOL	CIMZIA	35554		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe Crohn's disease?

   If yes, continue to #2.
   If no, continue to #4.

2. Has the drug been prescribed by or is the patient currently being supervised by a gastroenterologist?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a gastroenterologist, a diagnosis of moderate to severe Crohn's disease and trial of one or more conventional therapies (corticosteroids, azathioprine, mercaptopurine, methotrexate, or mesalamine).

3. Has the patient tried one or more conventional therapies for Crohn's disease such as: corticosteroids, azathioprine, mercaptopurine, methotrexate, or mesalamine?

   If yes, **approve. Enter two authorizations as follows:**
   - **Approve for 1 fill of #1 Starter kit (= 6 prefilled syringes) OR #3 kits (= 6 vials or prefilled syringes) for the first month then,**
   - **Approve for 2 months of #1 kit (= 2 vials or prefilled syringes) per month.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a gastroenterologist, a diagnosis of moderate to severe Crohn's disease and a trial of one or more conventional therapies (corticosteroids, azathioprine, mercaptopurine, methotrexate, or mesalamine).

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INITIAL CRITERIA (CONTINUED)

4. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe rheumatoid arthritis, supervision by a rheumatologist, a trial of at least one recommended DMARD agent (disease-modifying antirheumatic drug), and concurrent methotrexate or a contraindication to methotrexate.

5. Has the drug been prescribed by or is the patient currently being supervised by a rheumatologist?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe rheumatoid arthritis, supervision by a rheumatologist, a trial of at least one recommended DMARD agent (disease-modifying antirheumatic drug), and concurrent methotrexate or a contraindication to methotrexate.

6. Has the patient tried or experienced intolerable side effects to at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, sulfasalazine?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe rheumatoid arthritis, supervision by a rheumatologist, a trial of at least one recommended DMARD agent (disease-modifying antirheumatic drug), and concurrent methotrexate or a contraindication to methotrexate.

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INITIAL CRITERIA (CONTINUED)

7. Is the patient taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, **approve. Enter two authorizations as follows:**
   - **Approve for 1 fill of #1 Starter kit (= 6 prefilled syringes) OR #3 kits (= 6 vials or prefilled syringes) for the first month then,**
   - **Approve for 2 months of #1 kit (= 2 vials or prefilled syringes) per month.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe rheumatoid arthritis, supervision by a rheumatologist, a trial of at least one recommended DMARD agent (disease-modifying antirheumatic drug), and concurrent methotrexate or a contraindication to methotrexate.

RENEWAL CRITERIA

1. Does the patient have Crohn's disease or rheumatoid arthritis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a gastroenterologist or a rheumatologist and a diagnosis of moderate to severe Crohn's disease or moderate to severe rheumatoid arthritis.

2. Has the drug been prescribed by or is the patient currently being supervised by a gastroenterologist or rheumatologist?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a gastroenterologist or a rheumatologist and a diagnosis of moderate to severe Crohn's disease or moderate to severe rheumatoid arthritis.

3. Does the patient have Crohn's disease?

   If yes, **approve for 12 months of #1 kit (= 2 vials or prefilled syringes) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, continue to #4.

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CERTOLIZUMAB PEGOL (PART D)

RENEWAL CRITERIA (CONTINUED)

4. Does the patient have rheumatoid arthritis?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a gastroenterologist or a rheumatologist and a diagnosis of moderate to severe Crohn's disease or moderate to severe rheumatoid arthritis.

5. Has the patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, a diagnosis of moderate to severe rheumatoid arthritis, that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy and that the patient is currently taking methotrexate or has a contraindication to methotrexate.

6. Is the patient currently taking methotrexate or does the patient have a contraindication to methotrexate?

   If yes, **approve for 12 months of #1 kit (= 2 vials or prefilled syringes) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, a diagnosis of moderate to severe rheumatoid arthritis, that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy and that the patient is currently taking methotrexate or has a contraindication to methotrexate.

RATIONALE

Ensure appropriate diagnostic, utilization and safety criteria are used for the management of prior authorization requests for certolizumab pegol.

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CERTOLIZUMAB PEGOL (PART D)

FDA APPROVED INDICATIONS

CIMZIA is indicated for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease that have had an inadequate response to conventional therapy. CIMZIA is also indicated for the treatment of moderately to severely active rheumatoid arthritis.

REFERENCES

- UCB, Inc. Cimzia product information, Smyrna, GA. May 2009.
- Bristol-Myers Squibb. Orencia product information. Princeton, NJ. August 2009.
- Amgen. Kineret product information. Thousand Oaks, CA. December 2009.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at https://www.thomsonhc.com/hcs/librarian. [Accessed: June 7, 2010].

Part D Effective: 04/01/13 Created: 05/08
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

CHENODIOL

Generic	Brand	HICL	GCN	Exception/Other
CHENODIOL	CHENODAL	01364		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is chenodiol being prescribed for the treatment of radiolucent gallstones?

   If yes, continue to #3.
   If no, continue to #2.

2. Is chenodiol being prescribed for cerebrotendinous xanthomatosis?

   If yes, **approve by HICL up to #3 per day per month for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of gallstones and trial of ursodiol, or a diagnosis of cerebrotendinous xanthomatosis.

3. Has the patient had a previous trial of or contraindication to the use of ursodiol?

   If yes, **approve by HICL up to #4 per day per month for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of gallstones and trial of ursodiol, or a diagnosis of cerebrotendinous xanthomatosis.

RATIONALE
Ensure appropriate utilization for chenodiol.

FDA APPROVED INDICATIONS
Chenodiol is indicated for patients with radiolucent stones in well-opacifying gallbladders, in whom selective surgery would be undertaken except for the presence of increased surgical risk due to systemic disease or age.

The likelihood of successful dissolution is far greater if the stones are floatable or small. For patients with nonfloatable stones, dissolution is less likely and added weight should be given to the risk that more emergent surgery might result from a delay due to unsuccessful treatment.

Safety of use beyond 24 months is not established. Chenodiol will not dissolve calcified (radiopaque) or radiolucent bile pigment stones.

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CHENODIOL

DOSAGE AND ADMINISTRATION

The recommended dose range for Chenodal (chenodiol tablets) is 13 to 16 mg/kg/day in two divided doses, morning and night, starting with 250 mg b.i.d. the first two weeks and increasing by 250 mg/day each week thereafter until the recommended or maximum tolerated dose is reached. If diarrhea occurs during dosage buildup or later in treatment, it usually can be controlled by temporary dosage adjustment until symptoms abate, after which the previous dosage usually is tolerated. Dosage less than 10 mg/kg usually is ineffective and may be associated with increased risk of cholecystectomy, so is not recommended.

REFERENCES

- Micromedex Healthcare Series [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 2008. Available at: https://www.thomsonhc.com/micromedex2/librarian. [Accessed: June 21, 2011].
- Manchester Pharmaceuticals. Chenodal™ package insert. Fort Collins, CO. September 2009.
- Petroni ML, Jazrawi RP, Pazzi P, et al. Ursodeoxycholic acid alone or with chenodeoxycholic acid for dissolution of cholesterol gallstones: a randomized multicentre trial. The British-Italian Gallstone Study group. Aliment Pharmacol. 2001; 15(1): 123-128.
- Verrips A, Wevers RA, Van Engelen BG, et al. Effect of simvastatin in addition to chenodeoxycholic acid in patients with cerebrotendinous xanthomatosis. Metabolism. 1999; 48(2): 233-238.
- Batta AK, Salen G, Tint GS. Hydrophilic 7 beta-hydroxy bile acids, lovastatin, and cholestyramine are ineffective in the treatment of cerebrotendinous xanthomatosis. Metabolism. 2004; 53(5): 556-562.

Part D Effective: 01/01/13 Created: 11/09
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

CHOLINESTERASE INHIBITORS

Generic	Brand	HICL	GCN	Exception/Other
DONEPEZIL	ARICEPT ARICEPT ODT	12259		
GALANTAMINE	RAZADYNE RAZADYNE ER RAZADYNE SOLN	16520		
RIVASTIGMINE TARTRATE	EXELON EXELON SOLN	18527		
RIVASTIGMINE	EXELON PATCH	34884		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient currently receiving cholinesterase inhibitor therapy (per MRF or claims history)?

   If yes, continue to #6.
   If no, continue to #2.

2. Is the request for Exelon (oral, solution or patch)?

   If yes, continue to #3.
   If no, continue to #4.

3. Is the patient diagnosed with dementia associated with Parkinson's disease or Alzheimer's disease?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of dementia associated with Parkinson's disease or Alzheimer's disease and Mini Mental State Exam (MMSE) score of 26 or less.

4. Is the patient diagnosed with dementia associated with Alzheimer's disease?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of dementia associated with Alzheimer's disease and Mini Mental State Exam (MMSE) score of 26 or less.

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GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a Mini Mental State Exam (MMSE) score of 26 or less?

   If yes, **approve as follows:**
   - **ARICEPT OR ARICEPT ODT: approve for 12 months, #1 per day per month by HICL**
   - **EXELON CAPSULES: approve for 12 months, #2 per day per month**
   - **EXELON ORAL SOLUTION: approve for 12 months, with a quantity limit of #2 bottles (240mL, 2 x 120mL bottle) per month**
   - **EXELON PATCH: approve for 12 months, #1 per day per month**
   - **RAZADYNE: approve for 12 months, #2 per day per month**
   - **RAZADYNE ER: approve for 12 months, #1 per day per month**
   - **RAZADYNE ORAL SOLUTION: approve for 12 months with a quantity limit of #2 bottles (200mL, 2 x 100mL bottle) per month**

   If no, do not approve.
   DENIAL TEXT: Approval requires a Mental State Exam (MMSE) score of 26 or less.

6. Is the patient diagnosed with dementia associated with Parkinson's disease or Alzheimer's disease?

   If yes, **approve as follows:**
   - **ARICEPT OR ARICEPT ODT: approve for 12 months, #1 per day per month by HICL**
   - **EXELON CAPSULES: approve for 12 months, #2 per day per month**
   - **EXELON ORAL SOLUTION: approve for 12 months, with a quantity limit of #2 bottles (240mL, 2 x 120mL bottle) per month**
   - **EXELON PATCH: approve for 12 months, #1 per day per month**
   - **RAZADYNE: approve for 12 months, #2 per day per month**
   - **RAZADYNE ER: approve for 12 months, #1 per day per month**
   - **RAZADYNE ORAL SOLUTION: approve for 12 months with a quantity limit of #2 bottles (200mL, 2 x 100mL bottle) per month**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of dementia associated with Parkinson's disease or Alzheimer's disease.

RATIONALE
To ensure appropriate utilization of cholinesterase inhibitors for the management of Alzheimer's or Parkinson's disease.

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CHOLINESTERASE INHIBITORS

FDA APPROVED INDICATIONS

ARICEPT and ARICEPT ODT are indicated for the treatment of mild to severe dementia of Alzheimer's type.
EXELON is indicated for the treatment of mild to moderate dementia associated with Parkinson's disease and treatment of mild to moderate dementia associated with Alzheimer's type.
RAZADYNE and EXELON are indicated for the treatment of mild to moderate dementia of the Alzheimer's type.

REFERENCES

- Eisai Co. Ltd. Aricept and Aricept ODT package insert. Woodcliff Lake, NJ. November 2010.
- Ortho-McNeil Neurologics, Inc. Razadyne and Razadyne ER package insert. Titusville, NJ. April 2008.
- Novartis Pharmaceuticals. Exelon capsule and solution package insert. East Hanover, NJ. June 2006.
- Novartis Pharmaceuticals. Exelon patch package insert. East Hanover, NJ. August 2010.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at https://www.thomsonhc.com/hcs/librarian. [Accessed: June 7, 2010].

Part D Effective: 01/01/13 Created: 05/97
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

CLOBAZAM

Generic	Brand	HICL	GCN	Exception/Other
CLOBAZAM	ONFI	06536		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Lennox-Gastaut Syndrome?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Lennox-Gastaut Syndrome; patient is at least 2 years old; and a trial of lamotrigine or topiramate.

2. Is the patient ≥ 2 years of age?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Lennox-Gastaut Syndrome; patient is at least 2 years old; and a trial of lamotrigine or topiramate.

3. Has the patient tried or does the patient have a contraindication to lamotrigine or topiramate?

   If yes, **approve for 12 months by HICL with a quantity limit of #60 tablets per 30 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Lennox-Gastaut Syndrome; patient is at least 2 years old: and a trial of lamotrigine or topiramate.

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CLOBAZAM

RATIONALE

Limit use to FDA approved indication of adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in patients 2 years and older. Usual dose starts at 5mg once or twice daily, and is titrated up based on weight to a max of 40mg per day. Doses above 5 mg/day should be administered in two divided doses. Dosage adjustments required in the elderly, CYP2C19 poor metabolizers, and hepatic impairment. Prefer use of generically available treatments also FDA approved for Lennox-Gastaut syndrome.

FDA APPROVED INDICATIONS

Adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in patients 2 years of age or older.

REFERENCES

- Lundbeck Inc. Onfi package insert. Deerfield, IL. October 2011.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2011. URL: http://cp.gsm.com. Updated December 2011.
- Leahy JT, Chu-Shore CJ, Fisher JL. (2011). Clobazam as an adjunctive therapy in treating seizures associated with Lennox–Gastaut syndrome*. Neuropsychiatric Disease and Treatment, 7,* 673–681.

Part D Effective: 01/01/13	Created: 02/12	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

COLLAGENASE INJECTION

Generic	Brand	HICL	GCN	Exception/Other
COLLAGENASE CLOSTRIDIUM HISTOLYTICUM	XIAFLEX		28257	ROUTE = INJECTION

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Has the prescriber completed Xiaflex training as provided by the REMS program (Xiaflex Xperience)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the prescriber has completed Xiaflex training as provided by the REMS program.

2. Does the patient have a diagnosis of Dupuytren's contracture with a palpable cord?

   If yes, **approve #1 vial per month for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Dupuytren's contracture with a palpable cord.

RATIONALE
Ensure appropriate utilization of Xiaflex. Xiaflex injections may be administered up to 3 times per cord at approximately 4-week intervals. Inject only one cord at a time. If a patient has other cords with contractures, inject each cord in sequential order.

FDA APPROVED INDICATION
Xiaflex is indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.

REFERENCES

- Auxilium Pharmaceuticals. Xiaflex™ (collagenase clostridium histolyticum) package insert. Malvern, PA. February 2010.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 21, 2011].

Part D Effective: 01/01/13 Created: 03/10
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

COMPOUNDED DRUGS FOR ERECTILE DYSFUNCTION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ALPROSTADIL	ALPROSTADIL	00177		
PHENTOLAMINE	PHENTOLAMINE	02100		
PAPAVERINE	PAPAVERINE	00170		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the product being used for erectile dysfunction?

   If yes, do not approve.
   DENIAL TEXT: Approval requires the use of this medication is not for the treatment of erectile dysfunction.
   If no, continue to #2.

2. **Approve by HICL for 12 months. (Note: Only ALPROSTADIL needs text.)**
   ALPROSTADIL APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE
To promote utilization for Part D indications only. Part D does not approve drugs used for erectile dysfunction.

WARNING Apnea is experienced by about 10 to 12% of neonates with congenital heart defects treated with Alprostadil Injection, USP. Apnea is most often seen in neonates weighing less than 2 kg at birth and usually appears during the first hour of drug infusion. Therefore, respiratory status should be monitored throughout treatment, and Alprostadil Injection, USP should be used where ventilatory assistance is immediately available.

FDA APPROVED INDICATIONS
ALPROSTADIL is indicated for patent ductus arteriosus and erectile dysfunction.

ALPROSTADIL INJECTION, USP is indicated for palliative, not definitive, therapy to temporarily maintain the patency of the ductus arteriosus until corrective or palliative surgery can be performed in neonates who have congenital heart defects and who depend upon the patent ductus for survival.

CONTINUED ON NEXT PAGE

FDA APPROVED INDICATIONS (CONTINUED)

ALPROSTADIL INJECTION, USP continued: Such congenital heart defects include pulmonary atresia, pulmonary stenosis, tricuspid atresia, tetralogy of Fallot, interruption of the aortic arch, coarctation of the aorta, or transposition of the great vessels with or without other defects.
In infants with restricted pulmonary blood flow, the increase in blood oxygenation is inversely proportional to pretreatment pO2 values; that is, patients with low pO2 values respond best, and patients with pO2 values of 40 torr or more usually have little response. Alprostadil injection should be administered only by trained personnel in facilities that provide pediatric intensive care.

PAPAVERINE is indicated for relief of cerebral and peripheral ischemia associated with arterial spasm and myocardial ischemia complicated by arrhythmias.
As an antispasmodic in the following conditions:

- Visceral spasm, e.g. gastrointestinal colic, biliary and urinary tract spasms.
- Peripheral vascular disease in which there is a vasospastic element.
- Vascular spasm associated with acute myocardial infarction, angina pectoris, peripheral and pulmonary embolism.

PHENTOLAMINE MESYLATE FOR INJECTION is indicated for the prevention or control of hypertensive episodes that may occur in a patient with pheochromocytoma as a result of stress or manipulation during preoperative preparation and surgical excision; for the prevention or treatment of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine; for the diagnosis of pheochromocytoma by the phentolamine blocking test.

PHENTOLAMINE MESYLATE FOR INJECTION is indicated for the prevention or control of hypertensive episodes that may occur in a patient with pheochromocytoma as a result of stress or manipulation during preoperative preparation and surgical excision.

PHENTOLAMINE MESYLATE FOR INJECTION is indicated for the prevention or treatment of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine.

PHENTOLAMINE MESYLATE FOR INJECTION is also indicated for the diagnosis of pheochromocytoma by the phentolamine blocking test.

REFERENCES

- Bedford Labs. Phentolamine package insert. Bedford, OH May 1999.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. Available at: http://www.clinicalpharmacology.com. Updated 2011. [Accessed: June. 10, 2011].
- Bedford Labs. Alprostadil package insert. Bedford, OH, August 2000.
- Teva Pharmaceutical. Papaverine package insert. Hungary. June 2007.

Part D Effective: 01/01/13 Created: 12/08
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

CORTICOSTEROID BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
BETAMET ACET/BETAMET NA PH BETAMETHASONE CORTISONE ACETATE DEXAMETHASONE DEXAMETHASONE ACETATE DEXAMETHASONE SOD PHOSPHATE HYDROCORTISONE HYDROCORTISONE SOD SUCC/PF HYDROCORTISONE SOD SUCCINATE METHYLPREDNISOLONE METHYLPREDNISOLONE ACETATE METHYLPREDNISOLONE SOD SUCC METHYLPREDNISOLONE SOD SUCC/PF PREDNISOLONE PREDNISOLONE ACETATE PREDNISOLONE SOD PHOSPHATE PREDNISONE TRIAMCINOLONE ACETONIDE TRIAMCINOLONE DIACETATE TRIAMCINOLONE HEXACETONIDE	VARIOUS			TCC = P5A, P5B, P5C GPID ≠ 26963, 27412, 28680, 28895, 28895, 30141, 99610 AND ROUTE ≠ INHALATION, INTRAOCULAR, RECTAL, MISCELL.

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the request for an organ transplant?

   If yes, continue to #2.
   If no, continue to #3.

CONTINUED ON NEXT PAGE

CORTICOSTEROID BVD DETERMINATION (PART D)

GUIDELINES FOR USE (CONTINUED)

2. Was the organ transplant approved by and paid for under Medicare?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #3. **(CSR: If unknown, ask the caller to submit MRF.)**

3. **Lifetime approval under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE

Corticosteroid therapy is covered under Part B for patients who received a Medicare covered organ transplant.

REFERENCES

- Medicare Prescription Drug Benefit Manual: Chapter 6 – Part D Drugs and Formulary Requirements

Part D Effective: 01/01/13	Created: 03/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

CORTICOTROPIN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CORTICOTROPIN	ACTHAR HP GEL	02830		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the product being ordered for diagnostic purposes?

   If yes, do not approve.
   DENIAL TEXT: Approval requires corticotropin not be used for diagnostic purposes. Please consider cosyntropin (Cortrosyn®).
   If no, continue to #2.

2. Is the patient being treated for acute exacerbation of multiple sclerosis?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried or does the patient have a contraindication to IV corticosteroids?

   If yes, **approve up to #120 units per day for up to 21 days.**
   PAC NOTE: Each 5mL vial of Acthar Gel contains 400 units. Approve 7 vials per 21 days treatment.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of infantile spasms in patients less than 2 years of age. All other FDA approved indications require a trial of IV corticosteroids.

4. Is the patient less than two years old and diagnosed with infantile spasms?

   If yes, **approve for 28 days with a maximum of #8 vials (each 5mL vial contains 400 units).**
   If no, continue to #5.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE (CONTINUED)

5. Is the patient diagnosed with a rheumatic disorder (such as psoriatic arthritis, rheumatoid arthritis including juvenile rheumatoid arthritis, or ankylosing spondylitis), systemic lupus erythematosus or systemic dermatomyositis (polymyositis), severe erythema multiforme (Stevens-Johnson syndrome), serum sickness, severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa (such as keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation), symptomatic sarcoidosis, or is the requested medication being used to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type, or that due to lupus erythematosus?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of infantile spasms in patients less than 2 years of age. All other FDA approved indications require a trial of IV corticosteroids.

6. Has the patient tried or does the patient have a contraindication to IV corticosteroids?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of infantile spasms in patients less than 2 years of age. All other FDA approved indications require a trial of IV corticosteroids.

RATIONALE

Ensure appropriate therapeutic use of this long acting corticotropin formulation.

The recommended regimen for use in infantile spasms is a daily dose of 150 units/m^2 (divided into twice daily intramuscular injections of 75 units/ m2) then a gradual taper over a 2-week period. A suggested taper schedule is 30 units/ m^2 every morning for 3 days, 15 units/ m^2 every morning for 3 days, 10 units/ m^2 every morning for 3 days, and then 10 units/ m^2 every other morning for 6 days.

8 vials per 28 days supply based on dosage of 150 units/m^2/day with an estimate of 0.7m^2 body surface area, estimated maximum for a child less than 40 pounds (two years old).

The American Academy of Neurology guidelines for treatment of infantile spasms state that response is usually within 2 weeks and current clinical data is insufficient to determine optimum dosage and duration.

Questcor states that the H.P. Acthar Gel vial expires 28 days after initial puncture, when stored under ideal conditions (per USP standard guidelines).

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CORTICOTROPIN (PART D)

FDA APPROVED INDICATIONS

Acthar Gel is indicated for the treatment of infantile spasms, for acute exacerbations of multiple sclerosis, and for numerous other diseases and disorders. (See below).

INFANTILE SPASMS: Monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

MULTIPLE SCLEROSIS: Treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

RHEUMATIC DISORDERS: As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), and ankylosing spondylitis.

COLLAGEN DISEASES: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus or systemic dermatomyositis (polymyositis).

DERMATOLOGIC DISEASES: Severe erythema multiforme (Stevens-Johnson syndrome).

ALLERGIC STATES: Serum sickness.

OPHTHALMIC DISEASES: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation.

RESPIRATORY DISEASES: Symptomatic sarcoidosis.

EDEMATOUS STATE: To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

REFERENCES

- Amphastar Pharmaceuticals, Inc. Cortrosyn package insert. Rancho Cucamonga, CA. September 2005.
- Baram TZ, Mitchell WG et al. High-dose corticotropin (ACTH) versus prednisone for infantile spasms; a prospective, randomized, blinded study. Pediatrics 1996; 97:375–379.
- CDC child growth charts (birth to 36 months for boys and girls). Last modified 4/20/2001. Accessible online at http://www.cdc.gov/growthcharts/data/set2clinical/cj41l067.pdf [Accessed June 28, 2011].

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REFERENCES (CONTINUED)

- Gettig J, Cummings J, and Matuszewski K. H.P. Acthar Gel and Cosyntropin Review. Pharmacy and Therapeutics 2009; 34 (5): 250-252.
- Mackay MT, Weiss, SK, Adams-Webber, T et al. Practice Parameter: Medical Treatment of Infantile Spasms Report of the American Academy of Neurology and the Child Neurology Society. Neurology 2004; 62:1668–1681. Accessible online at http://www.neurology.org/content/62/10/1668.full.pdf [Accessed June 28, 2011].
- Questcor Pharmaceuticals, Inc. HP Acthar Gel package insert. Hayward, CA. June 2011.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: http://www.thomsonhc.com/micromedex2/librarian. [Accessed: June 28, 2011].
- Riikonen R. A long-term follow-up study of 214 children with the syndrome of infantile spasms. Neuropediatrics. 1982; 13:14–23.

Part D Effective: 10/01/13 Created: 11/07
Commercial Effective: N/A Client Approval: 08/13 P&T Approval: 08/13

CRIZOTINIB

Generic	Brand	HICL	GCN	Exception/Other
CRIZOTINIB	XALKORI	37916		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of locally advanced or metastatic non small cell lung cancer (NSCLC)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of locally advanced or metastatic non small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK) positive.

2. Is the patient's tumor anaplastic lymphoma kinase (ALK) positive?

   If yes, **approve for 1 year with a quantity limit of #2 per day by HICL.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of locally advanced or metastatic non small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK) positive.

RATIONALE
To promote appropriate utilization of crizotinib for its FDA approved indication at its FDA approved dosage.

The recommended dose of crizotinib is 250mg twice daily with or without food. Dose reduction to 200mg twice daily or discontinuation is recommended in the presence of certain toxicities.

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CRIZOTINIB

FDA APPROVED INDICATIONS

Xalkori is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

This indication is based on response rate. There are no data available demonstrating improvements in patient reported outcomes or survival with Xalkori.

REFERENCE

- Pfizer Labs. Xalkori package insert. New York, NY August 2011.

Part D Effective: 01/01/13	Created: 09/11	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

CYCLOPHOSPHAMIDE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CYCLOPHOSPHAMIDE	CYTOXAN	03893		ROUTE = ORAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: For oral cyclophosphamide, this PA is for administrative Step Override purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the drug to be administered to treat a cancerous condition?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #2.

2. Is the request for an organ transplant?

   If yes, continue to #3.
   If no, continue to #4.

3. Was the organ transplant approved by and paid under Medicare?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #4. **(CSR: If unknown, ask the caller to submit MRF.)**

4. **Lifetime approval under Part D. (Populate the B vs. D field with a "D" in PA override field.)**

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CYCLOPHOSPHAMIDE BVD DETERMINATION (PART D)

RATIONALE
To determine whether cyclophosphamide is being used to treat a medical condition other than those for which it's use qualifies for coverage under Medicare Part B.

FDA APPROVED INDICATIONS
Acute lymphoid leukemia, acute myeloid leukemia, breast cancer, Burkitt's lymphoma, chronic lymphoid leukemia, chronic myeloid leukemia, Hodgkin's disease (stages III and IV, Ann Arbor staging system), Malignant histiocytosis, malignant lymphoma, Mantle cell lymphoma (stages III and IV, Ann Arbor staging system), minimal change disease in patients who fail to respond to or are unable to tolerate adrenocorticosteroid therapy, multiple myeloma, mycosis fungoides (advanced), neuroblastoma (disseminated disease), Non-Hodgkin's lymphoma, ovarian carcinoma, retinoblastoma.

Malignant Diseases
CYTOXAN, although effective alone in susceptible malignancies, is more frequently used concurrently or sequentially with other antineoplastic drugs. The following malignancies are often susceptible to CYTOXAN treatment:

1. Malignant lymphomas (Stages III and IV of the Ann Arbor staging system), Hodgkin's disease, lymphocytic lymphoma (nodular or diffuse), mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma.
2. Multiple myeloma.
3. Leukemias: Chronic lymphocytic leukemia, chronic granulocytic leukemia (it is usually ineffective in acute blastic crisis), acute myelogenous and monocytic leukemia, acute lymphoblastic (stem-cell) leukemia in children (CYTOXAN given during remission is effective in prolonging its duration).
4. Mycosis fungoides (advanced disease).
5. Neuroblastoma (disseminated disease).
6. Adenocarcinoma of the ovary.
7. Retinoblastoma.
8. Carcinoma of the breast.

REFERENCES

- Bristol-Myers Squibb. Cytoxan package insert. Princeton, NJ. September 2005.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13	Created: 09/05	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

CYCLOSPORINE OPHTHALMIC

Generic	Brand	HICL	GCN	Exception/Other
CYCLOSPORINE	RESTASIS		19216	ROUTE = OPHTHALMIC

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Has the treatment been prescribed or is it currently being supervised by an ophthalmologist, optometrist or rheumatologist?

   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have keratoconjunctivitis sicca (KCS) or dry eye disease?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the drug is prescribed by an ophthalmologist, optometrist or rheumatologist for patients with a diagnosis of keratoconjunctivitis sicca (KCS) or dry eye disease.

3. **Approve for 12 months with a quantity limit of #2 boxes of 30 vials per a box each (#60 vials) or #1 box of 60 vials per month.**

RATIONALE
To ensure cost-effective treatment of keratoconjunctivitis sicca.

FDA APPROVED INDICATIONS
Indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.

The safety and efficacy has not been established in pediatric patients below the age of 16.

REFERENCES

- Allergan Inc. Restasis package insert. Irvine, CA. February 2010.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard Inc.; 2010. Available at http://www.clinicalpharmacology.com. [Accessed June 8, 2010].

Part D Effective: 01/01/13 Created: 08/03
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

DABIGATRAN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
DABIGATRAN ETEXILATE MESYLATE	PRADAXA	35604		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of non-valvular atrial fibrillation (AF)?

   If yes, **approve for 12 months by HICL for #2 capsules per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of non-valvular atrial fibrillation (AF).

RATIONALE
To ensure appropriate use of dabigatran for the indication of prevention of stroke or systemic embolism in non-valvular atrial fibrillation.

FDA APPROVED INDICATIONS
Reduction of risk of stroke or systemic embolism in non-valvular atrial fibrillation.

REFERENCE
- Boehringer Ingelheim Pharmaceuticals, Inc. Pradaxa package insert. Ridgefield, CT. March 2011.

Part D Effective: 04/01/13 Created: 10/10
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

DABRAFENIB

Generic	Brand	HICL	GCN	Exception/Other
DABRAFENIB MESYLATE	TAFINLAR	40360		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic melanoma?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a $BRAF^{V600E}$ mutation.

2. Does patient have the genetic mutation called $BRAF^{V600E}$?

   If yes, **approve for 12 months with a quantity limit of #120 capsules per 30 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a $BRAF^{V600E}$ mutation.

RATIONALE
Ensure appropriate use of Tafinlar based on FDA approved indication.

The recommended dose for Tafinlar is 150 mg orally taken twice daily, approximately 12 hours apart, until disease progression or unacceptable toxicity occurs. The dose should be administered at least 1 hour before or at least 2 hours after a meal. A missed dose can be taken up to 6 hours prior to the next dose. Do not open, crush, or break Tafinlar capsules.

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RATIONALE (CONTINUED)
Dose modifications are recommended in the presence of certain adverse reactions as follows:

Dose Reductions	Dose and Schedule
First dose reduction	100 mg orally twice daily
Second dose reduction	75 mg orally twice daily
Third dose reduction	50 mg orally twice daily
If unable to tolerate 50 mg twice daily	Discontinue Tafinlar

Warnings and precautions include new primary cutaneous malignancies, tumor promotion in BRAF wild-type melanoma, serious febrile reactions, hyperglycemia, uveitis and iritis, glucose-6-phosphate dehydrogenase deficiency, and embryofetal toxicity. The most common adverse reactions (≥20%) for Tafinlar are hyperkeratosis, headache, pyrexia, arthralgia, papilloma, alopecia, and palmar-plantar erythrodysesthesia syndrome.

Concurrent administration of strong inhibitors or inducers of CYP3A4 or CYP2C8 is not recommended. Drugs that increase gastric pH may decrease dabrafenib concentrations. Concomitant use with agents that are substrates of CYP3A4, CYP2C8, CYP2C9, CYP2C19, or CYP2B6 may result in loss of efficacy of these agents.

Tafinlar is pregnancy category D. Female patients should use highly effective contraception during treatment and for 4 weeks following discontinuation of treatment. Male patients have a potential risk for impaired spermatogenesis. Nursing mothers are advised to discontinue drug or nursing.

Tafinlar (dabrafenib) joins Zelboraf (vemurafenib) as the second FDA approved inhibitor of BRAF V600E mutation approved for the treatment of advanced melanoma. They are both approved in combination with a companion diagnostic test; THxID BRAF Kit for Tafinlar and COBAS 4800 BRAF V600 Mutation Test for Zelboraf. BRAF V600E mutations are present about half of all metastatic melanomas.

In 2013, an estimated 76,690 Americans will be diagnosed melanoma and another 9,480 will die from it. There were approximately 822,770 Americans with history of melanoma in 2008. The lifetime risk of being diagnosed with melanoma is about 2 percent. The 5 year survival rate for metastatic disease is between 15 and 20 percent. Risk factors for melanoma include family history, genetic predisposition, and sun exposure.

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RATIONALE (CONTINUED)
At the time of this writing, Tafinlar is not yet included in the National Comprehensive Cancer Network (NCCN) melanoma treatment guidelines. Yervoy (ipilimumab), Zelboraf (for patients with a V600E mutation), and high dose Proleukin (aldesleukin) are the preferred systemic therapies for advanced or metastatic melanoma. Other active regimens include dacarbazine, temozolomide, Gleevec (for C-KIT mutated tumors), paclitaxel, and paclitaxel with carboplatin. The newer FDA agents Zelboraf and Yervoy are more commonly used than the other FDA approved agents Proleukin and dacarbazine. Hydroxyurea is FDA approved for the treatment of metastatic melanoma but no longer used. The commonly used off-label chemotherapy regimens have low objective tumor response rates and no evidence of improved survival.

Tafinlar was also studied for BRAF V600K mutation-positive cutaneous melanoma and for treatment of CNS metastases from BRAF V600E or K mutation-positive cutaneous melanoma in the BREAK-2 and BREAK-MB trials. The FDA reviewed data from these trials and determined that it did not constitute substantial evidence of effectiveness.

Mekinist (trametinib), a MEK 1 and MEK 2 inhibitor, was approved for metastatic melanoma with BRAF V600E or V600K mutations on the same day as Tafinlar. It is expected to be available in pharmacies later in 2013. The companion diagnostic test for Tafinlar is also approved for use with Mekinist. It detects for both the BRAF V600E or V600K mutations. While not yet approved as combination therapy, there are several ongoing trials investigating the use of Tafinlar in combination with Mekinist for the treatment of metastatic melanoma.

The FDA approval of Tafinlar was based on two studies.

The BREAK-3 trial (referred to as Trial 1 in Tafinlar's prescribing information) involved 250 patients with previously untreated BRAF V600E mutation-positive, unresectable, or metastatic melanoma. Patients were randomized to receive Tafinlar 150 mg by mouth twice daily or dacarbazine 1,000 mg/m^2 intravenously every 3 weeks. The main efficacy outcome measure was progression-free survival (PFS). Confirmed objective response rate (ORR) and duration of response were also measured.

The median duration of follow-up prior to initiation of alternative treatment in the Tafinlar arm was 5.1 months and in the dacarbazine arm was 3.5 months. Twenty-eight (44 percent) patients crossed over from the dacarbazine arm at the time of disease progression to receive Tafinlar. The Tafinlar arm demonstrated a statistically significant increase in progression-free survival (5.1 months median survival) compared to the dacarbazine arm (2.7 months median survival). The median duration of treatment was 4.9 months for Tafinlar and 2.8 months for dacarbazine treated patients.

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RATIONALE (CONTINUED)

Trial 1: Investigator-Assessed Progression-Free Survival and Confirmed Objective Response Results (from Tafinlar prescribing information)

	TAFINLAR N = 187	Dacarbazine N = 63
Progression-free Survival		
Number of Events (%)	78 (42%)	41 (65%)
Progressive Disease	76	41
Death	2	0
Median, months (95% CI)	5.1 (4.9, 6.9)	2.7 (1.5, 3.2)
HR[a] (95% CI)	0.33 (0.20, 0.54)	
P-value[b]	*P* <0.0001	
Confirmed Tumor Responses		
Objective Response Rate	52%	17%
(95% CI)	(44, 59)	(9, 29)
CR, n (%)	6 (3%)	0
PR, n (%)	91 (48%)	11 (17%)
Duration of Response		
Median, months (95% CI)	5.6 (5.4, NR)	NR (5.0, NR)

[a] Pike estimator, stratified by disease state.

[b] Stratified log-rank test.

CI = Confidence interval; CR = complete response; HR = hazard ratio; NR = not reached; PR = partial response

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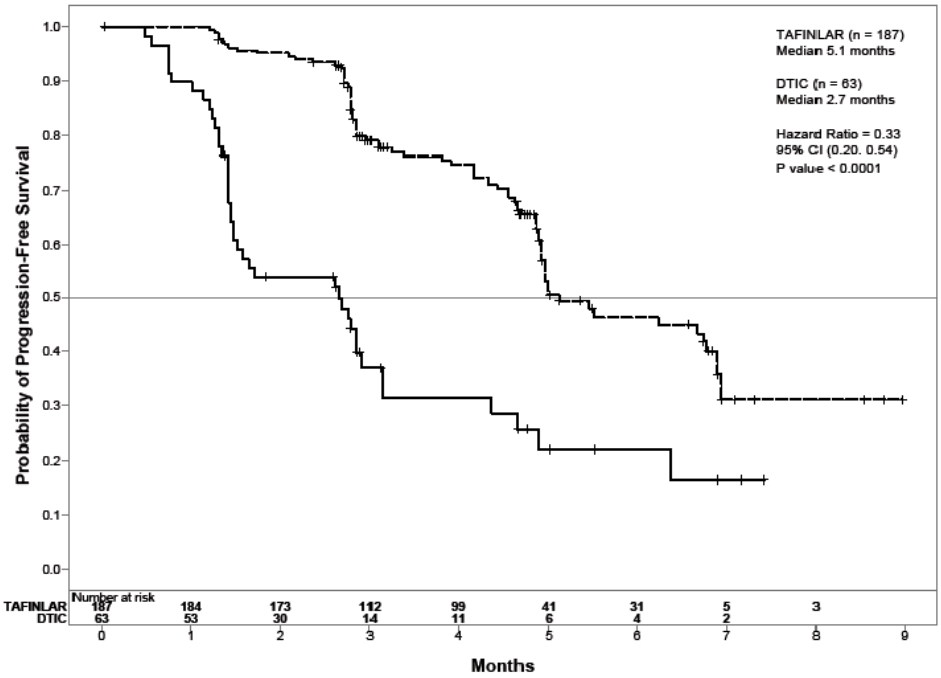
RATIONALE (CONTINUED)

Trial 1: Kaplan-Meier Curves of Investigator-Assessed Progression-Free Survival (from Tafinlar prescribing information)



Trial 2 was a single arm, open-label design of patients with BRAF V600E mutation-positive melanoma, metastatic to the brain. All patients received Tafinlar 150 mg twice daily. Patients in Cohort A (n=74) had received no prior local therapy for brain metastases, while patients in Cohort B (n=65) had received at least one local therapy for brain metastases, including, but not limited to, surgical resection, whole brain radiotherapy, or stereotactic radiosurgery such as gamma knife, linear accelerated-based radiosurgery, charged particles, or CyberKnife. In addition, patients in Cohort B were required to have evidence of disease progression in a previously treated lesion or an untreated lesion. The primary outcome measure was estimation of the overall intracranial response rate (OIRR) in each cohort.

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RATIONALE (CONTINUED)

Trial 2: Efficacy Results in Patients with BRAF V600E Melanoma Brain Metastases (from Tafinlar prescribing information)

	IRRC Assessed Response	
Endpoint	**Cohort A N = 74**	**Cohort B N = 65**
Overall Intracranial Response Rate (OIRR) % (95% CI)	18 (9.7, 28.2)	18 (9.9, 30.0)
Duration of OIRR Median, months (95% CI)	(N = 13) 4.6 (2.8, NR)	(N = 12) 4.6 (1.9, 4.6)

IRRC = Independent radiology review committee; CI = Confidence interval; NR = not reached

FDA APPROVED INDICATIONS

Tafinlar is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

Limitation of use: Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma

REFERENCES

- Tafinlar [Prescribing Information]. Research Triangle Park, NC: GlaxoSmithKline; May 2013.

Part D Effective: 10/01/13 Created: 06/13
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

DALFAMPRIDINE

Generic	Brand	HICL	GCN	Exception/Other
DALFAMPRIDINE	AMPYRA	13907		EXCLUDE ≠ MISCELL.; POWDER NON-DRUGS

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is this an initial request for Ampyra (dalfampridine)?

   If yes, continue to #2.
   If no, continue to #5.

2. Is the patient overseen by a neurologist?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is overseen by a neurologist, has a diagnosis of multiple sclerosis, and has symptoms of walking disability.

3. Does the patient have multiple sclerosis?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is overseen by a neurologist, has a diagnosis of multiple sclerosis, and has symptoms of walking disability.

4. Does the patient have symptoms of walking disability such as mild to moderate bilateral lower extremity weakness or unilateral weakness plus lower extremity or truncal ataxia?

   If yes, **approve #2 tablets per day per month for 3 months.**
   APPROVAL TEXT: Renewal requires that documentation of at least a 15% improvement in walking ability.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is overseen by a neurologist, has a diagnosis of multiple sclerosis, and has symptoms of walking disability.

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GUIDELINES FOR USE (CONTINUED)

5. Has the patient experienced or maintained at least a 15% improvement in walking ability?

   If yes, **approve #2 tablets per day per month for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient has experienced an improvement in walking ability.

RATIONALE
Ensure appropriate utilization for dalfampridine.

FDA APPROVED INDICATION
Dalfampridine is approved in patients with multiple sclerosis to improve walking.

REFERENCES

- Acorda Therapeutics. Ampyra package insert. Hawthorne, NY. January 2010.
- Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomized, double-blind, controlled trial. Lancet. 2009; 373:732-738.
- Kachuck NJ. Sustained release oral fampridine in the treatment of multiple sclerosis. Expert Opin Pharmacother. 2009; 10:2025-2035.
- Bever CT, Judge S. Sustained-release fampridine for multiple sclerosis. Expert Opin Investig Drugs. 2009; 18:1013-1024.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 6, 2011].

Part D Effective: 01/01/13 Created: 02/10
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

DENOSUMAB

Generic	Brand	HICL	GCN	Exception/Other
DENOSUMAB	PROLIA, XGEVA	37012		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the prescription for Prolia?

   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have a diagnosis of multiple myeloma?

   If yes, do not approve.
   XGEVA DENIAL TEXT: Approval requires that the requested medication is for prevention of skeletal related events in patients with a diagnosis of cancer with bone metastases from solid tumors or a diagnosis of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.
   If no, continue to #6.

3. Does the patient have osteoporosis?

   If yes, continue to #4.
   If no, continue to #7.

4. Does the patient have a history of osteoporotic fracture(s) or ≥ 2 risk factors for fracture (e.g. history of multiple recent low trauma fractures, BMD T-score ≤ -2.5, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)?

   If yes, **approve 2 fills by GPID for #1 pre-filled syringe per fill with an end date of 12 months.**
   If no, continue to #5.

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GUIDELINES FOR USE (CONTINUED)

5. Has the patient tried or have a contraindication to bisphosphonates (i.e., Fosamax, Actonel, or Boniva)?

   If yes, **approve 2 fills by GPID for #1 pre-filled syringe per fill with an end date of 12 months.**
   If no, do not approve.
   PROLIA DENIAL TEXT: Approval requires a diagnosis of osteoporosis and a trial of bisphosphonates; or treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer; or treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

6. Is Xgeva being used to treat skeletal-related events (e.g. bone fractures or bone pain requiring radiation) in a patient with diagnosis of cancer with bone metastases from solid tumors?

   If yes, **approve 12 fills by GPID for #1 vial per month with an end date of 12 months.**
   If no, continue to #11.

7. Is the patient a man receiving Prolia to increase bone mass?

   If yes, continue to #8.
   If no, continue to #9.

8. Is the patient at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer?

   If yes, **approve 2 fills by GPID for #1 pre-filled syringe per fill with an end date of 12 months.**
   If no, continue to #9.

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GUIDELINES FOR USE (CONTINUED)

9. Is the patient a woman receiving Prolia to increase bone mass?

   If yes, continue to #10.
   If no, do not approve.
   PROLIA DENIAL TEXT: Approval requires a diagnosis of osteoporosis and a trial of bisphosphonates; or treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer; or treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

10. Is the patient at high risk for facture receiving adjuvant aromatase inhibitor therapy for breast cancer?

    If yes, **approve 2 fills by GPID for #1 pre-filled syringe per fill with an end date of 12 months.**
    If no, do not approve.
    PROLIA DENIAL TEXT: Approval requires a diagnosis of osteoporosis and a trial of bisphosphonates; or treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer; or treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

11. Does the patient have a diagnosis of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity?

    If yes, **approve. Enter two authorizations by GPID as follows:**
    - **1 fill of #3 vials**
    - **11 fills of #1 vial with an end date of 12 months**

    If no, do not approve.
    XGEVA DENIAL TEXT: Approval requires that the requested medication is for prevention of skeletal related events in patients with a diagnosis of cancer with bone metastases from solid tumors or a diagnosis of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

RATIONALE
To ensure appropriate use of denosumab based on FDA approved indication and dosing.

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RATIONALE (CONTINUED)

Prolia Dosing:

- Prolia should be administered by a healthcare professional
- Administer 60 mg every 6 months as a subcutaneous injection in the upper arm, upper thigh, or abdomen
- Instruct patients to take calcium 1000 mg daily and at least 400 IU vitamin D daily

Xgeva Dosing:

- Bone Metastasis from Solid Tumors: Administer 120 mg every 4 weeks as a subcutaneous injection in the upper arm, upper thigh, or abdomen
- Giant Cell Tumor of Bone: Administer 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.
- Administer subcutaneously in the upper arm, upper thigh, or abdomen
- Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia

FDA APPROVED INDICATIONS

Prolia is a RANK ligand (RANKL) inhibitor indicated for:

- Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Treatment to increase bone mass in men with osteoporosis at high risk for fracture
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer
- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

Xgeva is a RANK ligand (RANKL) inhibitor indicated for:

- Prevention of skeletal-related events in patients with bone metastases from solid tumors
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity

Limitation of use: Xgeva is not indicated for the prevention of skeletal-related events in patients with multiple myeloma

REFERENCES

- Amgen. Prolia package insert. Thousand Oaks, CA. September 2012.
- Amgen. Xgeva package insert. Thousand Oaks, CA. June 2013.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 23, 2011].

Part D Effective: 10/01/13 Created: 07/10
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

DESIRUDIN

Generic	Brand	HICL	GCN	Exception/Other
DESIRUDIN	IPRIVASK	19072		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the request for Iprivask for the prevention (prophylaxis) of deep vein thrombosis (DVT) for a patient undergoing elective hip replacement surgery?

   If yes, **approve as follows:**

   - **For Commercial members (Enter 2 authorizations):**
     Approve for 12 days for #24 vials
     Also enter one fill for 23 days for #46 vials with a start date of 7 days following the initial approval (for a total of 35 days of treatment).
     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   - **For Part D members:**
     Approve for 12 days for #24 vials.
     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is receiving Iprivask for the prevention of deep vein thrombosis (DVT) undergoing elective hip replacement surgery.

RATIONALE
To ensure appropriate use of desirudin for the prevention of deep vein thrombosis (DVT) in patients undergoing hip replacement surgery. The desirudin prescribing information states that the average duration of treatment is 9 to 12 days. The 2008 ACCP guidelines recommend venous thromboembolism treatment of up to 35 days.

FDA APPROVED INDICATIONS
Prophylaxis of deep vein thrombosis (DVT) in elective hip replacement surgery.

CONTINUED ON NEXT PAGE

REFERENCES

- Canyon Pharmaceuticals, Inc. Iprivask package insert. Hunt Valley, MD. January 2010.
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: August 19, 2010].
- Geerts W, Bergquist D, and Pineo G et al. Prevention of Venous Thromboembolism supplement; The eighth ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2008; 133 (6 Suppl): 381S-453S.

Part D Effective: 01/01/13 Created: 08/10
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

DIMETHYL FUMARATE

Generic	Brand	HICL	GCN	Exception/Other
DIMETHYL FUMARATE	TECFIDERA	40168		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of relapsing-remitting multiple sclerosis (RRMS)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting multiple sclerosis, age of at least 18 years, and a trial of Copaxone and an interferon such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone) or rapidly progressing disease while on therapy with either a beta interferon or Copaxone.

2. Is the patient at least 18 years of age?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting multiple sclerosis, age of at least 18 years, and a trial of Copaxone and an interferon such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone) or rapidly progressing disease while on therapy with either a beta interferon or Copaxone.

3. Has the patient tried or does the patient have a contraindication to interferon therapy such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone) **AND** Copaxone?

   If yes, **approve for 12 months by HICL for #60 capsules in 30 days.**
   If no, continue to #4.

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient experienced rapid progression of disease while on interferon therapy or Copaxone?

   If yes, **approve for 12 months by HICL for #60 capsules in 30 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting multiple sclerosis, age of at least 18 years, and a trial of Copaxone and an interferon such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone) or rapidly progressing disease while on therapy with either a beta interferon or Copaxone.

RATIONALE

To ensure appropriate use aligned with FDA approved indication.

The starting dose for Tecfidera is 120 mg twice a day orally. After 7 days, the dose should be increased to the maintenance dose of 240 mg twice a day orally.

Multiple sclerosis is an autoimmune inflammatory demyelinating disease of the central nervous system characterized by instances of disease exacerbation (relapses). Relapses cause acute neurologic dysfunction, which can last a minimum of 24 hours and peak over the course of several days or weeks. After the relapse subsides, patients may fully recover or have permanent residual impairments. In RRMS, relapses are clearly defined and the disease does not progress during the time between each relapse. Although there are other types of multiple sclerosis, RRMS is the most common.

The safety and efficacy of Tecfidera was evaluated in two randomized, multi-national, double-blind, phase III trials. The first trial, CONFIRM, randomized 1400 adults with relapsing remitting multiple sclerosis (RRMS) to one of four groups: Tecfidera 240mg twice daily, Tecfidera 240mg three times daily, Copaxone 20mg daily, and placebo. The primary endpoint for CONFIRM was annualized relapse rate (ARR) at 2 years. Secondary endpoints included the proportion of patients with relapse at two years, disability progression at two years, number of new/enlarging hyperintense lesions on T2, and number of new/enlarging hypointense lesions on T1. Tertiary endpoints included a comparison of the relative benefits and risks of Tecfidera or Copaxone versus placebo and the number of gadolinium enhancing lesions. Approximately 29% of the patients had tried injectable therapy for RRMS before participating in the trial.

The second trial, DEFINE, randomized 1200 adults with RRMS to one of three groups: Tecfidera 240mg twice daily, Tecfidera 240mg three times daily, and placebo. The primary endpoint for DEFINE was the proportion of patients with relapse at 2 years. Secondary endpoints included the ARR at 2 years, disability progression at two years, number of new/enlarging hyperintense lesions on T2 and number of gadolinium enhancing lesions. Approximately 40% of the patients had tried injectable therapy for RRMS before participating in the trial.

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RATIONALE (CONTINUED)

Tecfidera significantly reduced ARR and the proportion of patients with relapse in both studies. However only DEFINE found a significant difference in disability progression. The ability of Tecfidera to reduce the risk of relapse is 34-49%. Copaxone reduced the risk of relapse by approximately 30%. All three MRI parameters (number of new/enlarging hyperintense lesions on T2, number of new/enlarging hypointense lesions on T1, and number of gadolinium enhancing lesions) were shown to be significant for CONFIRM. DEFINE also found significance in both of its MRI data (number of new/enlarging hyperintense lesions on T2 and number of gadolinium enhancing lesions). Post hoc analysis did not find a difference in efficacy between Tecfidera and Copaxone in any of the clinical and MRI data except that Tecfidera had significantly less hyperintense lesions on T2.

Tecfidera has a favorable safety profile compared to the other oral agents currently approved for RRMS; however, tolerability during the first month of treatment was an issue in clinical trials. The most common adverse reactions (incidence ≥10% and ≥2% more than placebo) for Tecfidera were flushing, abdominal pain, diarrhea, and nausea.

In clinical trials, approximately 40% of patients taking Tecfidera experienced flushing. Flushing symptoms were generally mild or moderate, began soon after drug initiation, and resolved over time. Taking Tecfidera with food may reduce symptoms. Three percent (3%) of patients discontinued Tecfidera for flushing.

Tecfidera caused gastrointestinal (GI) events that were observed early in the course of treatment (primarily in the first month) and usually decreased over time. The incidence of abdominal pain, diarrhea, and nausea in those taking Tecfidera was 18%, 14%, and 12%, respectively. In those taking placebo, the incidence of abdominal pain, diarrhea, and nausea was 10%, 11%, and 9%, respectively. Four percent (4%) of patients treated with Tecfidera and less than 1% of placebo patients discontinued due to GI events.

Tecfidera may decrease lymphocyte counts. During the first year, mean lymphocyte counts decreased by approximately 30% and then remained stable. Four weeks after stopping Tecfidera, mean lymphocyte counts increased but did not return to baseline. Six percent (6%) of Tecfidera patients and <1% of placebo patients experienced lymphocyte counts $<0.5x10^9$/L. The incidence of infections (60% vs. 58%) and serious infections (2% vs. 2%) was similar in patients treated with Tecfidera or placebo, respectively. Before initiation of therapy, it is recommended to check a recent complete blood cell count to identify patients with pre-existing low lymphocyte counts.

Tecfidera is a Pregnancy Category C.

FDA APPROVED INDICATIONS

Tecfidera is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

CONTINUED ON NEXT PAGE

DIMETHYL FUMARATE

REFERENCES

- Tecfidera [Prescribing Information]. Cambridge, MA: Biogen, Idec; March 2013.
- UpToDate, Inc. Treatment of relapsing-remitting multiple sclerosis in adults. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated January 30, 2013.
- UpToDate, Inc. Epidemiology and clinical features of multiple sclerosis in adults. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated December 6, 2012.

Part D Effective: 07/01/13 Created: 05/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 05/13

ELTROMBOPAG

Generic	Brand	HICL	GCN	Exception/Other
ELTROMBOPAG	PROMACTA	35989		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient being treated for chronic immune (idiopathic) thrombocytopenia purpura (ITP)?

   If yes, continue to #2.
   If no, continue to #6.

2. Is the patient currently taking Promacta as indicated on the MRF, claims history, or prior authorization history?

   If yes, continue to #4.
   If no, continue to #3.

3. Has the patient tried or does the patient have a contraindication to corticosteroids or immunoglobulins, or has had an insufficient response to a splenectomy?

   If yes, **approve for 1 month by GPID for #1 tablet (12.5mg, 25mg or 50mg) per day per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic immune (idiopathic) thrombocytopenia purpura (ITP) and either a trial of corticosteroids or immunoglobulins, or an insufficient response to a splenectomy; or a diagnosis of thrombocytopenia due to hepatitis C treatment consisting of interferon therapy.

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ELTROMBOPAG

GUIDELINES FOR USE (CONTINUED)

4. Did the patient have a clinical response, as defined by an increase in platelet count to ≥ $50X10^9$/L (≥ 50,000 per µl)?

   If yes, **approve for 12 months by HICL for #1 tablet per day per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #5.

5. Did the patient receive the maximum dose of 75mg for 4 consecutive weeks as indicated on the MRF, claims history, or prior authorization history?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a clinical response, as defined by an increase in platelet count to greater than or equal to $50X10^9$/L (greater than or equal to 50,000 per µl), after 4 weeks at maximum dose.
   If no, **approve for 1 month by GPID for #1 tablet (75mg) per day per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

6. Is the patient being treated for thrombocytopenia due to hepatitis C treatment consisting of interferon therapy?

   If yes, **approve for 12 months by HICL for #1 tablet per day.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic immune (idiopathic) thrombocytopenia purpura (ITP) and either a trial of corticosteroids or immunoglobulins, or an insufficient response to a splenectomy; or a diagnosis of thrombocytopenia due to hepatitis C treatment consisting of interferon therapy.

RATIONALE
To ensure safe and appropriate utilization of Promacta.

FDA APPROVED INDICATIONS
Promacta is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

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FDA APPROVED INDICATIONS (CONTINUED)
Promacta is indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy.

Limitations of use:
- Promacta should not be used in an attempt to normalize platelet counts.
- Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
- Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon therapy or limits the ability to maintain optimal interferon-based therapy.
- Safety and efficacy have not been established in combination with direct acting antiviral agents approved for treatment of chronic hepatitis C genotype 1 infection.

NOTE: Promacta is available only through a restricted distribution program called Promacta Cares (Network of Experts Understanding and Supporting Promacta and Patients) Program. Only prescribers, pharmacies and patients registered in the Promacta Cares program can receive, prescribe, or dispense Promacta. This program provides educational materials and a mechanism for the proper use of PROMACTA. PROMACTA *CARES*, 1-877-9-PROMACTA.

REFERENCES
- GlaxoSmithKline. Promacta package insert. Research Triangle Park, NC. November 2012.

Part D Effective: 04/01/13 Created: 01/09
Commercial Effective: 04/01/13 Client Approval: 02/13 P&T Approval: 02/13

ENDOTHELIN RECEPTOR ANTAGONISTS

Generic	Brand	HICL	GCN	Exception/Other
BOSENTAN	TRACLEER	22990		
AMBRISENTAN	LETAIRIS	34849		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the prescribing physician a cardiologist or pulmonologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a cardiologist or a pulmonologist, and a diagnosis of pulmonary arterial hypertension with New York Heart Association (NYHA) and World Health Organization (WHO) Class II to IV symptoms.

2. Does the patient have a diagnosis of pulmonary arterial hypertension with NYHA-WHO Functional Class II or greater?

   If yes, **approve as follows:**
   - **Tracleer: approve for 12 months #2 tablets per day per month by HICL.**
   - **Letairis: approve for 12 months #1 tablet per day per month by HICL.**

   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a cardiologist or a pulmonologist, and a diagnosis of pulmonary arterial hypertension with New York Heart Association (NYHA) and World Health Organization (WHO) Class II to IV symptoms.

RATIONALE
Ensure appropriate utilization of Tracleer and Letairis.

FDA APPROVED INDICATIONS
LETAIRIS is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA-WHO class II or III symptoms to improve exercise capacity and delay clinical worsening.

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ENDOTHELIN RECEPTOR ANTAGONISTS

FDA APPROVED INDICATIONS (CONTINUED)
TRACLEER is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA-WHO Class II to IV symptoms to improve exercise capacity and decrease clinical worsening.

REFERENCES

- Actelion Pharmaceuticals US, Inc. Tracleer package insert. South San Francisco, CA. August 2009.
- Gilead Sciences, Inc., Letairis package insert. Foster City, CA. March 2011.
- Badesch DB, Abman SH, Simonneau G, Rubin LJ, McLaughlin VV. Medical therapy for pulmonary arterial hypertension: updated ACCP evidence-based clinical practice guidelines. Chest 2007 Jun; 131(6):1917-28.

Part D Effective: 01/01/13 Created: 09/05
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

ENZALUTAMIDE

Generic	Brand	HICL	GCN	Exception/Other
ENZALUTAMIDE	XTANDI	39580		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic castration-resistant prostate cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic castration-resistant prostate cancer and a trial of docetaxel.

2. Has the patient tried, or does the patient have a contraindication to docetaxel?

   If yes, **approve for 12 months with a quantity limit of #120 capsules per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic castration-resistant prostate cancer and a trial of docetaxel.

RATIONALE
To ensure appropriate use of Xtandi consistent with FDA approved indication.

The recommended dosage is 160 mg (four 40 mg capsules) once daily with or without food. If a patient experiences a ≥ Grade 3 toxicity or an intolerable side effect, withhold dosing for one week or until symptoms improve to ≤ Grade 2, then resume at the same or a reduced dose (120 mg or 80 mg), if warranted. Concomitant use of strong CYP2C8 inhibitors such as gemfibrozil should be avoided if possible. If patients must be co-administered a strong CYP2C8 inhibitor, reduce the Xtandi dose to 80 mg once daily.

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RATIONALE (CONTINUED)

Xtandi is an oral once daily androgen receptor inhibitor for the treatment of metastatic castration-resistant prostate cancer. It decreases proliferation and induces cell death of prostate cancer. Xtandi joins Zytiga as the second oral agent available in this setting. While both are dosed once daily, Zytiga also requires twice daily prednisone dosing. The National Comprehensive Cancer Network (NCCN) guidelines recommend docetaxel as the preferred first-line treatment of symptomatic metastatic castration-resistant prostate cancer. There is no consensus for best second line treatment following docetaxel failure; however Zytiga, Jevtana, Provenge, and docetaxel rechallenge can all be considered.

Xtandi was evaluated in one phase 3 clinical trial that randomized metastatic castration-resistant prostate cancer patients who had received prior docetaxel-based therapy 2:1 to either Xtandi 160 mg once daily (n=800) or placebo (n=399). The primary endpoint was overall survival. All patients continued androgen deprivation therapy and were allowed to continue or initiate glucocorticoids. During the trial, 48% of patients on the Xtandi arm and 46% of patients on the placebo arm received glucocorticoids. At the pre-specified interim analysis of 520 events, Xtandi demonstrated a statistically significant improvement in overall survival compared to placebo, 18.4 vs. 13.6 months respectively (Hazard Ratio 0.63).

The most common adverse reactions observed in clinical trials were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression, cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 3 and higher adverse reactions were reported among 47% of Xtandi-treated patients and 53% of placebo-treated patients. Discontinuations due to adverse events were reported for 16% of patients treated with Xtandi compared to 18% in the placebo group. Seizure occurred in 0.9% of patients taking Xtandi in clinical trials. Xtandi is contraindicated in pregnancy and classified as pregnancy category X.

FDA APPROVED INDICATIONS

Xtandi is indicated for the treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel.

REFERENCES

- Xtandi [Prescribing Information]. Northbrook, IL: Astellas Pharma US, Inc.; August 2012.
- National Comprehensive Cancer Network. Prostate Cancer Guideline Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf [Accessed September 10, 2012].

Part D Effective: 01/01/13 Created: 09/12
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

ERIBULIN

Generic	Brand	HICL	GCN	Exception/Other
ERIBULIN MESYLATE	HALAVEN	37256		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer and previous treatment with an anthracycline [daunorubicin (Cerubidine), daunorubicin liposomal (Daunoxome), doxorubicin (Adriamycin), doxorubicin liposomal (Doxil), idarubicin (Idamycin), epirubicin (Ellence), or mitoxantrone (Novantrone) AND a taxane (docetaxel (brand Taxotere) or paclitaxel (brand Taxol or Abraxane)].

2. Have the previous treatments included an anthracycline [daunorubicin (Cerubidine), daunorubicin liposomal (Daunoxome), doxorubicin (Adriamycin), doxorubicin liposomal (Doxil), idarubicin (Idamycin), epirubicin (Ellence), or mitoxantrone (Novantrone) AND a taxane (docetaxel (brand Taxotere) or paclitaxel (brand Taxol or Abraxane)]?

   If yes, **approve for 12 months with a quantity limit of a total of #12 vials (maximum 3 vials per dose, maximum 4 doses) per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer and previous treatment with an anthracycline [daunorubicin (Cerubidine), daunorubicin liposomal (Daunoxome), doxorubicin (Adriamycin), doxorubicin liposomal (Doxil), idarubicin (Idamycin), epirubicin (Ellence), or mitoxantrone (Novantrone) AND a taxane (docetaxel (brand Taxotere) or paclitaxel (brand Taxol or Abraxane)].

RATIONALE
To ensure appropriate use of Halaven based on FDA indication and NCCN guidelines. NCCN lists eribulin as a preferred single agent for recurrent or metastatic breast cancer

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ERIBULIN

FDA APPROVED INDICATIONS

Halaven is indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

REFERENCES

- Eisai, Inc. Halaven package insert. Woodcliff Lake, NJ, November 2010.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 28, 2011].
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Breast Cancer v.2.2011.

Part D Effective: 10/01/13	Created: 11/10	
Commercial Effective: 10/01/13	Client Approval: 08/13	P&T Approval: 11/12

ERLOTINIB

Generic	Brand	HICL	GCN	Exception/Other
ERLOTINIB HCL	TARCEVA	26745		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of non-small cell lung cancer (NSCLC)?

   If yes, continue to #2.
   If no, continue to #4.

2. Do the patient's tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test?

   If yes, **approve for 12 fills by HICL of #30 tablets per 30 days.**
   If no, continue to #3.

3. Has the patient tried or does the patient have a contraindication to the use of IV chemotherapy?

   If yes, **approve for 12 fills by HICL of #30 tablets per 30 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of pancreatic cancer, and that requested agent is being used in combination with gemcitabine; or a diagnosis of non-small cell lung cancer (NSCLC) and, the tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test, or a trial of IV chemotherapy, which may be covered under the patient's medical benefit.

4. Does the patient have a diagnosis of pancreatic cancer?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of pancreatic cancer, and that requested agent is being used in combination with gemcitabine; or a diagnosis of non-small cell lung cancer (NSCLC) and, the tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test, or a trial of IV chemotherapy, which may be covered under the patient's medical benefit.

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ERLOTINIB

GUIDELINES FOR USE (CONTINUED)

5. Is erlotinib (Tarceva) being used in combination with gemcitabine?

   If yes, **approve for 12 fills by HICL of #30 tablets per 30 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of pancreatic cancer, and that requested agent is being used in combination with gemcitabine; or a diagnosis of non-small cell lung cancer (NSCLC) and, the tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test, or a trial of IV chemotherapy, which may be covered under the patient's medical benefit.

RATIONALE

To promote appropriate utilization of erlotinib based on FDA approved indications and NCCN guidelines. Erlotinib is recommended as first line therapy for non-small cell lung cancer that is EGFR mutation positive and as second line therapy for non-small cell lung cancer that is EGFR mutation negative. Erlotinib in combination with gemcitabine is recommended as treatment for metastatic pancreatic adenocarcinoma.

Dosage:
NSCLC: 150 mg orally, on an empty stomach, once daily
Pancreatic cancer: 100 mg orally, on an empty stomach, once daily

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ERLOTINIB

FDA APPROVED INDICATIONS

Tarceva is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.
- Maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- Treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Limitations of Use:

- Tarceva is not recommended for use in combination with platinum-based chemotherapy.
- Safety and efficacy of Tarceva have not been evaluated as first-line treatment in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

REFERENCES

- OSI Pharmaceuticals Inc. Tarceva package insert. Melville, NY May 2013.
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Version March 2011.
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma. Version February 2011.
- Azzoli CG et al. American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non-Small-Cell Lung Cancer. *Journal of Clinical Oncology* 2009 December 20; 27(36):6251-6266.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 24, 2011].

Part D Effective: 10/01/13	Created: 11/10	
Commercial Effective: 10/01/13	Client Approval: 08/13	P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

ERYTHROPOIESIS STIMULATING AGENTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
DARBEPOETIN	ARANESP	22890		
EPOETIN ALFA	EPOGEN PROCRIT	04553		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is this request for an emergency hospital billing or an unscheduled dialysis?

   If yes, **approve for 1 fill under part B. (Populate the B vs. D override field with "B". If MedImpact does not process Part B for the client, refer the caller/request back to the health plan.)**
   If no **or unknown**, continue to #2.

2. Is the patient identified as a Part D End Stage Renal Disease (ESRD) member? (In the Member Attributes screen if the Attribute Type is listed as PART_B_ESRD and the date of the request is between the start date and end date fields, then this patient is identified as Part D End Stage Renal Disease (ESRD) member.)

   If yes, do not approve.
   DENIAL TEXT: This medication is included in the bundled dialysis facility payment. Please contact the patient's dialysis treatment center.
   If no, continue to #3.

3. Is the patient diagnosed with End Stage Renal Disease (ESRD)?

   If yes, do not approve.
   DENIAL TEXT: This medication is included in the bundled dialysis facility payment. Please contact the patient's dialysis treatment center.
   If no, continue to #4.

4. Is the patient undergoing dialysis?

   If yes, do not approve.
   DENIAL TEXT: This medication is included in the bundled dialysis facility payment. Please contact the patient's dialysis treatment center.
   If no, continue to #5.

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GUIDELINES FOR USE (CONTINUED)

5. Is the request for Procrit?

   If yes, continue to #7.
   If no, continue to #6.

6. Has the patient tried or does the patient have a contraindication to the use of Procrit?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of Procrit, which may also require prior authorization.

7. Is the patient being treated for anemia associated with chronic renal failure?

   If yes, continue to #8.
   If no, continue to #12.

8. Is the patient currently taking the requested agent?

   If yes, continue to #9.
   If no, continue to #11.

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GUIDELINES FOR USE (CONTINUED)

9. Does the patient have a hemoglobin level less than 11g/dL if on dialysis or less than 10g/dL if not on dialysis?

   If yes, **approve for 12 months with the following quantity limits:**
   Aranesp:
   60mcg/0.3mL, 150mcg/0.3mL: 1.2mL per 28 days
   100mcg/0.5mL: 2mL per 28 days
   300mcg/0.6mL: 2.4mL per 28 days
   25mcg/mL, 40mcg/mL, 60mcg/mL, 100mcg/mL, 150mcg/0.75mL, 200mcg/mL, 300mcg/mL, 500mcg/mL: 4mL per 28 days
   40mcg/0.4mL, 200mcg/0.4mL: 1.6mL per 28 days
   25mcg/0.42mL: 1.68mL per 28 days
   Epogen:
   2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
   40,000U/mL: 6mL per 28 days
   Procrit:
   2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
   40,000U/mL: 6mL per 28 days

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #10.

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GUIDELINES FOR USE (CONTINUED)

10. Is the request for one of the following reasons:

a.) Hemoglobin has reached 11g/dL if on dialysis and dose reduction/dose interruption required to reduce the need for blood transfusions
b.) Hemoglobin has reached 10g/dL for patients not on dialysis and dose reduction/dose interruption is required to reduce the need for blood transfusions?

If yes, **approve for 12 months with the following quantity limits:**
Aranesp:
60mcg/0.3mL, 150mcg/0.3mL: 1.2mL per 28 days
100mcg/0.5mL: 2mL per 28 days
300mcg/0.6mL: 2.4mL per 28 days
25mcg/mL, 40mcg/mL, 60mcg/mL, 100mcg/mL, 150mcg/0.75mL, 200mcg/mL, 300mcg/mL, 500mcg/mL: 4mL per 28 days
40mcg/0.4mL, 200mcg/0.4mL: 1.6mL per 28 days
25mcg/0.42mL: 1.68mL per 28 days
Epogen:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days
Procrit:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

If no, do not approve.
DENIAL TEXT: Approval for reauthorization requires a level less than 11g/dL if on dialysis or less than 10g/dL if not on dialysis or the need for dose reduction required to reduce the need for blood transfusions for dialysis patients reaching Hgb of 11g/dL and patients not on dialysis who have reached a hemoglobin of 10g/dL.

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GUIDELINES FOR USE (CONTINUED)

11. Does the patient have hemoglobin level of less than 10g/dL?

    If yes, **approve for 12 months with the following quantity limits:**
    Aranesp:
    60mcg/0.3mL, 150mcg/0.3mL: 1.2mL per 28 days
    100mcg/0.5mL: 2mL per 28 days
    300mcg/0.6mL: 2.4mL per 28 days
    25mcg/mL, 40mcg/mL, 60mcg/mL, 100mcg/mL, 150mcg/0.75mL, 200mcg/mL, 300mcg/mL, 500mcg/mL: 4mL per 28 days
    40mcg/0.4mL, 200mcg/0.4mL: 1.6mL per 28 days
    25mcg/0.42mL: 1.68mL per 28 days
    Epogen:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days
    Procrit:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires a hemoglobin level of less than 10g/dL prior to initiating therapy.

12. Is the patient being treated for anemia due to the effect of concomitantly administered cancer chemotherapy?

    If yes, continue to #13.
    If no, continue to #15.

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GUIDELINES FOR USE (CONTINUED)

13. Is the patient currently taking requested agent and have a hemoglobin level between 10 and 12g/dL?

    If yes, **approve for 12 months with the following quantity limits:**
    Aranesp:
    60mcg/0.3mL, 150mcg/0.3mL: 1.2mL per 28 days
    100mcg/0.5mL: 2mL per 28 days
    300mcg/0.6mL: 2.4mL per 28 days
    25mcg/mL, 40mcg/mL, 60mcg/mL, 100mcg/mL, 150mcg/0.75mL, 200mcg/mL, 300mcg/mL, 500mcg/mL: 4mL per 28 days
    40mcg/0.4mL, 200mcg/0.4mL: 1.6mL per 28 days
    25mcg/0.42mL: 1.68mL per 28 days
    Epogen:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days
    Procrit:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, continue to #14.

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GUIDELINES FOR USE (CONTINUED)

14. Does the patient have a hemoglobin level of less than 11g/dL or has patient's hemoglobin decreased at least 2g/dL below their baseline level?

    If yes, **approve for 12 months with the following quantity limits:**
    Aranesp:
    60mcg/0.3mL, 150mcg/0.3mL: 1.2mL per 28 days
    100mcg/0.5mL: 2mL per 28 days
    300mcg/0.6mL: 2.4mL per 28 days
    25mcg/mL, 40mcg/mL, 60mcg/mL, 100mcg/mL, 150mcg/0.75mL, 200mcg/mL, 300mcg/mL, 500mcg/mL: 4mL per 28 days
    40mcg/0.4mL, 200mcg/0.4mL: 1.6mL per 28 days
    25mcg/0.42mL: 1.68mL per 28 days
    Epogen:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days
    Procrit:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires a hemoglobin level of less than 11g/dL or a decrease at least 2g/dL from baseline level.

15. Does the patient have anemia related to zidovudine therapy?

    If yes, continue to #16.
    If no, continues to #18.

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GUIDELINES FOR USE (CONTINUED)

16. Is the patient currently taking requested agent and have a hemoglobin level between 10 and 12g/dL?

    If yes, process as follows:
    Aranesp: Do not approve.
    DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease or concomitant cancer therapy.

    Epogen: Approve for 12 months with the following quantity limits:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    Procrit: Approve for 12 months with the following quantity limits:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, continue to #17.

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GUIDELINES FOR USE (CONTINUED)

17. Does the patient have a hemoglobin level of less than 10g/dL?

If yes, process as follows:
Aranesp: do not approve.
DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease or concomitant cancer therapy.

Epogen: Approve for 12 months with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

Procrit: Approve for 12 months with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

If no, do not approve.
DENIAL TEXT: Approval requires a hemoglobin level of less than 10g/dL.

18. Is the patient scheduled for elective, noncardiac, nonvascular surgery?

If yes, continue to #19.
If no, continue to #20.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE (CONTINUED)

19. Does the patient have a documented hemoglobin less than 13g/dL?

If yes, process as follows:
Aranesp: do not approve.
DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease or concomitant cancer therapy.

Epogen: Approve for one month with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

Procrit: Approve for one month with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

If no, do not approve.
DENIAL TEXT: Approval requires documented hemoglobin less than 13g/dL.

20. Does the patient have anemia due to concurrent hepatitis C treatment?

If yes, continue to #21.
If no, do not approve.
DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease, elective, noncardiac, nonvascular surgery, or concomitant zidovudine, cancer or hepatitis C therapy.

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GUIDELINES FOR USE (CONTINUED)

21. Is the patient currently taking requested agent and have a hemoglobin level between 10 and 12g/dL?

    If yes, process as follows:
    Aranesp: do not approve.
    DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease or concomitant cancer therapy.

    Epogen: Approve for 6 months with the following quantity limits:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    Procrit: Approve for 6 months with the following quantity limits:
    2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
    40,000U/mL: 6mL per 28 days

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, continue to #22.

22. Has the patient tried or does the patient have a contraindication to ribavirin dose reduction?

    If yes, continue to #23.
    If no, do not approve.
    DENIAL TEXT: Approval requires ribavirin dose reduction prior to receiving an erythropoiesis-stimulating agent.

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GUIDELINES FOR USE (CONTINUED)

23. Does the patient have a documented hemoglobin less than 10g/dL?

If yes, process as follows:
Aranesp: do not approve.
DENIAL TEXT: Approval requires a diagnosis of anemia related to chronic kidney disease or concomitant cancer therapy.

Epogen: Approve for 6 months with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/2mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

Procrit: Approve for 6 months with the following quantity limits:
2,000U/mL, 3,000U/mL, 4,000U/mL, 10,000U/mL, 20,000U/mL: 12mL per 28 days
40,000U/mL: 6mL per 28 days

APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

If no, do not approve.
DENIAL TEXT: Approval requires a documented hemoglobin less than 10g/dL.

RATIONALE
Ensure appropriate utilization and promote use of preferred ESA treatment. Patients identified as Part D End Stage Renal Disease (ESRD) undergoing dialysis will be directed to a dialysis treatment center and have their ESRD treatment related drug included in the bundled dialysis facility payment.

Anemia due to hepatitis C therapy is not an FDA approved indication for any ESA. AASLD does not recommend the use of ESAs, NIH/DHHS/NIDDKD state that the proper role and dose of ESAs has yet to be defined, and the AGA consider either ribavirin dose reduction or ESA use as viable options for managing treatment-related anemia. None of these guidelines provide specific hemoglobin levels at which to initiate or maintain hemoglobin levels for this patient population, so the hemoglobin levels selected for this diagnosis are based off of the recommendations for zidovudine therapy.

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ERYTHROPOIESIS STIMULATING AGENTS (PART D)

FDA APPROVED INDICATIONS

- CHRONIC KIDNEY DISEASE: the prescribing information of the ESAs and an FDA safety update recommend initiation of therapy only for patients with a hemoglobin of less than 10g/dL. They recommend reducing or interrupting the dose of ESA and using the lowest dose of an ESA sufficient to reduce the need for blood transfusions at a hemoglobin of 11g/dL for patients on dialysis or a hemoglobin of 10g/dL for patients not on dialysis.
- ANEMIA RELATED TO CANCER CHEMOTHERAPY: ASCO recommends initiating ESA therapy at hemoglobin levels at less than 10g/dL while NCCN recommends initiation at or below hemoglobin levels of 11g/dL. ASCO recommends maintaining hemoglobin levels between 10 and 12d/gL, while NCCN does not comment on a maintenance hemoglobin range.
- ANEMIA RELATED TO ZIDOVUDINE THERAPY: the clinical trials contained within the prescribing information of the ESAs recommend initiating therapy at a hemoglobin of less than 10g/dL and maintaining between 10 and 12g/dL.
- PATIENTS SCHEDULED FOR ELECTIVE, NONCARDIAC, NONVASCULAR SURGERY: the prescribing information of the ESAs recommends therapy only for those patients with a hemoglobin level at or below 13g/dL.

DARBEPOETIN is indicated for the treatment of anemia associated with chronic renal failure including patients on and not on dialysis and for anemia due to the effect of concomitantly administered chemotherapy in patients with non-myeloid malignancies.

EPOETIN ALFA is indicated for the treatment of anemia of chronic renal failure patients, including patients on dialysis and patients not on dialysis; treatment of anemia in zidovudine-treated HIV infected patients; treatment of anemia in cancer patients with metastatic, non-myeloid malignancies receiving chemotherapy; and reduction of allogenic blood transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

REFERENCES

- American Gastroenterological Association Medical Position Statement on the Management of Hepatitis C. Gastroenterology 2006; 130:225-230.
- Amgen, Aranesp product information. Thousand Oaks, CA, June 2011.
- Amgen. Epogen product information. Thousand Oaks, CA, June 2011.
- CMS Part C & D User Call: December 1, 2010, 3:30 PM ET. Available at: http://www.mscginc.com/materials/12_1_2010/CMSPartCDUserCallDec12010.pdf [Accessed December 22, 2010].
- Ghany MG, Strader DB et al. AASLD Practice Guidelines: Diagnosis, Management, and Treatment of Hepatitis C: An Update. Hepatology 2009:49 (4): 1335-1374.
- Locatelli F, Nissenson AR, et al. Clinical practice guidelines for anemia in chronic kidney disease: problems and solutions. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Available at: www.kidney-international.org. [Accessed January 12, 2011].

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REFERENCES (CONTINUED)

- Rizzo JD, Brouwers M, et al. American Society of Clinical Oncology / American Society of Hematology Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin in Adult Patients With Cancer. Available at www.ASCO.org. [Accessed January 12, 2011].
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. [Accessed January 13, 2011].
- Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies: An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology 2006; 105:198-208.
- U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Chronic Hepatitis C: Current Disease Management 2010. Available at: www.digestive.niddk.nih.gov. [Accessed January 13, 2011].
- U.S. Food and Drug Administration. FDA Drug Safety Communication: Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents (ESAs) in chronic kidney disease. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm259639.htm. [Accessed July 8 2011].

Part D Effective: 01/01/13	Created: 02/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

ESRD BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CALCITONIN,SALMON,SYNTHETIC	MIACALCIN		26431	
CALCITRIOL	CALCIJEX CALCITRIOL ROCALTROL	00999		GCN ≠13015
CALCIUM GLUCONATE	CAL-G CALCIUM GLUCONATE	00585		GCN ≠03850, 04989
DAPTOMYCIN	CUBICIN		20569	
DEFEROXAMINE MESYLATE	DESFERAL	01104		
DOXERCALCIFEROL	HECTOROL	20533		
HEPARIN SODIUM,PORCINE	HEPARIN SODIUM		25681, 25691, 25697, 46952, 46953	
HEPARIN SODIUM,PORCINE/PF			17635, 29477	
IBANDRONATE SODIUM	BONIVA		26368	
LEPIRUDIN,RECOMBINANT	REFLUDAN	18277		
LEVOCARNITINE	CARNITINE CARNITOR SF G-LEVOCARNITINE L-CARNITINE	00859		GCN ≠70382
LEVOCARNITINE (WITH SUCROSE)	CARNITOR	34794		
LIDOCAINE HCL	LIDOCAINE HCL XYLOCAINE		11830,11852, 11854,11857, 26886, 30510,	
LIDOCAINE HCL/PF	LIDOCAINE HCL/PF XYLOCAINE-MPF		26151, 26877	
LIDOCAINE-PRILOCAINE	EMLA LIDOCAINE-PRILOCAINE		5987	
LIDOCAINE/TETRACAINE	SYNERA		24965	
PAMIDRONATE DISODIUM	AREDIA	06250		
PARICALCITOL	ZEMPLAR	18250		
PROTAMINE SULFATE	PROTAMINE SULFATE		25860	
TETRACAINE HCL	PONTOCAINE		30561	
VANCOMYCIN HCL	VANCOMYCIN	04042		ROUTE = INTRAVEN.

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PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

ESRD BVD DETERMINATION (PART D)

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is this a request for an emergency hospital billing or an unscheduled dialysis?

   If yes, submit via Part B and **approve for 1 fill. (Populate the B vs. D override field with "B". If MedImpact does not process Part B for the client, refer the caller/request back to the health plan.)**
   If no **or unknown**, continue to #2.

2. Is the patient identified as a Part D End Stage Renal Disease (ESRD) member? (In the Member Attributes screen, if the Attribute Type is listed as "ESRD_DIALYSIS" and the value is listed as "PRTB_ESRD_DIAL" with the date of the request between the start date and end date fields, then this patient is identified as a Part D End Stage Renal Disease (ESRD) member.)

   If yes, continue to #4.
   If no, continue to #3.

3. Is the patient on hemodialysis?

   If yes, continue to #4.
   If no, **approve for up to 12 months under Part D. (Populate B vs. D field with "D" in the PA override field.)**

4. Is this a request for Cubicin (daptomycin) or vancomycin?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: This medication is included in the bundled dialysis facility payment. Please contact the patient's dialysis treatment center.

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ESRD BVD DETERMINATION (PART D)

GUIDELINES FOR USE (CONTINUED)

5. Is requested medication being used to treat an access site infection?

   If yes, do not approve.
   DENIAL TEXT: This medication is included in the bundled dialysis facility payment. Please contact the patient's dialysis treatment center.
   If no, **approve for up to 12 months under Part D. (Populate B vs. D field with "D" in the PA override field.)**

RATIONALE

Patients identified as Part D End Stage Renal Disease (ESRD) undergoing dialysis will be directed to a dialysis treatment center and have their ESRD treatment related drug included in the bundled dialysis facility payment.

FDA APPROVED INDICATIONS

REFERENCES

- CMS Part C & D User Call: December 1, 2010, 3:30 PM ET. Available at: http://www.mscginc.com/materials/12_1_2010/CMSPartCDUserCallDec12010.pdf [Accessed December 22, 2010].
- CMS memo: Clarification of Exclusion of Part D Payment for Drugs Included in the End-Stage Renal Disease Prospective Payment. February 17, 2011. From Cynthia G Tutor, Ph.D., Director Medicare Drug Benefit and C & D Data Group, Jeffrey A. Kelman, M.D., Medical Director, Center for Medicare.

Part D Effective: 01/01/13	Created: 02/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

ETANERCEPT (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ETANERCEPT	ENBREL	18830		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has this drug been prescribed by or is it currently being supervised by a rheumatologist or dermatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist or dermatologist; and a diagnosis of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, or plaque psoriasis; and trial of preferred formulary tumor necrosis factor(s) Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization.

2. Does the patient have active rheumatoid arthritis?

   If yes, continue to #3.
   If no, continue to #5.

3. Has the patient tried Humira (adalimumab) or Cimzia (certolizumab pegol)?

   If yes, continue to #4.
   If no, do not approve. (Ask the caller to submit a MRF for Humira or Cimzia.)
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of preferred formulary tumor necrosis factors Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization; and trial of one of the following DMARD (disease-modifying antirheumatic drug) agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

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INITIAL CRITERIA (CONTINUED)

4. Has the patient previously tried at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, for ACTIVE RHEUMATOID ARTHRITIS, **approve initially for 3 months for #8 of the 25mg syringes/vials (2 kits) per month or #4 of the 50mg syringes/vials (1 kit) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of preferred formulary tumor necrosis factors Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization; and trial of one of the following DMARD (disease-modifying antirheumatic drug) agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

5. Does the patient have active juvenile idiopathic arthritis?

   If yes, continue to #6.
   If no, continue to #8.

6. Has the patient tried Humira (adalimumab)?

   If yes, continue to #7.
   If no, do not approve. (Ask the caller to submit a MRF for Humira.)
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; and a trial of at least one DMARD (disease-modifying antirheumatic drug) agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

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INITIAL CRITERIA (CONTINUED)

7. Has the patient previously tried at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, for JUVENILE IDIOPATHIC ARTHRITIS, **approve initially for 3 months for #8 of the 25mg syringes/vials (2 kits) per month or #4 of the 50mg syringes/vials (1 kit) per.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist, a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; and a trial of at least one DMARD (disease-modifying antirheumatic drug) agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

8. Does the patient have ankylosing spondylitis?

   If yes, continue to #9.
   If no, continue to #10.

9. Has the patient tried Humira (adalimumab)?

   If yes, for ANKYLOSING SPONDYLITIS, **approve initially for 3 months for #8 of the 25mg syringes/vials (2 kits) per month or #4 of the 50mg syringes/vials (1 kit) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve. (Ask the caller to submit a MRF for Humira.)
   DENIAL TEXT: Approval requires supervision by a rheumatologist; and a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization.

10. Does the patient have active psoriatic arthritis?

    If yes, continue to #11.
    If no, continue to #13.

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INITIAL CRITERIA (CONTINUED)

11. Has the patient tried Humira (adalimumab)?

    If yes, continue to #12.
    If no, do not approve. (Ask the caller to submit a MRF for Humira.)
    DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; and a trial of at least one DMARD agents (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

12. Has the patient previously tried at least one of the following DMARD agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

    If yes, for PSORIATIC ARTHRITIS, **approve initially for 3 months for #8 of the 25mg syringes/vials (2 kits) per month or #4 of the 50mg syringes/vials (1 kit) per month.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; and a trial of at least one DMARD agents (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

13. Does the patient have chronic moderate to severe plaque psoriasis?

    If yes, continue to #14.
    If no, do not approve.
    DENIAL TEXT: Approval requires a diagnosis of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, or moderate to severe plaque psoriasis.

14. Has the patient tried Humira (adalimumab)?

    If yes, continue to #15.
    If no, do not approve. (Ask the caller to submit a MRF for Humira.)
    DENIAL TEXT: Approval requires supervision by a dermatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; diagnosis of plaque psoriasis, psoriatic lesions covering greater than 10% of BSA (Body Surface Area) or lesions on the hands, feet, or genital area; and a trial of or contraindication to one or more forms of preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate or cyclosporine.

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INITIAL CRITERIA (CONTINUED)

15. Does the plaque psoriasis involve greater than or equal to 10% body surface area (BSA) or do the psoriatic lesions affect the hands, feet, or genital area?

    If yes, continue to #16.
    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a dermatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization; diagnosis of plaque psoriasis, psoriatic lesions covering greater than 10% of BSA (Body Surface Area) or lesions on the hands, feet, or genital area; and a trial of or contraindication to one or more forms of preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate, or cyclosporine.

16. Has the patient tried or does the patient have a contraindication to one or more forms of preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), acitretin, methotrexate, or cyclosporine?

    If yes, for PLAQUE PSORIASIS, **approve initially for 3 months for #16 of the 25mg syringes/vials (4 kits) per month or #8 of the 50mg syringes/vials (2 kits) per month.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a dermatologist; a trial of a preferred formulary tumor necrosis factor Humira (adalimumab) which may also require a prior authorization; diagnosis of plaque psoriasis, psoriatic lesions covering greater than 10% of BSA (Body Surface Area) or lesions on the hands, feet, or genital area; and a trial of or contraindication to one or more forms of preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate or cyclosporine.

RENEWAL CRITERIA

1. Does the patient have active rheumatoid arthritis, psoriatic arthritis, or juvenile idiopathic arthritis?

    If yes, continue to #2.
    If no, continue to #3.

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RENEWAL CRITERIA (CONTINUED)

2. Has the patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count while on therapy?

   If yes, for RHEUMATOID ARTHRITIS OR JUVENILE IDIOPATHIC ARTHRITIS OR PSORIATIC ARTHRITIS, **approve for 12 months for #8 of the 25mg syringes/vials (2 kits) per month or #4 of the 50mg syringes/vials (1 kit) per month for 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of rheumatoid arthritis, psoriatic arthritis, or juvenile idiopathic arthritis and that the patient has experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count while on therapy.

3. Does the patient have chronic plaque psoriasis?

   If yes, continue to #4.
   If no, continue to #5.

4. Has the patient achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more?

   If yes, for CHRONIC PLAQUE PSORIASIS, **approve for 12 months for #8 of the 25mg syringes/vials (2 kits) per month for 12 months or #4 of the 50mg syringes/vials (1 kit) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of chronic plaque psoriasis and that the patient has achieved clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more.

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RENEWAL CRITERIA (CONTINUED)

5. Does the patient have ankylosing spondylitis?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of ankylosing spondylitis, and that the patient has experienced an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); rheumatoid arthritis, psoriatic arthritis, or juvenile idiopathic arthritis and that the patient has experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count while on therapy; or chronic plaque psoriasis and that the patient has achieved clear or minimal disease; or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more.

6. Has the patient experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)?

   If yes, for ANKYLOSING SPONDYLITIS, **approve for 12 months for #8 of the 25mg syringes/vials (2 kits) per month for 12 months or #4 of the 50mg syringes/vials (1 kit) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of ankylosing spondylitis, and that the patient has experienced an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).

RATIONALE
Ensure that appropriate diagnostic, utilization, and safety criteria are utilized for the management of requests for etanercept.

FDA APPROVED INDICATION
Rheumatoid arthritis, psoriatic arthritis, chronic moderate to severe plaque psoriasis, ankylosing spondylitis and juvenile rheumatoid arthritis.

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ETANERCEPT (PART D)

REFERENCES

- Immunex Corporation. Enbrel product information. Thousand Oaks, CA. November 2009.
- Braun J, Davis J et al. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with Ankylosing Spondylitis. Ann Rheum Dis. 2006; 65(3):316-20.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian. [Accessed: June 18, 2009].
- Smith CH, Anstey AV, et al. British association of dermatologists' guidelines for use of biological interventions in psoriasis 2005. Br J Dermatol 2005; 153:486-497.

Part D Effective: 03/08/13 Created: 02/03
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

EVEROLIMUS

Generic	Brand	HICL	GCN	Exception/Other
EVEROLIMUS	AFINITOR		20784 20844 28783 31396	
EVEROLIMUS	AFINITOR DISPERZ		34589 34590 34592	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, continue to #2.
   If no, continue to #3.

2. Has the patient tried or does the patient have a contraindication to sunitinib (Sutent) or sorafenib (Nexavar)?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Afinitor 2.5mg, 5mg: 1 tablet per day**
   - **Afinitor 7.5mg, 10mg: 2 tablets per day**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) with a trial of sunitinib (Sutent) or sorafenib (Nexavar), which may also require prior authorization, or subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS), or pancreatic neuroendocrine carcinomas (PNET), or renal angiomyolipoma, associated with tuberous sclerosis complex (TSC) that does not require immediate surgery, or for postmenopausal women with a diagnosis of advanced hormone receptor-positive, HER2-negative breast cancer (defined as IHC less than or equal to 3+ or FISH amplification ratio less than or equal to 2.0) in combination with exemestane after failure of treatment with letrozole or anastrozole.

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GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a diagnosis of subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS)?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Afinitor 2.5mg, 5mg: 1 tablet per day**
   - **Afinitor 7.5mg, 10mg: 2 tablets per day**
   - **Afinitor Disperz 2mg, 3mg, 5mg: 4 tablets per day**

   If no, continue to #4.

4. Does the patient have a diagnosis of pancreatic neuroendocrine carcinomas (PNET)?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Afinitor 2.5mg, 5mg: 1 tablet per day**
   - **Afinitor 7.5mg, 10mg: 2 tablets per day**

   If no, continue to #5.

5. Does the patient have a diagnosis of renal angiomyolipoma, associated with tuberous sclerosis complex (TSC) that does not require immediate surgery?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Afinitor 2.5mg, 5mg: 1 tablet per day**
   - **Afinitor 7.5mg, 10mg: 2 tablets per day**

   If no, continue to #6.

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GUIDELINES FOR USE (CONTINUED)

6. Is the patient a postmenopausal woman with a diagnosis of advanced hormone receptor-positive, HER2-negative breast cancer (defined as IHC less than or equal to 3+ or FISH amplification ratio less than or equal to 2.0)?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) with a trial of sunitinib (Sutent) or sorafenib (Nexavar), which may also require prior authorization, or subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS), or pancreatic neuroendocrine carcinomas (PNET), or renal angiomyolipoma, associated with tuberous sclerosis complex (TSC) that does not require immediate surgery, or for postmenopausal women with a diagnosis of advanced hormone receptor-positive, HER2-negative breast cancer (defined as IHC less than or equal to 3+ or FISH amplification ratio less than or equal to 2.0) in combination with exemestane after failure of treatment with letrozole or anastrozole.

7. Has the patient previously tried Femara (letrozole) or Arimidex (anastrozole)?

   If yes, continue to #8.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) with a trial of sunitinib (Sutent) or sorafenib (Nexavar), which may also require prior authorization, or subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS), or pancreatic neuroendocrine carcinomas (PNET), or renal angiomyolipoma, associated with tuberous sclerosis complex (TSC) that does not require immediate surgery, or for postmenopausal women with a diagnosis of advanced hormone receptor-positive, HER2-negative breast cancer (defined as IHC less than or equal to 3+ or FISH amplification ratio less than or equal to 2.0) in combination with exemestane after failure of treatment with letrozole or anastrozole.

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GUIDELINES FOR USE (CONTINUED)

8. Is the patient using Afinitor in combination with Aromasin (exemestane)?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Afinitor 2.5mg, 5mg: 1 tablet per day**
   - **Afinitor 7.5mg, 10mg: 2 tablets per day**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) with a trial of sunitinib (Sutent) or sorafenib (Nexavar), which may also require prior authorization, or subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS), or pancreatic neuroendocrine carcinomas (PNET), or renal angiomyolipoma, associated with tuberous sclerosis complex (TSC) that does not require immediate surgery, or for postmenopausal women with a diagnosis of advanced hormone receptor-positive, HER2-negative breast cancer (defined as IHC less than or equal to 3+ or FISH amplification ratio less than or equal to 2.0) in combination with exemestane after failure of treatment with letrozole or anastrozole.

RATIONALE
Ensure appropriate utilization of everolimus based on FDA approved indication and NCCN guidelines.

Dosage and Administration
Advanced HR+ BC, advanced PNET, advanced RCC, or renal angiomyolipoma with TSC:
- 10 mg once daily with or without food.
- For patients with hepatic impairment, reduce the Afinitor dose.
- If moderate inhibitors of CYP3A4 and/or P-glycoprotein (PgP) are required, reduce the Afinitor dose to 2.5 mg once daily; if tolerated, consider increasing to 5 mg once daily.
- If strong inducers of CYP3A4 are required, increase Afinitor dose in 5 mg increments to a maximum of 20 mg once daily.

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RATIONAL (CONTINUED)
SEGA with TSC:
- 4.5 mg/m^2 once daily; adjust dose to attain trough concentrations of 5-15 ng/mL.
- Assess trough concentrations approximately 2 weeks after initiation of treatment, a change in dose, a change in co-administration of CYP3A4 and/or PgP inducers or inhibitors, a change in hepatic function, or a change in dosage form between Afinitor tablets and Afinitor Disperz.
- For patients with severe hepatic impairment reduce the starting dose of Afinitor tablets or Afinitor Disperz.
- If concomitant use of moderate inhibitors of CYP3A4 and/or PgP is required, reduce the dose of Afinitor tablets or Afinitor Disperz by 50%.
- If concomitant use of strong inducers of CYP3A4 is required, double the dose of Afinitor tablets or Afinitor Disperz.

NCCN considers either immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH) tests as an acceptable method for making an initial determination of HER2 tumor status. Tumors are classified as HER2 positive if they are scored as 3+ by an IHC method.

FDA APPROVED INDICATION
AFINITOR is a kinase inhibitor indicated for the treatment of:
- postmenopausal women with advanced hormone receptor-positive, HER2negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole.
- adults with progressive neuroendocrine tumors of pancreatic origin (PNET) that are unresectable, locally advanced or metastatic. The safety and effectiveness of AFINITOR in the treatment of patients with carcinoid tumors have not been established.
- adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
- adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery. The effectiveness of AFINITOR in the treatment of renal angiomyolipoma is based on an analysis of durable objective responses in patients treated for a median of 8.3 months. Further follow-up of patients is required to determine long-term outcomes.

AFINITOR and AFINITOR DISPERZ are kinase inhibitors indicated for the treatment of:
- pediatric and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected. The effectiveness is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC has not been demonstrated.

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EVEROLIMUS

REFERENCES

- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 2.2011).
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Neuroendocrine Tumors. (Version 1.2011).
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. (Version 1.2012).
- Novartis Pharmaceuticals Corporation. Afinitor package insert. East Hanover, NJ. August 2012.

Part D Effective: 10/01/13 Created: 05/11
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

FENTANYL NASAL SPRAY (PART D)

Generic	Brand	HICL	GCN	Exception/Other
FENTANYL NASAL SPRAY	LAZANDA		27648 29146	ROUTE = NASAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain.

2. Is the patient on a maintenance dose of controlled release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires that a controlled-release pain medication is also being used, which may also require a prior authorization.

3. Has the patient tried, or does the patient have a contraindication to at least 1 immediate-release oral pain agent (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these)?

   If yes, continue to #5.
   If no, continue to #4.

4. Does the patient have difficulty swallowing tablets or capsules?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of or a contraindication to an oral immediate-release pain medication, which may also require a prior authorization.

5. **Approve for 6 months with a quantity limit of 15 per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

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FENTANYL NASAL SPRAY (PART D)

RATIONALE
To ensure use of nasal fentanyl spray is consistent with indication.

FDA APPROVED INDICATIONS
LAZANDA is an opioid analgesic indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

REFERENCES

- Archimedes Pharma US. Lazanda package insert. Bedminster, NJ. July 2011.

Part D Effective: 01/01/13 Created: 08/11
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

FENTANYL SUBLINGUAL SPRAY (PART D)

Generic	Brand	HICL	GCN	Exception/Other
FENTANYL SUBLINGUAL SPRAY	SUBSYS		31187, 31188, 31189, 31192, 31193, 31596, 31597	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), all of which may also require a prior authorization.

2. Is the patient on a maintenance dose of controlled release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), all of which may also require a prior authorization.

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FENTANYL SUBLINGUAL SPRAY (PART D)

GUIDELINES FOR USE (CONTINUED)

3. Has the patient tried or does the patient have a contraindication to at least 1 immediate-release oral pain agent (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these)?

   If yes, **approve for 6 months with a quantity limit of #120 per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #4.

4. Does the patient have difficulty swallowing tablets or capsules?

   If yes, **approve for 6 months with a quantity limit of #120 per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), all of which may also require a prior authorization.

RATIONALE
To ensure the use of fentanyl sublingual spray is consistent with the FDA approved indication.

FDA APPROVED INDICATIONS
SUBSYS is an opioid agonist indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

REFERENCES
- Insys Therapeutics, Subsys package insert. Phoenix, AZ. January 2012.

Part D Effective: 01/01/13	Created: 04/12	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

FENTANYL TRANSDERMAL PATCH

Generic	Brand	HICL	GCN	Exception/Other
FENTANYL	DURAGESIC		19200, 19201, 19202, 19203, 24635	GPID ≠ 25879

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Has the patient tried, or does the patient have a contraindication to at least one of the following agents: methadone or a sustained-release morphine product (e.g., Avinza, MS Contin, Kadian, or Oramorph SR)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of sustained-release morphine product such as generic MS Contin and that requested medication is not prescribed on an "as needed" basis.

2. Does the request form indicate that this medication will be used on an "as needed" or "PRN" basis?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a trial of sustained-release morphine product such as generic MS Contin and that requested medication is not prescribed on an "as needed" basis.
   If no, continue to #3.

3. Is the request for dosing more frequent than every 72 hours?

   If yes, continue to #4.
   If no, continue to #5.

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient tried or does the patient have a contraindication to transdermal fentanyl dosed every 72 hours?

   If yes continue to #5.
   If no, do not approve.
   - **For Part D: Enter a proactive approval by GPID for 12 months with the following quantity limits: 12mcg, 25mcg, 50mcg, 75mcg: #10 per 30 days.**
     100mcg: #20 per 30 days.
   - **For Commercial: Enter a proactive approval by GPID for 12 months with quantity limit of #10 per 30 days.**

   DENIAL TEXT: Approval requires a trial of or a contraindication to transdermal fentanyl dosed every 72 hours. A proactive Prior Authorization has been entered.

5. Is the patient currently taking more than one strength of transdermal fentanyl? (Based on information provided on request form, approved claims and active authorizations)

   If yes, send to Clinical for review.
   CLINICAL: If dose consolidation is possible, recommend the appropriate strength patch with a quantity limit of 10 patches per 30 days. If dose consolidation is not possible, please approve multiple strengths within the quantity limit of 10 patches per 30 days.
   If no, process as follows:
   - For every 72 hour dosing, continue to #6.
   - For every 48 hour dosing, continue to #7.

6. **Approve for 12 months by GPID with the following quantity limits:**
   - **For Part D: 12mcg, 25mcg, 50mcg, 75mcg: #10 per 30 days.**
     100mcg: #20 per 30 days.
   - **For Commercial: #10 per 30 days.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

7. **Approve for 12 months by GPID with the following quantity limits:**
   - **For Part D: 12mcg, 25mcg, 50mcg, 75mcg: #15 per 30 days.**
     100mcg: #20 per 30 days.
   - **For Commercial: #15 per 30 days.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

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FENTANYL TRANSDERMAL PATCH

RATIONALE
To ensure appropriate utilization of fentanyl transdermal patch after failure of a sustained-release morphine product. Fentanyl transdermal patch should not be used “as needed or PRN.”

FDA APPROVED INDICATION
Management of chronic pain in patients requiring continuous opioid analgesia for pain that cannot be managed by lesser means such as acetaminophen-opioid combinations, nonsteroidal analgesics, or PRN dosing with short-acting opioids.

REFERENCES

- Janssen Pharmaceuticals, Inc. Duragesic package insert. Titusville, NJ. July 2009.

Part D Effective: 01/01/13 Created: 02/03
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

FENTANYL TRANSMUCOSAL AGENTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
FENTANYL CITRATE	ACTIQ ABSTRAL FENTORA ONSOLIS	01747		ROUTE = BUCCAL, SUBLINGUAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), which also requires a prior authorization.

2. Is the patient on a maintenance dose of controlled release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), which also requires a prior authorization.

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GUIDELINES FOR USE (CONTINUED)

3. Has the patient tried, or does the patient have a contraindication to at least 1 immediate-release oral pain agent (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these)?

   If yes, **approve for 6 months with a quantity limit of #120 per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #4.

4. Does the patient have difficulty swallowing tablets or capsules?

   If yes, **approve for 6 months with a quantity limit of #120 per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cancer-related pain, and concurrent use with a controlled-release pain medication (MS Contin, Oxycontin, Oramorph SR, Duramorph, Roxanol SR, Duragesic, Kadian, Avinza or the generic forms of any of these drugs), and trial of an oral immediate-release pain medication (morphine sulfate immediate-release [MSIR], Percodan, Percocet, Vicodin, Tylenol with Codeine, Dilaudid, Demerol or the generic forms of any of these), which also requires a prior authorization.

RATIONALE
To ensure use of transmucosal fentanyl is consistent with indication.

FDA APPROVED INDICATIONS
ABSTRAL is an opioid analgesic indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

ACTIQ is indicated for breakthrough cancer pain in patients 16 years and older with malignancies who are already receiving and who are tolerant to opioid therapy for persistent cancer pain. Patients must remain on around-the-clock opioids when taking Actiq.

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FENTANYL TRANSMUCOSAL AGENTS (PART D)

FDA APPROVED INDICATIONS (CONTINUED)
FENTORA is indicated for breakthrough pain in patients with cancer who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid daily for a week or longer. This product must not be used in opioid non-tolerant patients because life-threatening hypoventilation and death could occur at any dose in patients not on a chronic regimen of opioids.

FENTORA is contraindicated in the management of acute or postoperative pain. Fentora is intended to be used only in the care of opioid tolerant cancer patients and only by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.

ONSOLIS is indicated for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

REFERENCES

- Cephalon, Inc. Actiq package insert. Frazer, PA. September 2009.
- Cephalon, Inc. Fentora package insert. Frazer, PA. January 2011.
- Meda Pharmaceuticals, Inc. Onsolis package insert. Somerset, NJ July 2009.
- ProStrakan Inc. Abstral package insert. Bedminster, NJ. January 2011.

Part D Effective: 01/01/13 Created: 02/03
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

FINGOLIMOD (PART D)

Generic	Brand	HICL	GCN	Exception/Other
FINGOLIMOD	GILENYA	37180		

This note pertains to Part D lines of business only:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis and a trial of both an interferon (such as Rebif) and Copaxone.

2. Has the patient tried, or does the patient have a contraindication to interferon therapy (Avonex, Betaseron, Extavia, or Rebif) **AND** Copaxone?

   If yes, **approve for 12 months #28 capsules per 28 days supply.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis and a trial of both an interferon (such as Rebif) and Copaxone.

RATIONALE
To prevent inappropriate utilization of fingolimod for clinically isolated syndrome (CIS) and encourage the use of Copaxone and preferred interferons.

FDA APPROVED INDICATION
Fingolimod is indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

REFERENCE

- Novartis Pharmaceutical Corporation. Gilenya package insert. East Hanover, NJ May 2011.

Part D Effective: 01/01/13 Created: 11/10
Commercial Effective: N/A Client Approval: 11/12 P&T Approval: 11/12

FONDAPARINUX

Generic	Brand	HICL	GCN	Exception/Other
FONDAPARINUX	ARIXTRA	23233		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
This note pertains to Part D lines of business only:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is this for prevention (prophylaxis) of deep vein thrombosis (DVT) after hip fracture surgery or hip replacement surgery?

   If yes, **approve one time for 2.5mg/0.5mL syringe: 16.5mL per 33 days.** ***(For the length of treatment of 33 days, one course of therapy allowed every 33 day period)***
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #2.

2. Is this for the prevention (prophylaxis) of deep vein thrombosis (DVT) after knee replacement surgery or prevention of venous thromboembolism (VTE) in patients undergoing abdominal surgery?

   If yes, **approve one time for 2.5mg/0.5mL syringe: 7mL per month.** ***(For the length of treatment of 14 days, one course of therapy allowed per month period)***
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #3.

3. Is the patient receiving fondaparinux for outpatient treatment of acute deep vein thrombosis (DVT) or acute pulmonary embolism (PE) administered in conjunction with warfarin?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires agent be used for prevention of deep vein thrombosis (DVT) after hip fracture or hip or knee replacement surgery, prevention of venous thromboembolism (VTE) in abdominal surgery, or outpatient treatment of acute DVT or pulmonary embolism (PE) administered in conjunction with warfarin.

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient established an oral anticoagulant effect with a therapeutic INR level between 2 to 3?

   If yes, do not approve.
   DENIAL TEXT: Approval requires patient to have acute deep vein thrombosis (DVT) or acute pulmonary embolism (PE) but have yet to establish a therapeutic INR level between 2 to 3. Per information provided patient's INR level is within therapeutic range.

   If no, **approve one time as follows *(For the length of treatment of 14 days, one course of therapy allowed per month period)*:**
   2.5mg/0.5mL syringe: 7mL per month
   5mg/0.4mL syringe: 5.6mL per month
   7.5mg/0.6mL syringe: 8.4mL per month
   10mg/0.8mL syringe: 11.2mL per month
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE
Ensure appropriate use of fondaparinux.

FDA APPROVED INDICATIONS
- Prevention of DVT in patients undergoing hip fracture surgery, hip replacement surgery, or knee replacement surgery.
- Treatment of acute DVT when administered in conjunction with warfarin.
- Treatment of acute PE when administered in conjunction with warfarin when initial therapy is administered in the hospital.
- Use in patients undergoing abdominal surgery who are at risk for thromboembolic complications.

REFERENCE
- GlaxoSmithKline. Arixtra package insert. Research Triangle Park, NC. June 2011.

Part D Effective: 01/01/13 Created: 02/03
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

GLP-1 ANALOGS

Generic	Brand	HICL	GCN	Exception/Other
EXENATIDE MICROSPHERES	BYDUREON	38451		
EXENATIDE	BYETTA	32893		
LIRAGLUTIDE	VICTOZA	36436		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have type 2 diabetes?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of type 2 diabetes.

2. Is the request for Victoza?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient failed to reach treatment goals with metformin (Glucophage), metformin ER (Glucophage XR), glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), a formulary oral sulfonylurea (e.g., glyburide, glipizide) or pioglitazone (Actos, Duetact, Actoplus Met, Actoplus Met XR), AND exenatide extended release (Bydureon)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of type 2 diabetes and documentation that the patient has failed to reach treatment goals with metformin (Glucophage), metformin ER (Glucophage XR), glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), a formulary oral sulfonylurea (e.g., glyburide, glipizide), or pioglitazone (Actos, Duetact, Actoplus Met, Actoplus Met XR), AND exenatide extended release (Bydureon).

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient failed to reach treatment goals with metformin (Glucophage), metformin ER (Glucophage XR), glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), a formulary oral sulfonylurea (e.g., glyburide, glipizide), or pioglitazone (Actos, Duetact, Actoplus Met, Actoplus Met XR)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of type 2 diabetes and documentation that the patient has failed to reach treatment goals with metformin (Glucophage), metformin ER (Glucophage XR), glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), a formulary oral sulfonylurea (e.g., glyburide, glipizide), or pioglitazone (Actos, Duetact, Actoplus Met, Actoplus Met XR).

5. **BYDUREON: Approve #4 vials per 28 days for 12 months.**
   BYETTA: Approve #1 pen (1.2mL or 2.4mL) per month for 12 months.
   VICTOZA: Approve up to #3 pens per month for 12 months.
   APPROVAL TEXT FOR BYDUREON AND VICTOZA: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE
Ensure appropriate use of Byetta and Victoza as second line therapy.

FDA APPROVED INDICATIONS
BYDUREON: As adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus in multiple clinical settings.
BYETTA: As adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
VICTOZA: As adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

REFERENCES

- Amylin Pharmaceuticals. Bydureon package insert. San Diego, CA. January 2012.
- Amylin Pharmaceuticals. Byetta package insert. San Diego, CA. September 2010.
- Novo Nordisk. Victoza package insert. Princeton, NJ. January 2010.
- AACE Diabetes Mellitus Guidelines, Endoc Pract. 2007; 13(Suppl 1) 2007.
- AACE/ACE Consensus Statement: Glycemic Control Algorithm, Endocr Pract. 2009;15(no.6) 541
- DIABETES CARE, Standards of Medical Care in Diabetes -2010, Volume 33, Supplement 1, January 2010.

Part D Effective: 07/01/13 Created: 05/05
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 11/12

GLYCEROL PHENYLBUTYRATE

Generic	Brand	HICL	GCN	Exception/Other
GLYCEROL PHENYLBUTYRATE	RAVICTI		34137	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a patient age of at least 2 months, a diagnosis of urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone, and a trial of Buphenyl.

2. Is the patient at least 2 months of age?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a patient age of at least 2 months, a diagnosis of urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone, and a trial of Buphenyl.

3. Has the patient tried or does the patient have a contraindication to Buphenyl?

   If yes, **approve for 12 months by GPID.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a patient age of at least 2 months, a diagnosis of urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone, and a trial of Buphenyl.

RATIONALE
To ensure appropriate use aligned with FDA approved indication.

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RATIONALE (CONTINUED)
Ravicti is supplied as a liquid for oral administration. It should be taken with food and administered directly into the mouth via oral syringe or dosing cup. Ravicti should be given in 3 equally divided dosages, each rounded up to the nearest 0.5 mL. The recommended dosages for patients switching from sodium phenylbutyrate to Ravicti and patients naïve to phenylbutyric acid are different.

Patients switching from sodium phenylbutyrate to Ravicti should receive the dosage of Ravicti that contains the same amount of phenylbutyric acid. The conversion is as follows:
Total daily dosage of Ravicti (mL) = total daily dosage of sodium phenylbutyrate (g) x 0.8

The recommended dosage range in patients naïve to phenylbutyrate (PBA), based upon body surface area, is 4.5 to 11.2 mL/m2/day (5 to 12.4 g/m2/day). For patients with some residual enzyme activity who are not adequately controlled with protein restriction, the recommended starting dosage is 4.5 mL/m2/day.

The maximum total daily dosage is 17.5 mL (19 g).

Ravicti (glycerol phenylbutyrate) joins Buphenyl (sodium phenylbutyrate) as the second FDA approved treatment for UCDs. Ravicti is a nearly tasteless and odorless liquid taken three times a day. In contrast, Buphenyl is poorly tolerated by patients due to its unpleasant taste and odor and along with the need to take up to 40 tablets a day. Over half of UCD patients do not take Buphenyl and it is believed that is largely due to the difficulties in tolerating the drug.

UCDs are genetic metabolic disorders present in an estimated 1 in 10,000 births in the United States. Patients with UCDs are deficient in one of the key enzymes that comprise the urea cycle, the body's primary vehicle for removing ammonia, a potent neurotoxin, from the bloodstream. Onset may occur at any age depending on the severity of the disorder. If left untreated, UCDs can cause dangerously heightened levels of ammonia in the bloodstream (hyperammonemia) resulting in brain damage, coma, and/or death.

Ravicti is a triglyceride containing 3 molecules of phenylbutyrate (PBA). Phenylacetate (PAA), the major metabolite of PBA, is the active moiety of Ravicti. PAA conjugates with glutamine (which contains 2 molecules of nitrogen) via acetylation in the liver and kidneys to form phenylacetylglutamine (PAGN), which is excreted by the kidneys. On a molar basis, PAGN, like urea, contains 2 moles of nitrogen and provides an alternate vehicle for waste nitrogen excretion.

The FDA approval of Ravicti was based on separate studies in adults and pediatrics.

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RATIONALE (CONTINUED)
A randomized, double-blind, active-controlled, crossover, non-inferiority study enrolled 45 subjects with UCDs who had been on sodium phenylbutyrate prior to enrollment. The trial was designed to compare Ravicti to sodium phenylbutyrate by evaluating venous ammonia levels. The primary endpoint was to establish non-inferiority in the 24-hour AUC (a measure of exposure to ammonia over 24 hours) for venous ammonia on days 14 and 28 when the drugs were expected to be at steady state. The subjects were randomized to sodium phenylbutyrate for 2 weeks followed by Ravicti for 2 weeks or Ravicti for 2 weeks followed by sodium phenylbutyrate for 2 weeks. The dose of Ravicti was calculated to deliver the same amount of PBA as the sodium phenylbutyrate dose the patients were taking when they entered the trial. Both treatments were administered three times daily with meals. Forty-four subjects were evaluable for analysis. Ravicti was non-inferior to sodium phenylbutyrate with respect to the 24-hour AUC for ammonia. Mean 24-hour AUCs for venous ammonia during steady-state dosing were 866 µmol/L hour and 977 µmol/L hour with Ravicti and sodium phenylbutyrate, respectively. Long term (12 month) studies in adults have demonstrated maintenance of normal ammonia serum values with Ravicti.

Two fixed-sequence, open-label, sodium phenylbutyrate to Ravicti switchover studies were conducted in pediatric patients ages 2 to 17 years. The first study was 7 days in duration and the second study was 10 days in duration. A total of 26 subjects were enrolled. The dose of Ravicti was calculated to deliver the same amount of PBA as the dose of sodium phenylbutyrate patients were taking when they entered the trial. Sodium phenylbutyrate or Ravicti was administered in divided doses with meals and the subjects adhered to a low-protein diet throughout the study. After a dosing period with each treatment, all subjects underwent 24 hours of venous ammonia measurements, as well as blood and urine PK assessments. The 24-hour AUCs for blood ammonia (AUC0-24h) in 11 pediatrics 6 to 17 years of age (Study 1) and 11 pediatrics 2 years to 5 years of age (Study 2) were similar between treatments. In children 6 to 17 years of age, the ammonia AUC0-24h was 604 µmol·h/L vs. 815 µmol·h/L on Ravicti versus sodium phenylbutyrate. In the patients between 2 years and 5 years of age, the ammonia AUC0-24h was 632 µmol·h/L vs. 720 µmol·h/L on Ravicti versus sodium phenylbutyrate. Long term (12 month) studies in pediatrics have also demonstrated maintenance of normal ammonia serum values with Ravicti.

The use of Ravicti in patients <2 months of age is contraindicated. Ravicti is not indicated for the treatment of acute hyperammonemia in patients with UCDs because more rapidly acting interventions are essential to reduce plasma ammonia levels. Warnings and precautions include nausea, vomiting, diarrhea, decreased appetite, hyperammonemia, dizziness, headache, upper abdominal pain, rash and fatigue. The most common adverse reactions (occurring in ≥10% of patients) reported during short-term treatment with Ravicti were diarrhea, flatulence, and headache. Ravicti is pregnancy category C. A voluntary patient registry will include evaluation of pregnancy outcomes in patients with UCDs.

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GLYCEROL PHENYLBUTYRATE

FDA APPROVED INDICATIONS

Ravicti is indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients ≥2 years of age with urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements).

Limitations of Use:

- Ravicti is not indicated for treatment of acute hyperammonemia in patients with UCDs.
- The safety and efficacy of Ravicti for the treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established.
- The use of Ravicti in patients <2 months of age is contraindicated

REFERENCES

- Ravicti [Prescribing Information]. South San Francisco, CA: Hyperion Therapeutics Inc.; January 2013.

Part D Effective: 07/01/13 Created: 02/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 05/13

GOLIMUMAB (PART D)

Generic	Brand	HICL	GCN	Exception/Other
GOLIMUMAB	SIMPONI	36278		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has this drug been prescribed by or is it currently being supervised by a rheumatologist or dermatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist or dermatologist; that the patient is at least 18 years of age; a diagnosis of rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis; and a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization.

2. Is the patient at least 18 years of age?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist or dermatologist; that the patient is at least 18 years of age; a diagnosis of rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis; and a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization.

3. Does the patient have active rheumatoid arthritis?

   If yes, continue to #4.
   If no, continue to #7.

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INITIAL CRITERIA (CONTINUED)

4. Has the patient tried or does the patient have a contraindication to at least one of the following DMARDs: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of one of the following DMARDs (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization; and that the patient is currently taking methotrexate.

5. Has the patient tried Humira (adalimumab) or Cimzia (certolizumab pegol)?

   If yes, continue to #6.
   If no, do not approve. (Ask the caller to submit a MRF for Humira).
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of one of the following DMARDs (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization; and that the patient is currently taking methotrexate.

6. Is the patient currently on methotrexate?

   If yes, for RHEUMATOID ARTHRITIS, **approve for 3 months for #1 prefilled SmartJect autoinjector or syringe per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a trial of one of the following DMARDs (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, sulfasalazine; a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization; and that the patient is currently taking methotrexate.

7. Does the patient have active psoriatic arthritis?

   If yes, continue to #8.
   If no, continue to #10.

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INITIAL CRITERIA (CONTINUED)

8. Has the patient tried or does the patient have a contraindication to at least one of the following DMARDs: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is at least 18 years of age; a diagnosis of active psoriatic arthritis; has tried at least one DMARD (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; and a trial of the preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization.

9. Has the patient tried Humira (adalimumab)?

   If yes, for PSORIATIC ARTHRITIS, **approve for 3 months for #1 prefilled SmartJect autoinjector or syringe per month.**
   If no, do not approve. (Ask the caller to submit a MRF for Humira).
   DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is at least 18 years of age; a diagnosis of active psoriatic arthritis; has tried at least one DMARD (disease-modifying antirheumatic drug): methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine; and a trial of the preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization.

10. Does the patient have active ankylosing spondylitis?

    If yes, continue to #11.
    If no, do not approve.
    DENIAL TEXT: Approval requires supervision by a rheumatologist or dermatologist; that the patient is at least 18 years of age; a diagnosis of rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis; and a trial of the preferred formulary tumor necrosis factors: Humira (adalimumab) or Cimzia (certolizumab pegol), which may also require a prior authorization.

11. Has the patient tried Humira (adalimumab)?

    If yes, for ANKYLOSING SPONDYLITIS, **approve for 3 months for #1 prefilled SmartJect autoinjector or syringe per month.**
    If no, do not approve. (Ask the caller to submit a MRF for Humira).
    DENIAL TEXT: Approval requires supervision by a rheumatologist; that the patient is at least 18 years of age; and a trial of the preferred formulary tumor necrosis factor Humira (adalimumab), which may also require a prior authorization.

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GOLIMUMAB (PART D)

RENEWAL CRITERIA

1. Does the patient have active rheumatoid arthritis?

   If yes, continue to #4.
   If no, continue to #2.

2. Does the patient have ankylosing spondylitis?

   If yes, continue to #6.
   If no, continue to #3.

3. Does the patient have psoriatic arthritis?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis.

4. Has the patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis; that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy; and that the patient is currently taking methotrexate.

5. Is the patient on concurrent methotrexate therapy?

   If yes, for RHEUMATOID ARTHRITIS, **approve for 12 months for #1 prefilled SmartJect autoinjector or syringe per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis; that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy; and that the patient is currently taking methotrexate.

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RENEWAL CRITERIA (CONTINUED)

6. Has the patient experienced or maintained an improvement of 20% or greater in the assessment in Ankylosing Spondylitis (ASAS20) criteria?

   If yes, for ANKYLOSING SPONDYLITIS, **approve for 12 months for #1 prefilled SmartJect autoinjector or syringe per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of ankylosing spondylitis and that the patient has experienced at least a 20% improvement from baseline on the Ankylosing Spondylitis (ASAS20) criteria.

7. Has the patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count?

   If yes, for PSORIATIC ARTHRITIS, **approve for 12 months for #1 prefilled SmartJect autoinjector or syringe per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of psoriatic arthritis and that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy.

RATIONALE
Ensure appropriate diagnostic, utilization and safety criteria are used for the management of prior authorization requests for golimumab.

FDA APPROVED INDICATIONS
SIMPONI in combination with methotrexate is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis.

Simponi, alone or in combination with methotrexate, is also indicated for adult patients with active psoriatic arthritis.

Simponi has a third indication for the treatment of adult patients with active ankylosing spondylitis.

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GOLIMUMAB (PART D)

REFERENCES

- Centocor Ortho Biotech, Inc. Simponi package insert. Horsham, PA. March 2011.
- Inman RD, Davis JC, Heijde D, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis. Arthritis & Rheumatism. 2008; 58(11): 3402-3412.
- Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new human tumor necrosis factor α antibody administered every four weeks as a subcutaneous injection in psoriatic arthritis. Arthritis & Rheumatism. 2009; 60(4): 976-986.
- Keystone EC, Genovese MC, Klareskog L, et al. Golimumab, a human antibody to tumor necrosis factor α antibody given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the GO-FORWARD study. Ann Rheum. 2009:68: 789-796.

Part D Effective: 03/08/13 Created: 06/09
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

HEPATITIS A VACCINE (INACTIVATED) BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
HEPATITIS A VACCINE	HAVRIX (HAV) VAQTA	07782 34417		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is this request for prevention of Hepatitis A? (i.e. active immunization for a person 12 months of age and older)

   If yes, **approve for up to 12 months under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   If no, continue to #2.

2. Is the drug to be administered to treat a member already exposed to Hepatitis A or member requiring both immediate and long-term protection?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, do not approve.
   DENIAL TEXT: Approval requires this medication is being used for the prevention of Hepatitis A, or for treatment of a patient who is already exposed to Hepatitis A or who requires both immediate and long-term protection.

RATIONALE

Hepatitis A vaccine, inactivated requires a Part B vs. Part D determination. This vaccine is Part D for active immunization of persons 12 months of age and older against disease caused by HAV and Part B if passive protection against Hepatitis A is required either following exposure to HAV or in persons requiring both immediate and long-term protection. Hepatitis A vaccine, inactivated may be co-administered with immune globulin.

FDA APPROVED INDICATION

It is indicated for immunization of persons 12 months of age and older against Hepatitis A.

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HEPATITIS A VACCINE (INACTIVATED) BVD DETERMINATION (PART D)

REFERENCES

- GlaxoSmithKline. Havrix package insert. Research Triangle Park, NC. May 2010.
- Merck & Co., Inc. Vaqta package insert. Whitehouse Station, NJ. December 2007.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13	Created: 02/08	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

HEPATITIS B VACCINE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
HEPATITIS B VIRUS VACCINE	RECOMBIVAX HB ENGERIX-B	21300 34649		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the drug to be administered to treat an individual at intermediate to high-risk of being infected with Hepatitis B?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #2.

2. Is the request for immunization against infection caused by Hepatitis B virus?

   If yes, **approve for 12 months under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   If no, do not approve.
   DENIAL TEXT: Approval requires this medication is being used for immunization against Hepatitis B viral infection, or for the treatment of an individual who is at intermediate to high-risk of being infected with Hepatitis B.

RATIONALE
Hepatitis B vaccine requires a Part B vs. Part D determination. This vaccine is Part D for immunization against disease caused by Hepatitis B virus. Part B if patients in all age groups are at intermediate to high-risk of being infected with Hepatitis B.

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HEPATITIS B VACCINE BVD DETERMINATION (PART D)

RATIONALE (CONTINUED)

High Risk Groups include:

- End-Stage Renal Disease (ESRD) patients;
- Hemophiliacs who receive Factor VIII or IX concentrates;
- Clients of institutions for the mentally retarded;
- Persons who live in the same household as a hepatitis B carrier;
- Homosexual men;
- Illicit injectable drug abusers; and
- Pacific Islanders (that is, those Medicare beneficiaries who reside on Pacific islands under U.S. jurisdiction, other than residents of Hawaii).
- Persons diagnosed with diabetes mellitus.

Intermediate Risk Groups include:

- Staff in institutions for the mentally retarded and classroom employees who work with mentally retarded persons;
- Workers in health care professions who have frequent contact with blood or blood-derived body fluids during routine work (including workers who work outside of a hospital and have frequent contact with blood or other infectious secretions); and
- Heterosexually active persons with multiple sexual partners (that is, those Medicare beneficiaries who have had at least two documented episodes of sexually transmitted diseases within the preceding 5 years).

FDA APPROVED INDICATION

Immunization against Hepatitis B.

REFERENCES

- Merck & Co., Inc. Recombivax package insert. Whitehouse Station, NJ. March 2010.
- GlaxoSmithKline. Engerix-B package insert. Research Triangle Park, NC. May 2010.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].
- Code of Federal Regulations/Title 42 – Public Health/Vol. 2/2006-10-01350. Section 410.63 – Hepatitis B vaccine and blood clotting factors: Conditions http://www.gpo.gov/fdsys/pkg/CFR-2006-title42-vol2/xml/CFR-2006-title42-vol2-sec410-63.xml
- Federal Register/Vol 77, No. 222/Friday, November 16, 2012/Rules and Regulations page 69328 [FR DOC # 2012-26900] http://www.gpo.gov/fdsys/pkg/FR-2012-11-16/pdf/2012-26900.pdf

Part D Effective: 02/01/13 Created: 09/05
Commercial Effective: N/A Client Approval: 01/13 P&T Approval: 11/12

HRM ANTICHOLINERGICS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
HYDROXYZINE HCL	HYDROXYZINE HCL		13932 13941 13943 13944 13881 13882	
HYDROXYZINE PAMOATE	HYDROXYZINE PAMOATE, VISTARIL		13951 13952 13953	
PROMETHAZINE HCL	PROMETHAZINE HCL, ANERGAN 50, PHENADOZ, PHENERGAN		14981 14983 14990 15003 15001 15002 15035 15042 15043 15044 41751	
BENZTROPINE MESYLATE	BENZTROPINE MESYLATE, COGENTIN		17610 17620 17621 17622 27379	
CARBINOXAMINE MALEATE	CARBINOXAMINE MALEATE, PALGIC, ARBINOXA	04483		
CLEMASTINE FUMARATE	CLEMASTINE FUMARATE	04512		CLASS = FEDERAL LEGEND
TRIHEXYPHENIDYL	TRIHEXYPHENIDYL	01900		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

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HRM ANTICHOLINERGICS (PART D)

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Does the patient have a diagnosis of pruritus, urticaria, seasonal or perennial allergy?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried or does the patient have a contraindication to levocetirizine?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of levocetirizine.

4. Does the patient have a diagnosis of insomnia?

   If yes, continue to #5.
   If no, continue to #6.

5. Has the patient tried or does the patient have a contraindication to both Rozerem AND Silenor?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of Rozerem and Silenor.

6. Does the patient have a diagnosis of anxiety?

   If yes, continue to #7.
   If no, continue to #8.

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GUIDELINES FOR USE (CONTINUED)

7. Has the patient tried or does the patient have a contraindication to two of the following: buspirone, paroxetine, or venlafaxine?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: buspirone, paroxetine, or venlafaxine.

8. Does the patient have a diagnosis of Parkinsonism?

   If yes, continue to #9.
   If no, continue to #10.

9. Has the patient tried or does the patient have a contraindication to two of the following: amantadine, carbidopa/levodopa, or selegiline?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: amantadine, carbidopa/levodopa, or selegiline.

10. Does the patient have a diagnosis of motion sickness?

    If yes, continue to #11.
    If no, continue to #12.

11. Has the patient tried or does the patient have a contraindication to meclizine?

    If yes, **approve for 1 year.**
    If no, do not approve.
    DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of meclizine.

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GUIDELINES FOR USE (CONTINUED)

12. Does the patient have a diagnosis of nausea or vomiting?

    If yes, continue to #13.
    If no, continue to #14.

13. Has the patient tried or does the patient have a contraindication to ondansetron?

    If yes, **approve for 1 year.**
    If no, do not approve.
    DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of ondansetron.

14. Does the patient have a diagnosis of extrapyramidal symptoms (EPS)?

    If yes, **approve for 1 year.**
    If no, do not approve.
    DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older.

RATIONALE

The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications. Treatment of cough is not covered under Part D.

In 2013, short acting benzodiazepines will be covered under Part D. At this time, lorazepam will be added as a therapeutic alternative for insomnia and anxiety.

FDA APPROVED INDICATIONS

ATARAX (HYDROXYZINE HCL) is indicated for the symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested. Useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatosis, and in histamine-mediated pruritus. As a sedative when used in premedication and following general anesthesia, hydroxyzine may potentiate meperidine and barbiturates, so their use in pre-anesthetic adjunctive therapy should be modified on an individual basis. The effectiveness of hydroxyzine as an anti-anxiety agent for long term use, that is more than 4 months, has not been assessed by systemic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

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FDA APPROVED INDICATIONS (CONTINUED)

VISTARIL (HYDROXYZINE PAMOATE) is indicated for the symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested. Useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatosis, and in histamine-mediated pruritus. As a sedative when used in premedication and following general anesthesia, hydroxyzine may potentiate meperidine and barbiturates, so their use in pre-anesthetic adjunctive therapy should be modified on an individual basis. The effectiveness of hydroxyzine as an anti-anxiety agent for long term use, that is more than 4 months, has not been assessed by systemic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

DIPHENHYDRAMINE is indicated for the following indications:

- Antihistaminic: For allergic conjunctivitis due to foods; mild, uncomplicated allergic skin manifestations of urticaria and angioedema; amelioration of allergic reactions to blood or plasma; dermatographism; as therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.
- Motion Sickness: For active and prophylactic treatment of motion sickness.
- Antiparkinsonism: For Parkinsonism (including drug-induced) in the elderly unable to tolerate more potent agents; mild cases of Parkinsonism (including drug-induced) in other age groups; in other cases of Parkinsonism (including drug-induced) in combination with centrally acting anti-cholinergic agents.
- Nighttime sleep-aid.

PROMETHAZINE HYDROCHLORIDE TABLETS are useful for: Perennial and seasonal allergies, vasomotor rhinitis, allergic conjunctivitis due to inhalant allergens and foods, mild, uncomplicated allergic skin manifestations of urticaria and angioedema, amelioration of allergic reactions to blood or plasma, dermographism, anaphylactic reactions, as adjunctive therapy to epinephrine and other standard measures, after the acute manifestations have been controlled, preoperative, postoperative, or obstetric sedation, prevention and control of nausea and vomiting associated with certain types of anesthesia and surgery, therapy adjunctive to meperidine or other analgesics for control of post-operative pain, sedation in both children and adults, as well as relief of apprehension and production of light sleep from which the patient can be easily aroused, active and prophylactic treatment of motion sickness, antiemetic therapy in postoperative patients.

BENZTROPINE MESYLATE is indicated for use as an adjunct in the therapy of all forms of Parkinsonism. Useful also in the control of extrapyramidal disorders (except tardive dyskinesia) due to neuroleptic drugs (e.g. phenothiazines).

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FDA APPROVED INDICATIONS (CONTINUED)

CARBINOXAMINE MALEATE is effective for the symptomatic treatment of:

- Seasonal and perennial allergic rhinitis.
- Vasomotor rhinitis.
- Allergic conjunctivitis due to inhalant allergens and foods.
- Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.
- Dermatographism.
- As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.
- Amelioration of the severity of allergic reactions to blood or plasma.

TRIHEXYPHENIDYL HCL is indicated as an adjunct in the treatment of all forms of Parkinsonism (post encephalitic, arteriosclerotic, and idiopathic). It is often useful as adjuvant therapy when treating these forms of Parkinsonism with levodopa. Additionally, it is indicated for the control of extrapyramidal disorders caused by central nervous system drugs such as the dibenzoxazepines, phenothiazines, thioxanthenes, and butyrophenones.

REFERENCES

- Roerig division of Pfizer, Inc. Atarax (hydroxyzine hcl tablets) package insert. NY, NY. June 2006.
- Pfizer Labs, division of Pfizer, Inc. Vistaril® (hydroxyzine pamoate capsules) package insert. NY, NY. April 2004.
- Barr Laboratories, Inc. Diphenhydramine package insert. Pomona, NY. May 1999.
- Watson Pharma, Inc. Promethazine tablets package insert. Corona, CA. June 2009.
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed October 23, 2012].

Part D Effective: 08/01/13 Created: 07/12
Commercial Effective: N/A Client Approval: 06/13 P&T Approval: 02/13

HRM ANTI-INFECTIVE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
NITROFURANTOIN	FURADANTIN		41870	
NITROFURANTOIN MACROCRYSTAL	MACRODANTIN		41820 41821 41822	
NITROFURANTOIN MONOHYDRATE/M-CRYSTAL	MACROBID		49001	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 12 months.**

2. Has the member received a cumulative (total) 90 days supply of any nitrofurantoin product within the current plan year (January to December of the current year) per claims history?

   If yes, continue to #3.
   If no, **approve for up to a 90 days supply (less any days supply in the current plan year) within a 12 month duration with the following quantity limits:**
   FURADANTIN: approve 80mL daily (maximum dose of 400mg per day)
   MACRODANTIN: approve #4 capsules daily (maximum dose of 400mg per day)
   MACROBID: approve #2 capsules daily (maximum dose of 200mg per day)

   PAC NOTE: Review claims history for previous fills of nitrofurantoin. Please deduct previous fills in the current plan year from the maximum approval criteria.

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GUIDELINES FOR USE (CONTINUED)

3. Has the patient tried or does the patient have a contraindication to sulfamethoxazole/trimethoprim (TMP-SMX) or trimethoprim?

   If yes, **approve for 12 months with the following quantity limits:**
   FURADANTIN: approve 80mL daily (maximum dose of 400mg per day)
   MACRODANTIN: approve #4 capsules daily (maximum dose of 400mg per day)
   MACROBID: approve #2 capsules daily (maximum dose of 200mg per day)
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval for longer than 90 days requires a trial of sulfamethoxazole/trimethoprim (TMP-SMX) or trimethoprim.

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS
Nitrofurantoin is indicated for prophylaxis and treatment of urinary tract infectious disease.

REFERENCES

- American Geriatric Society (AGS) Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (2012). Available at: http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012 [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: October 23, 2012].
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].

Part D Effective: 01/01/13	Created: 10/12	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

Generic	Brand	HICL	GCN	Exception/Other
GUANFACINE HCL	TENEX		32480 32481	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Has the patient tried or does the patient have a contraindication to two of the following: benazepril, benazepril-HCTZ, captopril, captopril-HCTZ, enalapril, enalapril-HCTZ, fosinopril, fosinopril-HCTZ, lisinopril, lisinopril-HCTZ, quinapril, ramipril, moexipril, moexipril-HCTZ, perindopril erbumine, quinapril, quinapril-HCTZ, trandolapril, trandolapril/verapamil, losartan, losartan-HCTZ, irbesartan, irbesartan-HCTZ, olmesartan, olmesartan-HCTZ, olmesartan-amlodipine-HCTZ (Benicar), valsartan, valsartan-HCTZ (Diovan), diltiazem HCL, diltiazem sustained release (generics only), verapamil, verapamil sustained release (generics only), atenolol, atenolol-chlorthalidone, bisoprolol, bisoprolol-HCTZ, carvedilol, carvedilol CR (Coreg CR), metoprolol tartrate, nadolol, acebutolol, betaxolol, labetalol, metoprolol succinate, metoprolol-HCTZ, pindolol, propranolol, propranolol-HCTZ, sotalol, timolol maleate, nebivolol (Bystolic)?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: benazepril, benazepril-HCTZ, captopril, captopril-HCTZ, enalapril, enalapril-HCTZ, fosinopril, fosinopril-HCTZ, lisinopril, lisinopril-HCTZ, quinapril, ramipril, moexipril, moexipril-HCTZ, perindopril erbumine, quinapril, quinapril-HCTZ, trandolapril, trandolapril/verapamil, losartan, losartan-HCTZ, irbesartan, irbesartan-HCTZ, olmesartan, olmesartan-HCTZ, olmesartan-amlodipine-HCTZ (Benicar), valsartan, valsartan-HCTZ (Diovan), diltiazem HCL, diltiazem sustained release (generics only), verapamil, verapamil sustained release (generics only), atenolol, atenolol-chlorthalidone, bisoprolol, bisoprolol-HCTZ, carvedilol, carvedilol CR (Coreg CR), metoprolol tartrate, nadolol, acebutolol, betaxolol, labetalol, metoprolol succinate, metoprolol-HCTZ, pindolol, propranolol, propranolol-HCTZ, sotalol, timolol maleate, nebivolol (Bystolic)?

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RATIONALE

The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure, Drugs to Avoid in the Elderly, and calculates the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS

Guanfacine is approved for the treatment of hypertension.

REFERENCES

- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/ [Accessed October 23, 2012]
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed October 23, 2012].

Part D Effective: 01/01/13 Created: 10/12
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

HRM CENTRAL NERVOUS SYSTEM (PART D)

Generic	Brand	HICL	GCN	Exception/Other
THIORIDAZINE HCL	THIORIDAZINE HCL		14860 14881 14882 14883 14880	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Has the patient tried or does the patient have a contraindication to two of the following: olanzapine, quetiapine, risperidone, ziprasidone?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: olanzapine, quetiapine, risperidone, ziprasidone.

RATIONALE

The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure, Drugs to Avoid in the Elderly, and calculates the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS

Thioridazine is approved for the treatment of schizophrenia in patients who fail to respond adequately to treatment with other antipsychotics.

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REFERENCES

- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/ [Accessed October 23, 2012].
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed October 23, 2012].

Part D Effective: 04/01/13 Created: 10/12
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

HRM DIGOXIN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
DIGOXIN	DIGITEK DIGOXIN LANOXIN		120 133 132	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 12 months.**

2. Has the member tried digoxin 125mcg once daily (per MRF or claims history of 1 tablet per day)?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers use of digoxin greater that 125mcg per day to be of high risk for patients 65 years old or older. Consider a trial of digoxin 125mcg once daily.

   (**Note:** Proactive PA is not needed for digoxin 0.125mg 1 tablet per day regardless of age).

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

The inappropriate drugs in the elderly measure for digoxin includes a patient if he/she received at least two (2) prescription fills for the medication and if the average daily dose is greater than 0.125mg.

FDA APPROVED INDICATIONS
Digoxin is indicated for the treatment of atrial fibrillation and heart failure.

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HRM DIGOXIN (PART D)

REFERENCES

- American Geriatric Society (AGS) Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (2012). Available at: http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012 [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed October 23, 2012].
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].

Part D Effective: 02/07/13	Created: 04/12	
Commercial Effective: N/A	Client Approval: 01/13	P&T Approval: 11/12

HRM ENDOCRINE ESTROGEN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CONJUGATED ESTROGENS	PREMARIN		10942 10943 19975 10944 10945 10947	
CONJUGATED ESTROGENS/MEDROXY-PROGESTERONE ACETATE	PREMPRO PREMPHASE		19739 20769 55730 55731 55733	
ESTROPIPATE	ESTROPIPATE		11080 11084 11085	
ESTRADIOL	DIVIGEL		10777 26659 98558	
ESTRADIOL	ESTRADIOL ESTRACE		10770 10771 10772	
ESTRADIOL	ESTRADIOL PATCH CLIMARA		20068 20069 28844 28845 28848 28853	
ESTRADIOL	ELESTRIN		98473	
ESTRADIOL	ESTRASORB		21816	
ESTRADIOL	ESTROGEL		22606	
ESTRADIOL	EVAMIST		98723	
ESTRADIOL	ALORA MINIVELLE VIVELLE-DOT		28840 28841 28842 28843 28846	
ESTRADIOL	MENOSTAR		22759	
ESTRADIOL ACETATE	FEMTRACE		25478 25479 25481	
DROSPIRENONE/ESTRADIOL	ANGELIQ	32896		

TABLE CONTINUED ON NEXT PAGE

HRM ENDOCRINE ESTROGEN (PART D) TABLE CONTINUED

Generic	Brand	HICL	GCN	Exception/Other
ESTRADIOL/NORETH AC	COMBIPATCH MIMVEY ACTIVELLA	07310		
ESTRADIOL/NORGESTIMATE	PREFEST ORTHO-PREFEST	20778		
ESTROGENS,CONJ.,SYNTHETIC A	CENESTIN	19951		
ESTROGENS,CONJ.,SYNTHETIC B	ENJUVIA	33540		
ESTROGENS,ESTERIFIED	MENEST	01429		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Is the requested medication for the treatment of vasomotor symptoms of menopause?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried or does the patient have a contraindication to Femring?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of Femring.

4. Is the requested medication for the treatment of vulvar or vaginal atrophy?

   If yes, continue to #5.
   If no, continue to #6.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE (CONTINUED)

5. Has the patient tried or does the patient have a contraindication to two of the following: Estrace vaginal cream, Premarin vaginal cream, Vagifem, or Femring?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: Estrace vaginal cream, Premarin vaginal cream, or Femring.

6. Is the requested medication for the treatment of osteoporosis?

   If yes, continue to #7.
   If no, defer to clinical for review.

7. Has the patient tried or does the patient have a contraindication to two of the following: alendronate, ibandronate, raloxifene?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: alendronate, ibandronate, raloxifene.

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure, Drugs to Avoid in the Elderly, and calculates the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

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HRM ENDOCRINE ESTROGEN (PART D)

FDA APPROVED INDICATIONS

PREMARIN is indicated for:

- Treatment of moderate to severe vasomotor symptoms due to menopause.
- Treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical products should be considered.
- Treatment of hypoestrogenism due to hypogonadism, castration or primary ovarian failure.
- Treatment of breast cancer (palliation only) in appropriately selected women and men with metastatic disease.
- Treatment of advanced androgen-dependent carcinoma of the prostate (for palliation only).
- Prevention of postmenopausal osteoporosis. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate.

PREMPRO is indicated for:

- Treatment of moderate to severe vasomotor symptoms due to menopause.
- Treatment of moderate to severe vulvar and vaginal atrophy due to menopause.
- Prevention of postmenopausal osteoporosis.

ESTROPIPATE is indicated for:

- Treatment of moderate to severe vasomotor symptoms associated with menopause.
- Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical products should be considered.
- Treatment of hypoestrogenism due to hypogonadism, castration or primary ovarian failure.
- Prevention of postmenopausal osteoporosis. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate.

REFERENCES

- Wyeth Pharmaceuticals Inc. Premarin® (conjugated estrogen tablets) package insert. Philadelphia, PA. October 2011.
- Wyeth Pharmaceuticals Inc. Prempro® (conjugated estrogen/medroxyprogesterone acetate tablets) package insert. Philadelphia, PA. May 2011.
- Watson Laboratories, Inc. Estropipate package insert. Corona, CA. Revised April 2006.
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].

Part D Effective: 02/07/13	Created: 06/12	
Commercial Effective: N/A	Client Approval: 01/13	P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

HRM ENDOCRINE GLYBURIDE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
GLYBURIDE	DIABETA MICRONASE		5710 5711 5712	
GLYBURIDE, MICRONIZED	GLYNASE		5713 5714 5715	
GLYBURIDE/METFORMIN HCL	GLUCOVANCE		89878 89879 92889	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Has the patient tried or have a contraindication to both glipizide AND glimepiride?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of both glipizide AND glimepiride.

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure, Drugs to Avoid in the Elderly, and calculates the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS
Glyburide is indicated for adjunctive therapy in the treatment of type 2 diabetes mellitus, where hyperglycemia cannot be controlled by diet and exercise alone.

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HRM ENDOCRINE GLYBURIDE (PART D)

REFERENCES

- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed October 23, 2012].

Part D Effective: 04/01/13 Created: 10/12
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

HRM NON-BENZODIAZEPINE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ESZOPICLONE	LUNESTA	26791		
ZOLPIDEM TARTRATE	AMBIEN AMBIEN CR EDLUAR INTERMEZZO ZOLPIMIST	07842		
ZALEPLON	SONATA	20347		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 12 months.**

2. Has the patient received any HRM non-benzodiazepine (eszopiclone, zolpidem, or zaleplon) or any combination of HRM non-benzodiazepine for more than 90 consecutive days in the current plan year (January to December of the current year) per claims history?

   PAC NOTE: Review claims history for previous fills of any HRM non-benzodiazepine. Please deduct previous fills in the current plan year from the 90 day maximum approval criteria.

   If yes, continue to #3.
   If no, **approve as follows:**
   - **ZOLPIMIST: approve for up to a maximum quantity of 3 spray pump containers (#23.1ml/3 spray pump containers) (less any quantity in the current plan year) within a 12 month duration; or,**
   - **LUNESTA, AMBIEN, AMBIEN CR, EDLUAR, INTERMEZZO, and SONATA: approve for up to a maximum quantity of #90 (less any quantity in the current plan year) within a 12 month duration.**

   LUNESTA: #90 per 365 days
   AMBIEN: #90 per 365 days
   AMBIEN CR: #90 per 365 days
   EDLUAR: #90 per 365 days
   INTERMEZZO: #90 per 365 days
   ZOLPIMIST: #23.1 mLs (3 spray pumps) (package size is 7.7mL) per 365 days
   SONATA: #90 per 365 days

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GUIDELINES FOR USE (CONTINUED)

3. Has the patient tried or does the patient have a contraindication to Rozerem or Silenor?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval for longer than 90 days requires a trial of Rozerem or Silenor. Silenor has a quantity limit of 30 tablets per 30 days.

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

FDA APPROVED INDICATIONS
AMBIEN is indicated for the short-term treatment of insomnia characterized by difficulty with sleep initiation.

AMBIEN CR is indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

EDLUAR is indicated for the short-term treatment of insomnia characterized by difficulty with sleep initiation.

INTERMEZZO is indicated for the treatment of insomnia when a middle of the night awakening is followed by difficulty returning to sleep.

LUNESTA is indicated for the treatment of insomnia.

SONATA is indicated for the short-term (generally 7-10 days) treatment of insomnia.

ZOLPIMIST is indicated for the treatment of insomnia when a middle of the night awakening is followed by difficulty returning to sleep.

CONTINUED ON NEXT PAGE

REFERENCES

- American Geriatric Society (AGS) Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (2012). Available at: http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012 [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: October 23, 2012].
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].

Part D Effective: 09/01/13	Created: 10/12	
Commercial Effective: N/A	Client Approval: 08/13	P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

HRM RESERPINE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
RESERPINE	RESERPINE		1351 1354	
RESERPINE/HYDRO CHLOROTHIAZIDE	HYDROCHLOROTHIAZIDE/ RESERPINE		51842 51843	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 12 months.**

2. Has the patient tried reserpine 0.1mg once daily (per MRF or claims history of 1 per day)?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers use of reserpine greater than 0.1mg daily to be of high risk for patients 65 years old or older. Consider a trial of reserpine 0.1mg once daily.

   (**Note:** Proactive PA is not needed for reserpine 0.1mg 1 tablet per day regardless of age.)

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

The inappropriate drugs in the elderly measure for reserpine includes a patient if he/she received at least two (2) prescription fills for the medication and if the average daily dose is greater than 0.1 mg.

FDA APPROVED INDICATIONS
Reserpine is indicated for treatment of hypertension and psychotic disorder.

CONTINUED ON NEXT PAGE

REFERENCES

- American Geriatric Society (AGS) Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (2012). Available at: http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012 [Accessed: October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed: October 23, 2012].
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: October 23, 2012].
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed: October 23, 2012].

Part D Effective: 02/07/13	Created: 04/12	
Commercial Effective: N/A	Client Approval: 01/13	P&T Approval: 11/12

HRM SKELETAL MUSCLE RELAXANTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
CARISOPRODOL	SOMA		17912 98857	
CHLORZOXAZONE	PARAFON FORTE DSC, LORZONE		17901 30715 30716	
CHLORZOXAZONE W/ACETAMINOPHEN	CHLORZOXAZONE W/ACETAMINOPHEN		73610	
CYCLOBENZAPRINE HCL	CYCLOBENZAPRINE AMRIX FEXMID FLEXERIL		12805 18020 97959 97960 98299	
METAXALONE	SKELAXIN		91765	
METHOCARBAMOL	ROBAXIN ROBAXIN-750		17881 17892 17893	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

2. Has the patient tried or does the patient have a contraindication to two of the following: prescription strength NSAID (such as diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamate, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, sulindac or tolmetin), hydrocodone, codeine, tramadol, baclofen, or tizanidine?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years older or older. Approval requires a trial of two of the following: prescription strength NSAID (such as diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamate, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, sulindac or tolmetin), hydrocodone, codeine, tramadol, baclofen, or tizanidine. When using an NSAID also consider the use of a proton pump inhibitor such as omeprazole or pantoprazole.

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RATIONALE

The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications.

Ketorolac and meperidine are considered to be HRM drugs by CMS.

FDA APPROVED INDICATIONS

SOMA (CARISOPRODOL) is indicated for the relief of discomfort with acute, painful musculoskeletal conditions. (Important limitations: should only be used for acute treatment periods up to two to three weeks. Not recommended in pediatric patients less than 16 years of age).

PARAFON FORTE DSC (CHLORZOXAZONE) is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

AMRIX, FEXMID & FLEXERIL (CYCLOBENZAPRINE) is indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions. (Flexeril should only be used for short periods (up to two to three weeks) because adequate evidence of effectiveness for more prolonged use is not available and because muscle spasm associated with acute, painful musculoskeletal conditions is generally of short duration and specific therapy for longer periods is seldom warranted. Flexeril has not been found effective in the treatment of spasticity associated with cerebral or spinal cord disease, or in children with cerebral palsy.

SKELAXIN (METAXALONE) is indicated as an adjunct to rest, physical therapy, and other measures for the relief or discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Metaxalone does not directly relax tense muscles in man.

ROBAXIN (METHOCARBAMOL) is indicated as an adjunct to rest, physical therapy, and other measures for the relief or discomfort associated with acute, painful musculoskeletal conditions. The mode of action of methocarbamol has not been clearly identified, but may be related to its sedative properties. Methocarbamol does not directly relax tense muscles in man.

CONTINUED ON NEXT PAGE

HRM SKELETAL MUSCLE RELAXANTS (PART D)

REFERENCES

- Meda Pharmaceuticals. Soma® (carisoprodol) package insert. Somerset, NJ. October 2009.
- Ortho-McNeil-Janssen Pharmaceuticals, Inc. Parafon Forte® DSC (chlorzoxazone) package insert. Raritan, NJ. October 2010.
- McNeil Consumer & Specialty Pharmaceuticals. Flexeril® (cyclobenzaprine) package insert. Fort Washington, NJ. February 2005.
- King Pharmaceuticals, Inc. Skelaxin® (metaxalone) package insert. Bristol, TN. April 2008.
- Schwarz Pharma, LLC. Robaxin® (methocarbamol tablets) package insert. Smyrna, GA. September 2009.
- Teva Pharmaceuticals, USA. Baclofen package insert. Sellersville, PA. May 2010.
- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012].

Part D Effective: 04/01/13 Created: 06/12
Commercial Effective: N/A Client Approval: 02/13 P&T Approval: 02/13

HRM TRICYCLIC ANTI-DEPRESSANTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
DOXEPIN HCL	DOXEPIN HCL		16563 16564 16565 16566 16567 16568 16571	
IMIPRAMINE HCL	IMIPRAMINE HCl TOFRANIL		16541 16542 16543	
IMIPRAMINE PAMOATE	IMIPRAMINE PAMOATE TOFRANIL-PM		16548 16549 16553 16554	
TRIMIPRAMINE MALEATE	SURMONTIL, TRIMIPRAMINE MALEATE		16592 16593 16594	
PERPHENAZINE/ AMITRIPTYLINE HCL	PERPHENAZINE- AMITRIPTYLINE HCL	13819		
AMITRIPTYLINE HCL	AMITRIPTYLINE HCL		16512 16515 16516 16517 16513	
CLOMIPRAMINE HCL	ANAFRANIL, CLOMIPRAMINE HCL		16602 16603 16604	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient 65 years of age or older?

   If yes, continue to #2.
   If no, **approve for 1 year.**

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GUIDELINES FOR USE (CONTINUED)

2. Is the patient requesting this medication for migraine prophylaxis?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried or does the patient have a contraindication to two of the following: propranolol, timolol, topiramate, valproic acid, or divalproex?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: propranolol, timolol, topiramate, valproic acid, or divalproex.

4. Does the patient have a diagnosis of depression?

   If yes, continue to #5.
   If no, continue to #6.

5. Has the patient tried or have a contraindication to two of the following: paroxetine, sertraline, venlafaxine, duloxetine, citalopram, escitalopram, fluoxetine, or trazodone?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: paroxetine, sertraline, venlafaxine, duloxetine, citalopram, escitalopram, fluoxetine, or trazodone.

6. Does the patient have a diagnosis of anxiety?

   If yes, continue to #7.
   If no, continue to #8.

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GUIDELINES FOR USE (CONTINUED)

7. Has the patient tried or does the patient have a contraindication to two of the following: paroxetine, venlafaxine, duloxetine (Cymbalta), or buspirone?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: paroxetine, venlafaxine, duloxetine (Cymbalta), or buspirone.

8. Does the patient have a diagnosis of postherpetic neuralgia?

   If yes, continue to #9.
   If no, continue to #10.

9. Has the patient tried or does the patient have a contraindication to both gabapentin AND pregabalin (Lyrica)?

   If yes, **approve for 1 year.**
   If no, do not approve.
   DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of both gabapentin and pregabalin (Lyrica).

10. Does the patient have a diagnosis of schizophrenia?

    If yes, continue to #11.
    If no, do not approve.
    DENIAL TEXT: Approval requires an FDA approved diagnosis and a trial of a medication not considered to be of high risk for patients 65 years old or older.

11. Has the patient tried or does the patient have a contraindication to two of the following: olanzapine, quetiapine, risperidone, or ziprasidone?

    If yes, **approve for 1 year.**
    If no, do not approve.
    DENIAL TEXT: Centers for Medicare & Medicaid Services (CMS) considers the requested medication to be of high risk for patients 65 years old or older. Approval requires a trial of two of the following: olanzapine, quetiapine, risperidone, or ziprasidone.

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HRM TRICYCLIC ANTI-DEPRESSANTS (PART D)

RATIONALE
The drug(s) is/are listed in the high risk medications in the elderly measurement used in the CMS STAR rating determination for plans. The measure is an adaptation of the HEDIS measure Drugs to Avoid in the Elderly and calculates: the percentage of patients 65 years or older who have received at least one prescription for a high-risk drug and the percentage of Medicare patients 65 years or older who received two or more different prescriptions for high risk medications. Treatment of cough is not covered under Part D.

FDA APPROVED INDICATIONS
DOXEPIN is approved for the treatment of major depression and/or anxiety, including psychotic depressive disorders with associated anxiety.

IMIPRAMINE is approved for the treatment of major depression.

TRIMIPRAMINE is approved for the treatment of major depression.

PERPHENAZINE is approved for the treatment of schizophrenia.

AMITRIPTYLINE is approved for the treatment of major depression (including patients with schizophrenia or psychosis with depressive symptoms).

CLOMIPRAMINE is approved for treatment of obsessive-compulsive disorder (OCD) or major depression.

REFERENCES

- Pharmacy Quality Alliance (PQA) http://www.pqaalliance.org/
- National Committee for Quality Assurance. HEDIS & Quality Measurement. Available at: http://www.ncqa.org/tabid/59/Default.aspx. [Accessed October 23, 2012].
- Centers for Medicare & Medicaid Services. Part D Performance Data. Available at: http://www.cms.gov/PrescriptionDrugCovGenIn/06_PerformanceData.asp [Accessed October 23, 2012]
- Clinical Pharmacology [database online]. Tampa, FL. Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed October 23, 2012].

Part D Effective: 04/01/13	Created: 10/12	
Commercial Effective: N/A	Client Approval: 02/13	P&T Approval: 02/13

HYDROMORPHONE ER

Generic	Brand	HICL	GCN	Exception/Other
HYDROMORPHONE ER	EXALGO		22056 28427 22098 33088	EXTENDED RELEASE ONLY

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS notes for processing.

GUIDELINES FOR USE

1. Has the patient tried or does the patient have a contraindication to at least one of the following: a sustained-release morphine product (e.g. Avinza, MS Contin, Kadian or Oramorph SR)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of a generic sustained-release morphine such as MS Contin and that the requested medication is not prescribed on an "as needed" basis.

2. Does the request form indicate that this medication will be used on an "as needed" or "PRN" basis?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a trial of a generic sustained-release morphine such as MS Contin and that the requested medication is not prescribed on an "as needed" basis.

   If no, **approve for 12 months with the following quantity limits:**
   - **8mg and 12mg: #1 per day per month**
   - **16mg: #4 per day per month**
   - **32mg: #2 per day per month**

RATIONALE
To position use of Exalgo after failure of less expensive oral opioid extended-release agents.

FDA APPROVED INDICATIONS
Management of moderate to severe pain in patients requiring continuous, around-the-clock opioid analgesia for an extended period of time. Exalgo is not to be used for PRN dosing. Exalgo is not indicated for the management of acute or postoperative pain.

REFERENCES
- Neuromed Pharmaceuticals, Exalgo package insert, Conshocken, PA. August 2012.

Part D Effective: 01/01/13 Created: 04/10
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

HYDROXYPROGESTERONE CAPROATE

Generic	Brand	HICL	GCN	Exception/Other
HYDROXYPROGESTERONE CAPROATE	MAKENA		11180	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have multiple gestations (twin, triplets, etc.)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient is (1) at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation, (2) has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes, and (3) a trial of compounded hydroxyprogesterone caproate.
   If no, continue to #2.

2. Does the patient have a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is (1) at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation, (2) has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes, and (3) a trial of compounded hydroxyprogesterone caproate.

3. Has the patient tried or does the patient have a contraindication to compounded hydroxyprogesterone caproate?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient is (1) at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation, (2) has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes, and (3) a trial of compounded hydroxyprogesterone caproate.
   Enter a proactive authorization for compounded hydroxyprogesterone caproate by GCN (18172) for 20 weeks with a quantity limit of 250mg/mL per week.

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GUIDELINES FOR USE (CONTINUED)

4. Process as follows based on how many weeks pregnant the patient is:

Weeks Pregnant	Action
< 16	Do not approve. **DENIAL TEXT:** Approval requires that the patient is (1) at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation, (2) and has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes.
16	**Approve 1 vial every 5 weeks for 5 fills.**
17-21	**Approve 1 vial every 5 weeks for 4 fills.**
22-26	**Approve 1 vial every 5 weeks for 3 fills.**
27-31	**Approve 1 vial every 5 weeks for 2 fills.**
32-36	**Approve 1 vial every 5 weeks for 1 fill.**
≥ 37	Do not approve. **DENIAL TEXT:** Approval requires that the patient is (1) at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation, (2) and has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes.

RATIONALE
Ensure appropriate use of Makena consistent with its FDA approved indication.

FDA APPROVED INDICATIONS
Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth.

REFERENCES
- Ther-Rx Corporation. Makena package insert. St. Louis, MO. February 2011.

Part D Effective: 01/01/13 Created: 05/11
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

IMIQUIMOD (PART D)

Generic	Brand	HICL	GCN	Exception/Other
IMIQUIMOD 5%	ALDARA	12998		
IMIQUIMOD 2.5% or 3.75%	ZYCLARA	12998		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

For Part D this prior authorization guideline will apply to NEW STARTS ONLY and does not affect stabilized members.

GUIDELINES FOR USE

1. Does the patient have perianal warts and is 12 years of age or older?

   If yes, process as follows:
   - **Aldara (imiquimod 5%): approve for 4 months with a quantity limit of #1 box (24 packets) per month.**
   - Zyclara (imiquimod 2.5% or 3.75%): continue to #9.

   If no, continue to #2.

2. Does the patient have external genital warts and is 12 years of age or older?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried or does the patient have a contraindication to podofilox (Condylox)?

   If yes, process as follows
   - **Aldara (imiquimod 5%): approve for 4 months with a quantity limit of #1 box (24 packets) per month.**
   - Zyclara (imiquimod 2.5%): do not approve.
     DENIAL TEXT FOR ZYCLARA 2.5%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis.
   - Zyclara (imiquimod 3.75%): continue to #9.

   If no, process as follows:
   - Aldara (imiquimod 5%): do not approve.
     DENIAL TEXT FOR ALDARA: Approval requires a trial or contraindication to podofilox.
   - Zyclara (imiquimod 2.5%): do not approve.
     DENIAL TEXT FOR ZYCLARA 2.5%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis.
   - Zyclara (imiquimod 3.75%): continue to #9.

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GUIDELINES FOR USE (CONTINUED)

4. Does the patient have primary superficial basal cell carcinoma no greater than 2cm in size and not on the face or lentigo maligna?

   If yes, process as follows:
   - Aldara (imiquimod 5%): continue to #5.
   - Zyclara (imiquimod 2.5%): do not approve.
     DENIAL TEXT FOR ZYCLARA 2.5%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis.
   - Zyclara (imiquimod 3.75%): do not approve.
     DENIAL TEXT FOR ZYCLARA 3.75%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis, or 12 years of age or older with a diagnosis of external genital or perianal warts.

   If no, continue to #6.

5. Has the treatment been prescribed or is it currently being supervised by a dermatologist or oncologist?

   If yes, **approve for 4 months with the following quantity limits:**
   - **ALDARA (imiquimod 5%): Quantity limit of #1 box (24 packets) per month.**

   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist or oncologist.

6. Is the patient 18 years of age or older with a diagnosis of actinic keratosis?

   If yes, continue to #7.
   If no, continue to #10.

7. Has the treatment been prescribed or is it currently being supervised by a dermatologist?

   If yes, continue to #8.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist.

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GUIDELINES FOR USE (CONTINUED)

8. Has the patient tried or does the patient have a contraindication to topical 5-fluorouracil (5-FU)?

   If yes, process as follows:
   - **Aldara (imiquimod 5%): approve for 4 months with a quantity limit of #1 box (24 packets) per month.**
   - Zyclara (imiquimod 2.5% or 3.75%): continue to #9.

   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of or contraindication to topical 5-fluorouracil.

9. Has the patient tried or does the patient have a contraindication to generic imiquimod 5%?

   If yes, **approve for 4 months with the following quantity limits:**
   - **Aldara (imiquimod 5%): Quantity limit of #1 box (24 packets) per month.**
   - **Zyclara (imiquimod 3.75%) Cream Packet: Quantity limit of #1 box (28 packets) per month.**
   - **Zyclara (imiquimod 2.5% or 3.75%) Cream Pump: Quantity limit of up to 15g (two 7.5g pumps or one 15g pump) per month.**

   If no, do not approve. **Enter a proactive approval for generic imiquimod 5% for 4 months with a quantity limit of #1 box (24 packets) per month.**
   DENIAL TEXT: Approval requires a trial of generic imiquimod 5%. A proactive Prior Authorization has been entered.

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GUIDELINES FOR USE (CONTINUED)

10. Does the patient have a diagnosis of molluscum contagiosum of the face?

If yes, process as follows:

- **Aldara (imiquimod 5%): approve for 4 months with a quantity limit of #1 box (24 packets) per month.**
- Zyclara (imiquimod 2.5%): do not approve.
  DENIAL TEXT FOR ZYCLARA 2.5%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis.
- Zyclara (imiquimod 3.75%): do not approve.
  DENIAL TEXT FOR ZYCLARA 3.75%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis, or 12 years of age or older with a diagnosis of external genital or perianal warts.

If no, do not approve.
DENIAL TEXT FOR ALDARA: Approval requires one of the following indications:
1.) External genital or perianal warts and the patient is 12 years of age or older.
2.) Actinic keratosis in a patient who is 18 years of age or older.
3.) Primary superficial basal cell carcinoma no greater than 2 cm in size that is not located on the face.
4.) Molluscum contagiosum of the face.
DENIAL TEXT FOR ZYCLARA 2.5%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis.
DENIAL TEXT FOR ZYCLARA 3.75%: Approval requires that the patient is 18 years of age or older with a diagnosis of actinic keratosis, or 12 years of age or older with a diagnosis of external genital or perianal warts.

RATIONALE
Ensure that Aldara is used as a second-line agent in the treatment of perianal genital warts, actinic keratosis, and superficial basal cell carcinoma.

Ensure that Zyclara is used as a second-line agent for actinic keratosis.

FDA APPROVED INDICATIONS
ALDARA is indicated for treatment of external genital and perianal warts (condyloma acuminata), actinic keratosis, and superficial basal cell carcinoma in patients 12 years of age or older.

ZYCLARA is indicated for the treatment of actinic keratosis in immunocompetent adult patients. It is also indicated for the treatment of external genital and perianal warts / condyloma acuminata in patients 12 years of age or older.

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IMIQUIMOD (PART D)

REFERENCES

- 3M Health Care Limited. Aldara package insert. Loughborough, England. April, 2009.
- 3M Health Care Limited. Zyclara package insert. Loughborough, England. March, 2011.
- Al-Mutrairi N, Al-Doukhi A et al. Comparative study on the efficacy, safety and acceptability of imiquimod 5% cream versus cryotherapy for molluscum contagiosum in children. Pediatr Dermatol. 2010 Jul-Aug; 27(4): 388-94.
- Micromedex® Healthcare Series [database online].Greenwood Village, Colo: Thomson Healthcare. Available at https://www.thomsonhc.com/hcs/librarian. [Accessed: March 29, 2011].

Part D Effective: 10/01/13 Created: 08/97
Commercial Effective: N/A Client Approval: 08/13 P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

IMMUNE GLOBULIN BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
IMMUNE GLOBULIN	GAMIMUNE, OTHERS	25631, 04202		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the patient receiving IVIG at the physician's office?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months by HICL. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #2. **(CSR: If unknown, ask the caller to submit MRF.)**

2. Is the patient receiving IVIG at home for a diagnosis of primary immune deficiency disease or is patient receiving IVIG at home and patient has ICD-9 diagnosis code of 279.04, 279.05, 279.06, 279.12, or 279.2?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months by HICL. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, continue to #3. **(CSR: If unknown, ask the caller to submit MRF.)**

3. **Approve as requested under Part D for up to 12 months by HICL. (Populate B vs. D field with "D" in the PA override field.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

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IMMUNE GLOBULIN BVD DETERMINATION (PART D)

RATIONALE

IVIG for use in physician's office or for use at home for patients with a diagnosis of primary immune deficiency disease, is covered via Part B. Intravenous immune globulin (IVIG) for the treatment of primary immune deficiency diseases in the home include ICD-9 diagnosis codes 279.04, 279.05, 279.12, and 279.2. Ensure use consistent with indications.

FDA APPROVED INDICATIONS

Immunodeficiency syndrome, ITP, CLL, Kawasaki Disease, Bone Marrow Transplants, Pediatric HIV.

REFERENCES

- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].
- Medicare Benefit Policy Manual Chapter 15 – Covered Medical and Other Health Services, Section 50.6. Rev 170, 05-10-13). http://www.cms.gov/

Part D Effective: 11/01/13	Created: 09/05	
Commercial Effective: N/A	Client Approval: 09/13	P&T Approval: 11/12

IMMUNOSUPPRESSANT BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
AZATHIOPRINE	AZASAN IMURAN			TCC = Z2E
BELATACEPT	NULOJIX			
CYCLOSPORINE	SANDIMMUNE			
CYCLOSPORINE, MODIFIED	GENGRAF NEORAL			
EVEROLIMUS	ZORTRESS			
MUROMONAB-CD3	ORTHOCLONE OKT-3			
MYCOPHENOLATE MOFETIL	CELLCEPT			
MYCOPHENOLATE SODIUM	MYFORTIC			
SIROLIMUS	RAPAMUNE			
TACROLIMUS	PROGRAF			
BASILIXIMAB	SIMULECT			TCC = Z2M
DACLIZUMAB	ZENAPAX			

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the request for an organ transplant?

   If yes, continue to #2.
   If no, continue to #3.

2. Was the organ transplant Medicare-approved?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #3. **(CSR: If unknown, ask the caller to submit MRF.)**

3. **Lifetime approval under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

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IMMUNOSUPPRESSANT BVD DETERMINATION (PART D)

RATIONALE

Immunosuppressant therapy is covered under Part B for patients who received a Medicare covered organ transplant.

REFERENCES

- Medicare Part B versus Part D Coverage Issues.

Part D Effective: 01/01/13 Created: 09/05
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

INFLIXIMAB (PART D)

Generic	Brand	HICL	GCN	Exception/Other
INFLIXIMAB	REMICADE	18747		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Is the patient being treated for moderate to severe Crohn's disease, ulcerative colitis or acute enterocutaneous fistula?

   If yes, continue to #2.
   If no, continue to #4.

2. Is therapy being initiated or recommended by a gastroenterologist?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe Crohn's disease, ulcerative colitis or acute enterocutaneous fistula, initiation or recommendation of therapy by a gastroenterologist and a trial of or a contraindication to one or more of the following preferred therapy agents: sulfasalazine, corticosteroids, methotrexate, azathioprine, olsalazine, Asacol, Pentasa, cyclosporine, or mercaptopurine.

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INITIAL CRITERIA (CONTINUED)

3. Has the patient tried or does the patient have a contraindication to one or more of the following preferred therapy agents: sulfasalazine, corticosteroids, methotrexate, azathioprine, olsalazine, Asacol, Pentasa, cyclosporine, or mercaptopurine?

   If yes, approve as follows:
   - Crohn's disease or acute enterocutaneous fistula: **enter two authorizations with a time frame of 4 months each as follows:**
     - **Approve one fill of #15 vials (100mg/20mL) with a duration of 6 weeks.**
     - **Approve one fill of #5 vials (100mg/20mL) with a duration of 8 weeks.**

     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   - Ulcerative colitis: **enter two authorizations as follows:**
     - **Approve one fill of #15 vials (100mg/20mL) with a duration of 6 weeks**
     - **Approve six fills of #5 vials (100mg/20mL) with a duration of 8 weeks with a time frame of 12 months.**

     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe Crohn's disease, ulcerative colitis or acute enterocutaneous fistula; initiation or recommendation of therapy by a gastroenterologist and a trial of or a contraindication to one or more of the following preferred therapy agents: sulfasalazine, corticosteroids, methotrexate, azathioprine, olsalazine, Asacol, Pentasa, cyclosporine, or mercaptopurine.

4. Is the patient diagnosed with moderate to severe rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis?

   If yes, continue to #5.
   If no, continue to #9.

CONTINUED ON NEXT PAGE

INITIAL CRITERIA (CONTINUED)

5. Is therapy being initiated or recommended by a rheumatologist?

   If yes, process as follows:
   - For psoriatic arthritis, continue to #6.
   - For rheumatoid arthritis, continue to #6.
   - For ankylosing spondylitis: **Enter two authorizations with a time frame of 4 months each as follows:**
     - **Approve one fill of #15 vials (100mg/20mL) with a duration of 6 weeks.**
     - **Approve one fill of #5 vials (100mg/20mL) with a duration of 6 weeks.**

     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis and initiation or recommendation of therapy by a rheumatologist.

6. Has the patient tried or does the patient have a contraindication to at least one of the following DMARD (disease-modifying antirheumatic drug) agents: methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine?

   If yes, process as follows:
   - For psoriatic arthritis, continue to #7.
   - For rheumatoid arthritis, continue to #8.

   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or recommendation of therapy by a rheumatologist, a diagnosis of psoriatic arthritis or rheumatoid arthritis, a trial of or a contraindication to one of the following DMARD (disease-modifying antirheumatic drug) agents such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.

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INITIAL CRITERIA (CONTINUED)

7. Has the patient tried Humira (adalimumab)?

   If yes, for psoriatic arthritis: **Enter two authorizations with a time frame of 4 months each as follows:**
   - **Approve one fill of #15 vials (100mg/20mL) with a duration of 6 weeks.**
   - **Approve one fill of #5 vials (100mg/20mL) with a duration of 8 weeks.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve. (Ask the caller to submit a MRF for Humira).
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a diagnosis of psoriatic arthritis; and a trial of a preferred formulary tumor necrosis factors Humira (adalimumab); which may also require prior authorization.

8. Has the patient tried Humira (adalimumab) or Cimzia (certolizumab pegol)?

   If yes, for rheumatoid arthritis: **Enter two authorizations with a time frame of 4 months each as follows:**
   - **Approve one fill of #9 vials (100mg/20mL) with a duration of 6 weeks.**
   - **Approve one fill of #3 vials (100mg/20mL) with a duration of 8 weeks.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve. (Ask the caller to submit a MRF for Humira or Cimzia).
   DENIAL TEXT: Approval requires supervision by a rheumatologist; a diagnosis of moderate to severe rheumatoid arthritis; and a trial of a preferred formulary tumor necrosis factor Humira (adalimumab) or Cimzia (certolizumab pegol); which may also require prior authorization.

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INITIAL CRITERIA (CONTINUED)

9. Does the patient have chronic severe plaque psoriasis of involving greater than or equal to 10% body surface area (BSA)?

   If yes, continue to #10.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of psoriasis with psoriatic arthritis or psoriatic lesions that affect the hands, feet, or genital area impacting quality of life; moderate to severe Crohn's disease; ulcerative colitis; acute enterocutaneous fistula; moderate to severe rheumatoid arthritis; psoriatic arthritis; or ankylosing spondylitis. Additional disease specific criteria also apply.

10. Does the patient have psoriatic lesions that affect the hands, feet, or genital area impacting quality of life?

    If yes, continue to #11.
    If no, do not approve.
    DENIAL TEXT: Approval requires initiation or recommendation of therapy by a dermatologist, a diagnosis of chronic severe plaque psoriasis involving greater than or equal to 10% body surface area (BSA) or psoriatic lesions that affect the hands, feet, or genital area impacting quality of life and trial of or a contraindication to one or more forms of preferred therapy such as PUVA, UVB, acitretin, methotrexate, or cyclosporine.

11. Has the treatment been prescribed or is it currently being supervised by a dermatologist?

    If yes, continue to #12.
    If no, do not approve.
    DENIAL TEXT: Approval requires initiation or recommendation of therapy by a dermatologist, a diagnosis of chronic severe plaque psoriasis involving greater than or equal to 10% body surface area (BSA) or psoriatic lesions that affect the hands, feet, or genital area impacting quality of life and trial of or a contraindication to one or more forms of preferred therapy such as PUVA, UVB, acitretin, methotrexate, or cyclosporine.

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INFLIXIMAB (PART D)

INITIAL CRITERIA (CONTINUED)

12. Has the patient tried or does the patient have a contraindication to one or more forms of preferred therapy (PUVA, UVB, acitretin, methotrexate, or cyclosporine)?

    If yes, for chronic severe plaque psoriasis: **Enter two authorizations with a time frame of 4 months each as follows:**
    - **Approve one fill of #15 vials (100mg/20mL) with a duration of 6 weeks.**
    - **Approve one fill of #5 vials (100mg/20mL) with a duration of 8 weeks.**

    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, do not approve.
    DENIAL TEXT: Approval requires initiation or recommendation of therapy by a dermatologist, a diagnosis of chronic severe plaque psoriasis of involving greater than or equal to 10% body surface area (BSA) or psoriatic lesions that affect the hands, feet, or genital area impacting quality of life and trial of or a contraindication to one or more forms of preferred therapy such as PUVA, UVB, acitretin, methotrexate, or cyclosporine.

RENEWAL CRITERIA

1. Is the patient being treated for moderate to severe Crohn's disease, ulcerative colitis or acute enterocutaneous fistula?

    If yes, **approve for a time frame of 12 months as follows:**
    - For Crohn's disease or acute enterocutaneous fistula: **Approve six fills of up to #10 vials (100mg/20mL) with a duration of 8 weeks each.**
      APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
    - For ulcerative colitis: **Approve six fills of for #5 vials (100mg/20mL) with a duration of 8 weeks each.**
      APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

    If no, continue to #2.

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RENEWAL CRITERIA (CONTINUED)

2. Does the patient have rheumatoid or psoriatic arthritis?

   If yes, continue to #3.
   If no, continue to #6.

3. Has patient experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of rheumatoid or psoriatic arthritis and patient to have experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count while on therapy.

4. Does the patient have psoriatic arthritis?

   If yes, for psoriatic arthritis: **Approve for a time frame of 12 months for six fills of #5 vials (100mg/20mL) with a duration of 8 weeks each.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #5.

5. Does the patient have rheumatoid arthritis?

   If yes, **approve for a time frame of 12 months for twelve fills of up to #10 vials (100mg/20mL) with a duration of 4 weeks each.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of rheumatoid or psoriatic arthritis and patient has experienced or maintained a 20% or greater improvement in tender joint count and swollen joint count while on therapy.

6. Does the patient have plaque psoriasis?

   If yes, continue to #7.
   If no, continue to #8.

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RENEWAL CRITERIA (CONTINUED)

7. Did the patient experience or maintain a Psoriasis Area and Severity Index (PASI-50: improvement greater than 50% in PASI score) or a significant improvement in Quality of Life observed by the physician and patient (i.e. Dermatology Life Quality Index)?

   If yes, for plaque psoriasis: **Approve for a time frame of 12 months for six fills of #5 vials (100mg/20mL) with a duration of 8 weeks each.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of plaque psoriasis and patient to have experienced a PASI-50 or a significant improvement in Dermatology Quality of Life measure while on therapy.

8. Does the patient have ankylosing spondylitis?

   If yes, continue to #9.
   If no, do not approve. Renewal criteria do not apply, refer to initial criteria.

9. Has the patient experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)?

   If yes, for ankylosing spondylitis: **Approve for a time frame of 12 months for eight fills of #5 vials (100mg/20mL) with a duration of 6 weeks each.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of ankylosing spondylitis and that the patient has experienced at least 50% or 2 unit improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy.

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INFLIXIMAB (PART D)

RATIONALE

To ensure the appropriate usage of infliximab according to diagnosis.

Infliximab is dosed by weight. The approval quantities are based on a patient with a weight of 100kg, which is approximately the 80th percentile for males in the US as of 2006.

CROHN'S DISEASE: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks. Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response.
ULCERATIVE COLITIS: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.
RHEUMATOID ARTHRITIS: In conjunction with methotrexate, 3 mg/kg at 0, 2 and 6 weeks, then every 8 weeks. Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks.
ANKYLOSING SPONDYLITIS: 5 mg/kg at 0, 2 and 6 weeks, then every 6 weeks.
PSORIATIC ARTHRITIS: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.
PLAQUE PSORIASIS: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.

FDA APPROVED INDICATIONS

Infliximab is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. It is also indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.

Infliximab is indicated for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

Infliximab, in combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis.

Infliximab is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

Infliximab is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.

Infliximab is indicated for the treatment of adult patients with chronic severe (i.e., extensive and /or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. It should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

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FDA APPROVED INDICATIONS (CONTINUED)

Black box warning: Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens. Infliximab should be discontinued if a patient develops a serious infection or sepsis during treatment. Perform test for latent TB; if positive, start treatment for TB prior to starting infliximab. Monitor all patients for active TB during treatment, even if initial latent TB test is negative. Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers. Post marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers. All cases reported in patients with Crohn's disease and ulcerative colitis, the majority of whom were adolescent or young adult males. This rare, aggressive T-cell lymphoma is fatal. All of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with infliximab at or prior to diagnosis.

REFERENCES

- Braun J, Davis J et al. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with ankylosing spondylitis. Ann Rheum Dis. 2006; 65(3):316-20.
- Centocor, Inc. Remicade package insert. Malvern, PA. April 2010.
- Machado NO, Chopra PJ, al Hamdani A. Crohn's disease of the appendix with enterocutaneous fistula post-appendectomy: An approach to management. North Am J Med Sci 2010; 2: 158-161.
- McDowell MA, Fryar CD et al. National Health Statistics Reports: Anthropometric Reference Data for Children and Adults: United States, 2003–2006. October 22, 2008. Available at: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf. [Accessed July 13, 2010].
- Smith CH, Anstey AV, et al. British association of dermatologist's guidelines for use of biological interventions in psoriasis 2005. Br J Dermatol 2005; 153:486-497.

Part D Effective: 01/01/13	Created: 02/03	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

INFUSIBLE DRUG BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
INFUSIBLE DRUGS	VARIOUS			ROUTE = INTRAVENOUS, INTRAMUSCULAR, INJECTION TCC ≠ P5A,P5B,P5C, Z2E, Z2M STC ≠ 0181, C318, 0330, 0180 HICL ≠ 33411, 24899, 37462, 04867, 36477, 21869, 36687, 18568, 00177, 02100, 00170, 02830, 22890, 04553, 00999, 00585, 01104, 20533, 18277, 00859, 34794, 06250, 18250, 04042, 07782, 34417, 21300, 34649, 25631, 04202, 15707, 24035, 21367, 04528, 18747, 37503, 26750, 36708, 04199, 16638, 35580, 36898, 02824, 04218, 36466, 16848, 37256, 01560, 01905, 01418, 01420, 01643, 01641, 01627, 01403, 01400, 01401, 40046 GCN ≠ 28257, 26431, 20569, 25681, 25691, 25697, 46952, 46953, 17635, 29477, 26368, 11830, 11852, 11854, 11857, 26886, 26151, 26877, 28273, 70151, 30918, 38750, 24231, 11180, 17881, 13881, 13882, 14981, 14983, 14990, 17610, 27379, 41751, 17724, 34983

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

NOTE: This PA guideline refers to injectable chemotherapeutic agents furnished and administered incident to a physician's medical service and other injectable drugs generally administered via a pump device.

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PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

INFUSIBLE DRUG BVD DETERMINATION (PART D)

GUIDELINES FOR USE

1. Is the drug administered via an implantable pump?

   If yes, continue to #3.
   If no, continue to #2.

2. Is the drug administered using an external pump?

   If yes, continue to #3.
   If no, continue to #4.

3. Is the drug specifically covered under the local coverage policy of the applicable Medicare DMERC? **(CSR: If Pharmacy/MD does not have information on the phone call, ask MD to submit a MRF.)**

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #4.

4. Is the drug on the formulary?

   If yes, **approve for up to 12 months under Part D**. **(Populate B vs. D field with "D" in the PA override field.)**
   If no, review using Standard Part D formulary exception process. **(CSR: Populate B vs. D field with "D" if approvable. If unknown, ask MD to submit a MRF.)**

RATIONALE

Infusible drugs furnished and administered at a provider's office are covered under Part B. Drugs administered via IV drip or push injection in the home or Long Term Care facility are covered under Part D. Drugs administered by an implantable pump are covered under Part B. Drugs administered via an external pump are covered under Part B if they are included under the local coverage policy of the applicable Medicare DMERC. Drugs administered via an external pump that are not included under the local coverage policy of the applicable Medicare DMERC are covered under Part D. A CMS website to assist with Local Coverage Determination for BvD review. is http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx

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INFUSIBLE DRUG BVD DETERMINATION (PART D)

REFERENCES

- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 10/01/13 Created: 08/05
Commercial Effective: N/A Client Approval: 08/13 P&T Approval: 11/12

INTERFERON AGENTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
INTERFERON ALFACON-1	INFERGEN	15707		
PEG-INTERFERON ALFA-2A	PEGASYS PEGASYS PROCLICK	24035		
PEG-INTERFERON ALFA-2B	PEGINTRON PEGINTRON REDIPEN	21367		GCN ≠ 29809, 29811, 29812
INTERFERON ALFA-2B	INTRON A	04528		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the request for continuation of current therapy (also consider continuation if member has a claim for the currently requested interferon in past 120 days) or a renewal?

   If yes, continue to #18.
   If no, continue to #2.

2. Is the request for Intron A?

   If yes, continue to #3.
   If no, continue to #4.

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GUIDELINES FOR USE (CONTINUED)

3. Is the patient being treated for one of the following?

    a. hairy cell leukemia, or
    b. condylomata acuminate, or
    c. AIDS-related Kaposi's sarcoma, or
    d. Chronic hepatitis B, or
    e. Non-Hodgkin's lymphoma, or
    f. Malignant melanoma, or
    g. Chronic phase, Philadelphia chromosome (Ph) positive chronic myelogenous leukemia (CML) patients who are minimally treated (within 1 year of diagnosis), or
    h. Follicular lymphoma, or
    i. Angioblastoma, or
    j. Carcinoid tumor, or
    k. Chronic myeloid leukemia, or
    l. Laryngeal papillomatosis, or
    m. Multiple myeloma, or
    n. Neoplasm of conjunctiva-neoplasm of cornea, or
    o. Ovarian cancer, or
    p. Polycythemia vera, or
    q. Renal cell carcinoma, or
    r. Skin cancer, or
    s. Thrombocytosis, or
    t. Vulvar vestibulitis

    If yes, continue to #17.
    If no, continue to #11.

4. Is the request for PegIntron or PegIntron Redipen?

    If yes, continue to #10.
    If no, continue to #5.

5. Is the request for Pegasys vial, kit or syringes AND is the patient 5 years of age or older?

    If yes, continue to #6.
    If no, continue to #7.

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GUIDELINES FOR USE (CONTINUED)

6. Is the patient being treated for chronic hepatitis B and currently supervised by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist)?

   If yes, continue to #17.
   If no, continue to #8.

7. Is the request for Infergen AND the patient is 18 years of age or older?

   If yes, continue #9.
   If no, do not approve.
   DENIAL TEXT: Approval requires age of 18 years or older.

8. Has the patient had a trial of peginterferon alfa-2b (PegIntron), or does the patient have a contraindication to peginterferon alfa-2b (PegIntron)?

   If yes, continue to #11.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of, or a contraindication to peginterferon alfa-2b which may also require a prior authorization.

9. Has the patient had a trial of Pegasys or PegIntron, or does the patient have a contraindication to peginterferon alfa-2 products?

   If yes, continue to #11.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of, or a contraindication to peginterferon alfa-2b which may also require a prior authorization.

10. Is the patient 3 years of age or older?

    If yes, continue to #11.
    If no, do not approve.
    DENIAL TEXT: Approval requires an age of 3 years or older.

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GUIDELINES FOR USE (CONTINUED)

11. Is the patient being treated for chronic hepatitis C and currently supervised by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist)?

    If yes, continue to #12.
    If no, do not approve.
    DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C and therapy is being supervised by a gastroenterologist, infectious disease specialist or a physician specializing in the treatment of hepatitis (e.g. hepatologist).

12. Is the request being used with ribavirin or does the patient have a contraindication to ribavirin?

    If yes, continue to #13.
    If no, do not approve.
    DENIAL TEXT: Approval requires combination therapy with ribavirin.

13. Does the patient have a detectable pretreatment HCV RNA level/viral load of ≥ 50 IU/mL?

    If yes, continue to #14.
    If no, do not approve.
    DENIAL TEXT: Approval requires a detectable pretreatment HCV RNA level/viral load of greater than or equal to 50 IU/mL.

14. Is the patient infected with genotype 1, 4, 5, or 6 hepatitis C?

    If yes, continue to #16.
    If no, continue to #15.

15. Is the patient infected with genotype 2 or 3 hepatitis C?

    If yes, continue to #17.
    If no, do not approve.
    DENIAL TEXT: Approval requires a diagnosis of hepatitis C with genotype 1, 2, 3, 4, 5, or 6.

16. **Approve for 16 weeks (4 months). (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**
    APPROVAL TEXT: Approval requires obtaining HCV RNA level at 12 weeks of treatment to determine if the patient has achieved at least a 2 log reduction (100 fold decrease) in HCV RNA.

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GUIDELINES FOR USE (CONTINUED)

17. **Approve for 24 weeks (6 months). (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**

18. Is the request for Intron A?

    If yes, continue to #27.
    If no, continue to #19.

19. Is the request for Pegasys?

    If yes, continue to #20.
    If no, continue to #21.

20. Is the request for continuing treatment of chronic hepatitis B?

    If yes, continue to #27.
    If no, continue to #21.

21. Is the request for combination therapy with ribavirin and an interferon, or does the patient have a contraindication to combination therapy with ribavirin?

    If yes, continue to #22.
    If no, do not approve.
    DENIAL TEXT: Renewal requires combination therapy with ribavirin.

22. Is the patient infected with genotype 1, 4, 5, or 6 hepatitis C?

    If yes, continue to #23.
    If no, do not approve.
    DENIAL TEXT: Renewal requires a diagnosis of hepatitis C with genotype 1, 4, 5, or 6.

23. Has the patient already received 24 weeks of treatment for hepatitis C?

    If yes, continue to #26.
    If no, continue to #24.

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GUIDELINES FOR USE (CONTINUED)

24. Did the patient achieve at least a 2 log reduction (100 fold decrease) in quantitative HCV RNA by week 12?

    If yes, continue to #25.
    If no, do not approve.
    DENIAL TEXT: Renewal requires at least a 2 log reduction (100 fold decrease) in quantitative HCV RNA by week 12.

25. Is the patient HCV RNA detectable (> 50 IU/mL) at 12 weeks?

    If yes, **approve for 8 weeks. (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**
    APPROVAL TEXT: Renewal requires re-testing at 24 weeks to determine if the patient will become HCV RNA negative by week 24 and if therapy will be continued
    If no, **approve 32 weeks for a total of 48 weeks treatment. (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**

26. Is the patient HCV RNA undetectable (< 50 IU/mL) at 24 weeks?

    If yes, **approve 48 weeks for a total of 72 weeks treatment. (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**
    If no, do not approve.
    DENIAL TEXT: Renewal criteria require HCV RNA to be undetectable (less than 50 IU/mL) after 24 weeks of treatment.

27. **Approve for 24 weeks (6 months). (Note: Approve by HICL for all requests except PegIntron and PegIntron Redipen which should be approved by GPID.)**

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INTERFERON AGENTS (PART D)

RATIONALE

Ensure that ribavirin and interferon are used for combination treatment of chronic hepatitis C. U.S. Clinical guidelines recommend combination the current standard of care therapy with a peginterferon alfa-2 agent and ribavirin. The 16 week initial approval for hepatitis C allow a sufficient length of time for the 12-week HCV RNA result (EVR) to be reported and evaluated by the physician. If the patient did not achieve undetectable viral load at 12 weeks then a total of 72 weeks may be considered if the 24-week HCV RNA is undetectable. Total therapy time for HCV genotypes 1, 4, 5 and 6 is 48 weeks, and for HCV genotypes 2 and 3 is 16 to 24 weeks.

FDA APPROVED INDICATIONS

INTRON A (Inteferon alfa-2b) is indicated for treatment of hairy cell leukemia, condylomata acuminata, AIDS-related Kaposi's sarcoma, hepatitis C (in combination), malignant melanoma, follicular lymphoma and chronic hepatitis B.

PEGASYS (peg-interferon alfa-2a) alone or in combination with COPEGUS (ribavirin) is indicated for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon or peginterferon alfa.

PEGASYS is also indicated for treatment of adults with chronic hepatitis C virus infection in patients with HIV/HCV co-infection.

PEGASYS is also indicated for treatment of adults with HBeAg positive and negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and inflammation.

PEGINTRON (peg-interferon alfa-2b) is indicated for use alone for the treatment of chronic hepatitis C in adults at least 18 years of age with compensated liver disease who have and those who have not been previously treated with interferon alfa.

PEG-INTRON (peg-interferon alfa-2b) in combination with REBETOL (ribavirin) is indicated for use in the treatment of chronic hepatitis C in adults and children at least 3 years of age with compensated liver disease.

INFERGEN is indicated for the treatment of chronic HCV infection in patients 18 years of age or older with compensated liver disease (retreatment).

REFERENCES

- Anon. National Institutes of Health Consensus Development Conference Statement. Management of Hepatitis C: 2002 [online]. Available at: <http://consensus.nih.gov/2002/2002HepatitisC2002116html.htm> [Accessed June 30, 2010].

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REFERENCES (CONTINUED)

- Bacon B, Shiffman M, Mendes F, et al. Retreating Chronic Hepatitis C with Daily Interferon alfacon-1/ribavirin after non-response to pegylated interferon/ribavirin: DIRECT Results. Hepatology 2009; 49:1838-1846.
- Ghany et al. AASLD Practice Guidelines. Diagnosis, Management, and Treatment of Hepatitis C. Hepatology 2009, 49(4) 1335-74.
- Fried MW et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. NEJM 2002, 347(13):975-82.
- Management and Treatment of Hepatitis C Virus Infection in HIV-Infected Adults: Recommendations from the Veterans Affairs Hepatitis C Resource Center Program and National Hepatitis C Program Office [online]. September 1, 2005. Available at: <http://hepatitis.va.gov/vahep?page=prtop04-00-rr> [Accessed June 30, 2010] and Am J Gastroenterol 2006; 101:2360-78.
- Merck/Schering Corporation. Intron A Product Information. Whitehouse Station, NJ. January 2011.
- Merck/Schering Corporation. PegIntron Product Information. Whitehouse Station, NJ. Available at, <http://www.spfiles.com/pipeg-intron.pdf> [Accessed January 2011].
- Roche Pharmaceuticals. Pegasys Product Information. Nutley, NJ. January 2011.
- Shiffman ML. Management of Patients with Chronic Hepatitis C Virus Infection and Previous Nonresponse. Rev Gastroenterol Disord 2004; 4(suppl1):S22-30.
- Shiffman M et al. 2006. Peginterferon alfa-2a (PEGASYS) plus ribavirin (COPEGUS) for 16 or 24 weeks in patients with HCV genotype 2 or 3 [abstract]. In: 41st Annual Meeting of The European Association for the Study of the Liver; 2006 April 26-30; Vienna, Austria.
- Three Rivers Pharmaceuticals. Infergen [Package Insert]. Warrendale, Pennsylvania. Available at <http://infergen.com/hc_prescribing.php > [Accessed January 2011].
- HCV Treatment Algorithm [online]. Available at <http://clinicaloptions.com/Hepatitis> [Accessed June 30, 2010].
- M H Nguyen and E B Keefe. Prevalence and Treatment of Hepatitis C virus Genotype 4, 5, and 6. Clinical Gastroenterology and Hepatology 3: Suppl 2:97-101. October 2005.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: January 12, 2011].
- D'heygere F, George C, Nevens F, et al. Patients infected with HCV-5 present the same response rate as patients infected with HCV-1: results from the Belgian Randomized Trial for Naïve and Relapsers (BERNAR-1). Program and Abstracts of the 40th Annual Meeting of the European Association for the Study of the Liver. Abstract 558.

Part D Effective: 01/01/13	Created: 12/09	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

IPILIMUMAB

Generic	Brand	HICL	GCN	Exception/Other
IPILIMUMAB	YERVOY	37503		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic melanoma?

   If yes, **enter two authorizations by GPID for 4 fills each as follows:**

   For Commercial members:
   - **Approve for 12 weeks for Yervoy 50mg vial, #2 vials every 3 weeks**
   - **Approve for 12 weeks for Yervoy 200mg vial, #1 vial every 3 weeks**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   For Part D members:
   - **Approve for 12 weeks for Yervoy 50mg vial, #3 vials every 3 weeks**
   - **Approve for 12 weeks for Yervoy 200mg vial, #2 vials every 3 weeks**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval criteria require a diagnosis of unresectable or metastatic melanoma.

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IPILIMUMAB

RATIONALE

To ensure appropriate utilization of ipilimumab consistent with its FDA approved indication. Ipilimumab is dosed by weight; 3mg/kg every 3 weeks for a total of 4 doses. This guideline approves ipilimumab dosing appropriate for patients weighing up to 100kg. For patients weighing over 100kg a clinical determination must be made. NCCN recommends ipilimumab as a systemic therapy option for advanced or metastatic melanoma.

Ipilimumab was approved based on the results of a trial involving patients who failed previous chemotherapy receiving ipilimumab 3mg/kg. A later trial dosed ipilimumab at 10mg/kg in combination with dacarbazine for treatment naïve patients. The FDA labeling has not been updated to reflect this alternative dosing regimen.

FDA APPROVED INDICATIONS

Ipilimumab is indicated for the treatment of unresectable or metastatic melanoma.

REFERENCES

- Bristol-Myers Squibb Company.Yervoy package insert. Princeton, NJ. March 2011.
- Hodi FS, O'Day SJ, McDermott DF et al. Improved Survival with Ipilimumab in Patients with Metastatic Melanoma. N Engl J Med 2010; 363:711-23.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Melanoma. (Version 4.2011).
- Robert C, Thomas L, Bondarenko I, et al. Ipilimumab plus Dacarbazine for Previously Untreated Metastatic Melanoma. N Engl J Med, 2011; 364.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 22, 2011].

Part D Effective: 10/01/13	Created: 04/11	
Commercial Effective: 10/01/13	Client Approval: 08/13	P&T Approval: 11/12

IVACAFTOR

Generic	Brand	HICL	GCN	Exception/Other
IVACAFTOR	KALYDECO	38461		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cystic fibrosis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cystic fibrosis, patient age of at least 6 years, and the presence of a *G551D* mutation.

2. Is the patient at least 6 years old?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cystic fibrosis, patient age of at least 6 years, and the presence of a *G551D* mutation.

3. Does the patient have a *G551D* mutation?

   If yes, **approve for 12 months with a quantity limit of #2 tablets per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cystic fibrosis, patient age of at least 6 years, and the presence of a *G551D* mutation.

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IVACAFTOR

RATIONALE

Promote appropriate utilization of Kalydeco based on FDA approved indication.

CF is an inherited chronic disease that affects about 30,000 patients in the US. A defective cystic fibrosis transmembrane conductance regulator (*CFTR*) protein leads to production of unusually thick, sticky mucus that clogs the lungs and prevents the body from breaking down and absorbing food. Ivacaftor increases chloride transport by potentiating the channel open probability of *G551D-CFTR* protein resulting in more fluid mucus. About 4-5% of CF patients have a *G551*D mutation. There is no cure for this disease however current treatments that offer symptomatic relief include the single source brands: Cayston, Pulmozyme, and Tobi.

Two double-blind trials randomized clinically stable patients with CF who have a *G551D* mutation to ivacaftor 150mg twice daily (n=109) or placebo (n=104) for 48 weeks. Patients could receive other CF treatments. Trial 1 involved patients 12 years of age and older while trial 2 involved patients who were 6 to 11 years of age. In both trials change from baseline in percent predicted pre-dose FEV1 through 24 weeks of treatment significantly increased: 10.6% in trial 1 and 12.5% in trial 2.

Common adverse reactions include headache, oropharyngeal pain, upper respiratory tract infection, nasal congestion, abdominal pain, nasopharyngitis, diarrhea, rash, nausea, and dizziness. Transaminases (ALT and AST) should be assessed prior to initiation of therapy, every 3 month during first year of treatment and annually thereafter.

Dosage: One 150mg tablet every 12 hours with fat-containing food. Reduce dose to 150mg twice weekly when co-administered with strong CYP3A inhibitors ad reduce dose to 150mg once daily when co-administered with moderate CYP3A inhibitors. Avoid food containing grapefruit or Seville oranges.

FDA APPROVED INDICATION

Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the *CFTR* gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *G551D* mutation.

Limitations of Use:

Not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene. Kalydeco has not been studied in other populations of patients with CF.

REFERENCES

- Vertex Pharmaceuticals Incorporated. Kalydeco package insert. Cambridge, MA. January 2012.

Part D Effective: 01/01/13	Created: 02/12	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

LOMITAPIDE

Generic	Brand	HICL	GCN	Exception/Other
LOMITAPIDE	JUXTAPID	39883		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of homozygous familial hypercholesterolemia (HoFH)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of homozygous familial hypercholesterolemia (HoFH) and that Juxtapid is being used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], or fenofibrate, niacin, etc.).

2. Will Juxtapid be used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], or fenofibrate, niacin, etc.)?
   If yes, **approve for 12 months by GPID as follows:**
   - **5mg capsule: #1 capsule per day**
   - **10mg capsule: #1 capsule per day**
   - **20mg capsule: #3 capsules per day**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of homozygous familial hypercholesterolemia (HoFH) and that Juxtapid is being used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], or fenofibrate, niacin, etc.).

RATIONALE
To ensure appropriate use of Juxtapid based on FDA approved indication.

Juxtapid should be taken once daily, whole with water and without food, at least 2 hours after evening meal.

Before starting treatment with Juxtapid (lomitapide): 1) measure ALT, AST alkaline phosphatase, and total bilirubin, 2) obtain a negative pregnancy test in females of reproductive potential, 3) initiate a low-fat diet supplying <20% of energy from fat.

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LOMITAPIDE

RATIONALE (CONTINUED)
The recommended dose titration schedule is detailed below:

Dosage	Duration of Administration Before Increase to Next Dosage
5 mg daily	At least 2 weeks
10 mg daily	At least 4 weeks
20 mg daily	At least 4 weeks
40 mg daily	At least 4 weeks
60 mg daily	Maximum recommended dosage

Dose modifications are recommended with cytochrome P450 3A4 inhibitors, elevated transaminases, and in patients with renal and hepatic impairment.

Juxtapid (lomitapide) is an orally administered first-in-class small-molecule inhibitor of microsomal triglyceride transfer protein (MTP), an intracellular enzyme critical to the assembly of apolipoprotein B (apoB)-containing lipoproteins in enterocytes and hepatocytes. Inhibition of MTP prevents the synthesis of chylomicrons and very-low-density lipoprotein (VLDL), which are precursors to the atherogenic low-density lipoprotein (LDL) particle. HoFH is a serious, rare genetic disease that impairs the function of the receptor responsible for removing LDL-C from the body. A loss of LDL receptor function results in extreme elevation of blood cholesterol levels resulting in premature and progressive atherosclerosis. In the United States, HoFH occurs in approximately one in one million individuals. For those with HoFH, heart attacks and death often occur before age 30. Juxtapid works by impairing the creation of the lipid particles that ultimately give rise to LDL. Although statins are the pharmacological agents of choice, individuals with HoFH have absent or dysfunctional LDL-receptors (LDL-R), which substantially attenuates the efficacy of statins. Extracorporeal removal of LDL-C (plasmapheresis or LDL apheresis) is the treatment of choice, but this therapy is not widely available, requires repeat procedures on a weekly or biweekly basis for life, and can be complicated by vascular access difficulties.

The FDA is requiring three postmarketing studies for Juxtapid: an animal study to evaluate the potential for toxicity in children and teens; a long-term registry of patients with HoFH treated with Juxtapid to determine the long-term safety; and an enhanced pharmacovigilance program to monitor reports of malignancy, teratogenicity, and hepatic abnormalities. Juxtapid is currently available through limited distribution and has a REMS program.

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RATIONALE (CONTINUED)
The safety and effectiveness of Juxtapid as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, were evaluated in a multinational, single-arm, open-label, 78-week trial involving 29 adults with HoFH. Concomitant lipid-lowering treatments at baseline included one or more of the following: statins (93%), ezetimibe (76%), nicotinic acid (10%), bile acid sequestrant (3%), and fibrate (3%); 18 (62%) were receiving apheresis. Concomitant lipid-lowering regimens and LDL apheresis schedules were not to be altered during the first 26 weeks of the trial. For those receiving LDL apheresis, efficacy was to be evaluated on the basis of pre-apheresis lipid levels.

After a six-week run-in period to stabilize lipid-lowering treatments, including the establishment of an LDL apheresis schedule if applicable, Juxtapid was initiated at 5 mg daily and titrated to daily doses of 10 mg, 20 mg, 40 mg, and 60 mg at weeks 2, 6, 10, and 14, respectively, based on tolerability and acceptable levels of transaminases. The maximum tolerated doses during the efficacy period were 5 mg (10%), 10 mg (7%), 20 mg (21%), 40 mg (24%), and 60 mg (34%). Patients were instructed to maintain a low-fat diet (<20% calories from fat) and to take dietary supplements that provided approximately 400 international units vitamin E, 210 mg alpha-linolenic acid (ALA), 200 mg linoleic acid, 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA) per day. After efficacy was assessed at Week 26, patients remained on Juxtapid for an additional 52 weeks to assess long-term safety. During this safety phase, the dose of Juxtapid was not increased above each patient's maximum tolerated dose established during the efficacy phase, but changes to concomitant lipid-lowering treatments were allowed.

Twenty-three (79%) patients completed the efficacy endpoint at Week 26, all of whom went on to complete 78 weeks of treatment. The primary efficacy endpoint was percent change in LDL-C from baseline to Week 26. At Week 26, the mean and median percent changes in LDL-C from baseline were -40% (paired t-test $p<0.001$) and -50%, respectively, based on the intent-to-treat population with last observation carried forward (LOCF) for patients who discontinued prematurely. Mean LDL-C was 336mg/dl at baseline despite subjects taking maximally tolerated lipid-lowering therapy. At week 26/LOCF, the mean LDL-C was 190mg/dl.

Of the 29 subjects who started the trial, 20 (69%) achieved ≥15% reduction in LDL-C from baseline to week 26/LOCF, 19 (66%) achieved ≥25%, and 14 (48%) achieved ≥50%. Eight (35%) of the 23 subjects who completed the efficacy period had an LDL-C level <100mg/dl at week 26, with one subject having a level <70mg/dl.

The Juxtapid label contains a boxed warning describing the risk of hepatotoxicity with Juxtapid therapy, including elevations in transaminases levels and the risk of hepatic steatosis. Because of the risk of hepatotoxicity, Juxtapid is available only through a restricted program called the Juxtapid REMS Program that includes prescriber and pharmacy certification and documentation of safe-use conditions consisting of a prescription authorization form that will be required to accompany each new prescription.

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RATIONALE (CONTINUED)

Contraindications to therapy with Juxtapid include pregnancy, concomitant use with strong or moderate CYP3A4 inhibitors, and concomitant use with strong or moderate CYP3A4 inhibitors. Warnings and precautions include embryo-fetal toxicity, and gastrointestinal adverse reactions that could affect absorption of concomitant oral medications. Juxtapid increases plasma level concentrations of warfarin, simvastatin and lovastatin and P-gp substrates, dosing adjustments are recommended.

The most common adverse reactions were gastrointestinal, reported by 27 (93%) of 29 patients. Adverse reactions reported by ≥8 (28%) patients in the HoFH clinical trial included diarrhea, nausea, vomiting, dyspepsia, and abdominal pain. Other common adverse reactions, reported by 5 to 7 patients (17-24%), included weight loss, abdominal discomfort, abdominal distension, constipation, flatulence, increased ALT, chest pain, influenza, nasopharyngitis, and fatigue. Five (17%) of the 29 patients with HoFH that participated in the clinical trial discontinued treatment due to an adverse reaction.

FDA APPROVED INDICATIONS

Juxtapid is indicated as an adjunct to a low-fat diet and other lipid lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apoB), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

REFERENCES

- Juxtapid [Prescribing Information]. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; December 2012.
- US Food and Drug Administration. FDA News Release. December 26, 2012. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333285.htm [Accessed January 21, 2013].
- US Food and Drug Administration. FDA Briefing Document. October 17, 2012. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM323841.pdf [Accessed January 21, 2013].

Part D Effective: 04/01/13 Created: 01/13
Commercial Effective: 04/01/13 Client Approval: 02/13 P&T Approval: 02/13

MEASLES VIRUS LIVE VACCINE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
MEASLES VACCINE-LIVE	ATTENUVAX	04187		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is this drug to be administered to an individual of 12 months of age or older for vaccination against measles (not for immediate exposure to measles)?

   If yes, **approve for 12 months under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   If no, continue to #2.

2. Is the drug to be administered within 72 hours to treat an individual who has had immediate exposure to natural measles?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, do not approve.
   DENIAL TEXT: Approval requires that requested medication is administered to an individual at least 1 year old for vaccination against measles or for treatment of immediate exposure to natural measles.

RATIONALE
Measles virus vaccine, live requires a Part B vs. Part D determination. The vaccine is Part D for vaccination against measles in persons 12 months of age or older. The vaccine is Part B for post exposure vaccination: The measles virus vaccine given immediately after exposure to natural measles may provide some protection if the vaccine can be administered within 72 hours of exposure.

FDA APPROVED INDICATION
Vaccination against measles in person 12 months of age or older.

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MEASLES VIRUS LIVE VACCINE BVD DETERMINATION (PART D)

REFERENCES

- Attenuvax Product Information, Merck & Co, February 2006.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13	Created: 02/08	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

METHOTREXATE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
METHOTREXATE SODIUM	TREXALL RHEUMATREX METHOTREXATE	03905		ROUTE = ORAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: For oral methotrexate, this PA is for administrative Step Override purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Has the patient received an organ transplant that was approved by and paid under Medicare?

   If yes, **submit via Part B for lifetime. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #2. **(CSR: If unknown, ask the caller to submit MRF.)**

2. Is the drug to be administered to treat a cancerous condition?

   If yes, **submit via Part B for lifetime. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, **approve for lifetime under Part D. (Populate the B vs. D field with "D" in PA override field.)**

RATIONALE
To determine whether methotrexate is being used to treat a medical condition other than those for which it's use qualifies for coverage under Medicare Part B.

FDA APPROVED INDICATIONS
Rheumatoid arthritis, breast cancer, choriocarcinoma, gestational trophoblastic neoplasms, head and neck cancer, acute lymphocytic leukemia, Burkitt's lymphoma, mycosis fungoides, non-metastatic osteosarcoma, psoriasis.

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METHOTREXATE BVD DETERMINATION (PART D)

REFERENCES

- Thomson Healthcare. Methotrexate. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 20, 2011].
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 02/07/13	Created: 08/05	
Commercial Effective: N/A	Client Approval: 01/13	P&T Approval: 11/12

METHYLNALTREXONE

Generic	Brand	HICL	GCN	Exception/Other
METHYLNALTREXONE	RELISTOR	35611		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient receiving palliative care?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient has constipation due to an opioid pain medication (i.e. morphine or methadone) with a diagnosis of a terminal illness in a patient receiving palliative care.

2. Does patient have constipation due to treatment with an opioid (i.e. morphine or methadone)?

   If yes, **approve for up to 6 months with a quantity of #1 vial, kit or syringes per day by HICL.**
   If no, do not approve.
   DENIAL TEXT: Approval requires that the patient has constipation due to an opioid pain medication (i.e. morphine or methadone) with a diagnosis of a terminal illness in a patient receiving palliative care.

RATIONALE

Promote cost-effective and clinically appropriate utilization of methylnaltrexone for its FDA approved indication. In both pivotal trials included in the package insert, methylnaltrexone was studied in patients with advanced illness with a life expectancy of less than 6 months who were receiving care to control their symptoms. The recommended dose of methylnaltrexone is 8mg for patients weighing 38 to less than 62kg or 12mg for patients weighing 62 to 114kg. Patients whose weight falls outside of these ranges should be dosed at 0.15mg/kg. Traditional treatment of opioid-induced constipation (OIC) includes the use of a stimulant and a stool softener. Metoclopramide can also be considered. Methylnaltrexone shows promise in treating OIC, but further data will be required to fully assess its place in therapy.

FDA APPROVED INDICATION

Treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient.

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METHYLNALTREXONE

REFERENCES

- Wyeth Pharmaceuticals Inc. Relistor package insert. Philadelphia, PA. September 2010.
- DeHaven-Hudkins DL, Dehaven RN, Little PJ, Techner LM. The involvement of the μ-opioid receptor in gastrointestinal pathophysiology: Therapeutic opportunities for antagonism at this receptor. *Pharmacology & Therapeutics*. 2007; 117(2008): 162-187.
- Becker G, Galandi D, Blum HE. Peripherally Acting Opioid Antagonists in the Treatment of Opiate-Related Constipation: A Systematic Review. *Journal of Pain and Symptom Management*. 2007; 34(5): 547-565.
- McNicol ED, Boyce D, Schumann R, Carr DB. Mu-opioid antagonists for opioid-inducted bowel dysfunction. *Cochrane Database of Systematic Reviews*. 2008, Issue 2. Art. No.:CD006332. DOI: 10.1002/14651858.CD006332.pub2.
- National Comprehensive Cancer Network. NCCN Practice Guidelines in Oncology: Palliative Care – v.1.2008.
- Locke GR, Pemberton JH, Phillips SF. American Gastroenterological Association Medical Position Statement: Guidelines on Constipation. *Gastroenterology*. 2000; 119(6):1761-1766.
- Locke GR, Pemberton JH, Phillips SF. American Gastroenterological Association AGA Technical Review on Constipation. *Gastroenterology*. 2000; 119(6):1766-1778.

Part D Effective: 01/01/13	Created: 11/08	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

MIFEPRISTONE

Generic	Brand	HICL	GCN	Exception/Other
MIFEPRISTONE	KORLYM		31485	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of endogenous Cushing's syndrome?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval of Korlym requires a diagnosis of endogenous Cushing's syndrome, a failure of surgery for treatment of Cushing's syndrome, as well as type 2 diabetes mellitus or glucose intolerance.

2. Does the patient have a diagnosis of diabetes type 2 or glucose intolerance?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval of Korlym requires a diagnosis of endogenous Cushing's syndrome, a failure of surgery for treatment of Cushing's syndrome, as well as type 2 diabetes mellitus or glucose intolerance.

3. Has the patient failed surgical treatment for Cushing's syndrome or is not a candidate for surgery?

   If yes, **approve for 1 year, by GCN up to #4 tablets per day.**
   APPROVAL TEXT: Please note this medication has an important FDA Safety Warning; pregnancy must be excluded before the initiation of treatment with Korlym or when therapy is interrupted for more than 14 days. For more information, discuss with your physician or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval of Korlym requires a diagnosis of endogenous Cushing's syndrome, a failure of surgery for treatment of Cushing's syndrome, as well as type 2 diabetes mellitus or glucose intolerance.

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MIFEPRISTONE

RATIONALE
To ensure appropriate use of Korlym.

FDA APPROVED INDICATIONS
- Korlym is a cortisol receptor antagonist indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.
- Korlym should not be used for the treatment of diabetes type 2 unrelated to endogenous Cushing's syndrome.

REFERENCE
- Korlym [Prescribing Information]. Menlo Park, CA: Corcept Therapeutics; March 2012.

Part D Effective: 01/01/13 Created: 04/12
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

MIPOMERSEN SODIUM

Generic	Brand	HICL	GCN	Exception/Other
MIPOMERSEN SODIUM	KYNAMRO	40041		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of homozygous familial hypercholesterolemia (HoFH)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of homozygous familial hypercholesterolemia, that Kynamro is being used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], fenofibrate, niacin, or a bile acid sequestrant [cholestyramine, colestipol, colesevelam]), and that the patient is not concurrently receiving LDL apheresis.

2. Will Kynamro be used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], fenofibrate, niacin, or bile acid sequestrant [cholestyramine, colestipol, colesevelam])?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of homozygous familial hypercholesterolemia, that Kynamro is being used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], fenofibrate, niacin, or a bile acid sequestrant [cholestyramine, colestipol, colesevelam]), and that the patient is not concurrently receiving LDL apheresis.

3. Is Kynamro being prescribed in conjunction with LDL apheresis?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of homozygous familial hypercholesterolemia, that Kynamro is being used in combination with other lipid-lowering treatments (such as a statin [simvastatin, atorvastatin], fenofibrate, niacin, or a bile acid sequestrant [cholestyramine, colestipol, colesevelam]), and that the patient is not concurrently receiving LDL apheresis.
   If no, **approve for 12 months for #4 syringes per 28 day supply.**

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MIPOMERSEN SODIUM

RATIONALE

To ensure appropriate use of Kynamro based on FDA approved indication and prescribing information.

The recommended dosage is 200mg injected subcutaneously once weekly. The first dose should be administered under the supervision of a healthcare provider. Prior to initiating therapy, patient ALT, AST, alkaline phosphatase, and total bilirubin should be measured.

Kynamro may increase risk of hepatic toxicity. Kynamro contains a boxed warning regarding the risk of elevated transaminases and hepatic steatosis. Kynamro also has a mandatory REMS program to educate prescribers about the risk of hepatotoxicity and the importance of monitoring patients while taking Kynamro as well as to limit the use of Kynamro to patients with HoFH.

FDA APPROVED INDICATION

Kynamro (mipomersen) is indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use:

- The safety and effectiveness of Kynamro have not been established in patients with hypercholesterolemia who do not have HoFH.
- The effect of Kynamro on cardiovascular morbidity and mortality has not been determined.
- The use of Kynamro as an adjunct to LDL apheresis is not recommended.

REFERENCES

- Kynamro (mipomersen) [Prescribing Information]. Cambridge, MA: Genzyme Corp.; January 2013.
- Ito M, McGowan M, and Moriarty P. Management of Familial Hypercholesterolemia in adult patients: Recommendations from the National Lipid Association Expert panel on Familial Hypercholesterolemia. Journal of Clinical Lipidology 2011 (5): S38-S45.
- Raal F, Santos R, Blom D, Marais D, Charng M, et al. Mipomersen, an apolipoprotein B synthesis inhibitor for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolemia: a randomized, double-blind, placebo-controlled trial. Lancet 2010; 375:998-1006.
- UpToDate, Inc. Primary disorders of LDL-cholesterol metabolism. UpToDate [database online]. Waltham, MA. Available at: http://www.uptodate.com/home/index.html. Updated August 21, 2012.

Part D Effective: 07/01/13 Created: 03/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 05/13

MODAFINIL AND ARMODAFINIL (PART D)

Generic	Brand	HICL	GCN	Exception/Other
MODAFINIL	PROVIGIL	10865		
ARMODAFINIL	NUVIGIL	34868		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the prior authorization request for modafinil?

   If yes, continue to #2.
   If no, continue to #3.

2. Is the patient diagnosed with shift work sleep disorder or chronic fatigue syndrome related to multiple sclerosis?

   If yes, **approve modafinil for 12 months #2 tablets per day per month by HICL.**
   MODAFINIL APPROVAL TEXT: The FDA maximum recommended dose is 400mg per day.
   If no, continue to #4.

3. Is the patient diagnosed with a shift work sleep disorder?

   If yes, **approve Nuvigil (armodafinil) for 12 months as follows:**
   - **50mg: #3 tablets per day per month.**
   - **150mg or 250mg: #1 tablet per day per month.**

   If no, continue to #4.

4. Is the patient diagnosed with obstructive sleep apnea/hypopnea syndrome?

   If yes, process as follows:
   - **Modafinil: approve for 12 months #2 tablets per day per month by HICL.**
     MODAFINIL APPROVAL TEXT: The FDA maximum recommended dose is 400mg per day.

   - **Nuvigil (armodafinil) 50mg: approve for 12 months #3 tablets per day per month.**
   - **Nuvigil (armodafinil) 150mg or 250mg: approve for 12 months #1 tablet per day per month.**

   If no, continue to #5.

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MODAFINIL AND ARMODAFINIL (PART D)

GUIDELINES FOR USE (CONTINUED)

5. Is the patient diagnosed with narcolepsy?

   If yes, process as follows.
   - **Modafinil: approve for 12 months #2 tablets per day per month by HICL.**
     MODAFINIL APPROVAL TEXT: The FDA maximum recommended dose is 400mg per day.

   - **Nuvigil (armodafinil) 50mg: approve for 12 months #3 tablets per day per month.**
   - **Nuvigil (armodafinil) 150mg or 250mg: approve for 12 months #1 tablet per day per month.**

   If no, do not approve.
   MODAFINIL DENIAL TEXT: Approval requires a diagnosis of shift work sleep disorder or chronic fatigue syndrome related to multiple sclerosis, obstructive sleep apnea/hypopnea syndrome, or narcolepsy.
   ARMODAFINIL DENIAL TEXT: Approval requires a diagnosis of shift work sleep disorder, obstructive sleep apnea/hypopnea syndrome, or narcolepsy.

RATIONALE
To promote the most cost-efficient and clinically appropriate utilization for modafinil and armodafinil.

Although some studies have shown efficacy of modafinil over placebo for pediatric use in ADHD, there have been reports of erythema multiforme major (EMM) and Stevens-Johnson syndrome (SJS) in pediatric clinical trials for modafinil (see “Pediatric Use” section in Provigil prescribing information). At this time, ADHD treatment guidelines do not recommend off label use of modafinil or armodafinil for treatment of ADHD in the pediatric population.

FDA APPROVED INDICATIONS
Modafinil and armodafinil are indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder.

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MODAFINIL AND ARMODAFINIL (PART D)

REFERENCES

- Cephalon. Provigil product information. Frazer, PA. October 2010.
- Cephalon. Nuvigil product information. Frazer, PA. October 2010.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. Available at: http://www.clinicalpharmacology.com. Updated August 2006. [Accessed: June 2, 2009].
- Thomson Healthcare. Modafinil. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 12, 2011].
- Thomson Healthcare. Armodafinil. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 12, 2011].
- Rammohan KW, Rosenberg JH, Lynn DJ, et al: Efficacy and safety of modafinil (Provigil(R)) for the treatment of fatigue in multiple sclerosis: a two centre phase 2 study. J Neurol Neurosurg Psychiatry 2002; 72:179-183.
- Harsh, JR, et al. The efficacy and safety of armodafinil as treatment for adults with excessive daytime sleepiness associated with narcolepsy. Current Medical Research and Opinion 2006; 22(4):761-774.

Part D Effective: 01/01/13 Created: 06/09
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

NATALIZUMAB

Generic	Brand	HICL	GCN	Exception/Other
NATALIZUMAB	TYSABRI	26750		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
This note pertains to Part D lines of business only:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient being treated for multiple sclerosis (MS)?

   If yes, continue to #3.
   If no, continue to #2.

2. Is the patient being treated for Crohn's disease (CD)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of multiple sclerosis or Crohn's disease.

3. Is this a renewal request for a patient with MS?

   If yes, **approve for 12 months, for one 15mL (300mg) vial every 4 weeks.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, continue to #4.

4. Did the patient have an inadequate response to, or is unable to tolerate one of the interferons used for multiple sclerosis (e.g., Avonex, Betaseron, or Rebif) or Copaxone?

   If yes, **approve for 12 months, for one 15mL (300mg) vial every 4 weeks.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a trial with an interferon used for multiple sclerosis (Avonex, Betaseron, or Rebif) or Copaxone.

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GUIDELINES FOR USE (CONTINUED)

5. Is this a new start for a patient with Crohn's disease?

   If yes, continue to #6.
   If no, continue to #7.

6. Did the patient have an inadequate response to at least one TNF-alpha inhibitor (e.g., Remicade, Humira, or Cimzia)?

   If yes, **approve for 24 weeks, for one 15mL (300 mg) vial every 4 weeks.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a trial with a TNF-alpha inhibitor such as Remicade, Humira, or Cimzia.

7. Is this a renewal request for a patient with Crohn's disease that has received at least 12 months of therapy?

   If yes, continue to #8.
   If no, continue to #9.

8. Has the patient required more than 3 months of corticosteroids within the past 12 months, while on natalizumab, for control of Crohn's disease?

   If yes, do not approve.
   DENIAL TEXT: Patients who require at least 3 months of corticosteroid use to control their disease while on natalizumab should be discontinued off of natalizumab.

   If no, **approve for 12 months, for one 15mL (300mg) vial every 4 weeks.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE (CONTINUED)

9. Is this a renewal request for a patient with Crohn's disease that has received 24 weeks of therapy?

   If yes, continue to #10.
   If no, **approve for a duration sufficient for the patient to have a total of 24 weeks of treatment and place a quantity limit of 15mL (300mg) vial every 4 weeks.**
   Note to Reviewer: To determine approval duration, subtract 24 weeks from total weeks patient already received per claims or MRF information.
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

10. Is the patient currently on corticosteroids?

    If yes, do not approve.
    DENIAL TEXT: Approval requires that patients are tapered off of corticosteroids during the first 24 weeks of therapy with natalizumab.

    If no, **approve for 12 months one 15mL (300mg) vial every 4 weeks.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

RATIONALE
To ensure appropriate utilization of Tysabri.

FDA APPROVED INDICATIONS
TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations.

TYSABRI is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α. TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α. **NOTE:** Only prescribers registered in the TOUCH™ Prescribing Program may prescribe TYSABRI.

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NATALIZUMAB

REFERENCES

- Biogen Idec Inc. Tysabri Product Information, Cambridge, MA. March 2011.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 6, 2011].
- Polman C, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. NEJM 2006; 354:899-910.
- Targan SR et al. Natalizumab for the treatment of active Crohn's disease: Results of the ENCORE Trial. Gastro. 2007; 132:1672-1683.
- Yoursry T et al., Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. NEJM 2006; 354:924-33.

Part D Effective: 07/01/13 Created: 08/06
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 11/12

NEBULIZER BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ACETYLCYSTEINE	ACETYLCYSTEINE		2400, 2401	
ALBUTEROL SULFATE	ALBUTEROL SULFATE, ACCUNEB, VENTOLIN		41680 14634 14633 41681	
ARFORMOTEROL TARTRATE	BROVANA	34087		
BUDESONIDE	BUDESONIDE, PULMICORT		17957 17958 62980	
CROMOLYN SODIUM	CROMOLYN SODIUM		46780	
DORNASE ALFA	PULMOZYME		27200	
FORMOTEROL FUMERATE	PERFOROMIST		98776	
ILOPROST	VENTAVIS	26287		
IPRATROPIUM BROMIDE	IPRATROPIUM BROMIDE		42235	
IPRATROPIUM/ALBUTEROL SULFATE	IPRATROPIUM/ALBUTEROL SULFATE, DUONEB		13456	
LEVALBUTEROL HCL	LEVALBUTEROL HCL, LEVALBUTEROL CONCENTRATE XOPENEX XOPENEX CONCENTRATE		23146 15665 24540 24541 15665	
METHACHOLINE CHLORIDE	PROVOCHOLINE		44840	
PENTAMIDINE ISETHIONATE	NEBUPENT		42980	
RIBAVIRIN	VIRAZOLE		43490	
SODIUM CHLORIDE FOR INHALATION	SODIUM CHLORIDE, NEBUSAL, HYPER-SAL		98520 29531 31137	
TOBRAMYCIN/0.25 NORMAL SALINE	TOBI		61551	
TREPROSTINIL	TYVASO	36541		
TREPROSTINIL/NEB ACCESSORIES		36539		
TREPROSTINIL/NEBULIZER/ACCESOR		36537		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

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PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

NEBULIZER BVD DETERMINATION (PART D)

GUIDELINES FOR USE

1. Is the request from a long term care facility?

   If yes, **approve for up to 12 months under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and provide lifetime approval. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**

RATIONALE

Nebulizer therapy is covered under Part D for patients when claims are submitted from a long term care facility. Claims not from a long term care facility e.g. retail pharmacy are covered under Part B.

REFERENCES

- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 07/01/13 Created: 03/11
Commercial Effective: N/A Client Approval: 05/13 P&T Approval: 11/12

OFATUMUMAB

Generic	Brand	HICL	GCN	Exception/Other
OFATUMUMAB	ARZERRA	36708		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is ofatumumab being prescribed for chronic lymphocytic leukemia (CLL)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic lymphocytic leukemia (CLL) and a trial of both fludarabine and alemtuzumab.

2. Has the patient tried treatment with fludarabine (Fludara) and alemtuzumab (Campath)?

   If yes, **approve for total length of approval equal to 6 months and a total of #223 vials.**
   - **INITIAL: Approve #3 (100mg/5mL) vials for the first dose.**
     APPROVAL TEXT: The renewal will be approved if the initial dose is tolerated.

   - **RENEWAL: Approve for 6 months for up to #80 (100mg/5mL) vials per month.**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic lymphocytic leukemia (CLL) and a trial of both fludarabine and alemtuzumab.

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OFATUMUMAB

RATIONALE
Ensure appropriate utilization for FDA approved indication. NCCN recommends use in the relapsed/refractory therapy setting following first line regimens containing fludarabine, alemtuzumab, or rituximab.

FDA APPROVED INDICATION
Ofatumumab is a CD 20-directed cytolytic monoclonal antibody indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) refractory to fludarabine and alemtuzumab.

The effectiveness of ofatumumab is based on the demonstration of durable objective responses. No data demonstrate an improvement in disease related symptoms or increased survival.

REFERENCES

- GlaxoSmithKline. Arzerra package insert. Research Triangle Park, NC. September 2010.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 27, 2011].
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. Version 3.2011.

Part D Effective: 10/01/13 Created: 11/09
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 11/12

OMACETAXINE MEPESUCCINATE

Generic	Brand	HICL	GCN	Exception/Other
OMACETAXINE MEPESUCCINATE	SYNRIBO	24243		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of chronic myeloid leukemia (CML)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic myeloid leukemia (CML) and a trial of at least two of the following therapies: Gleevec, Sprycel, Tasigna, Bosulif, or Iclusig.

2. Is this for induction therapy?

   If yes, continue to #3.
   If no, continue to #5.

3. Has the patient previously tried at least two of the following or does the patient have a contraindication to Gleevec, Sprycel, Tasigna, Bosulif, or Iclusig?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic myeloid leukemia (CML) and a trial of at least two of the following therapies: Gleevec, Sprycel, Tasigna, Bosulif, or Iclusig.

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient received less than 6 fills for Synribo?

   If yes, **approve for 3 fills by HICL with a quantity limit of #28 vials per 28 days supply. PAC Note: Patient should receive a maximum of 6 fills of Synribo when used as induction therapy.**
   If no, do not approve.
   DENIAL TEXT: Approval of Synribo beyond 6 treatment cycles requires evidence of a hematologic response.

5. Has the patient achieved a hematologic response (defined as an absolute neutrophil count (ANC) greater than or equal to 1.5 x 10(9)/L, AND platelets greater than or equal to 100 x 10(9)/L, AND no blood blasts; OR bone marrow blasts less than 5%)?

   If yes, **approve for 12 fills by HICL with a quantity limit of #14 vials per 28 days supply.**
   If no, **approve for 3 fills by HICL with a quantity limit of #28 vials per 28 days supply.**

RATIONALE
Ensure appropriate utilization of Synribo based on FDA approved indication and dosage. Synribo should be prepared in a healthcare facility and administered by a healthcare professional. The recommended induction dosing schedule is 1.25 mg/m^2 administered subcutaneously twice daily for 14 consecutive days every 28 days, over a 28-day cycle, and should be repeated every 28 days until patients achieve a hematologic response.

The recommended maintenance schedule is 1.25 mg/m^2 administered subcutaneously twice daily for 7 consecutive days every 28 days, over a 28-day cycle, and should continue as long as patients are clinically benefiting from therapy.

Complete blood counts (CBCs) should be performed weekly during induction and initial maintenance cycles followed by every two weeks thereafter, or as clinically indicated. If a patient experiences Grade 4 neutropenia (absolute neutrophil count (ANC) <0.5 x 10^9/L) or Grade 3 thrombocytopenia (platelet counts <50 x 10^9/L) during a cycle, the next cycle should be delayed until the ANC is >1.0 x 10^9/L and platelet count is >50 x 10^9/L, and the number of dosing days should be reduced by two days (for example to 12 or 5 days).

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RATIONALE (CONTINUED)
Synribo is a first-in-class cephalotaxine that functions as a protein synthesis inhibitor in CML. CML is a malignant clonal disorder that results in rapid growth of myeloid stem cells in the bone marrow. It is usually associated with a chromosomal abnormality that results from the fusion of the BCR and ABL1 genes, called the Philadelphia (Ph) chromosome. Normally, the ABL1 gene produces a protein with tyrosine kinase catalytic activity that is tightly regulated. The fused BCR-ABL1 gene in the Ph chromosome however, produces a protein with deregulated and constitutively active kinase activity that is fundamental to the pathogenesis of CML. The mainstay of treatment in CML over the last decade has been inhibition of the enzymatic activity of those proteins, and thus the TKIs Gleevec, Sprycel, and Tasigna are designated as first line treatment of CML in the National Comprehensive Cancer Network clinical practice guidelines. Another TKI, Bosulif, was approved earlier this year for treatment-resistant patients. It is currently being studied in a phase III open-label trial versus Gleevec for patients with newly diagnosed CML. However, because there are patients that fail, cannot tolerate, or are resistant to TKI therapy, new therapies, such as Synribo, are being explored. Synribo is unique in that it inhibits protein synthesis independently of direct BCR-ABL1 binding, and therefore, provides a different mechanism to help control the cancer and delay its progression to an acute leukemia for those who have already tried TKI based therapy.

Synribo was approved under the FDA's accelerated approval program. The accelerated approval allows the FDA to approve a drug to treat a serious disease based on clinical data showing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients. All accelerated approvals come with the caveat that the manufacturer must conduct additional clinical studies to confirm the drug's clinical benefit and safe use.

Effectiveness was based on data from two Phase II, open-label, multicenter, single-arm trials enrolling a combined cohort of 111 patients with chronic phase CML or accelerated phase CML who had received 2 or more approved TKIs and had, at a minimum, documented evidence of resistance or intolerance to dasatinib and/or nilotinib.

The efficacy endpoint for the 76 patients in chronic phase CML was major cytogenetic response (MCyR) as demonstrated by a reduction in the percentage of cells expressing the Philadelphia chromosome genetic mutation. MCyR was achieved in 14 out of 76 patients (18.4 percent) with a mean onset time of 3.5 months and Kaplan-Meier estimated median reduction duration of 12.5 months.

For the 35 patients in accelerated phase CML, the efficacy endpoints of MCyR or major hematologic response (MaHR) as demonstrated by either normalization of white blood cell counts (complete hematologic response [CHR]) or no evidence of leukemia (NEL) were evaluated. Five out of the 35 patients (14.3 percent) achieved MaHR with a mean response onset time of 2.3 months and Kaplan-Meier estimated median duration of 4.7 months. MCyR was not achieved in any of the 35 patients.

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OMACETAXINE MEPESUCCINATE

RATIONALE (CONTINUED)

Warnings and precautions for Synribo include: myelosuppression, including severe and fatal thrombocytopenia, neutropenia and anemia; bleeding, including fatal cerebral hemorrhage and severe, non-fatal gastrointestinal hemorrhage; hyperglycemia, including glucose intolerance and hyperosmolar non-ketotic hyperglycemia; and embryo-fetal toxicity.

The most common adverse reactions observed in clinical trials include thrombocytopenia, anemia, neutropenia, including febrile neutropenia, diarrhea, nausea, weakness and fatigue, injection site reaction, and lymphopenia. Synribo is pregnancy category D and may cause fetal harm. Females of reproductive potential should avoid pregnancy while undergoing Synribo treatment. Clinical drug interaction trials were not performed on Synribo based on the lack of interactions seen during in vitro studies.

FDA APPROVED INDICATIONS

Treatment of adult patients with chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKI) based upon response rate. There are no trials verifying an improvement in disease-related symptoms or increased survival with Synribo.

REFERENCES

- Synribo [Prescribing Information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2012.
- FDA News Release. FDA approves Synribo for chronic myelogenous leukemia. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm325895.htm [Accessed November 19, 2012].
- National Comprehensive Cancer Network. Chronic Myelogenous Leukemia 4.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf [Accessed April 23, 2013]
- Teva News Release. Teva Receives Approval For SYNRIBO™ (Omacetaxine Mepesuccinate) for Injection. Available at http://ir.tevapharm.com/phoenix.zhtml?c=73925&p=irol-newsArticle&ID=1750668&highlight [Accessed November 20, 2012].
- Omacetaxine: issues you may want to know. Available at: http://www.omacetaxine.info/ [Accessed November 20, 2012].
- Van Etten, RA. Clinical manifestations and diagnosis of chronic myeloid leukemia. In: UpToDate, Larson, RA (Ed), UpToDate, Waltham, MA, 2012.
- Tefferi, A. Overview of the myeloproliferative neoplasms. In: UpToDate, Schrier, SL (Ed), UpToDate, Waltham, MA, 2012.
- Negrin, RS., Schiffer, CA. Overview of the treatment of chronic myeloid leukemia. In: UpToDate, Larson, RA (Ed), UpToDate, Waltham, MA, 2012.

Part D Effective: 10/01/13 Created: 12/12
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 05/13

OMALIZUMAB

Generic	Brand	HICL	GCN	Exception/Other
OMALIZUMAB	XOLAIR	25399		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
This note pertains to Part D lines of business only:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is a physician specializing in Allergy or Pulmonary Medicine currently prescribing or supervising treatment?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or supervision of therapy by a physician specializing in Allergy or Pulmonary Medicine.

2. Is the patient 12 years of age or older?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires an age of 12 years or older.

3. Does the patient have a measured forced expiratory volume in one second (FEV_1) of less than 80 percent?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of moderate to persistent asthma with a measured forced expiratory volume in one second (FEV_1) of less than 80 percent.

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INITIAL CRITERIA (CONTINUED)

4. Does the patient have a positive skin prick or RAST test to a perennial aeroallergen?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a positive skin prick or RAST test to a perennial aeroallergen.

5. Has the patient demonstrated therapeutic failure to an inhaled or oral corticosteroid product combined with a second asthma controller agent such as a long-acting inhaled $beta_2$-agonist (Serevent, Foradil or Advair), leukotriene modifier (Singulair or Accolate), or theophylline?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a therapeutic failure to an inhaled corticosteroid product combined with a long-acting inhaled $beta_2$-agonist (Serevent, Foradil or Advair), leukotriene modifier (Singulair or Accolate), or theophylline.

6. Is the patient's baseline IgE serum level greater than or equal to greater than or equal to 30IU/mL?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires baseline IgE serum level greater than or equal to 30 IU/mL.

7. **Approve for 12 months with a quantity limit of 30 mL (#6 vials) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

RENEWAL CRITERIA

1. In the previous year, has the patient experienced at least a 25 percent reduction in asthma exacerbations (for example, hospitalizations, urgent or emergent care visits, use of rescue medications, etc.) from their pre-Xolair baseline?

   If yes, continue to #5.
   If no, continue to #2.

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RENEWAL CRITERIA (CONTINUED)

2. Was the patient receiving maintenance therapy with an oral corticosteroid prior to initiation of Xolair?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient been able to reduce their oral corticosteroid dose from their pre-Xolair baseline or to less than or equal to 5 mg daily?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a reduction in oral corticosteroid dose from baseline or to less than or equal to 5 mg daily.

4. Has the patient been able to reduce their inhaled corticosteroid dose from their pre-Xolair dose?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a reduction in inhaled corticosteroid dose from baseline.

5. **Approve for 12 months with a quantity limit of 30 mL (6 vials) per month.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

RATIONALE
Ensure appropriate diagnostic and utilization criteria.

FDA APPROVED INDICATIONS
Adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

CONTINUED ON NEXT PAGE

REFERENCES

- Busse W, Corren J, Lanier BQ, McAlary MA, Fowler-Tayler A, et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol 2001; 108:184-90.
- Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention. Bethesda, MD: National Institutes of Health; Updated 2007.
- Holgate S, Bousquet J, Wenzel S, Fox H, Liu J, et al. Efficacy of omalizumab, an anti-immunoglobulin E antibody in patients with allergic asthma at high risk of serious asthma-related morbidity and mortality. Curr Med Res Opin 2001; 17(4):233-240.
- NAEPP Expert Panel Report: Guidelines for the diagnosis and management of asthma-update on selected topics 2002. Bethesda, MD: National Institutes of Health; 2002: Publication No. 02-5075.
- Soler M, Matz J, Townley R, Buhl R, O'Brien J, et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. Eur Respir J 2001; 18(2):254-61.
- Genentech, INC. Xolair package insert. South San Francisco, CA. January 2010.
- National Heart, Lung, and Blood Institute National Asthma Education and Prevent Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. August 28, 2007.

Part D Effective: 10/01/13 Created: 08/03
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

OPIOID DEPENDENCY AGENTS (PART D)

Generic	Brand	HICL	GCN	Exception/Other
BUPRENORPHINE	SUBUTEX	01762		ROUTE = SUBLINGUAL
BUPRENORPHINE /NALOXONE	SUBOXONE	24846		ROUTE = SUBLINGUAL

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of opioid addiction?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of opioid addiction.

2. Will the patient also undergo psychosocial counseling?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires that this medication is used along with psychosocial counseling as part of a comprehensive addiction treatment program.

3. Is the request for Suboxone?

   If yes, **approve for 6 months.**
   If no, continue to #4.

4. Is the request for induction therapy with Subutex?

   If yes, **approve one time maximum of a month supply.**
   If no, continue to #5.

5. Does the patient have a contraindication or is unable to tolerate naloxone in combination with buprenorphine?

   If yes, **approve for 6 months.**
   If no, do not approve
   DENIAL TEXT: Approval requires a contraindication or intolerance to naloxone.
   .

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OPIOID DEPENDENCY AGENTS (PART D)

RATIONALE
Avoid use for unapproved indications. Ensure counseling is part of a comprehensive addiction treatment program. Avoid use of Subutex for maintenance therapy.

FDA APPROVED INDICATION
Treatment of opioid dependence.

PLEASE NOTE: The physician must obtain a unique ID# from the DEA prior to prescribing Suboxone and Subutex.

REFERENCES

- Reckitt Benckiser Pharmaceuticals, Inc. Subutex and Suboxone product information. Richmond, VA., September 2006.
- Frequently Asked Questions. Suboxone.com. Available from: http://suboxone.com/hcp/pharmacists/pharmacists_faqs.aspx [Accessed May 27 2010].
- Clinical Pharmacology [database online]. Tampa, Fl: Gold Standard, Inc.; 2010. Available at: http://www.clinicalpharmacology.com. Updated March 2010. [Accessed May 27, 2010].

Part D Effective: 01/01/13	Created: 08/03	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

PAZOPANIB

Generic	Brand	HICL	GCN	Exception/Other
PAZOPANIB	VOTRIENT	36709		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, **approve for 12 months with a quantity limit of #4 per day.**
   If no, continue to #2.

2. Does the patient have a diagnosis of adipocytic soft tissue sarcoma (STS) or gastrointestinal stromal tumors (GIST)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) or advanced soft tissue sarcoma (STS) and previous chemotherapy. Votrient is not covered for adipocytic soft tissue sarcoma (STS) and gastrointestinal stromal tumors (GIST).
   If no, continue to #3.

3. Does the patient have a diagnosis of advanced soft tissue sarcoma (STS)?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) or advanced soft tissue sarcoma (STS) and previous chemotherapy. Votrient is not covered for adipocytic soft tissue sarcoma (STS) and gastrointestinal stromal tumors (GIST).

4. Has the patient tried or does the patient have a contraindication to chemotherapy (including anthracycline treatment)?

   If yes, **approve for 12 months with a quantity limit of #4 per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) or advanced soft tissue sarcoma (STS) and previous chemotherapy. Votrient is not covered for adipocytic soft tissue sarcoma (STS) and gastrointestinal stromal tumors (GIST).

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PAZOPANIB

RATIONALE
Ensure appropriate utilization of pazopanib based on FDA approved indication and NCCN guidelines.

FDA APPROVED INDICATIONS
Pazopanib is indicated for the treatment of advanced renal cell carcinoma and advanced soft tissue sarcoma (STS) in patients who have received prior chemotherapy.

Limitation of use: the efficacy of pazopanib for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors (GIST) has not been demonstrated.

REFERENCES

- GlaxoSmithKline. Votrient package insert. Research Triangle Park, NC. April, 2012.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 2.2011).

Part D Effective: 01/01/13	Created: 05/11	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

PDE5 INHIBITORS FOR PULMONARY ARTERIAL HYPERTENSION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
SILDENAFIL	REVATIO		24758, 28273	
TADALAFIL	ADCIRCA		26587	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the request for Adcirca (tadalafil)?

   If yes, continue to #2.
   If no, continue to #3.

2. Has the patient had a trial of Revatio (sildenafil) or a contraindication to this product?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a trial of Revatio (sildenafil) prior to approval for Adcirca (tadalafil).

3. Is the prescribing physician a cardiologist or pulmonologist?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a cardiologist or a pulmonologist.

4. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of pulmonary arterial hypertension.

5. **REVATIO: Approve for 12 months with a quantity limit of up to #3 tablets or 37.5mL (#3 vials) per day.**
   ADCIRCA: Approve for 12 months with a quantity limit of up to #2 tablets per day.

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PDE5 INHIBITORS FOR PULMONARY ARTERIAL HYPERTENSION (PART D)

RATIONALE

Ensure appropriate utilization of PDE5 inhibitors, Revatio and Adcirca. FDA indicated dosage for Revatio tablets in the treatment of PAH is 20mg three times daily. For Revatio injection, the dosage is 10mg (12.5mL) three times daily administered as an IV bolus injection. The 10mg dose of Revatio injection is predicted to provide an equivalent pharmacological effect of 20mg Revatio tablet. For Adcirca, the dosage is 40mg once daily.

FDA APPROVED INDICATIONS

Revatio and Adcirca are indicated for treatment of pulmonary artery hypertension (WHO Group 1) to improve exercise capacity and delay clinical worsening.

World Health Organization Classification of Pulmonary Hypertension Group 1:

- Idiopathic (familial)
- Congenital systemic-to-pulmonary shunts
- HIV infection
- Collagen vascular disease
- Portal Hypertension
- Drugs and toxins

REFERENCES

- Pfizer, Inc. Revatio® (Sildenafil) package insert. New York, NY. November 2009.
- Eli Lilly and Company. Adcirca™ (Tadalafil) package insert. Indianapolis, IN. May 2009.

Part D Effective: 01/01/13 Created: 01/08
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

PEG-INTERFERON ALFA-2B

Generic	Brand	HICL	GCN	Exception/Other
PEG-INTERFERON ALFA-2B	SYLATRON SYLATRON 4-PACK		29809 29811 29812	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
This note pertains to Part D lines of business only:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient currently taking requested medication?

   If yes, continue to #2.
   If no, continue to #3.

2. Has the patient received 5 years of therapy with Sylatron?

   If yes, do not approve.
   DENIAL TEXT: Duration of therapy is limited to 5 years per FDA approved indication.
   If no, **approve as follows:**
   - **COMMERCIAL MEMBERS: Approve for 12 months with a quantity limit of one 296mcg 4-pack or four 296mcg single dose kits per month.**
     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   - **PART D MEMBERS: Approve for 12 months with a quantity limit of one 4-pack or four single dose kits per month.**
     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

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PEG-INTERFERON ALFA-2B

GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a diagnosis of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection?

   If yes, **approve. Enter two authorizations as follows:**
   - **2 months with a quantity limit of one 4-pack or four single dose kits per month, AND**
   - **10 months with a quantity limit of one 296mcg 4-pack or four 296mcg single dose kits per month with a start date 1 week prior to the end date of the authorization for 2 months.**

     APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.

   DENIAL TEXT: Approval requires a diagnosis of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection.

RATIONALE

Ensure appropriate utilization of Sylatron based on FDA approved indication and NCCN guidelines. Peg-interferon in combination with wide excision is recommended for the treatment of Melanoma. Sylatron's dosing is weight based as follows: 6mcg/kg/week for 8 doses followed by 3mcg/kg/week subcutaneously for up to 5 years. This guideline approves the appropriate quantities for a patient weighing up to 98kg. Patients weighing over 98kg should be reviewed by clinical to determine the appropriate dose.

FDA APPROVED INDICATION

Sylatron is indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

REFERENCES

- Eggermont AMM, Sucio S, Santinami M et al. Adjuvant therapy with pegylated interferon alfa-2b versus observation alone in resected stage III melanoma: final results of EORTC 18991, a randomised phase III trial. Lancet 200; 372:117-126.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Melanoma. (Version 4.2011).
- Schering Corporation. Sylatron package insert. Kenilworth, NJ. March 2011.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 22, 2011].

Part D Effective: 01/01/13 Created: 05/11
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

PLERIXAFOR

Generic	Brand	HICL	GCN	Exception/Other
PLERIXAFOR	MOZOBIL	36021		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the prescription written or currently being supervised by a hematologist or an oncologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or supervision by a hematologist or an oncologist and a diagnosis of non-Hodgkin's lymphoma or multiple myeloma.

2. Is the patient diagnosed with non-Hodgkin's lymphoma or multiple myeloma?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or supervision by a hematologist or an oncologist and a diagnosis of non-Hodgkin's lymphoma or multiple myeloma.

3. Is the request for more than 4 vials?

   If yes, obtain patient's weight in kg.
   - If greater than 100kg, then **approve for one fill up to #8 vials (24mg/1.2mL) for 1 day supply**
   - If less than or equal to 100kg, then **approve for one fill up to #4 vials (24mg/1.2mL) for 1 day supply**

   If no, **approve for one fill up to #4 vials (24mg/1.2mL) for 1 day supply.**

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PLERIXAFOR

RATIONALE
Ensure appropriate utilization based on FDA approved indication.

FDA APPROVED INDICATIONS
Plerixafor is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.

REFERENCES

- Genzyme Corporation. Mozobil package insert, Cambridge, Massachusetts, April 2010.
- Stewart DA, Smith C, et al. Pharmacokinetics and pharmacodynamics of plerixafor in patients with non-Hodgkin lymphoma and multiple myeloma. Biol Blood Marrow Transplant. 2009 Jan; 15(1):39-46.
- Stiff P, Micallef I, et al. Treatment with plerixafor in non-Hodgkin's lymphoma and multiple myeloma patients to increase the number of peripheral blood stem cells when given a mobilizing regimen of G-CSF: implications for the heavily pretreated patient. Biol Blood Marrow Transplant. 2009 Feb; 15(2):249-56.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 27, 2011].

Part D Effective: 10/01/13 Created: 02/09
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 11/12

POMALIDOMIDE

Generic	Brand	HICL	GCN	Exception/Other
POMALIDOMIDE	POMALYST	39996		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multiple myeloma?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of multiple myeloma and prior trial with at least two therapies including Revlimid and Velcade.

2. Has the patient received at least two prior therapies including Revlimid and Velcade?

   If yes, **approve for 12 fills by HICL with a quantity limit of #21 capsules per 28 days.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of multiple myeloma and prior trial with at least two therapies including Revlimid and Velcade.

RATIONALE
To ensure appropriate use of pomalidomide aligned with FDA approved indication.

The recommended starting dose is 4 mg once daily orally on days 1-21 of repeated 28-day cycles until disease progression. Pomalyst may be given in combination with dexamethasone and/or with water. The capsules should not be broken, chewed, or opened. Pomalyst should be taken at least 2 hours before or 2 hours after a meal. Dose interruption and modification to 1mg less than the previous dose is recommended in the presence of neutropenia, thrombocytopenia, or any other Grade 3 or 4 toxicity.

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RATIONALE (CONTINUED)
Pomalyst is a second generation oral, once-daily thalidomide analogue that may be administered in combination with low-dose dexamethasone for treatment of relapsed and refractory multiple myeloma (MM) patients who have received at least two prior therapies. Both Thalomid (thalidomide) and Revlimid (lenalidomide) are thalidomide analogues with FDA approval for MM; Thalomid as first line therapy and Revlimid as second line therapy. Velcade (bortezomib) and Kyprolis (carfilzomib) are proteasome inhibitors also approved for MM (Kyprolis as third line only) given intravenously. Additionally there are multiple traditional chemotherapy agents used in the treatment of MM.
MM is a plasma cell neoplasm characterized by the presence of monoclonal (or myeloma) protein, also known as M protein. The malignant proliferation of plasma cells, or activated B cells, leads to accumulation in the bone marrow resulting in bone marrow failure and also bone destruction. It is estimated that in 2012 there were 21,270 new cases of MM and 10,710 deaths in the United States. The majority of MM patients are over 60 years old. The 5 year survival rate for MM has improved with the availability of newer therapies and was estimated to be 34% in 2003.

Pomalyst inhibited proliferation and induced apoptosis of hematopoietic tumor cells. Additionally, Pomalyst inhibited the proliferation of Revlimid-resistant multiple myeloma cell lines and synergized with dexamethasone in both lenalidomide-sensitive and lenalidomide-resistant cell lines to induce tumor cell apoptosis. Pomalyst enhanced T cell- and natural killer (NK) cell-mediated immunity and inhibited production of pro-inflammatory cytokines (e.g., TNF-α and IL-6) by monocytes. Pomalyst demonstrated anti-angiogenic activity in a mouse tumor model and in the in vitro umbilical cord model. Thalomid and Revlimid work in a similar fashion. The proteasome inhibitors increase the sensitization of malignant cells to apoptosis.

The National Comprehensive Cancer Network (NCCN) guidelines do not include Pomalyst at the time of this review. They do list several preferred regimens for MM, categorized by stage in therapy and transplant candidacy.

Treatment regimens utilizing alkylating agents such as melphalan should be avoided in stem cell transplant candidates since they compromise marrow hemopoiesis and may make the harvesting of adequate numbers of hemopoietic stem cells impossible. The preferred primary therapy regimens for transplant candidates are:

- Velcade (bortezomib) with dexamethasone
- Velcade with cyclophosphamide and dexamethasone
- Velcade with doxorubicin and dexamethasone
- Velcade with Revlimid and dexamethasone
- Velcade with Thalomid and dexamethasone
- Revlimid with dexamethasone

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RATIONALE (CONTINUED)
The preferred primary therapy regimens for non-transplant candidates are:

- Velcade with dexamethasone
- Revlimid with low-dose dexamethasone
- Melphalan with prednisone and Velcade
- Melphalan with prednisone and Revlimid
- Melphalan with prednisone and Thalomid

The preferred primary therapies for maintenance therapy are:

- Velcade
- Revlimid
- Thalomid

The preferred primary therapy regimens for salvage therapy are:

- Velcade
- Velcade with dexamethasone
- Velcade with Revlimid and dexamethasone
- Velcade with liposomal doxorubicin
- Velcade with Thalomid and dexamethasone
- Kyprolis
- Velcade with cyclophosphamide and dexamethasone
- Revlimid with cyclophosphamide and dexamethasone
- Dexamethasone, cyclophosphamide, etoposide, cisplatin (DCEP)
- Dexamethasone with Thalomid, cisplatin, doxorubicin, cyclophosamide, and etoposide (DT-PACE) with or without Velcade (VTD-PACE)
- High-dose cyclophosphamide
- Revlimid with dexamethasone
- Thalomid with dexamethasone

Pomalyst is being studied in combination with Velcade and low-dose dexamethasone (OPTIMISMM trial) and Kyprolis with dexamethasone for relapsed and refractory MM. It is also being investigated for the treatment of graft vs. host disease, myelofibrosis, and several other cancers. Pomalyst will likely be used as salvage therapy in practice, which is aligned with its FDA approved indication.

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POMALIDOMIDE

RATIONALE (CONTINUED)
The pivotal trial (trial 1 included in the prescribing information) was a phase 2, multicenter, randomized open label study in patients with relapsed MM who were refractory to their last myeloma therapy and had received both Revlimid and Velcade. Patients were considered relapsed if they had achieved at least stable disease for at least one cycle of treatment to at least one prior regimen and then developed progressive disease. Patients were considered refractory if they experienced disease progression on or within 60 days of their last therapy. Patients (N=221) were randomized to receive Pomalyst (4mg once daily for 21 of 28 days, until disease progression) alone or in combination with low dose dexamethasone (40 mg per day given only on Days 1, 8, 15 and 22 of each 28-day cycle for patients 75 years or younger, or 20mg per day given only on Days 1, 8, 15 and 22 of each 28-day cycle for patients greater than 75 years of age). Patients in the Pomalyst alone arm were allowed to add dexamethasone upon disease progression.

Baseline characteristic for the Pomalyst alone and Pomalyst with low dose dexamethasone were as follows: age (61 vs. 64 years), male (57 vs. 62 percent), Caucasian (86 vs. 92 percent), number of prior therapies (5 in both groups), and refractory to bortezomib and lenalidomide (59.3 vs. 61.1 percent).

The overall response rate was greater among patients treated with Pomalyst and low dose dexamethasone compared to Pomalyst alone (29.2 vs. 7.4 percent).

Pomalyst was also studied in the phase III, open-label MM-003 study, which examined Pomalyst plus low-dose dexamethasone (given weekly) compared with high-dose dexamethasone alone (given on days 1-4, 9-12 and 17-20 of each 28-day cycle) in patients (N=455) with refractory multiple myeloma who have failed therapy with both Revlimid and Velcade, administered either alone or in combination. The top line results demonstrated significantly longer progression free survival in patients who received Pomalyst plus low-dose dexamethasone compared with those who received high-dose dexamethasone (median 3.6 months vs. 1.8 months).

Pomalyst has boxed warnings for embryo-fetal toxicity and venous thromboembolism. It is only available through a restricted program called the Pomalyst REMS program, which includes prescriber certification, pharmacy certification, and a signed patient-prescriber agreement. Pomalyst is contraindicated in pregnancy (pregnancy category X) and nursing mothers are advised to discontinue either Pomalyst or nursing. It should also be avoided in patients with serum creatinine >3.0 mg/dL. Patients with a prior history of serious hypersensitivity associated with thalidomide or lenalidomide may be at higher risk of hypersensitivity. No formal drug interaction studies have been conducted with Pomalyst. It is primarily metabolized by CYP1A2 and CYP3A. It is also a substrate for P-glycoprotein (P-gp).

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POMALIDOMIDE

RATIONALE (CONTINUED)
The most common adverse reactions (≥30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain and pyrexia. Neutropenia was the most frequently reported Grade 3/4 adverse event. Monitor patients for hematologic toxicities, especially neutropenia.

FDA APPROVED INDICATIONS
Pomalyst (pomalidomide) is indicated for patients with multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

REFERENCES

- Pomalyst [Prescribing Information]. Summit, NJ: Celgene Corporation; February 2013.
- Celgene. Phase III Study (MM-003) of Pomalidomide Plus Low-Dose Dexamethasone Demonstrates Significant Progression-Free and Overall Survival Improvement for Patients with Relapsed or Refractory Multiple Myeloma. Available at: http://ir.celgene.com/phoenix.zhtml?c=111960&p=RssLanding&cat=news&id=1766190 [Accessed February 19, 2013].
- National Comprehensive Cancer Network. NCCN Guidelines Version 1.2013 Multiple Myeloma. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf [Accessed February 19, 2013].
- Safety and Efficacy of Pomalidomide, Bortezomib and Low-dose Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma (OPTIMISMM). Available at: http://www.clinicaltrials.gov/ct2/show/NCT01734928?term=pomalidomide&rank=8 [Accessed February 19, 2013].
- Carfilzomib, Pomalidomide, and Dexamethasone in Treating Patients With Relapsed or Refractory Multiple Myeloma Available at: http://www.clinicaltrials.gov/ct2/show/NCT01665794?term=pomalidomide&rank=23 [Accessed February 19, 2013].
- Ruxolitinib and Pomalidomide Combination Therapy in Patients With Primary and Secondary MF (POMINC) Available at: http://www.clinicaltrials.gov/ct2/show/NCT01644110?term=pomalidomide&rank=34 [Accessed February 19, 2013].
- Pomalidomide for Chronic Graft-versus-Host Disease Available at: http://www.clinicaltrials.gov/ct2/show/NCT01688466?term=pomalidomide&rank=41 [Accessed February 19, 2013].

Part D Effective: 07/01/13 Created: 02/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 05/13

PONATINIB

Generic	Brand	HICL	GCN	Exception/Other
PONATINIB HCL	ICLUSIG	39859		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML)?

   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have a diagnosis of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or a diagnosis of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) and a trial of Bosulif, Gleevec, Sprycel, or Tasigna, which may also require prior authorization.

3. Has the patient previously tried or does the patient have a contraindication to Gleevec, Sprycel, Tasigna, or Bosulif?

   If yes, **approve for 12 fills by GPID as requested with the following quantity limits:**
   - **Iclusig 45mg: #30 tablets per 30 days**
   - **Iclusig 15mg: #60 tablets per 30 days**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or a diagnosis of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) and a trial of Bosulif, Gleevec, Sprycel, or Tasigna, which may also require prior authorization.

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RATIONALE
Ensure appropriate utilization of ponatinib based on FDA approved indication and dosage. The recommended dosage is 45mg once daily with or without food. Tablets should be swallowed whole.

Continue treatment as long as the patient does not show evidence of disease progression or unacceptable toxicity. Dose modifications to 30mg and then 15mg daily are recommended for neutropenia and thrombocytopenia unrelated to leukemia; hepatic toxicity; or pancreatitis and lipase elevation. The recommended dose should be reduced to 30 mg once daily when administering Iclusig with strong CYP3A inhibitors.

Iclusig (ponatinib) is the fifth tyrosine kinase inhibitor (TKI) approved for the treatment of CML. It blocks the activity of ABL (including the T315I mutation) to treat CML and Ph+ALL. Iclusig also inhibited the in vitro activity of additional kinases involved in the growth and development of cancer cells. These include members of the VEGFR, PDGFR, FGFR, EPH receptors, the SRC families of kinases, and KIT, RET, TIE2, and FLT3.

CML is a malignant clonal disorder that results in rapid growth of myeloid stem cells in the bone marrow. It is usually associated with a chromosomal abnormality that results from the fusion of the BCR and ABL1 genes, called the Philadelphia (Ph) chromosome. Normally, the ABL1 gene produces a protein with tyrosine kinase catalytic activity that is tightly regulated. The fused BCR-ABL1 gene in the Ph chromosome however, produces a protein with deregulated and constitutively active kinase activity that is fundamental to the pathogenesis of CML. The presence of the T315I “gatekeeper” mutation has been associated with resistance to currently approved TKIs including Gleevec, Sprycel, Tasigna, and Bosulif.

The mainstay of treatment in CML over the last decade has been inhibition of the enzymatic activity of those proteins, and thus the TKIs Gleevec, Sprycel, and Tasigna are designated as first line treatment of CML in the National Comprehensive Cancer Network clinical practice guidelines. NCCN recommends that Bosulif, another TKI, be considered as a second line treatment. It is currently being studied in the phase III open-label BELA trial versus Gleevec for patients with newly diagnosed CML. Synribo, a first-in-class cephalotaxine that inhibits protein synthesis independently of direct BCR-ABL1 binding, was also approved in 2012 for patients that fail, cannot tolerate, or are resistant to TKI therapy. NCCN recommends its use for patients who failed two or more TKIs or have a T315I mutation. EPIC is an ongoing randomized trial comparing Iclusig to Gleevec in patients with newly diagnosed CML. EPIC began in June 2012 and has an estimated study completion date of June 2021. Initially Iclusig will likely be used as a second line agent (similar to Bosulif) except for those patients with the T315I mutation where it may be considered as a first line therapy (similar to Synribo). Depending on the results of the EPIC trial, Iclusig may be considered a first line agent for all patients regardless of mutation type.

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RATIONALE (CONTINUED)

The PACE trial (n=444) studied Iclusig in patients with CML and Ph+ALL whose disease was considered to be resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy. This was a single-arm, open-label, international, multicenter trial. All patients were administered a starting dose of 45 mg of Iclusig once daily. Patients were assigned to one of six cohorts based on disease phase (chronic phase CML [CP-CML]; accelerated phase CML [AP-CML]; or blast phase CML [BP-CML]/Ph+ALL), resistance or intolerance (R/I) to prior TKI therapy, and the presence of the T315I mutation. All patients had previously been on at least one FDA approved or investigational TKI therapy: 7% had 1 TKI therapy, 37% had 2 TKI therapies, and 56% had 3 or more TKI therapies.

Resistance in CP-CML while on prior TKI therapy, was defined as failure to achieve either a complete hematologic response (by 3 months), a minor cytogenetic response (by 6 months), or a major cytogenetic response (by 12 months). Patients with CP-CML who experienced a loss of response or development of a kinase domain mutation in the absence of a complete cytogenetic response or progression to AP-CML or BP-CML at any time on prior TKI therapy were also considered resistant. Resistance in AP-CML, BP-CML, and Ph+ALL was defined as failure to achieve either a major hematologic response (by 3 months in AP-CML, and by 1 month in BP-CML and Ph+ALL), loss of major hematologic response (at any time), or development of a kinase domain mutation in the absence of a complete major hematologic response while on prior TKI therapy. Intolerance was defined as the discontinuation of prior TKI therapy due to toxicities despite optimal management in the absence of a complete cytogenetic response in patients with CP-CML or major hematologic response for patients with AP-CML, BP-CML, or Ph+ALL.

The primary endpoint of major cytogenetic response (which combines both complete (no detectable Ph+ cells) and partial (1% to 35% Ph+ cells in at least 20 metaphases) cytogenetic responses) for CP-CML was 54% overall and 70% in the T315I cohort. At the time of analysis, the median duration of Iclusig treatment was 281 days in patients with CP-CML and the median duration of major cytogenetic response was not reached.

The results of the primary endpoint of overall major hematologic response (which combines complete hematologic responses and no evidence of leukemia) for AP-CML, BP-CML, and Ph+ALL were 52%, 31% and 41%, respectively. At the time of analysis, the median duration of Iclusig treatment was 286 days in patients with AP-CML, 89 days in patients with BP-CML, and 81 days in patients with Ph+ALL. The median time to overall, major hematologic response in patients with AP-CML, BP-CML, and Ph+ALL was 21 days, 29 days, and 20 days, respectively. The median duration of overall major hematologic response for patients with AP-CML, BP-CML, and Ph+ALL was 9.5 months, 4.7 months, and 3.2 months, respectively.

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RATIONALE (CONTINUED)

Iclusig has a boxed warning for arterial thrombosis and hepatotoxicity. Patients should be monitored for signs and symptoms of congestive heart failure, hypertension, pancreatitis, hemorrhage, fluid retention, cardiac arrhythmias, myelosuppression, tumor lysis syndrome, gastrointestinal perforation, and compromised wound healing. The most common non-hematologic adverse reactions (≥ 20%) were hypertension, rash, abdominal pain, fatigue, headache, dry skin, constipation, arthralgia, nausea, and pyrexia. Hematologic adverse reactions included thrombocytopenia, anemia, neutropenia, lymphopenia, and leukopenia. Iclusig is pregnancy category D and can cause fetal harm.

FDA APPROVED INDICATIONS

Iclusig is indicated for the treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) that is resistant or intolerant to prior tyrosine kinase inhibitor therapy or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) that is resistant or intolerant to prior tyrosine kinase inhibitor therapy.

REFERENCES

- Iclusig [Prescribing Information]. Cambridge, MA: ARIAD Pharmaceuticals, Inc.; December 2012.
- National Comprehensive Cancer Network. Chronic Myelogenous Leukemia 3.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf [Accessed January 2, 2013].
- Center for Drug Evaluation and Research. Application Number: 203469Orig1s000 Summary Review. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203469Orig1s000SumR.pdf [Accessed January 2, 2013].
- Ariad Investors/News. ASH 2012 PACE 12-Month Update on Ponatinib. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01650805?term=ponatinib+imatinib&rank=1 http://phx.corporate-ir.net/phoenix.zhtml?c=118422&p=irol-IRhome [Accessed January 2, 2013]
- Ponatinib in Newly Diagnosed Chronic Myeloid Leukemia (CML) (EPIC). Available at: http://www.clinicaltrials.gov/ct2/show/NCT01650805?term=ponatinib+imatinib&rank=1 [Accessed January 2, 2013].
- Van Etten, RA. Clinical manifestations and diagnosis of chronic myeloid leukemia. In: UpToDate, Larson, RA (Ed), UpToDate, Waltham, MA, 2012.
- Tefferi, A. Overview of the myeloproliferative neoplasms. In: UpToDate, Schrier, SL (Ed), UpToDate, Waltham, MA, 2012.
- Negrin, RS., Schiffer, CA. Overview of the treatment of chronic myeloid leukemia. In: UpToDate, Larson, RA (Ed), UpToDate, Waltham, MA, 2012.

Part D Effective: 07/01/13 Created: 01/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 02/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

QUININE SULFATE

Generic	Brand	HICL	GCN	Exception/Other
QUININE SULFATE	QUALAQUIN	04142		

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Has the patient been diagnosed with malaria?

   If yes, **approve for 12 months by HICL with a quantity limit of a maximum of #42 capsules.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of malaria.

RATIONALE
Ensure appropriate use of FDA-approved quinine sulfate products only. The FDA has warned that off label use of quinine for leg cramps is not appropriate due to the risk of serious hematological reactions.

FDA APPROVED INDICATIONS
- Treatment of uncomplicated *Plasmodium falciparum* Malaria. Quinine sulfate has been shown to be effective in geographical regions where resistance to chloroquine has been documented.
- Qualaquin oral capsules are not approved for:
  - treatment of severe or complicated *P. falciparum* malaria
  - prevention of malaria
  - treatment or prevention of nocturnal leg cramps

REFERENCES

- AR Scientific, Inc. Qualaquin package insert. Philadelphia, PA. April 2011.
- FDA. Qualaquin (quinine sulfate): New Risk Evaluation and Mitigation Strategy- Risk of serious hematological reactions. Available at: http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm218424.htm [Accessed July 5 2011].

Part D Effective: 01/01/13 Created: 11/07
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

RABIES VACCINE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
RABIES VACCINE	IMOVAX RABAVERT	04199 16638 35580		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the request for pre-exposure immunization for rabies?

   If yes, **approve for 1 year under Part D. (Populate the B vs. D field with "D" in PA override field.)**
   If no, continue to #2.

2. Is this drug to be administered as prophylaxis to a member as a result of being exposed to Rabies (i.e. post-exposure prophylaxis)?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of post-exposure Rabies prophylaxis.

RATIONALE
Rabies vaccine requires a Part B vs. Part D determination. The vaccine is Part D for pre-exposure vaccination. The vaccine is Part B if used for post exposure prophylaxis against rabies in all age groups.

FDA APPROVED INDICATION
It is indicated for induction of active immunity against rabies virus either before or after viral exposure.

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RABIES VACCINE BVD DETERMINATION (PART D)

REFERENCES

- Sanofi Pasteur SA. Imovax package insert. Lyon, France. December 2005.
- Novartis Vaccines & Diagnostics Gmbh & Co. KG. Rabavert prescribing information. Marburg, Germany. October 2006.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13	Created: 02/08	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

REGORAFENIB

Generic	Brand	HICL	GCN	Exception/Other
REGORAFENIB	STIVARGA		33363	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic colorectal cancer?

   If yes, continue to #2.
   If no, continue to #5.

2. Is the colorectal cancer KRAS wild type?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient tried, or does the patient have a contraindication to an anti-EGFR therapy such as Erbitux or Vectibix?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic colorectal cancer and a trial of an anti-VEGF therapy such as Avastin or Zaltrap AND a fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy such as: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, and FOLFOXIRI. Wild type KRAS colorectal cancer also requires a trial of an anti-EGFR therapy such as Erbitux or Vectibix. Alternatively, approval requires a diagnosis of locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) and a trial of Gleevec and Sutent. These prior therapies may be covered under the medical benefit and/or may require prior authorization.

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REGORAFENIB

GUIDELINES FOR USE (CONTINUED)

4. Has the patient tried, or does the patient have a contraindication to an anti-VEGF therapy such as Avastin or Zaltrap AND a fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy such as: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, and FOLFOXIRI?

   If yes, **approve for 12 fills of #84 tablets per 28 days supply.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic colorectal cancer and a trial of an anti-VEGF therapy such as Avastin or Zaltrap AND a fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy such as: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, and FOLFOXIRI. Wild type KRAS colorectal cancer also requires a trial of an anti-EGFR therapy such as Erbitux or Vectibix. Alternatively, approval requires a diagnosis of locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) and a trial of Gleevec and Sutent. These prior therapies may be covered under the medical benefit and/or may require prior authorization.

5. Does the patient have a diagnosis of locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST)?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic colorectal cancer and a trial of an anti-VEGF therapy such as Avastin or Zaltrap AND a fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy such as: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, and FOLFOXIRI. Wild type KRAS colorectal cancer also requires a trial of an anti-EGFR therapy such as Erbitux or Vectibix. Alternatively, approval requires a diagnosis of locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) and a trial of Gleevec and Sutent. These prior therapies may be covered under the medical benefit and/or may require prior authorization.

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REGORAFENIB

GUIDELINES FOR USE (CONTINUED)

6. Has the patient tried or does the patient have a contraindication to Gleevec and Sutent?

   If yes, **approve for 12 fills of #84 tablets per 28 days supply.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic colorectal cancer and a trial of an anti-VEGF therapy such as Avastin or Zaltrap AND a fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy such as: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, and FOLFOXIRI. Wild type KRAS colorectal cancer also requires a trial of an anti-EGFR therapy such as Erbitux or Vectibix. Alternatively, approval requires a diagnosis of locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) and a trial of Gleevec and Sutent. These prior therapies may be covered under the medical benefit and/or may require prior authorization.

RATIONALE
To ensure appropriate use of Stivarga consistent with FDA approved indication.

The recommended dose of Stivarga is 160 mg orally (four 40mg tablets), once daily for the first 21 days of each 28-day cycle with a low-fat breakfast. Do not take two doses of Stivarga on the same day to make up for a missed dose from the previous day. Treatment should be interrupted and dose reduction to 120mg and then 80mg daily should be considered in the presence of certain grade 2-4 adverse reactions.

Stivarga is a once daily oral medication for treatment-resistant metastatic colorectal cancer. It is an inhibitor of multiple kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment. Stivarga is structurally similar to sorafenib, leading to its moniker of “son of Nexavar”. It is also in a phase III trial for treatment-resistant metastatic and / or unresectable gastrointestinal stromal tumors (GIST).

Colorectal cancer originates in either the colon or rectum typically as a polyp that slowly develops over many years. About 50% to 60% of patients diagnosed with colorectal cancer will eventually develop metastases. The American Cancer Society estimates that there will be 103,170 new cases of colon cancer and 40,290 new cases of rectal cancer in 2012.

According to the National Comprehensive Cancer Network (NCCN) colon and rectal cancer guidelines, options for treatment of metastatic disease consist of 5-fluorouracil with leucovorin (5-FU/LV), irinotecan, capecitabine, oxaliplatin, bevacizumab, cetuximab, and panitumumab. Five chemotherapy regimens are recommended as initial treatment of metastatic disease: FOLFOX, FOLFIRI, CapeOx, infusional 5-FU/LV or capecitabine, or FOLFOXIRI.

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RATIONALE (CONTINUED)
Vascular endothelial growth factor (VEGF) inhibitor Avastin (bevacizumab), and the epidermal growth factor receptor (EGFR) antagonists Erbitux (cetuximab) and Vectibix (panitumumab) are newer biologic therapies that may also be used as part of initial therapy. KRAS gene mutation status is predictive of poor response to Erbitux and Vectibix. Stivarga is not yet included in the current version of the NCCN guidelines. Zaltrap (ziv-aflibercept), a novel VEGF inhibitor, was also recently approved for the treatment of metastatic colorectal cancer in patients who have been previously treated with other therapies.

Stivarga was evaluated in a trial that randomized 760 patients with previously treated metastatic colorectal cancer to receive 160 mg of regorafenib orally once daily (n=505) plus Best Supportive Care (BSC) or placebo (n=255) plus BSC for the first 21 days of each 28-day cycle. Stivarga was administered with a low-fat breakfast that contained less than 30% fat. Treatment continued until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall survival (OS); supportive efficacy outcome measures included progression-free survival (PFS); and objective tumor response rate.

History of KRAS evaluation was reported for 729 (96%) patients; 430 (59%) of these patients were reported to have KRAS mutation. All patients received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, and with bevacizumab. Patients received a median of three prior lines of therapy for metastatic disease.

The median OS for Stivarga with BSC was 6.4 months compared to 5.0 months for placebo with BSC. Stivarga also improved PFS (2.0 vs. 1.7 months) and overall response rate (1% vs. 0.4%) as compared to placebo.

Warnings and precautions include hepatotoxicity, hemorrhage, dermatological toxicity, hypertension, cardiac ischemia and infarction, reversible posterior leukoencephalopathy syndrome, gastrointestinal perforation or fistulae, and wound healing complications. The Stivarga label contains a Boxed Warning alerting patients and health care professionals that severe and fatal liver toxicity occurred in patients treated with Stivarga during clinical studies.

The most common side effects of Stivarga are asthenia/fatigue, decreased appetite and food intake, hand-foot skin reaction (HFSR) [palmar-plantar erythrodysesthesia (PPE)], diarrhea, mucositis, weight loss, infection, hypertension, and dysphonia. Stivarga is Pregnancy Category D and can cause fetal harm when administered to a pregnant woman. Avoid concomitant use of strong CYP3A4 inducers (e.g. rifampin, phenytoin, carbamazepine, phenobarbital, and St. John's Wort) and strong CYP3A4 inhibitors (e.g. clarithromycin, grapefruit juice, itraconazole, ketoconazole, posaconazole, telithromycin, and voriconazole).

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REGORAFENIB

FDA APPROVED INDICATIONS

Stivarga is a kinase inhibitor indicated for the treatment of patients with:

- Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy.
- Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.

Anti-VEGF therapies approved for the treatment of colorectal cancer include Avastin and Zaltrap.
Anti-EGFR therapies approved for the treatment of colorectal cancer include Erbitux and Vectibix.

REFERENCES

- Stivarga [Prescribing Information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc, February 2013.
- National Comprehensive Cancer Network. Colon Cancer Guideline Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf [Accessed October 1, 2012].
- National Comprehensive Cancer Network. Rectal Cancer Guideline Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf [Accessed October 1, 2012].
- American Cancer Society. Colorectal Cancer Overview. Available at: http://www.cancer.org/Cancer/ColonandRectumCancer/OverviewGuide/colorectal-cancer-overview-what-is-colorectal-cancer. [Accessed October 1, 2012].
- ClinicalTrials.gov. Study of Regorafenib as a 3rd-line or Greater Treatment for Gastrointestinal Stromal Tumors (GIST) (GRID). Available at: http://clinicaltrials.gov/ct2/show/NCT01271712?term=regorafenib&rank=19 [Accessed October 1, 2012].

Part D Effective: 07/01/13	Created: 10/12	
Commercial Effective: 07/01/13	Client Approval: 05/13	P&T Approval: 05/13

RIFAXIMIN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
RIFAXIMIN	XIFAXAN	20401		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient being treated for travelers' diarrhea (TD)?

   If yes, continue to #2.
   If no, continue to #4.

2. Is the patient at least 12 years old?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of traveler's diarrhea for patients at least 12 years old with a previous trial of ciprofloxacin or azithromycin, or a diagnosis of hepatic encephalopathy for patients at least 18 years old with trial of lactulose or concurrent lactulose therapy.

3. Has the patient had a previous trial of ciprofloxacin or azithromycin?

   If yes, **approve 200mg strength tablets for one fill by GPID with a quantity limit of #9.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of traveler's diarrhea for patients at least 12 years old with a previous trial of ciprofloxacin or azithromycin, or a diagnosis of hepatic encephalopathy for patients at least 18 years old with trial of lactulose or concurrent lactulose therapy.

4. Is the patient being treated for the prevention or treatment of hepatic encephalopathy (HE)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of traveler's diarrhea for patients at least 12 years old with a previous trial of ciprofloxacin or azithromycin, or a diagnosis of hepatic encephalopathy for patients at least 18 years old with trial of lactulose or concurrent lactulose therapy.

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GUIDELINES FOR USE (CONTINUED)

5. Has the patient had a trial of lactulose or currently on lactulose monotherapy?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of traveler's diarrhea for patients at least 12 years old with a previous trial of ciprofloxacin or azithromycin, or a diagnosis of hepatic encephalopathy for patients at least 18 years old with trial of lactulose or concurrent lactulose therapy.

6. Is the patient at least 18 years old?

   If yes, **approve 550mg strength tablets for 12 months by GPID with a quantity limit of #60 tablets per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of traveler's diarrhea for patients at least 12 years old with a previous trial of ciprofloxacin or azithromycin, or a diagnosis of hepatic encephalopathy for patients at least 18 years old with trial of lactulose or concurrent lactulose therapy.

RATIONALE

To ensure appropriate utilization of Xifaxan for traveler's diarrhea (TD) and hepatic encephalopathy (HE).

In 2001, the ACG developed practice guidelines for the diagnosis and treatment of HE. Pharmacological treatment was recommended to reduce the nitrogenous load in patients with HE. Lactulose was recommended as the first line agent and that remains the recommendation today. Neomycin and metronidazole are listed as alternative agents when lactulose is ineffective or not tolerated. However, these antibiotics can be associated with adverse effects when administered over a long period of time. Rifaximin was not mentioned in the guidelines. The guidelines also state that flumazenil and bromocriptine may have a therapeutic role in select patients. Xifaxan is FDA approved for HE at 550mg twice daily.

Xifaxan is FDA approved for TD at 200mg three times daily for 3 days. Infectious Diseases Society of America (IDSA) 2006 Guidelines recommend the following agents for prophylaxis: bismuth subsalicylate (tablets 4 times daily), norfloxacin (400mg daily) ciprofloxacin (500mg daily), or rifaximin (200mg daily or twice daily). For antibiotic treatment they recommend the following with a duration of 1 to 3 days: norfloxacin (400mg twice daily), ciprofloxacin (500mg twice daily), ofloxacin 200mg twice daily), levofloxacin (500mg daily), azithromycin (1000mg once), or rifaximin (200mg three times daily).

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RATIONALE (CONTINUED)
Xifaxan (550mg three times daily for 2 weeks) was studied for the treatment of irritable bowel syndrome (IBS). The FDA issued a complete response letter for this indication, requiring additional information on retreatment. The 2009 ACG Position Statement suggests several agents for the treatment of IBS including psyllium, polyethylene glycol, loperamide, neomycin, Lotronex (alosetron), Amitiza (lubiprostone), and low dose TCAs.

FDA APPROVED INDICATIONS
Xifaxan 200mg is indicated for the treatment of patients 12 years of age and older with travelers' diarrhea caused by non-invasive strains of *Escherichia coli*.

Limitation of use: Xifaxan tablets should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli*.

Xifaxan 550mg is indicated for reduction in risk of overt hepatic encephalopathy in adult patients 18 years of age and older.

Diarrhea evidence favors efficacy based on 121 patients. (Della Marchina M, Renzi G, & Palazzini E: Infectious diarrhea in the aged: controlled clinical trial of rifaximin. Chemioterapia 1988; 7:336-340.)

Diverticular disease evidence favors efficacy based on 108 patients (Giaccari S, Tronci S, Falconieri M, et al: Long-term treatment with rifaximin and lactobacilli in post-diverticulitis stenosis of the colon. Eur Rev Med Pharmacol Sci 1993; 15:29-34.)

Irritable bowel syndrome without constipation evidence favors efficacy (TARGET 1 and TARGET 2, n=1260) (Pimentel H, Lembo A, Chey W, et al: Rifaximin therapy for patients with Irritable Bowel Syndrome without constipation. N Engl J Med 2011; 364(1):22-32.)

REFERENCES
- Salix Pharmaceuticals, Inc. Xifaxan package insert. Morrisville, NC. November 2010.
- Hill DR, Ericsson CD, Pearson RD et al. The Practice of Travel Medicine: Guidelines by the Infectious Diseases Society of America. Clinical Infectious Diseases 2006;43;1499-1539.
- Blei AT, Cordoba J. The Practice Parameters Committee of the American College of Gastroenterology. Hepatic Encephalopathy Practice Guidelines. Am J Gastroenterology. 2001 July; 96 (7): 1968-1976.
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare; Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 7 2011].

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REFERENCES (CONTINUED)

- Gerard L, Garey K and Dupont H. Rifaximin: a nonabsorbable rifamycin antibiotic for use in nonsystemic gastrointestinal infections. Expert Rev. Anti Infect. Ther 2005: 3(2): 201-211.
- Gasbarrini A, Lauritano EC Gabrielli M et al. Small Intestinal Bacterial Overgrowth: Diagnosis and Treatment. Dig Dis 2007: 25: 237-240.
- Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. N Engl J Med 2010; 362:1071-1081.
- Salix Pharmaceuticals, Inc. Salix Receives Anticipated FDA Complete Response Letter on Xifaxan 550mg Tablets Non-C IBS Supplemental New Drug Application. Available at: http://www.salix.com/news-media/news/index/salix-receives-anticipated-fda-complete-response-letter-on-xifaxan%C2%AE-550-mg-tablets-non-c-ibs-supplemental-new-drug-application.aspx. [Accessed July 7 2011].
- American College of Gastroenterology IBS Task Force. An Evidence-Based Position Statement on the Management of Irritable Bowel Syndrome. *American Journal of Gastroenterology* 2009; 104:S1-S7.
- Pimentel H, Lembo A, Chey W, et al: Rifaximin therapy for patients with Irritable Bowel Syndrome without constipation. *New England Journal of Medicine* 2011; 364(1):22-32.

Part D Effective: 02/07/13 Created: 02/05
Commercial Effective: N/A Client Approval: 01/13 P&T Approval: 11/12

RITUXIMAB

Generic	Brand	HICL	GCN	Exception/Other
RITUXIMAB	RITUXAN	16848	70151	

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have active rheumatoid arthritis?

   If yes, continue to #6.
   If no, continue to #2.

2. Is the patient being treated for Non Hodgkin's Lymphoma (NHL) in combination with chemotherapy and being supervised by an oncologist?

   If yes, **approve for #1 fill with end date 1 month from today.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist
   If no, continue to #3.

3. Is the patient being treated for Chronic Lymphocytic Leukemia (CLL) in combination with chemotherapy and being supervised by an oncologist?

   If yes, **approve up to #6 fills with end date 6 months from today.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist
   If no, continue to #4.

4. Is the patient diagnosed with Wegner's Granulomatosis (WG) or Microscopic Polyangiitis (MPA)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of; Non Hodgkin's Lymphoma, Chronic Lymphocytic Leukemia in combination with chemotherapy, rheumatoid arthritis, Wegner's Granulomatosis (WG), or Microscopic Polyangiitis (MPA) with concurrent glucocorticoid therapy.

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GUIDELINES FOR USE (CONTINUED)

5. Is the patient taking concurrent glucocorticoids (such as methylprednisone or prednisone)?

   If yes, **approve for #4 fills with end date 1 month from today.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval for the treatment of Wegner's Granulomatosis (WG) or Microscopic Polyangiitis (MPA) requires concurrent glucocorticoid therapy.

6. Has the treatment been prescribed by or is it being supervised by a rheumatologist?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation of therapy or supervision by a rheumatologist.

7. Has the patient been treated with this agent before or had a previous prior authorization?

   If yes, continue to #10.
   If no, continue to #8.

8. Is the patient currently on methotrexate?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Approval requires concomitant therapy with methotrexate.

9. Is the patient intolerant to or has the patient failed at least one of the following TNF blockers: Enbrel, Humira, Remicade, Simponi, or Cimzia?

   If yes, **approve for #1 fill with end date 4 months from today.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist
   If no, do not approve.
   DENIAL TEXT: Approval requires a previous therapy trial with at least one of the following TNF blockers such as Enbrel, Humira, Remicade, Simponi, or Cimzia, which may also require a prior authorization.

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GUIDELINES FOR USE (CONTINUED)

10. Has the patient experienced or maintained at least a 20% improvement in tender joint count and swollen joint count?

    If yes, **approve for #1 fill with end date 4 months from today.**
    APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
    If no, do not approve.
    DENIAL TEXT: Renewal requires a 20% improvement in tender joint count and swollen joint count from baseline while on therapy.

RATIONALE
Ensure appropriate utilization of rituximab based on FDA approved indications.

FDA APPROVED INDICATION
Rituximab is a CD20-directed cytolytic antibody indicated for the treatment of patients with:
- Non-Hodgkin's Lymphoma (NHL)
- Chronic Lymphocytic Leukemia (CLL)
- Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to-severely-active RA who have inadequate response to one or more TNF antagonist therapies
- Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids

Limitations of Use: Not recommended for use in patients with severe, active infections.

REFERENCES
- Genentech. Rituxan product information, South San Francisco, CA. April 2011.

Part D Effective: 01/01/13 Created: 01/09
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

ROMIDEPSIN

Generic	Brand	HICL	GCN	Exception/Other
ROMIDEPSIN	ISTODAX	36898		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient being treated for cutaneous T-cell lymphoma (also known as Mycosis Fungoides/Sezary Syndrome)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cutaneous T-cell lymphoma and trial of Zolinza (vorinostat) or that the patient is unable to tolerate oral medications and at least one form of systemic therapy (for example, retinoids, interferons, denileukin diftitox, methotrexate, liposomal doxorubicin, gemcitabine, chlorambucil).

2. Has the patient tried or has a contraindication to Zolinza (vorinostat)?

   If yes, **approve for up to 12 months.**
   If no, continue to #3.

3. Is the patient able to tolerate oral medications?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cutaneous T-cell lymphoma and trial of Zolinza (vorinostat) or that the patient is unable to tolerate oral medications and at least one form of systemic therapy (for example, retinoids, interferons, denileukin diftitox, methotrexate, liposomal doxorubicin, gemcitabine, chlorambucil).
   If no, continue to #4.

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ROMIDEPSIN

GUIDELINES FOR USE (CONTINUED)

4. Has the patient tried at least one form of systemic therapy (see table below)?

   If yes, **approve for up to 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of cutaneous T-cell lymphoma and trial of Zolinza (vorinostat) or that the patient is unable to tolerate oral medications and at least one form of systemic therapy (e.g. retinoids, interferons, denileukin diftitox, methotrexate, liposomal doxorubicin, gemcitabine, chlorambucil).

RATIONALE
Ensure cost effective and appropriate utilization of Istodax. Istodax and Zolinza are both histone deacetylase (HDAC) inhibitors approved for cutaneous T-cell lymphoma. Zolinza is administered orally and Istodax is administered intravenously. NCCN recommends romidepsin as second-line therapy for relapsed or refractory peripheral T-Cell Lymphoma (PTCL).

FDA APPROVED INDICATIONS
Istodax is indicated for primary cutaneous T-cell lymphoma (CTCL), following at least one prior systemic therapy.

SYSTEMIC TREATMENT OPTIONS	
Retinoids (bexarotene, retinoic acid, isotretinoin, acitretin)	Chlorambucil (Leukeran)
Interferons (Intron A)	Pentostatin
Extracorporeal photopheresis	Etoposide (VePesid)
Denileukin diftitox (Ontak)	Cyclophosphamide (Cytoxan)
Methotrexate	Temozolomide (Temodar)
Liposomal doxorubicin (Doxil)	Bortezomib (Velcade)
Gemcitabine (Gemzar)	

REFERENCES

- Gloucester Pharmaceuticals, Istodax product information. Cambridge, MA. November 2009.
- Merck Sharp & Dohme Corp, Zolinza product information. Whitehouse Station, NJ. February 2010.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 27, 2011].
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. Version 3.2011.

Part D Effective: 10/01/13 Created: 02/10
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 11/12

ROMIPLOSTIM

Generic	Brand	HICL	GCN	Exception/Other
ROMIPLOSTIM	NPLATE	35798		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient being treated for chronic immune (idiopathic) thrombocytopenia purpura (ITP)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic immune (idiopathic) thrombocytopenia purpura (ITP) AND a trial of corticosteroids or immunoglobulin (or an insufficient response to splenectomy).

2. Is the patient currently taking romiplostim as indicated on MRF, claims history, or prior authorization history?

   If yes, continue to #4.
   If no, continue to #3.

3. Did the patient have inadequate response to corticosteroids, immunoglobulins, or splenectomy?

   If yes, **approve #8 (250mcg or 500mcg) single-use vials per month x 2 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires either a trial of corticosteroids or immunoglobulins, or an insufficient response to a splenectomy as well as a diagnosis of chronic ITP.

4. Did the patient have a clinical response, as defined by an increase in platelet count to ≥ 50 X 10^9/L?

   If yes, **approve #8 (250mcg or 500mcg) single-use vials per month x 12 months.**
   If no, continue to #5.

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GUIDELINES FOR USE (CONTINUED)

5. Did the patient receive the maximum dose of 10mcg/kg for 4 consecutive weeks?

   If yes, do not approve.
   DENIAL TEXT: Renewal requires a clinical response after 4 weeks at maximum dosing.
   If no, **approve #8 (250mcg or 500mcg) single-use vials per month x 1 month.**

RATIONALE
To ensure safe and appropriate utilization of NPlate.

Maximum Dosage Limits based on 100kg patient:
Adults: 10mcg/kg/week.
Elderly: 10mcg/kg/week.
Adolescents and Children: Safety and efficacy have not been established.

FDA APPROVED INDICATIONS
NPlate is indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. NPlate should be used in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. NPlate should not be used in an attempt to normalize platelet counts.

NOTE: NPlate is available only through a restricted distribution program called NPlate NEXUS (Network of Experts Understanding and Supporting NPlate and Patients) Program. Only prescribers and patients registered in the NEXUS program can receive, prescribe, or administer NPlate. NPlate NEXUS Program, 1-877-675-2831.

REFERENCES
- Amgen Inc. NPlate package insert. Thousand Oaks, CA. January 2011.
- Thomson Healthcare. Romiplostim. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 30, 2011].

Part D Effective: 01/01/13 Created: 10/08
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

RUXOLITINIB

Generic	Brand	HICL	GCN	Exception/Other
RUXOLITINIB	JAKAFI	38202		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of intermediate or high-risk myelofibrosis, such as primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of intermediate or high-risk myelofibrosis, such as primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis.

2. Has the patient been taking the requested medication for at least 6 months?

   If yes, continue to #3.
   If no, **approve for 6 months #2 tablets per day by HICL.**

3. Did the patient experience or maintain symptom improvement [such as a 50% or greater reduction in total symptom score on the modified Myelofibrosis Symptom Assessment Form (MFSAF) v2.0], 50% or greater reduction in palpable spleen length, or spleen reduction of 35% or greater from baseline spleen volume after 6 months of therapy?

   If yes, **approve for 12 months #2 tablets per day by HICL**
   If no, do not approve.
   DENIAL TEXT: Renewal requires symptom improvement [such as a 50% or greater reduction in total symptom score on the modified Myelofibrosis Symptom Assessment Form (MFSAF) v2.0], 50% or greater reduction in palpable spleen length, or spleen reduction of 35% or greater from baseline spleen volume after 6 months of therapy.

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RUXOLITINIB

RATIONALE

Promote appropriate utilization and dosing of Jakafi for its FDA approved indication of intermediate or high-risk myelofibrosis.

The recommended starting dose of Jakafi is based on platelet count. Jakafi is dosed twice daily: patients with a platelet count greater than or equal to 125 X 10^9/L are recommended to start at 20mg twice daily, while those with a platelet count from 100 X 10^9/L to 200 X 10^9/L should start at 15mg twice daily. The maximum recommended dose is 25mg twice daily. If platelet count falls to less than 50 X10^9/L treatment should be interrupted and restarted between 5mg twice daily and 20mg twice daily depending on current platelet count.

The modified Myelofibrosis Symptom Assessment Form MFSAF is a daily diary capturing the core symptoms of myelofibrosis (abdominal discomfort, pain under left ribs, night sweats, itching, bone/muscle pain and early satiety). Symptom scores ranged from 0 to 10 with 0 representing symptoms “absent” and 10 representing “worst imaginable” symptoms. These scores were added to create the daily total score, which has a maximum of 60.

FDA APPROVED INDICATIONS

Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis.

REFERENCES

- Incyte Corporation. Jakafi package insert. Wilmington, DE. November 2011.

Part D Effective: 01/01/13	Created: 12/11	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

SOMATROPIN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
SOMATROPIN	GENOTROPIN HUMATROPE NUTROPIN NUTROPIN AQ NUTROPIN AQ NUSPIN NORDITROPIN NORDITROPIN FLEXPRO NORDITROPIN NORDIFLEX OMNITROPE SAIZEN SEROSTIM TEV-TROPIN ZORBTIVE	02824		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is Somatropin being prescribed for athletic enhancement or anti-aging purposes?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that Somatropin not be used for athletic enhancement or anti-aging purposes.
   If no, continue to #2.

2. Is the medication being prescribed by an endocrinologist?

   If yes, **approve for 12 months.**
   If no, continue to #3.

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GUIDELINES FOR USE (CONTINUED)

3. Does the patient have one of the following:

   - Growth failure due to chronic renal insufficiency (CRI), continue to #4.
   - HIV/AIDS-wasting syndrome, continue to #8.
   - Short-bowel syndrome, continue to #13.
   - Idiopathic Short Stature, **approve for 12 months.**

   If yes, continue as indicated above.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of growth failure due to chronic renal insufficiency (CRI), HIV/AIDS-wasting syndrome, or short-bowel syndrome, and for patients with growth hormone deficiency (GHD), idiopathic short stature, small for gestational age (SGA), Turner Syndrome, Prader Willi Syndrome, Noonan Syndrome, or SHOX deficiency growth hormone therapy must be supervised by an endocrinologist.

4. Has the patient undergone renal transplantation?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that Somatropin is used for chronic renal insufficiency up to the time of renal transplantation.
   If no, continue to #5.

5. Is the patient's epiphysis closed (as confirmed by radiograph of the wrist and hand)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that Somatropin not be used in pediatric patients with closed epiphyses.
   If no and induction, continue to #6.
   If no and renewing, continue to #7.

6. Is the patient's height at ≥ 2 standard-deviations (SD) below the mean height for normal children of the same age and gender?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval requires the height standard deviation score is -2 or lower.

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GUIDELINES FOR USE (CONTINUED)

7. Does the patient have one or more of the following:

   - A lack of response defined as gain of growth velocity by ≤ 2cm compared with that observed during the previous year;
   - Patient has reached 50th percentile for target height following growth hormone therapy?

   If yes, do not approve.
   DENIAL TEXT: Renewal requires a gain of growth velocity by greater than or equal to 2cm or patient has not reached a target height within the 50th percentile.
   If no, **approve for 12 months.**

8. Is the patient on antiviral therapy?

   If yes, continue to #9.
   If no, do not approve.
   DENIAL TEXT: Approval requires patient is being treated with HIV antiviral therapy concurrently.

9. Does the patient meet one of the following criteria:

   - 10% unintentional weight loss over 12 months
   - 7.5% unintentional weight loss over 6 months
   - 5% body cell mass (BCM) loss within 6 months
   - In men: BCM <35% of total body weight and body mass index (BMI) <27kg/m^2
   - In women: BCM <23% of total body weight and BMI <27kg/m^2
   - BMI <20kg/m^2

   If yes, continue to #10.
   If no, do not approve.
   DENIAL TEXT: Approval requires that patient must have exhibited signs of HIV wasting.

10. Is the patient currently using this drug?

    If yes, continue to #12.
    If no, continue to #11.

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GUIDELINES FOR USE (CONTINUED)

11. Has the patient had an inadequate response to previous therapy (i.e., exercise training, nutritional supplements, appetite stimulants or anabolic steroids)?

    If yes, **approve for 3 months.**
    If no, do not approve.
    DENIAL TEXT: Approval requires an inadequate response to previous therapy such as exercise training, nutritional supplements, appetite stimulants or anabolic steroids.

12. Has the patient shown a net clinical benefit from growth hormone replacement therapy, such as an increase in body weight of at least 1.5kg or an increase in lean body mass of at least 3kg?

    If yes, **approve for an additional 3 months.**
    If no, do not approve.
    DENIAL TEXT: Approval requires an increase in clinical benefits such as an increase in muscle mass and weight.

13. Is the patient currently on specialized nutritional support (i.e. consisting of a high carbohydrate, low-fat diet)?

    If yes, continue to #14.
    If no, do not approve.
    DENIAL TEXT: Approval requires concurrent specialized nutritional support (high carbohydrate, low fat diet).

14. Is this initial therapy for the patient or renewal?

    If initial therapy, **approve for 4 weeks.**
    If renewal, do not approve.
    DENIAL TEXT: Approval requires that Somatropin not be administered for more than 4 weeks in patients with short bowel syndrome because it has not been adequately studied.

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SOMATROPIN (PART D)

RATIONALE
Ensure appropriate use of growth hormones with respect to evidence based guidelines.

FDA APPROVED INDICATIONS
GENOTROPIN is indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in of either adult or child onset. **Adult Onset:** Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. **Childhood Onset:** Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. Genotropin is also indicated for pediatric patients for the treatment of inadequate secretion of endogenous growth hormone, growth failure due to Prader-Willi syndrome, growth failure in children born small for gestational age who fail to manifest catch-up growth by the age of 2, for growth failure associated with Turner syndrome in patients with open epiphyses and for idiopathic short stature (ISS).

HUMATROPE is indicated for **Pediatric Patients:** Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature, SHOX deficiency, and failure to catch up in height after small for gestational age birth. **Adult Patients:** Treatment of adults with either childhood-onset or adult-onset GH deficiency.

NORDITROPIN, FLEXPRO, AND NORDIFLEX are indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, the treatment of children with short stature born small for gestational age (SGA) with no catch up growth by age 2-4 years and for the replacement of endogenous growth hormone in adults with growth hormone deficiency either alone, or associated with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or childhood onset: patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

NUTROPIN, NUTROPIN AQ, NUTROPIN AQ NUSPIN are indicated in the replacement of endogenous growth hormone in adults with growth hormone deficiency in either adult or child onset. **Adult Onset:** Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary diseases, hypothalamic disease, surgery, radiation therapy, or trauma. **Childhood Onset:** Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired or idiopathic causes. These are also indicated in pediatric patients for the treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone for the treatment of short stature associated with Turner syndrome, for the treatment of idiopathic short stature, and for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation.

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SOMATROPIN (PART D)

FDA APPROVED INDICATIONS (CONTINUED)
OMNITROPE is indicated for the treatment of pediatric and adult growth hormone deficiency

SAIZEN is indicated for the treatment of pediatric and adult growth hormone deficiency.

SEROSTIM is indicated in the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight and improve physical endurance with concomitant antiretroviral therapy.

TEV-TROPIN is indicated for the treatment of children who have growth hormone failure due to an inadequate secretion of normal endogenous growth hormone.

ZORBTIVE is indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support.

REFERENCES

- American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. Endocr Pract 2003; 9(1):64-76.
- Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCE & M 2000; 85(11):3990-3.
- Bengtsson B, et al. Treatment of Growth Hormone Deficiency in Adults. JCE & M 2000; 85(3): 933-42.
- Wilson, T et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003; 143:314-21.
- National Kidney Foundation (2000). Clinical practice guidelines for nutrition in chronic renal failure. Available at: www.kidney.org/professionals/kdoqi/guidelines_updates/nut_p10.html. [Accessed July 21, 2009].
- Vance M, Mauras N. Growth hormone therapy in adults and children. NEJM 1999; 341(16):1206-16.
- Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clinical Infectious Disease 2003; 36:S69-78.
- Corcoran C, Grinspoon S. Treatments for Wasting in Patients with the Acquired Immunodeficiency Syndrome. NEJM 1999; 340:1740-50.
- Hintz R, et al. Effect of Growth Hormone Treatment on Adult Height of Children with idiopathic Short Stature. NEJM 1999; 340:502-7.
- Haffner D, et al. Effect of Growth Hormone Treatment on the Adult Height of Children with Chronic Renal Failure. NEJM 2000; 343:923-30.
- Weiming Z, Ning L, Jieshou L. Effect of Recombinant Human Growth Hormone and Enteral Nutrition on Short Bowel Syndrome. JPEN 2004; 28(6): 377-81.

CONTINUED ON NEXT PAGE

REFERENCES (CONTINUED)

- Vetter Pharma-Fertigung GmBH & Co. KG. Genotropin package insert. Ravensburg, Germany. August 2009.
- Eli Lilly and Company. Humatrope package insert. Indianapolis, IN. August 2009.
- Novo Nordisk, Inc. Norditropin package insert. Princeton, NJ. March 2010.
- Genentech, Inc. Nutropin package insert. South San Francisco, CA. June 2006.
- Genentech, Inc. Nutropin AQ package insert. South San Francisco, CA. January 2008.
- EMD Serono, Inc. Saizen package insert. Rockland, MA. September 2007.
- EMD Serono, Inc. Serostim package insert. Rockland, MA. September 2007.
- Bio-Technology General (Israel) LTD. Tev-Tropin package insert. Be'er Tuvia, Israel. October 2007.
- EMD Serono, Inc. Zorbtive package insert. Rockland, MA. March 2009.
- Sandoz GmbH. Omnitrope package insert. Austria. June 2010.

Part D Effective: 01/01/13 Created: 05/04
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

SORAFENIB

Generic	Brand	HICL	GCN	Exception/Other
SORAFENIB TOSYLATE	NEXAVAR	33400		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, **approve for 12 months with a quantity limit of #4 per day.**
   If no, continue to #2.

2. Does the patient have a diagnosis of unresectable hepatocellular carcinoma?

   If yes, **approve for 12 months with a quantity limit of #4 per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC) or unresectable hepatocellular carcinoma.

RATIONALE
Ensure appropriate utilization of sorafenib based on FDA approved indication and NCCN guidelines.

FDA APPROVED INDICATION
Sorafenib is indicated for the treatment of unresectable hepatocellular carcinoma and advanced renal cell carcinoma.

REFERENCES

- Bayer HealthCare Pharmaceuticals Inc. Nexavar package insert. Wayne, NJ. November 2010.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. (Version 1.2011).
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 2.2011).

Part D Effective: 01/01/13 Created: 05/11
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

SUNITINIB

Generic	Brand	HICL	GCN	Exception/Other
SUNITINIB MALATE	SUTENT	33445		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, **approve for 12 months and enter up to three authorizations by GPID for the strengths requested as follows:**
   - **Sutent 12.5mg: #1 per day and**
   - **Sutent 25mg: #1 per day and**
   - **Sutent 50mg: #1 per day.**

   If no, continue to #2.

2. Does the patient have a diagnosis of gastrointestinal stromal tumor (GIST)?

   If yes, continue to #3.
   If no, continue to #4.

3. Has the patient previously tried or does the patient have a contraindication to imatinib mesylate (Gleevec)?

   If yes, **approve for 12 months and enter up to three authorizations by GPID for the strengths requested as follows:**
   - **Sutent 12.5mg: #1 per day and**
   - **Sutent 25mg: #1 per day and**
   - **Sutent 50mg: #1 per day.**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC), pancreatic neuroendocrine carcinoma (PNET) or gastrointestinal stromal tumor (GIST) following a trial of Gleevec, which may also require a prior authorization.

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GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of pancreatic neuroendocrine carcinoma (PNET)?

   If yes, **approve for 12 months and enter two authorizations by GPID as follows:**
   - **Sutent 12.5mg: #1 per day and**
   - **Sutent 25mg: #1 per day.**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC), pancreatic neuroendocrine carcinoma (PNET) or gastrointestinal stromal tumor (GIST) following a trial of Gleevec, which may also require a prior authorization.

RATIONALE
Ensure appropriate utilization of sunitinib based on FDA approved indication and NCCN guidelines.

FDA APPROVED INDICATION
Sunitinib is indicated for the treatment of gastrointestinal stromal tumor after disease progression or intolerance to imatinib mesylate. It is also indicated for the treatment of advanced renal cell carcinoma.

REFERENCES
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 2.2011).
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Neuroendocrine Tumors. (Version 1.2011).
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Soft Tissue Sarcoma. (Version 1.2011).
- Pfizer Labs. Sutent package insert. New York, NY. July 2010.

Part D Effective: 01/01/13	Created: 05/11	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

TADALAFIL (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TADALAFIL	CIALIS		20736 99409	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Benign Prostatic Hyperplasia (BPH)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Benign Prostatic Hyperplasia (BPH) and a trial of a formulary alpha blocker (e.g., doxazosin, terazosin, or tamsulosin) AND finasteride.

2. Has the patient tried a formulary alpha blocker (e.g., doxazosin, terazosin, or tamsulosin) AND finasteride?

   If yes, **approve Cialis 2.5mg or 5mg (whichever is requested) for 12 months with a quantity limit of 30 per month by GPID.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of Benign Prostatic Hyperplasia (BPH) and a trial of a formulary alpha blocker (e.g., doxazosin, terazosin, or tamsulosin) AND finasteride.

RATIONALE
To limit the coverage of Cialis to the CMS covered indication of benign prostatic hyperplasia (BPH) and exclude coverage for erectile dysfunction (ED). The recommended dose for the treatment of BPH is 5mg daily. A starting dose of 2.5mg daily is recommended for patients with a creatine clearance of 30 to 50mL/min.

FDA APPROVED INDICATIONS
Cialis is indicated for the treatment of ED, the signs and symptoms of BPH, and ED and the signs and symptoms of BPH. Cialis may be administered once daily or on an as needed basis for the treatment of ED. For the treatment of BPH, Cialis is recommended to be administered on a daily basis.

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TADALAFIL (PART D)

REFERENCES

- AUA practice guidelines Committee. AUA guideline on management of benign prostatic hyperplasia. Chapter 1: Guideline on the Management of Benign Prostatic Hyperplasia. 2010: American Urological Association Education and Research, Inc.
- Eli Lilly and Company. Cialis package insert. Indianapolis, IN. October 2011.
- MICROMEDEX® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare; Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 8, 2010].

Part D Effective: 01/01/13	Created: 11/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

TEDUGLUTIDE

Generic	Brand	HICL	GCN	Exception/Other
TEDUGLUTIDE	GATTEX	39890		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Short Bowel Syndrome (SBS)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 18 years of age with a diagnosis of Short Bowel Syndrome (SBS) that is dependent on intravenous parenteral nutrition, defined as requiring parenteral nutrition at least three times per week.

2. Is the patient dependent on intravenous parenteral nutrition, defined as requiring parenteral nutrition at least three times per week?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 18 years of age with a diagnosis of Short Bowel Syndrome (SBS) that is dependent on intravenous parenteral nutrition, defined as requiring parenteral nutrition at least three times per week.

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GUIDELINES FOR USE (CONTINUED)

3. Is the patient at least 18 years old?

   If yes, **approve as follows:**

   - **For Commercial members:**
     Approve for 12 months by NDC as follows:
     - **Gattex 5 mg one vial kit: quantity limit of #30 per 30 days or,**
     - **Gattex 5 mg thirty vial kit: quantity limit of #1 per 30 days**

   - **For Part D members:**
     Approve for 12 months by NDC.

   If no, do not approve.
   DENIAL TEXT: Approval requires the patient to be at least 18 years of age with a diagnosis of Short Bowel Syndrome (SBS) that is dependent on intravenous parenteral nutrition, defined as requiring parenteral nutrition at least three times per week.

RATIONALE
To ensure appropriate use of Gattex based on FDA approved indication.

The recommended daily dose of Gattex is 0.05mg/kg body weight administered by subcutaneous injection once daily. Gattex should not be administered intravenously or intramuscularly. Patients should be advised to alternate sites of injection. Recommended sites of administration include: thighs, arms and quadrants of the abdomen. Missed doses should be taken as soon as possible that day but patients should not take 2 doses on the same day.

A 50% dose reduction is recommended in patient with moderate and severe renal impairment (creatine clearance < 50ml/min) and ESRD. There is potential for increased absorption of concomitant oral medications, which should be considered if these drugs require titration or have a narrow therapeutic index.

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RATIONALE (CONTINUED)
Gattex is the first GLP-2 analog indicated for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support. SBS is a condition that results from the partial or complete surgical removal of the small and/or large intestine. A normal human small intestine ranges between 3 and 8 m in length. SBS is defined in adults as < 200cm of small intestine. Extensive loss of the small intestine can lead to poor absorption of fluids and nutrients from food needed to sustain life. As a result, patients with SBS often receive parenteral nutrition. The number of patients with SBS in the United States is unknown but extrapolating from European data the estimated incidence is 2 per million individuals.

Teduglutide is an analog of naturally occurring human glucagon-like peptide-2 (GLP-2), a peptide secreted by L-cells of the distal intestine. GLP-2 is known to increase intestinal and portal blood flow, and inhibit gastric acid secretion. Teduglutide binds to the glucagon-like peptide-2 receptors located in intestinal subpopulations of enteroendocrine cells, subepithelial myofibroblasts and enteric neurons of the submucosal and myenteric plexus. Activation of these receptors results in the local release of multiple mediators including insulin-like growth factor (IGF)-1, nitric oxide and keratinocyte growth factor (KGF).

Gattex joins two other agents that are FDA approved for SBS. Zorbtive [somatropin (rDNA origin)] was approved in 2003 and is a human growth hormone (hGH) produced by recombinant DNA technology. Intestinal mucosa contains receptors for growth hormone and for insulin-like growth factor-I (IGF-I), which is known to mediate many of the cellular actions of growth hormone. Thus, the actions of growth hormone on the gut may be direct or mediated via the local or systemic production of IGF. In human clinical studies the administration of growth hormone has been shown to enhance the transmucosal transport of water, electrolytes, and nutrients. NutreStore (glutamine) was approved in 2004 and is an amino acid indicated for the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication. Another differentiating factor besides mechanism of action of these agents is duration of use. Administration over 4 weeks has not been studied for Zorbtive whereas Gattex has been studied out to 1 ½ years.

Gattex was approved based on the evaluation of two clinical trials and two extension studies.

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RATIONALE (CONTINUED)
Study 1 was a randomized, double-blind, placebo-controlled, parallel-group, multi-national, multi-center clinical trial in n=86 adults with SBS who were dependent on parenteral nutrition/intravenous (PN/I.V.) support for at least 12 months and required PN at least 3 times per week. Optimization and stabilization of PN/IV fluid volumes were achieved before randomization to treatment (Gattex 0.05mg/kg/day) or placebo. Gattex was administered subcutaneously once daily for 24 weeks. The primary endpoint was defined as a subject achieving at least 20% reduction in weekly PN/I.V. volume from baseline (prior to randomization) to both 20 and 24 weeks. At week 24 the mean reduction in weekly PN/I.V. volume was 4.4 Liters for Gattex-treated subjects (from pre-treatment baseline of 12.9 Liters) versus 2.3 Liters for placebo-treated subjects (from pre-treatment baseline of 13.2 Liters/week) ($p<0.001$). Twenty-one subjects on Gattex (53.8%) versus 9 on placebo (23.1%) achieved at least a one-day reduction in PN/I.V. support. Study 2 was the ongoing two-year open-label extension of Study 1. The extension study demonstrated continuous response after one year, further reductions in parenteral support as well as the ability for a small number of patients to discontinue PN/I.V. support.

Study 3 was similar to Study 1 in terms of design and the patient inclusion criteria. After similar optimization and stabilization as in Study 1, subjects were randomized for 24 weeks to either Gattex 0.05mg/kg/day (n=35), Gattex 0.10 mg/kg/day (n=32), or placebo (n=16). The high dose of Gattex 0.10mg/kg/day did not reach statistical significance. Further evaluation of PN/I.V. volume reduction using the endpoint of response (defined as at least 20% reduction in PN/I.V. fluid from Baseline to Weeks 20 and 24) showed that 46% of subjects on Gattex 0.05 mg/kg/day responded versus 6% on placebo. Subjects on Gattex at both dose levels experienced a 2.5 L/week reduction in parenteral support requirements versus 0.9 L/week for placebo at 24 weeks. Two subjects in the Gattex 0.05 mg/kg/day dose group were weaned off parenteral support by Week 24. Study 4 was a blinded, uncontrolled extension of Study 3 with n=65 subjects. Subjects were treated for an additional 28 weeks. Of responders in Study 3 who entered Study 4, 75% sustained response on Gattex after one year of treatment. The mean reduction of weekly PN/I.V. volume was 4.9 L/week (52% reduction from baseline) after one year of continuous Gattex treatment.

Gattex has warnings and precautions that include neoplastic growth, colorectal polyps, intestinal obstruction, biliary and pancreatic disease and fluid overload. Patients may also experience an increase of absorption of concomitant oral medications.

The most commonly reported adverse drug reactions (≥10%) are abdominal pain, injection site reactions, nausea, headaches, abdominal distension and upper respiratory tract infection. A 50% dose reduction is recommended in patient with moderate and severe renal impairment (creatinine clearance < 50ml/min) and ESRD. Gattex is pregnancy category B; no well-controlled studies have been conducted in pregnant women.

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RATIONALE (CONTINUED)
Immunogenicity was seen in patients on Gattex and increased in incidence over time. Anti-Gattex antibodies did not appear to have an impact on efficacy or safety in patients who were treated up to 1.5 years, but long-term impact is unknown.

The FDA is requiring a REMS program for Gattex consisting of a communication plan and training for prescribers, and a post marketing study of SBS patients treated with the drug to evaluate future risk of colorectal cancer and other conditions.

FDA APPROVED INDICATIONS
Gattex (teduglutide [rDNA origin]) for injection is indicated for the treatment of adult patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

REFERENCES

- Gattex [Prescribing Information]. Bedminister, NJ: NPS Pharmaceutical; December 2012.
- Buchman, Alan L. Etiology and Initial Management of Short Bowel Syndrome. Gastroenterology; 2006; 130; S5-S15.
- Zorbtive [Prescribing Information]. Rockland, MA: EMD Serono, Inc.; November 2003.
- NutreStore [Prescribing Information]. Torrance, CA: Emmaus Medical, Inc.; 2010.
- FDA News Release. FDA approves Gattex to treat short bowl syndrome. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333171.htm [Accessed on Jan 28th, 2013].

Part D Effective: 07/01/13 Created: 02/13
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 02/13

TELAPREVIR (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TELAPREVIR	INCIVEK	37629		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the requested medication being used with ribavirin **AND** peginterferon alfa?
   Note: The patient must have an active prior authorization for peginterferon alfa before proceeding.

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not currently taking rifampin.

2. Is the patient currently taking the requested medication as indicated on the MRF, claims history, or prior authorization history?

   If yes, continue to #9.
   If no, continue to #3.

3. Does the patient have a diagnosis of chronic hepatitis C, genotype 1?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not currently taking rifampin.

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GUIDELINES FOR USE (CONTINUED)

4. Is the patient at least 18 years old?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not currently taking rifampin.

5. Is the patient currently supervised by a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (e.g. hepatologist), or specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not currently taking rifampin.

6. Has the patient completed a prior course of therapy with telaprevir (Incivek) or boceprevir (Victrelis) and not achieved a sustained virologic response (SVR)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient has not failed therapy with telaprevir (Incivek) or boceprevir (Victrelis). Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa. Approval requires that the patient is not currently taking rifampin.
   If no, continue to #7.

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GUIDELINES FOR USE (CONTINUED)

7. Is the patient currently taking rifampin?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient is not currently taking rifampin. Approval requires a diagnosis of chronic hepatitis C, genotype 1, a minimum age of 18 years old, current supervision by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist), and concurrent use of ribavirin and peginterferon alfa.
   If no, continue to #8.

8. Does the patient have coinfection with hepatitis B or have a history of a previous solid organ transplant?

   If yes, do not approve.
   DENIAL TEXT: Approval requires that the patient does not have coinfection with hepatitis B or have a history of a previous solid organ transplant.
   If no, **approve #6 tablets per day for 8 weeks.**
   PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = 6 tablets and a duration of 56 days.
   APPROVAL TEXT: Renewal requires HCV RNA level at baseline and at 4 weeks of telaprevir therapy (level 1,000 IU/mL or less). Drugs that are contraindicated with Incivek include alfuzosin, rifampin, ergot derivatives, cisapride, St. John's wort, atorvastatin, lovastatin, simvastatin, pimozide, sildenafil or tadalafil (when used for pulmonary arterial hypertension [PAH]), orally administered midazolam and triazolam.

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GUIDELINES FOR USE (CONTINUED)

9. **Renewal criteria for treatment week 9, the patient has an approved PA for telaprevir:** Did the patient have a HCV RNA level/viral load of 1,000 IU/mL or less at 4 weeks of telaprevir therapy?

   If yes, **approve #6 tablets per day for 4 weeks. Maximum of telaprevir therapy is not to exceed 12 weeks.**
   PAC: The days supply is based on the benefit structure. Enter the Maximum Daily Dose (MDD) = 6 tablets and a duration of 28 days; total telaprevir therapy duration not to exceed 84 days (12 weeks).
   APPROVAL TEXT: Drugs that are contraindicated with Incivek include alfuzosin, rifampin, ergot derivatives, cisapride, St. John's wort, atorvastatin, lovastatin, simvastatin, pimozide, sildenafil or tadalafil (when used for pulmonary arterial hypertension [PAH]), orally administered midazolam and triazolam.

   If no, do not approve.
   DENIAL TEXT: Renewal requires HCV RNA level/viral load of less than 1,000 IU/mL at 4 weeks of telaprevir therapy.

   CLINICAL SPECIALISTS: If HCV RNA level greater than 1,000 IU/mL at week 4, triple therapy will be discontinued at this time. Review the prior authorization history and close peginterferon PA (and ribavirin PA, if applicable).

   CLINICAL SPECIALISTS: Please review peginterferon/ribavirin dosing regimens:
   - For treatment-naïve and prior relapse patients with undetectable HCV-RNA at weeks 4 and 12, dual therapy is for a total treatment duration of 24 weeks.
   - For treatment-naïve and prior relapse patients with detectable (1,000 IU/mL or less) HCV-RNA at weeks 4 and/or 12, dual therapy is for a total duration of 48 weeks.
   - For prior partial and null responder patients dual therapy is for a total duration of 48 weeks.
   - For treatment-naïve patients with cirrhosis who have undetectable HCV-RNA levels at week 4 and 12, dual therapy for a total duration of 48 weeks would be beneficial.

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TELAPREVIR (PART D)

From the Incivek package insert (Vertex):

Table 1: Recommend Treatment Duration (See also Table 2 for Treatment Futility Rules)

Treatment-Naïve and Prior Relapse Patients			
HCV RNA*	**Triple Therapy** INCIVEK, peginterferon alfa and ribavirin	**Dual Therapy** Peginterferon alfa and ribavirin	**Total Treatment Duration**
Undetectable (Target Not Detected) at Weeks 4 and 12	First 12 weeks	Additional 12 weeks	24 weeks
Detectable (1000 IU/mL or less) at Weeks 4 and/or 12	First 12 weeks	Additional 36 weeks	48 weeks
Prior Partial and Null Responder Patients			
	Triple Therapy INCIVEK, peginterferon alfa and ribavirin	**Dual Therapy** Peginterferon alfa and ribavirin	**Total Treatment Duration**
All Patients	First 12 weeks	Additional 36 weeks	478 weeks

*In clinical trials, HCV RNA in plasma was measured using a COBAS® TaqMan® assay with a lower limit of quantification of 25 IU/mL and a limit of detection of 10 IU/mL. *See Laboratory Tests (5.6)* for a description of HCV-RNA assay recommendations.

Table 2: Treatment Futility Rules: All Patients

HCV RNA	**Action**
Week 4 or Week 12: Greater than 1000 IU/mL	Discontinue INCIVEK and peginterferon alfa and ribavirin (INCIVEK treatment complete at 12 weeks)
Week 24: Detectable	Discontinue peginterferon alfa and ribavirin

If peginterferon alfa or ribavirin is discontinued for any reason, INCIVEK must also be discontinued.

RATIONALE

Ensure appropriate utilization of telaprevir based on FDA approved indication.

FDA APPROVED INDICATION

Incivek, in combination with peginterferon alfa and ribavirin, is indicated for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve (patients who have not received interferon-based drug therapy for their infection), or who have previously been treated with interferon-based treatment and not responded adequately, including prior null responders, partial responders, and relapsers.

FDA APPROVED DOSAGE

Incivek 750mg (two 375mg tablets) orally three times daily is added to peginterferon alfa and ribavirin for the first twelve weeks of therapy.

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TELAPREVIR (PART D)

OTHER INFORMATION

Currently AASLD treatment guidelines recommend that any use of telaprevir in HIV-coinfected or transplant populations infected with HCV should be done with caution and under close clinical monitoring. A clinical trial evaluating use of telaprevir triple therapy in HCV/HIV co-infected patients showed significantly higher rates of SVR than in patients treated with peginterferon/ribavirin alone.

Note on HCV RNA levels defined by lab as undetectable versus detectable but not quantifiable: Commercially available quantitative HCV RNA assays may have differing limits for quantification and detection. The lower limit of detection is 10 or 50 IU/mL HCV RNA (depends on assay used by lab). The FDA suggests that labs testing HCV RNA levels for patients taking protease inhibitors must use an assay with a lower limit of quantification of 25 IU/mL or less, and a lower limit of detection of 10-15 IU/mL. Generally patients with detectable but not quantifiable levels of HCV RNA will have lower SVR rates with triple therapy; a detectable but not quantifiable HCV RNA level should not be considered equivalent to an undetectable level. When the product package insert (or MedImpact PA guideline) specifies "undetectable HCV RNA level", generally an undetectable HCV RNA result is required.

REFERENCES

- Arora S, Thornton K, Murata G, et al. Outcomes of Treatment for Hepatitis C Virus Infection by Primary Care Providers. NEJM 364; 23: 2199-2207.
- Dietrich D, et al. 19th Conference on Retroviruses and Opportunistic Infections (CROI): Abstract 47: Presented March 6, 2012.
- Ghany M, Nelson D, Strader D, Thomas D, and Seeff L. An Update on Treatment of Genotype I Chronic Hepatitis C Virus Infection: 2011 Practice Guidelines by the American Association for the Study of Liver Diseases. Hepatology 2011; 54 (4): 1433-1443. Accessed online March 9, 2012 at http://www.aasld.org/practiceguidelines/Documents/2011UpdateGenotype1HCVbyAASLD24641.pdf
- Harrington P, Zeng W, and Naeger L. Clinical relevance of detectable but not quantifiable hepatitis C virus RNA during boceprevir or telaprevir treatment. Hepatology 2012; Apr 55 (4): 1048-1057.
- Vertex Pharmaceuticals. Incivek package insert. Cambridge, MA. May 2011.

Part D Effective: 01/01/13	Created: 06/11	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

TEMOZOLOMIDE – IV (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TEMOZOLOMIDE	TEMODAR		17724	

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have one of the following diagnoses: metastatic melanoma, anaplastic astrocytoma, or glioblastoma multiforme?

   If yes, **approve by GPID for 12 months**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic melanoma, anaplastic astrocytoma, or glioblastoma multiforme.

RATIONALE
Approve for FDA approved indications of glioblastoma multiforme and anaplastic astrocytoma and CMS compendia recognized indication of metastatic melanoma. NCCN considers temozolomide to be a systemic therapy option for advanced or metastatic melanoma. No quantity limit is included within this guideline since there are multiple dosing regimens available, all of which are based on body surface area.

Oral Temodar is covered under Part B, while IV Temodar is covered under Part D.

FDA APPROVED INDICATIONS
Temodar is an alkylating drug indicated for the treatment of adult patients with:
- Newly diagnosed glioblastoma multiforme (GBM) concomitantly with radiotherapy and then as maintenance treatment.
- Refractory anaplastic astrocytoma patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

REFERENCES

- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology Melanoma. (Version 3.2012).
- Schering Corporation, a subsidiary of Merck & Co., Inc. Temodar package insert. Whitehouse Station, NJ. February 2011.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: January 24, 2012].

Part D Effective: 10/01/13 Created: 02/12
Commercial Effective: N/A Client Approval: 08/13 P&T Approval: 08/13

TERIFLUNOMIDE

Generic	Brand	HICL	GCN	Exception/Other
TERIFLUNOMIDE	AUBAGIO	39624		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis and a trial of Copaxone and an interferon such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone).

2. Has the patient tried or does the patient have a contraindication to interferon therapy such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone) **AND** Copaxone?

   If yes, **approve for 12 months by HICL with a quantity limit of #28 tablets per 28 days.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of relapsing-remitting, secondary-progressive or progressive-relapsing multiple sclerosis and a trial of Copaxone and an interferon such as Rebif (the interferons Avonex, Betaseron, and Extavia require prior use of Rebif and Copaxone).

RATIONALE
To ensure appropriate use of Aubagio consistent with FDA approved indication.

The recommended dose of Aubagio is 7 mg or 14 mg orally once daily, with or without food.

Aubagio is the second oral medication approved by the U.S. Food and Drug Administration (FDA) to treat relapsing forms of multiple sclerosis. It is an immunomodulatory agent that inhibits dihydroorotate dehydrogenase, an enzyme involved in pyrimidine synthesis. The drug reduces T- and B- cell activation, proliferation and function in response to auto antigens. Aubagio is the active metabolite of leflunomide, an agent used for rheumatoid arthritis, which has been on the market since 1998.

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RATIONALE (CONTINUED)

The relapsing remitting form of multiple sclerosis accounts for roughly 85% of the total multiple sclerosis population. Guidelines and consensus statements from the American Academy of Neurology and National Clinical Advisory Board of the National Multiple Sclerosis Society do not indicate preference of first line agents. Current first line treatments available for relapsing forms of multiple sclerosis include: interferon beta-1a (Avonex, Rebif), interferon beta-1b (Betaseron, Extavia), and glatiramer acetate (Copaxone).

The FDA approval of Aubagio stems from one large phase III study and another smaller phase III imaging study.

Study 1 (TEMSO) was a double-blind, placebo-controlled study that evaluated teriflunomide 7mg and 14mg versus placebo in 1088 patients with relapsing forms of multiple sclerosis over 108 weeks. Inclusion criteria included a definite diagnosis of MS and at least 1 relapse over the year preceding the trial or 2 relapses over the 2 years preceding the trial. MRI was performed at screening and at various time points thereafter. Upon entry to the trial, the patient's Expanded Disability Status Scale (EDSS) score was ≤ 5.5. The primary endpoint of the study was the annualized relapse rate (ARR).

The ARR was reduced in both the 7mg (ARR= 0.370) and 14mg (ARR=0.369) treatment arms compared with placebo (ARR= 0.539), which was statistically significant (p=0.0005 and p=0.0002, respectively). The disability progression measurement assessed by EDSS at week 108 was only statistically significant in the 14mg arm (20.2%) versus placebo (27.3%). MRI endpoints included median change from baseline in total lesion volume and mean number of Gd-enhancing T1-lesions per scan. Teriflunomide 7mg and 14 mg demonstrated statistically significant decreases in both lesion volume and fewer Gd-enhancing lesions versus placebo.

Study 2 was a randomized, double blind, placebo-controlled study in 179 patients treated for 36 weeks that further demonstrated the effects of teriflunomide on MRI activity. The primary endpoint of average number of unique active lesions per MRI scan was lower in the teriflunomide 7mg and 14mg arms (0.98, 1.06) compared to placebo (2.69; p=0.0052 and p=0.0234, respectively).

Aubagio has a black box warning for hepatotoxicity and risk of teratogenicity, and is contraindicated in patients with severe hepatic impairment and in pregnant women. Aubagio is classified as pregnancy category X. Women of childbearing potential must not be started on Aubagio until pregnancy is excluded and it has been confirmed that they are using reliable contraception.

Warnings and precautions include hepatotoxicity, bone marrow and immunosuppression, risk of infections, malignancy, peripheral neuropathy, acute renal failure, hyperkalemia, dermatological toxicity, increases in blood pressure, and respiratory disease. The most common side effects seen with Aubagio are ALT elevations, alopecia, diarrhea, influenza, nausea and paresthesia. Co-administration with leflunomide is contraindicated. Aubagio may increase levels of CYP2C8 substrates and oral contraceptives, and decrease levels of warfarin and CYP1A2 substrates.

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TERIFLUNOMIDE

FDA APPROVED INDICATIONS
Aubagio is indicated for the treatment of patients with the relapsing forms of multiple sclerosis.

REFERENCES

- Aubagio [Prescribing Information]. Cambridge, MA: Genzyme Corporation; September 2012.
- Goodin DS et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002;58(2):169-178.
- National Clinical Advisory Board of the National Multiple Sclerosis Society. MS Disease Management Consensus Statement. 2007. Available at: http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx [Accessed October 1, 2012].

Part D Effective: 07/01/13 Created: 10/12
Commercial Effective: 07/01/13 Client Approval: 05/13 P&T Approval: 05/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

TESTOSTERONE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TESTOSTERONE	ANDRODERM ANDROGEL AXIRON FORTESTA STRIANT TESTIM TESTOPEL	01403		
TESTOSTERONE CYPIONATE	DEPO-TESTOSTERONE	01400		
TESTOSTERONE ENANTHATE	DELATESTRYL	01401		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient a male and have a diagnosis of primary or secondary hypogonadism (hypotestosteronism or low testosterone)?

   If yes, continue to #2.
   If no, continue to #4.

2. Does the patient have a previously approved PA for testosterone or has the patient been on any form of testosterone replacement therapy as indicated on the MRF or claims history?

   If yes, continue to #6.
   If no, continue to #3.

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GUIDELINES FOR USE (CONTINUED)

3. Does the patient have one or more of the following laboratory values confirming low testosterone level:

   - total serum testosterone level of less than 300ng/dL, or
   - a low total serum testosterone level as indicated by a lab result, with a reference range, obtained within 90 days, or
   - a free serum testosterone level of less than 50ng/L (174 pmol/L)?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval criteria requires that the diagnosis of hypogonadism be accompanied by appropriate lab values such as: total serum testosterone level of less than 300ng/dL; or a low total serum testosterone level as indicated by a lab result, with a reference range, obtained within 90 days; or a free serum testosterone level of less than 50ng/L (174 pmol/L).

4. Is the patient a male and have a diagnosis of delayed puberty not secondary to a pathological disorder?

   If yes, continue to #6.
   If no, continue to #5.

5. Is the patient female and have a diagnosis of metastatic breast cancer?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of hypogonadism (primary or secondary), delayed puberty not secondary to a pathological disorder in a male patient, or metastatic breast cancer in a female patient.

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GUIDELINES FOR USE (CONTINUED)

6. **Approve for 12 months with appropriate quantity limits.**
   - **AndroGel 1% (testosterone):** 2.5 gram packet: up to 5 grams per day per 30 days; 5 gram packet: up to 10 grams per day per 30 days; or up to 4 x 75 gram pumps.
   - **AndroGel 1.62% (testosterone):** 1.25 gram packet: up to 1.25 grams per day per 30 days; 2.5 gram packet: up to 5 grams per day per 30 days; up to 2 x 75 gram pumps per 30 days.
   - **Androderm (testosterone):** 2mg patches: 30 patches per 30 days; 2.5mg patches: 60 patches per 30 days; 4mg patches: 30 patches per 30 days; or 5mg patches: 30 patches per 30 days.
   - **Axiron (testosterone):** 30mg per pump, 60 pumps per container: up to 180mL per 30 days (2 x 90mL metered-dose pumps) per 30 days.
   - **Depo-Testosterone (testosterone cypionate):** no quantity limit.
   - **Delatestryl (testosterone enanthate):** 200mg/mL, 5mL vial: one 5mL vial per 30 days.
   - **Delatestryl (testosterone enanthate):** 200mg/mL, 1mL syringe: two 1mL syringes per 30days.
   - **Fortesta (testosterone):** up to 120 grams per 30 days (2 x 60 gram pumps).
   - **Striant (testosterone):** 60 systems (tablets) per 30 days.
   - **Testim (testosterone):** up to 300 grams per 30 days (5 gram tube).
   - **Testopel (testosterone):** up to 6 pellets per 90 days.

RATIONALE

Ensure appropriate diagnostic, utilization, and safety criteria. Normal testosterone level is defined for males as between 300 -1,200ng/dL per the National Institute on Aging. Low free serum testosterone level is defined as less than 50ng/L per Adult Men with Androgen Deficiency Syndrome: An Endocrine Society Clinical Practice Guideline.

FDA APPROVED INDICATIONS

ANDRODERM (testosterone transdermal system) is indicated for testosterone replacement therapy in men for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter's Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations accompanied by gonadotropins (FSH, LH) above the normal range.
- Secondary, i.e., hypogonadotropic hypogonadism (congenital or acquired) - idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low serum testosterone concentrations without associated elevation in gonadotropins.

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FDA APPROVED INDICATIONS (CONTINUED)

ANDROGEL, an androgen, is indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary Hypogonadism (Congenital or Acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone levels and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic Hypogonadism (Congenital or Acquired) - idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum levels but have gonadotropins in the normal or low range.

AXIRON, an androgen is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterones: Primary hypogonadism (congenital or acquired); Hypogonadotropic hypogonadism (congenital or acquired). Not indicated in males <18 years of age.

DEPO-TESTOSTERONE INJECTION is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy.
- Hypogonadotropic hypogonadism (congenital or acquired) - idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

DELATESTRYL (Testosterone Enanthate Injection, USP) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

FORTESTA is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone including primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired). Important limitation of use: safety and efficacy of FORTESTA in males <18 years old have not been established.

STRIANT is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone levels and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired) - idiopathic gonadotropin or LHRH deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation. These patients have low serum testosterone levels but have gonadotropins in the normal or low range.

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FDA APPROVED INDICATIONS (CONTINUED)

TESTIM is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone levels and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired) - idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum levels but have gonadotropins in the normal or low range. Testim has not been clinically evaluated in males less than 18 years of age.

TESTOPEL

Androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome: or orchidectomy.
- Hypogonadotropic hypogonadism (congenital or acquired) - idiopathic or gonadotropic LHRH deficiency, or pituitary- hypothalamic injury from tumors, trauma or radiation.
- Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.

CONTINUED ON NEXT PAGE

REFERENCES

- Lilly USA, LLC. Axiron Package Insert. Indianapolis, IN. July, 2011.
- Auxilium Pharmaceuticals, Inc. Testim package insert. Malvern, PA. September 2009.
- Bartor Pharmacal Co.; Inc. Testopel package insert. Rye, NY. January 2009.
- Columbia Laboratories, Inc. Striant package insert. Livingston, NJ. February 2007.
- Conway AJ, Handelsman DJ, Lording DW, Stuckey B, Zajac JD. Use, misuse and abuse of androgens. MJA. 2000; 172:220-224.
- Endo Pharmaceuticals. Fortesta package insert. Chadds Ford, PA. April, 2011.
- Francis S. Greenspan and David G. Gardner eds. Lange Basic and Clinical Endocrinology. 7th ed. McGraw-Hill Companies, Inc.; 2004.
- Gould DC, Petty R, Jacobs HS. The male menopause: does it exist? BMJ. 2000; 320:858-861.
- Endo Pharmaceuticals, Inc. Delatestryl package insert. Chadds Ford, PA. June, 2011.
- Lui PY, Swerdloff RS, Wang C. Relative testosterone deficiency in older men: Clinical definition and presentation. Endocrinol Metab Clin N Am. 2005; 34:957-72.
- Miller KK. Special Articles: Hormones and Reproductive Health. J Clin Endocrinol Metab 2001; 86(6):2395-2401.
- National Institute on Aging. Scientific task force to examine usefulness of testosterone replacement therapy in older men [online]. NIH News Release. November 6, 2002. Available at: http://www.nia.nih.gov/NewsAndEvents/PressReleases/PR20021106ScientificTask.htm [Accessed July 21, 2009].
- Petak SM. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients-2002 Update. Endocrine Practice. 2002; 8 (6): 439-456.
- Pharmacia & Upjohn Company. Depo-Testosterone package insert. New York, NY. September 2006.
- Shalender B, Glenn, Cunningham, FJ, et al. Adult Men with Androgen Deficiency Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, June 2010, 95(6):2536–2559. Available at: http://www.endo-society.org/guidelines/final/upload/final-androgens-in-men-standalone.pdf [Accessed July 25, 2011].
- The Formulary Monograph Service, Facts and Comparisons, St Louis, Missouri, 2003.
- Abbott Laboratories. Androgel 1% package insert. North Chicago, IL. November, 2011.
- Abbott Laboratories. Androgel 1.62% package insert. North Chicago, IL. April, 2011.
- Watson Pharma, Inc. Androderm package insert. Parsippany, NJ. October 2011.

Part D Effective: 01/01/13 Created: 02/01
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

TETANUS TOXOID VACCINE BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TETANUS TOXOID,ADSORBED	TE ANATOXAL BERNA TETANUS TOXOID ADSORBED	04218		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding.

GUIDELINES FOR USE

1. Is the request for prevention of tetanus (i.e. active immunization) for a patient with an age of at least 7 years?

   If yes, **approve for 12 months under Part D by HICL. (Populate the B vs. D field with "D" in PA override field.)**
   If no, continue to #2.

2. Is this drug to be administered to a patient with an age of at least 7 years for wound management (i.e. post-exposure to tetanus)?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months by HICL. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of tetanus prevention or wound management in a patient with an age of at least 7.

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TETANUS TOXOID VACCINE BVD DETERMINATION (PART D)

RATIONALE

Tetanus Toxoid requires a Part B vs. Part D determination. Part D for active immunization of children 7 years of age or older, and adults, for prevention of tetanus. Part B if for wound management in patients 7 years of age and older.

FDA APPROVED INDICATIONS

Aventis-Pasteur Tetanus Toxoid Absorbed is indicated for active immunization of children 7 years of age or older, and adults, for prevention of tetanus. For immunization of infants and children younger than 7 years of age against tetanus and diphtheria, refer to the manufacturers' package inserts for Diphtheria and Tetanus Toxoids and Accellular Pertussis Vaccine Absorbed (DTaP) and for Diptheria and Tetanus Toxoids Absorbed (for Pediatric Use) (DT). It is not to be used for the treatment of active tetanus disease. For the use of this vaccine for tetanus prophylaxis in wound management, refer to DOSAGE AND ADMINISTRATION.

REFERENCES

- Aventis Pasteur. Tetanus Toxoid package insert., Aventis Pasteur, July 2005.
- Aventis Pasteur. Tetanus Toxoid Adsorbed package insert. Swiftwater, PA. July 2005.
- Tetanus Toxoid Adsorbed package insert. Lederle, December 1998.
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011]

Part D Effective: 01/01/13	Created: 02/08	
Commercial Effective: N/A	Client Approval: 10/12	P&T Approval: 11/12

TETRABENAZINE

Generic	Brand	HICL	GCN	Exception/Other
TETRABENAZINE	XENAZINE	07350		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Has the prescription been prescribed or is it recommended by a neurologist?

   If yes, **approve by HICL for 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #2.

2. Does the patient have a diagnosis of chorea (involuntary movements) associated with Huntington's disease?

   If yes, **approve by HICL for 12 months.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more
   information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of chorea (involuntary movements) associated with Huntington's disease.

RATIONALE

Ensure appropriate diagnostic, utilization and safety criteria are used for the management of tetrabenazine.

Proper dosing of XENAZINE involves careful titration of therapy to determine an individualized dose or each patient. Doses should be individualized. For CYP2D6 extensive/immediate metabolizers doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg. For CYP2D6 poor metabolizers, the recommended maximum single dose is 25 mg, and the maximum recommended daily dose is 50 mg.

FDA APPROVED INDICATION

Xenazine is indicated for the treatment of chorea associated with Huntington's disease.

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TETRABENAZINE

REFERENCES

- Ovation Pharmaceuticals, Inc. Xenazine package insert. Deerfield, IL. September, 2009.
- Thomson Healthcare. Tetrabenazine. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 30, 2011].

Part D Effective: 01/01/13 Created: 02/09
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

THIAZOLIDINEDIONE (PART D)

Generic	Brand	HICL	GCN	Exception/Other
ROSIGLITAZONE	AVANDIA	20214		
ROSIGLITAZONE /METFORMIN	AVANDAMET	24353		
ROSIGLITAZONE /GLIMEPIRIDE	AVANDARYL	33371		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have type 2 diabetes?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of type 2 diabetes and a trial of, or contraindication to metformin (Glucophage), metformin ER, glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), or a formulary oral sulfonylurea (such as glyburide, glipizide, chlorpropamide, glimepiride, tolazamide, tolbutamide), AND pioglitazone (such as Actos, pioglitazone/glimepiride [*Duet*act], pioglitazone/metformin [ACTO*plus* Met, ACTO*plus* Met XR]).

2. Has the patient tried or does the patient have a contraindication to metformin (Glucophage), metformin ER, glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), or a sulfonylurea (such as glyburide, glipizide, chlorpropamide, glimepiride, tolazamide, tolbutamide), AND pioglitazone (such as Actos, pioglitazone/glimepiride [*Duet*act], pioglitazone/metformin [ACTO*plus* Met, ACTO*plus* Met XR])?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of type 2 diabetes and trial of, or contraindication to metformin (Glucophage), metformin ER, glyburide/metformin (Glucovance), glipizide/metformin (Metaglip), or a formulary oral sulfonylurea (such as glyburide, glipizide, chlorpropamide, glimepiride, tolazamide, tolbutamide), AND pioglitazone (such as Actos, pioglitazone/glimepiride [*Duet*act], pioglitazone/metformin [ACTO*plus* Met, ACTO*plus* Met XR]).

3. **Approve for 12 months by HICL with the following quantity limits:**
   - **Avandia: #1 per day per month**
   - **Avanda*met*: #2 per day per month**
   - **Avandaryl: #1 per day per month**

   APPROVAL TEXT: Please note that these drugs have important FDA safety warnings. For more information, please contact your doctor or pharmacist.

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RATIONALE

Ensure that rosiglitazone is not used for type 1 diabetes, ensure use as a second-line agent (after metformin) for type 2 diabetes, ensure that rosiglitazone containing products (Avandia, Avandaryl and Avanda*met*) are not approved for patients who are not already taking rosiglitazone or rosiglitazone containing products or have not tried/failed other diabetes medications including pioglitazone (Actos, *Duet*act, ACTO*plus* Met).

FDA APPROVED INDICATIONS

AVANDIA is indicated after consultation with a healthcare professional who has considered and advised the patient of the risks and benefits of AVANDIA, this drug is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are already taking AVANDIA, or not already taking AVANDIA and are unable to achieve adequate glycemic control on other diabetes medications, and, in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS) for medical reasons.
Due to its mechanism of action, Avandia is active only in the presence of endogenous insulin. Therefore, Avandia should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. The coadministration of Avandia and insulin is not recommended. The use of Avandia with nitrates is not recommended.

AVANDA*MET* is indicated after consultation with a healthcare professional who has considered and advised the patient of the risks and benefits of AVANDIA, this drug is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are already taking AVANDIA, or not already taking AVANDIA and are unable to achieve adequate glycemic control on other diabetes medications, and, in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS) or pioglitazone-containing products (ACTOS*PLUS* MET, ACTO*PLUS* MET XR, *DUET*ACT) for medical reasons. Due to its mechanism of action, rosiglitazone is active only in the presence of endogenous insulin. Therefore, Avanda*met* should not be used in patients with type 1 diabetes. The use of Avanda*met* with nitrates is not recommended. Coadministration of Avanda*met* with insulin is not recommended,

AVANDARYL is indicated after consultation with a healthcare professional who has considered and advised the patient of the risks and benefits of AVANDIA, this drug is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are already taking AVANDIA, or not already taking AVANDIA and are unable to achieve adequate glycemic control on other diabetes medications, and, in consultation with their healthcare provider, have decided not to take pioglitazone (ACTOS) or pioglitazone-containing products (ACTOS*PLUS* MET, ACTO*PLUS* MET XR, *DUET*ACT) for medical reasons. Due to its mechanism of action, rosiglitazone is active only in the presence of endogenous insulin. Therefore, Avandaryl should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. The use of Avandaryl with nitrates is not recommended. The coadministration of Avandaryl and insulin is not recommended.

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THIAZOLIDINEDIONE (PART D)

REFERENCES

- AACE Diabetes Mellitus Guidelines, Endoc Pract. 2007; 13(Suppl 1) 2007.
- AACE/ACE Consensus Statement: Glycemic Control Algorithm, Endocr Pract. 2009; 15(no.6) 541.
- DIABETES CARE, Standards of Medical Care in Diabetes -2010, Volume 33, Supplement 1, January 2010.
- GlaxoSmithKline. Avanda*met* package insert. Research Triangle Park, NC. May 2011.
- GlaxoSmithKline. Avandaryl package insert. Research Triangle Park, NC. May 2011.
- GlaxoSmithKline. Avandia package insert. Research Triangle Park, NC. May 2011.
- US FDA Safety Announcement: Rosiglitazone REMS Program. Accessed: http://www.fda.gov/Drugs/DrugSafety/ucm255005.htm, on June 9, 2011.
- Nesto RW, Bell D, Bonow RO, Fonseca V, Grundy SM, et al. Thiazolidinedione Use, Fluid Retention and Congestive Heart Failure: A Consensus Statement from the American Heart Associated and American Diabetes Association. Circulation 2003; 180:2941-48.
- Takeda Pharmaceuticals America, Inc. Actos package insert. Deerfield, IL. January 2011.
- Takeda Pharmaceuticals America, Inc. ACTO*plus* Met and ACTO*plus* Met XR package insert. Deerfield, IL. December 2010.
- Takeda Pharmaceuticals America, Inc. *Duet*act package insert. Deerfield, IL. July 2009.

Part D Effective: 01/01/13 Created: 11/99
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

TOCILIZUMAB

Generic	Brand	HICL	GCN	Exception/Other
TOCILIZUMAB	ACTEMRA	36466		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of active rheumatoid arthritis?

   If yes, continue to #2.
   If no, continue to #3.

2. Is the patient currently taking the requested medication?

   If yes, continue to #7.
   If no, continue to #5.

3. Does the patient have a diagnosis of active systemic juvenile idiopathic arthritis or active polyarticular juvenile arthritis?

   If yes, continue to #4.
   If no, do not approve
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis following a trial with at least one of the following TNF blockers such as Enbrel, Humira, Remicade, Simponi, or Cimzia, which may also require prior authorization; or active systemic juvenile idiopathic arthritis or active polyarticular juvenile arthritis for patients 2 years of age and older; and supervision by a rheumatologist.

4. Is the patient at least 2 years of age?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis following a trial with at least one of the following TNF blockers such as Enbrel, Humira, Remicade, Simponi, or Cimzia, which may also require prior authorization; or active systemic juvenile idiopathic arthritis or active polyarticular juvenile arthritis for patients 2 years of age and older; and supervision by a rheumatologist.

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GUIDELINES FOR USE (CONTINUED)

5. Has the treatment been prescribed by or is it currently being supervised by a rheumatologist?

   If yes, process by indication as follows:
   - ACTIVE RHEUMATOID ARTHRITIS: continue to #6.
   - **ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: Approve for 12 months for #2 vials per month.**
   - **ACTIVE POLYARTICULAR JUVENILE ARTHRITIS: Approve for 12 months for #2 vials per month.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of active rheumatoid arthritis following a trial with at least one of the following TNF blockers such as Enbrel, Humira, Remicade, Simponi, or Cimzia, which may also require prior authorization; or active systemic juvenile idiopathic arthritis or active polyarticular juvenile arthritis for patients 2 years of age and older ; and supervision by a rheumatologist.

6. Is the patient intolerant to or has the patient failed at least one of the following TNF blockers: Enbrel, Humira, Remicade, Simponi, or Cimzia?

   If yes, **approve a maximum of #2 vials per fill x 6 fills with an end date 24 weeks from today.**
   APPROVAL TEXT: Renewal requires a 20% or greater improvement in tender joint count and swollen joint count. Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

   If no, do not approve and recommend use of a TNF blocker such as Enbrel, Humira, Remicade, Simponi, or Cimzia.
   DENIAL TEXT: Approval requires a previous therapy trial with at least one of the following TNF blockers such as Enbrel, Humira, Remicade, Simponi or Cimzia, which may also require prior authorization.

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GUIDELINES FOR USE (CONTINUED)

7. Has the patient experienced or maintained at least a 20% improvement in tender joint count and swollen joint count from baseline?

   If yes, **approve a maximum of #2 vials per fill x 6 fills with an end date 24 weeks from today.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Renewal requires the patient to have experienced or maintained at least a 20% improvement in tender joint count and swollen joint count while on therapy.

RATIONALE
Ensure appropriate utilization criteria are met for the management of requests for tocilizumab for use as monotherapy or in combination with methotrexate or other non-biologic DMARD.

Actemra may be used alone or in combination with methotrexate: and in RA, other DMARDs may be used.

RHEUMATOID ARTHRITIS
When used in combination with DMARDs or as monotherapy the recommended starting dose is 4 mg per kg every 4 weeks followed by an increase to 8 mg per kg every 4 weeks based on clinical response.

POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS
Recommended PJIA Dosage Every 4 Weeks
- Patients less than 30 kg weight 10 mg per kg
- Patients at or above 30 kg weight 8 mg per kg

SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS
- Less than 30 kg weight 12 mg per kg
- Patients at or above 30 kg weight 8 mg per kg

General Dosing Information
- It is recommended that Actemra not be initiated in patients with an absolute neutrophil count (ANC) below 2000 per mm^3, platelet count below 100,000 per mm^3, or who have ALT or AST above 1.5 times the upper limit of normal (ULN).
- Actemra doses exceeding 800 mg per infusion are not recommended in RA patients.

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RATIONALE (CONTINUED)

Administration

- For adults, PJIA and SJIA patients at or above 30 kg, dilute to 100 mL in 0.9% Sodium Chloride for intravenous infusion using aseptic technique.
- For PJIA and SJIA patients less than 30 kg, dilute to 50 mL in 0.9% Sodium Chloride for intravenous infusion using aseptic technique.
- Administer as a single intravenous drip infusion over 1 hour; do not administer as bolus or push.

Dose Modifications

- Recommended for management of certain dose-related laboratory changes including elevated liver enzymes, neutropenia, and thrombocytopenia.

FDA APPROVED INDICATION

Actemra is an interleukin-6 (IL-6) receptor antagonist indicated for treatment of:

- Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.

REFERENCE

- Genentech. Actemra package insert. South San Francisco, CA. April 2013.

Part D Effective: 10/01/13 Created: 02/10
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

TOFACITINIB

Generic	Brand	HICL	GCN	Exception/Other
TOFACITINIB CITRATE	XELJANZ	39768		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is this for initial therapy of Xeljanz?

   If yes, continue to #2.
   If no, continue to #5.

2. Does the patient have a diagnosis of rheumatoid arthritis?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of rheumatoid arthritis, a trial of or contraindication to methotrexate and a trial of the preferred formulary tumor necrosis factors Humira (adalimumab) and Cimzia (certolizumab pegol), which may also require a prior authorization.

3. Has the patient had a trial of or does the patient have a contraindication to methotrexate?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT Approval requires a diagnosis of rheumatoid arthritis, a trial of or contraindication to methotrexate and a trial of the preferred formulary tumor necrosis factors Humira (adalimumab) and Cimzia (certolizumab pegol), which may also require a prior authorization.

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GUIDELINES FOR USE (CONTINUED)

4. Has the patient tried Humira (adalimumab) and Cimzia (certolizumab pegol)?

   If yes, **approve for 3 months by HICL with a quantity limit of #2 tablets per day.**
   If no, do not approve. (Ask the caller to submit a MRF for Humira or Cimzia).
   DENIAL TEXT: Approval requires a diagnosis of rheumatoid arthritis, a trial of or contraindication to methotrexate and a trial of the preferred formulary tumor necrosis factors Humira (adalimumab) and Cimzia (certolizumab pegol), which may also require a prior authorization.

5. Has the patient experienced or maintained a 20% improvement in tender or swollen joint count while on therapy?

   If yes, **approve for 12 months by HICL with a quantity limit of #2 tablets per day.**
   If no, do not approve.
   DENIAL TEXT: Renewal requires that the patient has experienced or maintained a 20% improvement in tender or swollen joint count while on therapy.

RATIONALE
To ensure appropriate use of Xeljanz consistent with FDA approved indication.

The recommended dose of Xeljanz is 5 mg orally twice daily with or without food. Dosage modifications are needed for patients with moderate hepatic impairment, moderate to severe renal impairment, concomitant use of potent inhibitors of CYP2C19, concomitant use of moderate/potent inhibitors/inducers of CYP3A4, lymphopenia, neutropenia and anemia.

Xeljanz, an oral agent, is the first selective inhibitor of Janus kinase (JAK) 1 and JAK3 available for the treatment of RA. JAKs are intracellular kinases which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence intracellular immune processes. Xeljanz inhibits the signaling of several cytokine members simultaneously and is therefore being studied for use in the treatment of other autoimmune disorders including ulcerative colitis. While Xeljanz is FDA approved as first line therapy following failure of a DMARD, initially its utilization is expected to be limited to those patients who have failed or are not candidates for injectable biologic therapy (i.e., TNF inhibitors).

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RATIONALE (CONTINUED)
The American College of Rheumatology RA treatment guidelines recommend DMARDs (i.e. MTX, hydroxychloroquine, leflunomide, minocycline and sulfasalazine) as first line pharmacological treatment. Failure with a DMARD is followed by a trial of one or more TNF inhibitors (Humira, Cimzia, Enbrel, Simponi, and Remicade) followed by a non-TNF biologic such as abatacept (T-cell costimulation modulator), Rituximab (B-cell CD20 antagonist) and tocilizumab (IL-6 receptor antagonist). The TNF and non-TNF inhibitor biologics currently on the market today are administered via subcutaneous (SC) injection or intravenous (IV) infusion.

The safety and efficacy of Xeljanz was studied in five phase 3, double-blind, controlled, multicenter trials, in adult patients with moderate to severe active RA who had an inadequate response (IR) to previous DMARD treatment. Studies included IR to MTX, IR to TNF inhibitors and IR to any DMARD (biologic and nonbiologic). The trials ranged from 6 months to an ongoing 2-year trial and totaled 3,315 patients. The primary endpoints for all of the studies were proportion of patients who achieved an ACR 20 response, change in Health Assessment Questionnaire-Disability Index (HAQ-DI), and rates of Disease Activity Score DAS28-4 (ESR) less than 2.6. One study also included mean change from baseline in van der Heijde-modified total Sharp Score (mTSS) as another co-primary endpoint. All of the studies had different time points for primary endpoints ranging from 3 months to 6 months.

In all trials, patients treated with 5 mg twice daily Xeljanz had higher ACR20, ACR50, and ACR70 response rates versus placebo, with or without background non-biologic DMARD treatment, at Month 3 and Month 6. Higher ACR20 response rates were observed within 2 weeks compared to placebo. In the 12-month trials, ACR response rates in Xeljanz -treated patients were consistent at 6 and 12 months.

Study III, known in the literature as the Oral Standard trial, was the only trial to have an active comparator arm (Humira). Study duration was 12 months. Patients (N=792) were on stable doses of MTX and were randomly assigned to receive Xeljanz 5 mg or 10 mg twice daily, Humira 40 mg once every two weeks, or placebo. The ACR20 response rates for Xeljanz 5 mg, Humira and placebo were 51.5%, 47.2% and 28.3% respectively ($p<0.001$ for all comparison groups vs. placebo). The mean change from baseline in the HAQ-DI score at month 3 and percentage of patients with a DAS28-4 (ESR) below 2.6 at month 6 were also significantly greater with the active treatment versus placebo. The study was not designed or powered to directly compare the efficacy of Xeljanz versus Humira.

Xeljanz has black box warnings of serious infections and malignancies. Prior to starting Xeljanz patients should be tested for latent tuberculosis (TB) and all patients should be monitored for active TB during treatment even if the initial TB test was negative. Other warnings and precautions include gastrointestinal perforations, hepatic impairment, concurrent use of live vaccines, and the necessity to monitor specific laboratory parameters including lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipids. The most common adverse reactions reported in >2% of patients treated with Xeljanz monotherapy or in combination with DMARDs were upper respiratory tract infections, headache, diarrhea and nasopharyngitis.

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RATIONALE (CONTINUED)

As Xeljanz undergoes hepatic metabolism via the Cytochrome P450 enzymes CYP3A4 and CYP2C19, drug-drug interactions with inhibitors/inducers of those enzymes can occur. Xeljanz is pregnancy category C.

FDA APPROVED INDICATIONS

Xeljanz is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs)

Xeljanz should not be used in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine.

REFERENCES

- Xeljanz [Prescribing Information]. New York, NY: Pfizer; August 2012.
- FDA News Release. US Food and Drug Administration. Available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm327152.htm [Accessed 11/12/12].
- American College of Rheumatology Committee to Reevaluate Improvement Criteria. A proposed revision to the ACR20: the hybrid measure of American College of Rheumatology response. Arthritis Rheum 2007;57:193-202
- Sokka T. Radiographic scoring in rheumatoid arthritis. Bulletin of the NYU Hospital for Joint Diseases 2008;66:166-168.
- Kyttaris, VC. Kinase inhibitors: a new class of antirheumatic drugs. Drug Design, Development and Therapy 2012:6 245–250.
- McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011;365:2205–19.
- van Vollenhoven RF, Fleischmann R, Cohen S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. N Engl J Med 2012;367:508-19.

Part D Effective: 04/01/13 Created: 11/12
Commercial Effective: 04/01/13 Client Approval: 02/13 P&T Approval: 0213

TOTAL PARENTERAL NUTRITION AGENT BVD DETERMINATION (PART D)

Generic	Brand	HICL	GCN	Exception/Other
AMINO ACIDS	CLINIMIX, OTHERS			STC 0181 & C318 AND ROUTE = "INTRAVEN."
FAT EMULSIONS	INTRALIPID, OTHERS			STC 0330 AND ROUTE = "INTRAVEN."
INVERTED SUGARS	TRAVERT, OTHERS			STC 0180 AND ROUTE = "INTRAVEN."

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

NOTE: This PA is for administrative purposes to determine Medicare Part B versus Medicare Part D funding and applies to all TPN products.

GUIDELINES FOR USE

1. Is the patient receiving total parenteral nutrition (TPN) because of a non-functioning digestive tract?

   If yes, **submit via Part B. (Populate the B vs. D field with "B" in PA override field and approve for 12 months. If MI does not process Part B for the client, refer the caller/request back to the Health plan.)**
   If no, continue to #2. **(CSR: If unknown, ask the caller to submit MRF.)**

2. **Approve as requested for up to 12 months under Part D. (Populate B vs. D field with "D" in the PA override field.)**

RATIONALE
TPN for patients due to a non-functioning digestive tract is covered under Part B.

FDA APPROVED INDICATION
Sources of nutrition in patients requiring total parenteral nutrition.

REFERENCE
- Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Appendix C- Summary of Coverage Policy Medicare Part B Versus Part D Coverage Issues. Rev 10, 02-19-10. Available at: http://www.cms.gov/PrescriptionDrugCovContra/12_PartDManuals.asp. [Accessed July 20, 2011].

Part D Effective: 01/01/13 Created: 09/05
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

TRAMETINIB

Generic	Brand	HICL	GCN	Exception/Other
TRAMETINIB DIMETHYL SULFOXIDE	MEKINIST	40361		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic melanoma?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a BRAF V600E or BRAF V600K mutation and no prior BRAF inhibitor therapy (such as Zelboraf or Tafinlar).

2. Has the patient received prior BRAF inhibitor therapy (such as Zelboraf or Tafinlar)?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a BRAF V600E or BRAF V600K mutation and no prior BRAF inhibitor therapy (such as Zelboraf or Tafinlar).
   If no, continue to #3.

3. Does patient have the genetic mutation called BRAF V600E or BRAF V600K?

   If yes, **approve for 12 months by GPID as requested with the following quantity limits:**
   - **Mekinist 2mg #30 tablets per 30 days**
   - **Mekinist 0.5mg #90 tablets per 30 days**

   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a BRAF V600E or BRAF V600K mutation and no prior BRAF inhibitor therapy (such as Zelboraf or Tafinlar).

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TRAMETINIB

RATIONALE

Ensure appropriate use of Mekinist based on FDA approved indication.

The recommended Mekinist dose is 2 mg orally once daily until disease progression or unacceptable toxicity. Take at least 1 hour before or 2 hours after a meal. Do not take a missed dose within 12 hours of the next dose. Dose reduction to 1.5 or 1mg daily is recommended in the presence of certain adverse reactions.

Warnings and precautions include cardiomyopathy, retinal pigment epithelial detachment (RPED), retinal vein occlusion (RVO), interstitial lung disease (ILD), serious skin toxicity, and embryofetal toxicity. The most common adverse reactions (≥ 20 percent) for Mekinist include rash, diarrhea, and lymphedema.

No formal clinical studies have been conducted to evaluate human cytochrome P450 (CYP) enzyme-mediated drug interactions with Mekinist. Mekinist is pregnancy category D. Female patients should use highly effective contraception during treatment and for 4 months following discontinuation of treatment. Nursing mothers are advised to discontinue drug or nursing.

Mekinist (trametinib), the first MEK 1 and MEK 2 inhibitor, was approved for metastatic melanoma with BRAF V600E or V600K mutations on the same day as Tafinlar (dabrafenib). Tafinlar joins Zelboraf (vemurafenib) as the second FDA approved inhibitor of BRAF V600E mutation approved for the treatment of advanced melanoma. MEK1 and MEK 2 are kinases that work downstream of BRAF in an extracellular pathway that promotes cellular proliferation. Both Mekinist and Tafinlar are approved in combination with the THxID BRAF Kit companion diagnostic test, which detects for both the BRAF V600E or V600K mutations. BRAF V600E mutations are present in about half of all metastatic melanomas and V600K mutations are present in up to 10 percent of cases. While not yet approved as combination therapy, there are several ongoing trials investigating the use of Tafinlar in combination with Mekinist for the treatment of metastatic melanoma.

In 2013, an estimated 76,690 Americans will be diagnosed melanoma and another 9,480 will die from it. There were approximately 822,770 Americans with a history of melanoma in 2008. The lifetime risk of being diagnosed with melanoma is about 2 percent. The 5 year survival rate for metastatic disease is between 15 and 20 percent. Risk factors for melanoma include family history, genetic predisposition, and sun exposure.

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RATIONALE (CONTINUED)
At the time of this writing, Mekinist and Tafinlar are not yet included in the National Comprehensive Cancer Network (NCCN) melanoma treatment guidelines. Yervoy (ipilimumab), Zelboraf (for patients with a V600E mutation), and high dose Proleukin (aldesleukin) are the preferred systemic therapies for advanced or metastatic melanoma. Other active regimens include dacarbazine, temozolomide, Gleevec (for C-KIT mutated tumors), paclitaxel, and paclitaxel with carboplatin. The newer FDA agents Zelboraf and Yervoy are more commonly used than the other FDA approved agents Proleukin and dacarbazine. Hydroxyurea is FDA approved for the treatment of metastatic melanoma but no longer used. The commonly used off-label chemotherapy regimens have low objective tumor response rates and no evidence of improved survival.

The FDA approval of Mekinist was based on the METRIC study (referred to as Trial 1 in Mekinist's prescribing information). This open label trial randomized 322 patients with BRAF V600E or V600K mutation-positive, unresectable or metastatic melanoma to Mekinist 2mg once daily or chemotherapy consisting of either dacarbazine 1000mg/m^2 intravenously every 3 weeks or paclitaxel 175mg/m^2 intravenously every 3 weeks. Patients were excluded if they had more than one prior chemotherapy regimen for advanced or metastatic disease, or prior treatment with a BRAF inhibitor or MEK inhibitor. The distribution of BRAF V600 mutations was BRAF V600E (87 percent), V600K (12 percent), or both (<1 percent).

The median durations of follow-up prior to initiation of alternative treatment were 4.9 months for patients treated with Mekinist and 3.1 months for patients treated with chemotherapy. Fifty one (47 percent) patients crossed over from the chemotherapy arm at the time of disease progression to receive Mekinist. Mekinist improved progression free survival (PFS) by 3.3 months over chemotherapy (4.8 versus 1.5 months). Overall survival at 6 months was 81 percent in the Mekinist arm and 67 percent in the chemotherapy arm despite crossover.

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RATIONALE (CONTINUED)

Trial 1: Investigator-Assessed Progression-Free Survival and Confirmed Objective Response Results (from Mekinist prescribing information)

	MEKINIST N = 214	Chemotherapy N = 108
PFS	117 (55%)	77 (71%)
Number of Events (%)	107 (50%)	70 (65%)
Progressive Disease Death	10 (5%)	7 (6%)
Median, month (95% CI)	4.8 (4.3, 4.9)	1.5 (1.4, 2.7)
HR[a] (95% CI)	0.47 (0.34, 0.65)	
P value (log-rank test)	*P*<0.0001	
Confirmed Tumor Responses		
Objective Response Rate	22%	8%
(95% CI)	(17, 28)	(4, 15)
CR, n (%)	4 (2%)	0
PR, n (%)	43 (20%)	9 (8%)
Duration of Response		
Median, months (95% CI)	5.5 (4.1, 5.9)	NR (3.5, NR)

[a] Pike estimator.

CI = confidence interval; CR = complete response; HR = Hazard Ratio; NR = Not reached, PFS = Progression-free Survival; PR = partial response.

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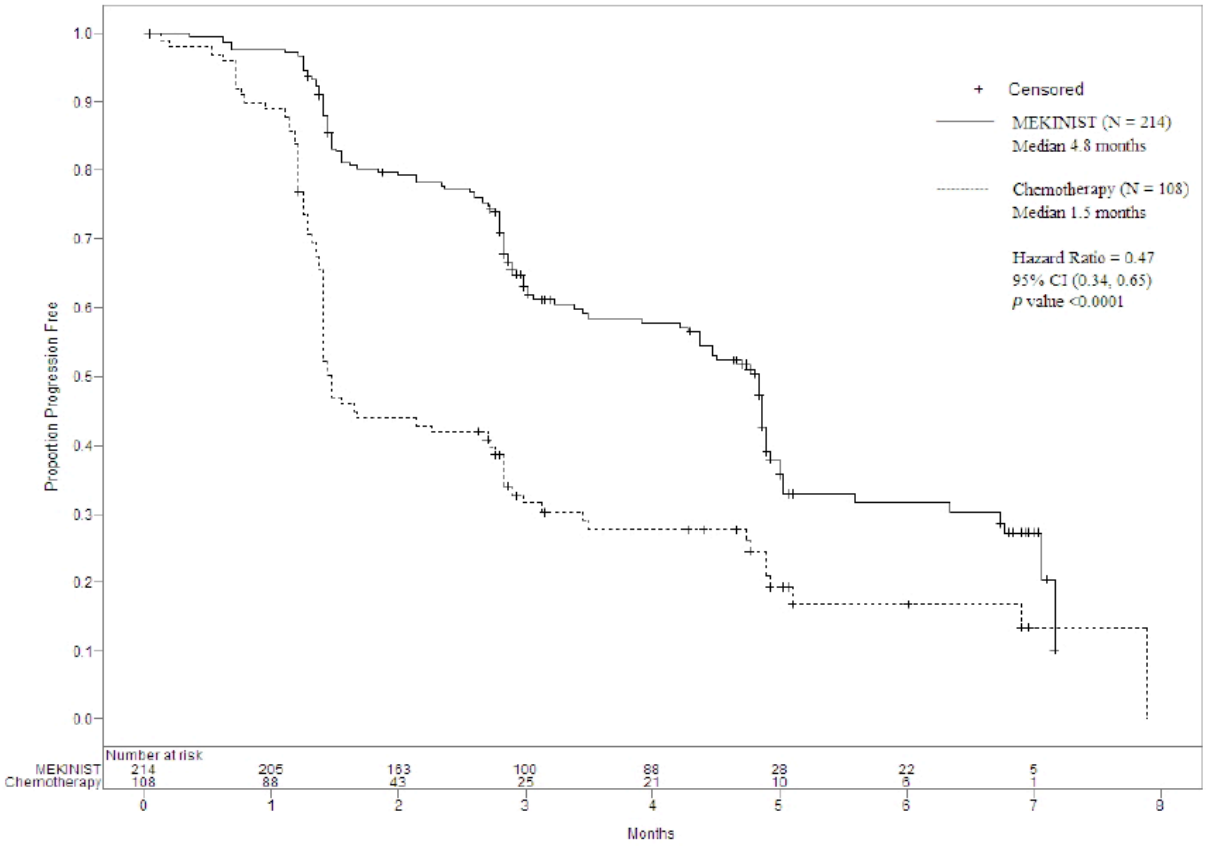
RATIONALE (CONTINUED)

Trial 1: Kaplan-Meier Curves of Investigator-Assessed Progression-Free Survival (ITT population) (from Mekinist prescribing information)



Trial 2 was a single-arm trial of 40 patients with BRAF V600E or V600K mutation-positive, unresectable or metastatic melanoma who had received prior treatment with a BRAF inhibitor. All patients received Mekinist 2mg once daily until disease progression or unacceptable toxicity. The distribution of BRAF V600 mutations was V600E (83 percent), V600K (10 percent), and the remaining patients had multiple V600 mutations (5 percent), or unknown mutational status (2%). No patient in Trial 2 achieved a confirmed partial or complete response as determined by the clinical investigators.

FDA APPROVED INDICATIONS

Mekinist is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test.

Limitation of use: Mekinist is not indicated for the treatment of patients who have received prior BRAF inhibitor therapy.

CONTINUED ON NEXT PAGE

REFERENCES

- Mekinist [Prescribing Information]. Research Triangle Park, NC: GlaxoSmithKline; May 2013.
- Center for Drug Evaluation and Research Summary Review. Application number 204114Orig1s000. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204114Orig1s000SumR.pdf [Accessed June 24, 2013].
- Tafinlar [Prescribing Information]. Research Triangle Park, NC: GlaxoSmithKline; May 2013.
- Center for Drug Evaluation and Research Summary Review. Application number 202806Orig1s000. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202806Orig1s000SumR.pdf [Accessed: June 17, 2013].
- American Cancer Society. Melanoma Skin Cancer Detailed Guide. Available at: http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/skin-cancer-melanoma-detailed-guide-toc [Accessed June 17, 2013].
- NCCN Clinical Practice Guidelines in Oncology. Melanoma Version 2.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf [Accessed June 17, 2013]
- ClinicalTrials.gov. Available at: http://www.clinicaltrials.gov/ct2/results?term=dabrafenib+AND+trametinib&Search=Search [Accessed June 17, 2013].
- Rubinstein JC, Sznol M, Pavlick AC, et al. Incidence of the V600K mutation among melanoma patients with BRAF mutations, and potential therapeutic response to the specific BRAF inhibitor PLX4032. *J Transl Med*. 2010; 8: 67. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917408/ [Accessed June 24, 2013].
- Flaherty KT, Robert C, Hersey P, et al. Improved Survival with MEK Inhibitor in BRAF-Mutated Melanoma. *N Engl J Med* 367; 2. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1203421 [Accessed June 24, 2013].

Part D Effective: 10/01/13 Created: 07/13
Commercial Effective: 10/01/13 Client Approval: 08/13 P&T Approval: 08/13

TRETINOIN (PART D)

Generic	Brand	HICL	GCN	Exception/Other
TRETINOIN	ATRALIN AVITA RETIN-A TRETIN-X	02468		ROUTE = TOPICAL
TRETINOIN MICROSPHERES	RETIN-A MICRO RETIN-A MICRO PUMP	32888		

Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the request for a cosmetic indication such as melasma, photoaging or wrinkles?

   If yes, do not approve.
   DENIAL TEXT: Approval requires a non-cosmetic diagnosis.
   If no, continue to #2.

2. Is the request for a generic formulation of tretinoin?

   If yes, **approve for 12 months.**
   If no, continue to #3.

3. Has patient had a trial of or contraindication to a generic formulation of tretinoin?

   If yes, **approve for 12 months.**
   If no, do not approve.
   DENIAL TEXT: Approval of branded tretinoin formulations requires a trial of a generic formulation.

RATIONALE
To prevent use of tretinoin products for the treatment of cosmetic conditions and encourage use of generic formulations.

FDA APPROVED INDICATION
Tretinoin is indicated for the topical treatment of acne vulgaris.

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TRETINOIN (PART D)

REFERENCES

- DPT Laboratories. Atralin package insert. San Antonio, TX, July 2007.
- Ortho-Dermatological. Retin-A package insert. Skillman, NJ, April 2007.
- Ortho-Neutrogena. Retin-A Micro package insert. Los Angeles, CA, May 2006.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: www.thomsonhc.com/hcs/librarian/. [Accessed: June 20, 2011].

Part D Effective: 01/01/13 Created: 02/02
Commercial Effective: N/A Client Approval: 10/12 P&T Approval: 11/12

USTEKINUMAB

Generic	Brand	HICL	GCN	Exception/Other
USTEKINUMAB	STELARA	36187		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Has this drug been prescribed by or is it recommended by a dermatologist or rheumatologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist or rheumatologist, a diagnosis of moderate to severe plaque psoriasis covering 10 percent or more of Body Surface Area or PASI (Psoriasis Area and Severity Index) score greater than or equal 12, and a trial of one or more forms of a preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate, or cyclosporine, and trial of Humira.

2. Does the patient have moderate to severe plaque psoriasis of greater than or equal to 10% Body Surface Area (BSA) or PASI (Psoriasis Area and Severity Index) score greater than or equal 12?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist or rheumatologist, a diagnosis of moderate to severe plaque psoriasis covering 10 percent or more of Body Surface Area or PASI (Psoriasis Area and Severity Index) score greater than or equal 12, and a trial of one or more forms of a preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate, or cyclosporine, and trial of Humira.

3. Has the patient tried or does the patient have a contraindication to one of the following forms of a preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), acitretin, methotrexate, or cyclosporine?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist or rheumatologist, a diagnosis of moderate to severe plaque psoriasis covering 10 percent or more of Body Surface Area or PASI (Psoriasis Area and Severity Index) score greater than or equal 12, and a trial of one or more forms of a preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate, or cyclosporine, and trial of Humira.

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INITIAL CRITERIA (CONTINUED)

4. Has the patient tried or does the patient have a contraindication to Humira?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by a dermatologist or rheumatologist, a diagnosis of moderate to severe plaque psoriasis covering 10 percent or more of Body Surface Area or PASI (Psoriasis Area and Severity Index) score greater than or equal 12, and a trial of one or more forms of a preferred therapy such as PUVA (Psoralen Ultraviolet Light A), UVB (Ultraviolet Light B), methotrexate or cyclosporine, and trial of Humira.

5. Does the patient weigh 100kg (220 lbs) or less?

   If yes, continue to #6.
   If no, continue to #7.

6. **Total initial approval equal to 4 months:**
   Approve #2 x 45mg/0.5mL prefilled syringes or vials the first month, then #1 x 45mg/0.5mL prefilled syringe or vial every 3 months.
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist. Renewal requires documentation that the patient has achieved clear or minimal disease (Physician's Global Assessment equal to zero or one) or documentation of the percentage of decrease in PASI (Psoriasis Area and Severity Index).

7. **Total initial approval equal to 4 months:**
   Approve #2 x 90mg/mL prefilled syringes or vials the first month, then #1 x 90mg/mL prefilled syringe or vial every 3 months.
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist. Renewal requires documentation that the patient has achieved clear or minimal disease (Physician's Global Assessment equal to zero or one) or documentation of the percentage of decrease in PASI (Psoriasis Area and Severity Index).

RENEWAL CRITERIA

1. Does the patient have moderate to severe plaque psoriasis?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Renewal requires a diagnosis of moderate to severe plaque psoriasis.

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RENEWAL CRITERIA (CONTINUED)

2. Has the patient achieved clear or minimal disease (Physician's Global Assessment equal to zero or one) or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50 percent or more?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Renewal requires patient has achieved clear or minimal disease (Physician's Global Assessment equal to zero or one) or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50 percent or more.

3. Does the patient weigh 100kg (220 lbs) or less?

   If yes, continue to #4.
   If no, continue to #5.

4. **Total renewal approval:**
   Approve for 1 year for up to #2 x 45mg/0.5mL prefilled syringes or vials every 12 weeks.
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

5. **Total renewal approval:**
   Approve for 1 year for up to #1 x 90mg/mL prefilled syringe or vial every 12 weeks.
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

RATIONALE

Ensure that appropriate diagnostic, utilization, and safety criteria are utilized for the management of ustekinumab. Promote use of preferred agent Humira when appropriate.

The Psoriasis Area Severity Index (PASI) is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. The PASI produces a numeric score that can range from zero to seventy-two.

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RATIONAL (CONTINUED)
The Physician's Global Assessment (PGA) is used to determine the subject's psoriasis lesions overall at a given time point. Overall lesions are graded for induration, erythema, and scaling based on a scale from zero or five, with higher scores indicating greater severity.

Total PGA Scores
0 = Cleared
1 = Minimal
2 = Mild
3 = Moderate
4 = Marked
5 = Severe

FDA APPROVED INDICATIONS
Treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

REFERENCES

- Centocor Ortho Biotech. Stelara package insert. Horsham, PA. December 2009.
- Centocor Ortho Biotech. Stelara Dossier. Horsham, PA. September 2009.
- Feldman SF, Koo JY, et al. The psoriasis and psoriatic pocket guide: treatment algorithms and management options. National Psoriasis Foundation. Available from: www.psoriasis.org. [Accessed: October 8, 2009].
- Menter A, Gottlieb A, et al. Guidelines of care for the management of psoriasis and psoriatic Arthritis: section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol* 2008;58: 826-850.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: October 8, 2009].

Part D Effective: N/A | Created: 10/09
Commercial Effective: 10/01/13 | Client Approval: 08/13 | P&T Approval: 08/13

PLUS DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

VANDETANIB

Generic	Brand	HICL	GCN	Exception/Other
VANDETANIB	CAPRELSA	37531		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Is the patient a Part D member?

   If yes, continue to #2.
   If no, continue to #3.

2. Is the patient currently stable on requested medication?

   If yes, **approve as follows:**
   - If the request is for 300mg tablets: **approve for 12 months #1 per day per month.**
   - If the request is for 100mg tablets: **approve for 12 months up to #2 per day per month.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #3.

3. Does the patient have diagnosis of symptomatic or progressive medullary thyroid cancer with unresectable locally advanced or metastatic disease?

   If yes, **approve as follows:**
   - If the request is for 300mg tablets: **approve for 12 months #1 per day per month.**
   - If the request is for 100mg tablets: **approve for 12 months up to #2 per day per month.**

   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of symptomatic or progressive medullary thyroid cancer with unresectable locally advanced or metastatic disease.

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VANDETANIB

RATIONALE

Ensure appropriate utilization of vandetanib based on FDA approved indication and NCCN guidelines. Vandetanib is recommended as an option for the treatment of recurrent or persistent medullary thyroid carcinoma.

FDA APPROVED INDICATION

Vandetanib is indicated for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease.

REFERENCES

- AstraZeneca Pharmaceuticals LP. Vandetanib package insert. Wilmington, DE. April 2011.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Thyroid Carcinoma. (Version 2.2011).
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 22, 2011].

Part D Effective: 01/01/13	Created: 05/11	
Commercial Effective: 01/01/13	Client Approval: 10/12	P&T Approval: 11/12

VEMURAFENIB

Generic	Brand	HICL	GCN	Exception/Other
VEMURAFENIB	ZELBORAF	37837		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

4. Does the patient have a diagnosis of unresectable or metastatic melanoma?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a $BRAF^{V600E}$ mutation.

5. Does patient have the genetic mutation called $BRAF^{V600E}$?

   If yes, **approve for 12 months with a quantity limit of #8 tablets per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of unresectable or metastatic melanoma with a $BRAF^{V600E}$ mutation.

RATIONALE
Ensure appropriate use of vemurafenib based on FDA approved indication.
The recommended dose of vemurafenib is 960mg (four 240mg tablets) twice daily. Dose reduction is recommended in the presence of QTc prolongation.

FDA APPROVED INDICATIONS
Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with $BRAF^{V600E}$ mutation as detected by an FDA-approved test.

Limitation of Use: Zelboraf is not recommended for use in patients with wild-type BRAF melanoma.

REFERENCES
- Genentech, Inc. Zelboraf package insert. South San Francisco, CA. August 2011.

Part D Effective: 01/01/13 Created: 08/11
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

VISMODEGIB

Generic	Brand	HICL	GCN	Exception/Other
VISMODEGIB	ERIVEDGE	38455		

FOR COMMERCIAL CLIENTS:
This drug requires a written request for prior authorization.

FOR PART D CLIENTS:
Do not review Part D guidelines with physicians; if the caller wishes to initiate an oral request then a verbal MRF must be completed. Please check the applicable CS note for processing.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic basal cell carcinoma?

   If yes, **approve for 12 months with a quantity limit of #1 capsule per day.**
   If no, continue to #2.

2. Does the patient have a diagnosis of locally advanced basal cell carcinoma that has recurred following surgery or is the patient not a candidate for surgery or radiation?

   If yes, **approve for 12 months with a quantity limit of #1 capsule per day.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic basal cell carcinoma or locally advanced basal cell carcinoma that has recurred following surgery or the patient is not a candidate for surgery or radiation.

RATIONALE
To promote appropriate utilization of Erivedge based on its FDA approved indication.

Vismodegib is an inhibitor of the Hedgehog signaling pathway. This pathway is important in embryonic development and becomes reactivated in cancer. Because this pathway is not required in most adult tissues, inhibitors selectively attack tumor cells. Vismodegib is the first drug approved for advanced BCC. BCC is the most common type of skin cancer and is typically localized, slow-growing and painless. Localized disease is usually curable by surgery and radiation treatment. Advanced disease is more deadly and has no other FDA approved treatment options.

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RATIONALE (CONTINUED)
A single-arm, open-label trial was conducted in patients with either mBCC (n=33) or laBCC (n=71) who received 150mg vismodegib daily until disease progression or unacceptable toxicity. Objective response rates were 30.3% for mBCC and 42.9% for laBCC. No mBCC patients achieved complete response, while 20.6% of laBCC patients had a complete response. Median response duration was 7.6 months for both mBCC and laBCC.

The common adverse reactions are muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, diarrhea, decreased appetite, constipation, arthralgias, vomiting, and ageusia.

There is a **black box warning** for embryo-fetal death and severe birth defects. Pregnancy Category D.

Dosage: One 150mg capsule once daily with or without food.

FDA APPROVED INDICATION
Erivedge is indicated for the treatment of adults with metastatic basal cell carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

REFERENCES
- Genentech, Inc. Erivedge package insert. South San Francisco, CA. January 2012.

Part D Effective: 01/01/13 Created: 02/12
Commercial Effective: 01/01/13 Client Approval: 10/12 P&T Approval: 11/12

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