

**PHARMACY PRIOR AUTHORIZATION
Clinical Guideline**

Proton Pump Inhibitors (PPIs)

**Prilosec® (omeprazole), Prilosec (omeprazole) OTC™, Zegerid® (omeprazole),
Protonix® (pantoprazole), Prevacid® (lansoprazole), Aciphex® (rabeprazole),
Nexium® (esomeprazole)**

FDA Indications (label and off-label*)

- Duodenal ulcer
- Dyspepsia
- Gastric ulcer
- *Helicobacter pylori* (*H. pylori*) infection in combination with an appropriate antibiotic regimen
- Gastroesophageal reflux disease (GERD)
- Esophagitis
- Hypersecretory conditions (i.e., Zollinger–Ellison syndrome)
- Stress ulcer prophylaxis in critically ill patients
- **Other commonly accepted uses***:
 - Esophageal stricture
 - Barrett’s esophagus
 - Risk reduction of nonsteroidal anti-inflammatory drug (NSAID)–associated gastric ulcer (risk factors include: >60 yrs of age, documented history of peptic ulcer disease/gastric ulcer/upper gastrointestinal bleed, or concomitant oral glucocorticoid or anticoagulant therapy)
 - To improve pancreatic enzyme absorption in cystic fibrosis patients with intestinal malabsorption

*Off-label use based on peer-reviewed clinical studies

Dosage Forms

Rx omeprazole, Prilosec - 10 mg, 20 mg, 40 mg delayed-release capsules
Rx Prilosec – 2.5 mg, 10 mg delayed-release powder for oral suspension
OTC Prilosec/omeprazole OTC – 20 mg delayed-release tablets
Protonix, pantoprazole – 20 mg, 40 mg delayed-release tablet
Protonix – 40mg delayed-release granules for oral suspension
Prevacid

- 15 mg, 30 mg delayed-release capsules
- 15 mg, 30 mg Solutab (orally disintegrating), delayed-release tablets

Aciphex – 20 mg delayed-release tablets
Nexium

- 20 mg, 40 mg delayed-release capsules
- 10 mg, 20 mg, 40 mg delayed-release powder for oral suspension

Zegerid

- 20mg, 40 mg immediate-release capsules (with sodium bicarbonate 1,100 mg)
- 20 mg, 40 mg powder for oral suspension (with sodium bicarbonate 1,680 mg)

Dosage

Omeprazole, Prilosec, Prilosec OTC/omeprazole OTC

- Adults: 20 mg – 40 mg once daily for most indications, up to 120 mg 3 times daily for hypersecretory conditions
- Children 1 – 16 years of age:
 - Weight 5<10kg= 5mg daily
 - Weight 10<20kg = 10mg daily
 - Weight ≥ 20kg = 20mg daily

Pantoprazole, Protonix - Adults: 40 mg once daily, up to 240 mg daily for hypersecretory conditions

Prevacid

- Adults: 15 mg – 30 mg once daily, up to 90 mg twice daily for hypersecretory conditions
- Children 1 - 11 years of age:
 - Weight < 30kg = 15mg daily, up to 30mg twice daily
 - Weight > 30kg = 30mg daily, up to 30mg twice daily

Aciphex - Adults: 20 mg once daily, up to 120 mg daily for hypersecretory conditions

Nexium

- Adults: 20 mg – 40 mg once daily
- Adolescents and Children 12—17 years: 20 mg or 40 mg once daily, for up to 8 weeks.
- Children 1—11 years of age:
 - < 20 kg: 10 mg PO once daily for up to 8 weeks
 - ≥20 kg: 10 mg or 20 mg once daily for up to 8 weeks

Zegerid – Adults 20 mg-80 mg daily

Authorization Guidelines

Inclusions

Medicaid Plans (MCY, MHG)

Note: MHG -Prilosec OTC – not covered due to OTC status

- **Prilosec OTC/omeprazole OTC, omeprazole Rx capsules: Approve up to 4 per day [120/month], when filled with a prescription:**
 - **Step-therapy** after 2 consecutive fills of therapeutic dose formulary H2-antagonist within the last 6 months, by Rx claims history or
 - **Member has filled omeprazole/omeprazole OTC/Prilosec OTC** in the last year by Rx claims history (step-therapy had been met in the past) or
 - **Medical records** documenting failure of H2-antagonists or
 - **GI specialist:** Prescribing physician/physician assistant/nurse practitioner is a gastroenterology specialist, or
 - **Appropriate diagnosis** documented in medical records (e.g., progress notes, EGD results, or laryngoscopic exam):
 - Duodenal ulcer or gastric ulcer
 - Erosive esophagitis, Barrett's esophagus, or esophageal stricture

- GERD-related laryngitis
- Hypersecretory conditions (e.g., Zollinger-Ellison syndrome)
- Cystic fibrosis patients with intestinal malabsorption
- To reduce NSAID-associated gastric ulcer for members who need to continue taking NSAIDS. Must have at least 1 of the following risk factors:
 - 1) >60 years of age
 - 2) Documented history of peptic ulcer disease/gastric ulcer/upper gastrointestinal bleed
 - 3) High dose NSAID
 - 4) Concurrent use of corticosteroids (chronic use)
 - 5) Concurrent use of anticoagulants

*Note: Omeprazole/OTC/Prilosec OTC will automatically process if NSAIDs are filled twice in the last 90 days

- **Approve 28 tablets for a 2-week course of therapy for the treatment of *H.pylori* with documentation (e.g., positive IgG serology, Urea Breath Test, pathology).**
Note: Combination products such as Prevpac and Helidac are not covered. Please refer to formulary for individual agents in combination with PPI.

- **Pantoprazole**

- Approve after 2 consecutive month fills of omeprazole 80 mg daily or
- Approve after 2 consecutive month fills of maximum, tolerated dose of omeprazole or
- Approve for failure of omeprazole (any dose) per medical records

- **Prevacid Solutab or omeprazole** approve for children 1-17 years of age

- After trial of any dose H2 antagonists, or
- If prescriber is pediatric/adult gastroenterology or pediatric/adult pulmonologist

Exclusions

None

Prior Authorization Requirements

Initial Approval

- **Review pharmacy claims history** (for medications that require step-therapy)
- **Review medical records** (e.g., progress notes, EGD report, *H. pylori* test results)
- **Duration of approval based on indication:**
 - *H. pylori* infection – approve for 2 weeks-1 month (as requested)
 - Prevention of NSAID-induced gastropathy-approve for 6 months
 - All other indications
 - Adults – approve indefinitely
 - Children – approve (3-6 months)

Renewal

- **Review pharmacy claims history for compliance**
- **Review medical records if member has been non-compliant with rx fills**
- **Duration of approval based on indication:**
 - post-*H. pylori* treatment without indication for PPI: step therapy with H2-antagonists is required
 - Prevention of NSAID-induced gastropathy- approve indefinitely

➤ Children – approve (3-6 months) at a time

Additional Information

H. pylori tests:

IgG serology is an indicator of ongoing *H. pylori* gastritis with a sensitivity and specificity of greater than 90%. The results of a serologic test are usually reported as a qualitative result (positive, negative, indeterminate) based upon a predetermined cutoff value in EIA units. The quantitative result (expressed in EIA units) falls slowly following successful treatment with antibiotics and a 20% decline in titer over 6 months has been shown to correlate with successful eradication.

Urea Breath Test: Proton pump inhibitors, antibiotics and bismuth may cause false negative breath tests and it is recommended that patients be off of antibiotics and bismuth for 1 month prior to the breath test. Proton pump inhibitors must be discontinued 1 week prior to breath testing.

FDA Approved Regimens for *H.pylori* Eradication:

1. Bismuth 525mg qid + metronidazole 250mg qid + tetracycline 500 mg qid × 2 wk + H2RA as directed× 4 wk.
2. Lansoprazole 30 mg b.i.d. + clarithromycin 500 mg b.i.d. + amoxicillin 1 g b.i.d. × 10 days.
3. Omeprazole 20 mg b.i.d. + clarithromycin 500 mg b.i.d. + amoxicillin 1 g b.i.d. × 10 days.
4. esomeprazole 40 mg q.d. + clarithromycin 500 mg b.i.d. + amoxicillin 1 g b.i.d. × 10 days.
5. Rabeprazole 20 mg b.i.d. + clarithromycin 500 mg b.i.d. + amoxicillin 1 g b.i.d. × 7 days.

First-Line Regimens for *Helicobacter pylori* Eradication (Am J Gastroenterol 2007;102:1808-1825)

Regimen	Duration	Eradication Rates	Comments
Standard dose PPI b.i.d. (esomeprazole is q.d.), clarithromycin 500 mg b.i.d., amoxicillin 1,000 mg b.i.d.	10-14 days	70-85%	Consider in nonpenicillin allergic patients who have not previously received a macrolide
Standard dose PPI b.i.d., clarithromycin 500 mg b.i.d. metronidazole 500 mg b.i.d.	10-14 days	70-85%	Consider in penicillin allergic patients who have not previously received a macrolide, or are unable to tolerate bismuth quadruple therapy
Bismuth subsalicylate 525 mg p.o. q.i.d. metronidazole 250 mg p.o. q.i.d., tetracycline 500 mg p.o. q.i.d., ranitidine 150 mg p.o. b.i.d. or standard dose PPI q.d. to b.i.d.	10-14 days	75-90%	Consider in penicillin allergic patients
PPI + amoxicillin 1 g b.i.d. x 5 days followed by: PPI, clarithromycin 500 mg, tinidazole 500 mg b.i.d. x 5 days	10 days total	>90%	Requires validation in North America

Standard dosages for PPIs are as follows: lansoprazole 30 mg p.o., omeprazole 20 mg p.o., pantoprazole 40 mg p.o., rabeprazole 20 mg p.o., esomeprazole 40 mg p.o.

H. pylori treatment regimens available at: <http://www.gi.org/physicians/guidelines/ManagementofHpylori.pdf>
<http://www.cdc.gov/ulcer/keytocure.htm#fda>

PPI dosing for infants < 1 year old:

Drug	Dose	Comments
Esomeprazole	1-12 months of age: 0.25 mg/kg and 1 mg/kg	Age < 1 yr: safety and efficacy has not been established J Pediatr Gastroenterol Nutr. 2007 Nov;45(5):530-7

Lansoprazole	≥3 mos: Limited data, single-dose studies, range used: 0.5 to 1.6 mg/kg.	Age <1 yr: safety and efficacy has not been established 0. 2-0. 3 mg/kg/day in infants <10 weeks of age, or 1-1. 5 mg/kg/day in infants >10 weeks of age 3-7 months: 15mg once daily or 7.5mg BID
Omeprazole	Per limited, short-term data, 1 to 3.3 mg/kg/day is effective and safe.	Age <1 yr: safety and efficacy has not been established
Pantoprazole	Limited short-term data indicates that 0.5 to 1 mg/kg/day once daily is effective and safe	safety and efficacy in children has not been established
Rabeprazole, Zegerid	N/A	safety and efficacy in children has not been established

Plavix and PPIs:

Clopidogrel requires hepatic biotransformation via CYP2C19 isoenzymes to its active metabolite; omeprazole is both a substrate and an inhibitor of the CYP2C19 isoenzyme. As a result, omeprazole may decrease the hepatic metabolism of clopidogrel to its active metabolite. In a randomized study (n=140), patients undergoing elective coronary stent implantation were treated with clopidogrel (loading dose 300 mg, followed by 75 mg/day) plus aspirin (75 mg/day) and randomized to receive omeprazole (20 mg/day) or placebo. On day 7 of treatment, 60.9% of patients in the omeprazole group were considered poor responders compared to 26.7% in the placebo group (p <0.0001). Because other proton pump inhibitors (PPIs) are also CYP2C19 isoenzyme substrates, it is possible that any PPI may decrease the conversion of clopidogrel to its active metabolite thereby reducing effectiveness. It should be noted that conflicting results have been reported and that the manufacturer is working with the FDA to conduct additional studies to better understand the clinical significance of this interaction. Nevertheless, clinicians should carefully evaluate the need for initiating or continuing PPI therapy in patients being treated with clopidogrel.

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