

Aciphex Sprinkle (rabeprazole sodium)

STRENGTH	DOSAGE FORM	ROUTE	GPID
5 and 10mg	delayed release sprinkle capsule	oral	34467, 34468

MANUFACTURER

Eisai Inc.

INDICATION(S)

Aciphex is a proton-pump inhibitor (PPI) indicated in adults for:

- Healing of erosive or ulcerative Gastroesophageal Reflux Disease (GERD)
- Maintenance of healing of erosive or ulcerative GERD
- Treatment of symptomatic GERD
- Healing of duodenal ulcers
- Helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence
- Treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome

In adolescent patients 12 years of age and older for:

- Short-term treatment of symptomatic GERD

In pediatric patients 1 to 11 years of age for:

- Treatment of GERD

DRUG CLASS

UPPER GASTROINTESTINAL DISORDERS - ULCER DISEASE; PROTON-PUMP INHIBITORS

PLACE IN THERAPY

Aciphex Sprinkle is a delayed-release capsule that joins generically available Aciphex (rabeprazole sodium) delayed-release tablet and other proton pump inhibitors (PPIs) such as Prilosec (omeprazole) and Prevacid (lansoprazole). Other oral, non-solid formulations of PPIs include Nexium packets, Prilosec suspension and Prevacid Solutab (all single source brand products). Prilosec and Prevacid are available as generic delayed-release capsules and share the same FDA-approved labeling as Aciphex (which includes pediatric dosing) plus a few additional indications. Prevacid and Prilosec capsules can also be used for patients that may have difficulty swallowing capsules; the Prevacid and Prilosec package inserts recommend that patients who have difficulty swallowing delayed-release capsules should open the capsules and sprinkle the intact granules onto 15mL of applesauce. The granules should be mixed with the applesauce and swallowed immediately with liquid thereafter to ensure complete swallowing of the granules. Aciphex Sprinkle is available in a lower dosage (5mg, 10mg) than Aciphex tablets (20mg) which allows for administration to children unable to swallow capsules when its capsule contents are sprinkled onto soft food or liquid.

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EFFICACY

The use of Aciphex Sprinkle in pediatric patients 1 to 11 years of age is supported by a two-part, multicenter, randomized, double-blind, parallel 2 dose arms clinical trial which was conducted in 127 pediatric patients with endoscopic and histologic evidence of GERD prior to study treatment. Part 1 was 12 weeks in duration. Patients were randomized to one of two Aciphex Sprinkle dose levels based on body weight. Patients weighing 6.0 to 14.9 kg received either 5 or 10 mg Aciphex Sprinkle and those with body weight 15 kg received either 10 or 20 mg of Aciphex Sprinkle. For Part 1, rates of endoscopic healing were calculated and are shown in the table below.

SHORT-TERM (12-WEEK) HEALING RATES IN 1 to 11 YEAR OLD CHILDREN (PART 1)

Endoscopic Classification of GERD At Baseline	Healing Rate at 12 weeks		
	Body Weight <15 kg		Body Weight ≥15 kg
	5 mg dose	10 mg dose	10 mg dose
Erosive ^a	88% (7/8)	83% (5/6)	71% (12/17)
Non-erosive ^b	78% (7/9)	100% (10/10)	81% (17/21)

^a Hetzel-Dent score ≥2

^b Hetzel-Dent score = 1

Obtained from Aciphex package insert

Part 2 was a 24-week double-blinded extension of Part 1 (on same dose assigned in Part 1). Endoscopic evaluations were performed at 12 weeks (Part 1) and 36 weeks (Part 2) to assess esophageal healing. No pre-specified formal hypothesis testing was conducted. Of the 87 patients with healing in Part 1, 64 patients were enrolled into Part 2. The absence of a placebo group does not allow assessment of sustained efficacy through 36 weeks. Of the 52 patients with available data, healing was observed in 47 (90%) patients at 36 weeks.

SAFETY

In the adult studies (4 to 8 weeks), adverse reactions that occurred at a rate greater than 2% and greater than placebo included pain, pharyngitis, flatulence, infection and constipation. In studies of pediatric and adolescent patients (ages 1 to 16 years, and up to 36 weeks exposure) adverse reactions that occurred at a rate of 5% of patients included abdominal pain, diarrhea and headache.

As with all PPIs, their use has been associated with an increased risk of *Clostridium difficile*-associated diarrhea, bone fracture, and hypomagnesemia. Also, PPIs inhibit gastric acid secretion which may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, iron salts and digoxin).

Patients taking warfarin need to be monitored since Aciphex has been noted to increase INR and prothrombin times. Aciphex may reduce the plasma levels of atazanavir, inhibit cyclosporine and increase serum level of methotrexate.

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DOSAGE

Patients between the ages of 1 to 11 years old with GERD should use 5 mg daily if weighing less than 15 kg and 10mg daily if weighing 15kg or more. Patients aged 12 years and older with GERD and adults with duodenal ulcers should use 20mg daily. Patients with pathological hypersecretory conditions, including Zollinger-Ellison Syndrome, should be initiated on 60mg and the dose adjusted per patient needs.

Aciphex Sprinkle delayed-release capsules should be opened and the granule contents sprinkled on a spoonful of soft food or liquid (e.g., applesauce). Whole dose should be taken within 15 minutes of being sprinkled. The granules should not be chewed or crushed. Dose should be taken 30 minutes before a meal.

COST

Drug	Cost/unit	Cost per 30 Days
Aciphex Sprinkle (rabeprazole sodium) 5 &10mg delayed-release sprinkle capsules	AWP=\$14 (flat priced)	\$420*
Aciphex (rabeprazole sodium)20mg delayed- release tablet	MAC=\$ pending	
lansoprazole delayed-release capsule 15&30mg	MAC=\$0.79-\$1.09	\$24-33*
omeprazole delayed- release capsule 10&20mg	MAC=\$0.10-\$0.26	\$3-8*
Nexium (esomeprazole) 2.5mg, 5mg, 10mg, 20mg, 40mg delayed-release packet	AWP=\$8.93	\$268
Prilosec (omeprazole magnesium) delayed-release suspension (packet) 2.5mg, 10mg	AWP=\$6.84	\$205-\$410*

*Cost is calculated using package labeled dosing for 1-11 year olds which is as follows:

- Lansoprazole 30mg daily if over 30kg (15mg daily if 30Kg or less)
- Omeprazole 20mg daily for 20Kg or more, 10mg for 10-19Kg, and 5mg for 5-9kg.

FORMULARY PLACEMENT RECOMMENDATIONS

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

REFERENCES

- Aciphex Sprinkle [Prescribing Information]. Woodcliff Lake, NJ: Eisai Inc., March 2013.
- Prilosec [Prescribing Information]. Wilmington, DE: AstraZeneca, May 2013.
- Prevacid [Prescribing Information]. Deerfield, IL: Takeda Pharmaceuticals, September 2012.