

Myalept (metreleptin)

STRENGTH	DOSAGE FORM	ROUTE	GPID
5 mg/ml	vial	subcutaneous	36398

MANUFACTURER

Bristol-Meyers Squibb Company

INDICATION(S)

Myalept is a leptin analog indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Limitations of Use:

- The safety and effectiveness of Myalept for the treatment of complications of partial lipodystrophy have not been established.
- The safety and effectiveness of Myalept for the treatment of liver disease including nonalcoholic steatohepatitis (NASH) have not been established.
- Myalept is not indicated for use in patients with HIV-related lipodystrophy.
- Myalept is not indicated for use in patients with metabolic disease, without concurrent evidence of generalized lipodystrophy.

DRUG CLASS

ENDOCRINE DISORDER – OTHER; LEPTIN HORMONE ANALOGS

PLACE IN THERAPY

Myalept, an analog of leptin made through recombinant DNA technology, is the first agent to gain FDA approval for treating complications associated with generalized lipodystrophy. Considered an orphan disease, generalized lipodystrophy is characterized by a lack of fat tissue. This lack of fat tissue impairs proper fat storage and processing, often leading to elevated triglyceride levels and metabolic abnormalities such as insulin resistance and diabetes. Generalized lipodystrophy can be congenital (Seip-Berardinelli syndrome) or acquired (Lawrence syndrome) with an estimated prevalence of less than one case per one million people. Other available agents, such as Egrifta, specifically target HIV associated lipodystrophy and lipoatrophy as opposed to the complications associated with generalized lipodystrophy.

EFFICACY

Safety and efficacy of Myalept was evaluated in a single open-label, single-arm study involving 48 patients with congenital or acquired generalized lipodystrophy and diabetes mellitus, hypertriglyceridemia, and/or increased fasting insulin. Patients were followed for a median of 2.7 years (ranging from 3.6 months to 10.9 years). The majority of enrolled patients had congenital generalized lipodystrophy (67%), were female (75%), and Caucasian (46%). Median age at baseline was 15 years (range 1-68 years) with 35% of patients being less than 18 years of age. Efficacy results at 12 months are

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presented below in table 1. Change in hemoglobin A1C (HbA_{1c}), fasting glucose, and triglycerides observed at month 4 were similar to those at 1 year. Concomitant anti-hyperglycemic and lipid-altering medication dosage regimens were not held constant during the study (e.g., insulin doses were increased, decreased or discontinued altogether during the course of the study).

Table 1. Efficacy results in an open-label, single-arm study in patients with generalized lipodystrophy treated with Myalept.

Parameter	n	Baseline	Change from Baseline at Month 12
		Mean (SD)	Mean (SD)
HbA _{1c} (%)	35	8.7 (2)	-2 (1.5)
Fasting Glucose (mg/dL)	37	174 (85)	-49 (75)
		Median (Q1, Q3)	Median Change (Q1, Q3)
Fasting Triglycerides (mg/dL)	36	348 (176, 769)	-184 (-643, -21)
			Median Percent Change (Q1, Q3)
			-55 (-77, -20)%

SD = standard deviation; Q = quartile

Among 28 patients with generalized lipodystrophy who had a baseline HbA_{1c} 7% or greater and data available at Month 12, the mean (SD) baseline HbA_{1c} was 9.3 (1.5)% and the mean reduction in HbA_{1c} at Month 12 was 2.4%.

Among 12 patients with generalized lipodystrophy who had a baseline triglyceride level 500 mg/dL or greater and data available at Month 12, the median baseline triglyceride level was 1527 mg/dL and the median reduction in triglycerides at Month 12 was 1117 mg/dL.

SAFETY

Myalept carries a black box warning for risk of anti-metreleptin antibodies and risk of lymphoma. For this reason, Myalept is only available through the Myalept Risk Evaluation and Mitigation Strategy (REMS) program. Antibody formation may lead to loss of action of endogenous leptin and loss of efficacy of Myalept. T-cell lymphoma has been reported in patients treated with Myalept. The FDA will require several post-marketing studies to ascertain the incidence of antibody formation and lymphoma development.

Use of Myalept is contraindicated in patients with general obesity not associated with congenital leptin deficiency. Use is also contraindicated in patients with hypersensitivity to Myalept or any of the product components.

Use caution in patients taking insulin or insulin secretagogues concomitantly with Myalept. Significant dose reductions of these agents may be necessary to reduce risk of hypoglycemia.

Adverse reactions most common in clinical trials (≥10%) include headache, hypoglycemia, decreased weight and abdominal pain.

Myalept has been studied in patients as young as 1 year old. No clinically meaningful efficacy or safety differences were observed between the adult and pediatric population. There was not a sufficient

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number of geriatric patients included in the Myalept study population to determine difference in response. Use caution in elderly patients.

No data exists to determine need for adjusted dosing in hepatic or renal impairment.

No drug interaction studies were performed.

Myalept is considered pregnancy category C. It is not known if Myalept is excreted in human milk. Consider risk to infant and mother when determining whether to continue Myalept therapy in nursing mothers.

DOSAGE

Myalept is administered as a once-daily subcutaneous injection. Recommended starting doses, dose adjustments and maximum daily dose is based on weight and gender (see table 2). Dose may be increased or decreased based on clinical response (i.e., metabolic control) and other factors (i.e., tolerability and weight loss). Vials may be reconstituted with sterile water for injection (for newborns and infants) or bacteriostatic water for injection, which can be stored in the refrigerator and used within 3 days.

Table 2: Myalept dose recommendations based on weight and gender.

Baseline Weight	Starting Daily Dose (injection volume)	Dose Adjustments (injection volume)	Maximum Daily Dose (injection volume)
Less than or equal to 40 kg (males and females)	0.06 mg/kg (0.012 mL/kg)	0.02 mg/kg (0.004 mL/kg)	0.13 mg/kg (0.026 mL/kg)
Males greater than 40 kg	2.5 mg (0.5 mL)	1.25 mg (0.25 mL) to 2.5 mg (0.5 mL)	10 mg (2 mL)
Females greater than 40 kg	5 mg (1 mL)	1.25 mg (0.25 mL) to 2.5 mg (0.5 mL)	10 mg (2 mL)

COST

Drug	Cost/unit	Cost per 30 Days
Myalept (metreleptin) 11.3 mg vial (5 mg/ml); dosing based on age and gender	\$1766.4/vial	\$52,992*
Egrifta 2 mg vial; 2 mg SQ daily	\$99.69/vial	\$2990.07

*Based on a 70 kg male

FORMULARY PLACEMENT RECOMMENDATIONS

Based on this initial assessment of available clinical and financial information, consider **NOT ADDING** Myalept to the formulary pending complete review by the appropriate oversight committee for the plan.

REFERENCES

- Myalept [Prescribing Information]. Princeton, NJ: Bristol-Meyers Squibb Company; April 2014

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- Food and Drug Administration. (2014). FDA approves Myalept to treat rare metabolic disease. <http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm387060.htm> (Accessed on April 28, 2014)
- Mantzoros C. Lipodystrophic Syndromes. In: UpToDate, Waltham, MA. (Accessed on April 28, 2014.)