BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.50.001

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	December 7, 2011
Subject:	Proton Pump Inhibitors	**Page:**	1 of 7

Last Review Date: March 8, 2024

Proton Pump Inhibitors

Description

Aciphex*, Aciphex Sprinkle* (rabeprazole*)
Dexilant, Dexilant Solutabs (dexlansoprazole)
Esomeprazole Strontium, Nexium* (esomeprazole magnesium)
Prevacid*, Prevacid Solutab*, First-Lansoprazole suspension* (lansoprazole)
Protonix*, First-Pantoprazole suspension* (pantoprazole)
Zegerid* (omeprazole / sodium bicarbonate)

*Prior authorization for certain formulations applies only to formulary exceptions due to being a non-covered medication. Please review plan formulary options.

Background
Omeprazole, esomeprazole, lansoprazole, dexlansoprazole, rabeprazole, and pantoprazole belong to a class of medications called proton pump inhibitors (PPI) that are used to decrease the amount of acid produced in the stomach. This reduction helps aid in the healing of acid-related damage to the lining of the esophagus caused by acid reflux. They also work to aid in the healing of ulcers (1-10).

Regulatory Status
The individual agent proton pump inhibitor products addressed by this policy are FDA-approved for use in one or more of the following conditions:

- Duodenal ulcer
- Gastric ulcer

- Gastroesophageal reflux disease (GERD)
- Erosive esophagitis (EE)
- *Helicobacter pylori* eradication to reduce the risk of duodenal ulcer recurrence
- Pathological hypersecretory conditions, including Zollinger-Ellison Syndrome
- Relief of heartburn

Zegerid (omeprazole / sodium bicarbonate); FDA-approved indications:

- Short-term treatment of active duodenal ulcer
- Short-term treatment of active benign gastric ulcer
- Treatment of gastroesophageal reflux disease (GERD)
- Maintenance of healing of erosive esophagitis
- Reduction of risk of upper GI bleeding in critically ill patients (9)

The safety and effectiveness of Zegerid Powder for Oral Suspension and Capsules in pediatric patients (<18 years of age) have not been established (10).

Proton Pump therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated (1-10).

Proton pump inhibitor therapy may be associated with an increased risk of *Clostridium difficile* associated diarrhea (CDAD) and hypomagnesemia. Low magnesium levels may occur in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. Discontinuation of the PPI may be required. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that cause hypomagnesemia, healthcare professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically (1-10).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Proton Pump Inhibitors may be considered **medically necessary** it the conditions indicated below are met.

Proton Pump Inhibitors may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Esophagitis
    a. Barrett's*
    b. Erosive*
    c. GERD (includes laryngeal and pharyngeal)
    d. Sclerodermal (part of CREST syndrome) *
2. Gastropathy
    a. Medication related
    b. NSAID related*
3. GI Bleed
4. H. Pylori – currently undergoing treatment and in combination with antibiotic therapy
5. Hypersecretory disease such as Zollinger-Ellison Syndrome*
6. Ulcer – duodenal, gastric or peptic

OR

1. **ANY** GI related diagnosis

    AND ONE of the following**:**

    a. Failure of therapy with one H2 blocker
    b. Failure of therapy with one of the other PPI
    c. Prescriber is **ONE** of the following
        i. Gastroenterologist
        ii. Ear, Nose and Throat Specialist
        iii. Pulmonologist

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Quantity 90 units
Age ≤6 **only**: 900 ml of First-Lansoprazole (3 mg/ml) suspension
Age ≤6 **only**: 900 ml of First-Pantoprazole (4 mg/ml) suspension

Duration 365 days

Prior - Approval Limits

Quantity

Medication/Strength	Quantity
All non-FE medications	3 units per day

Medication/Strength **with Approved Formulary Exception only**	Quantity
First-Lansoprazole (3 mg/mL) suspension	2,700 mL every 90 days
First-Pantoprazole (4 mg/mL) suspension	2,700 mL every 90 days
All other FE medications	3 units per day

Duration 12 months
*These diagnoses may be approved for 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Proton pump inhibitors are the potent suppressors of gastric acid secretion. In typical doses, they diminish the daily production of acid by 80-95%. PPIs are generally safe, although caution

should be used in patients being treated concurrently with anticoagulants, tacrolimus, theophylline, and methotrexate. Proton Pump therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Proton pump inhibitor therapy may be associated with an increased risk of *Clostridium difficile* associated diarrhea (CDAD) and hypomagnesemia (1-10).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of the proton pump inhibitors while maintaining optimal therapeutic outcomes.

References

1. Aciphex [package insert] Woodcliff Lake, NJ: Eisai Inc.; November 2020.
2. Dexilant [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; November 2020.
3. Esomeprazole Strontium [package insert]. Glasgow, KY: Amneal Pharmaceuticals; January 2021.
4. Nexium [package insert]. Wilmington DE: AstraZeneca LP; November 2020.
5. Nexium IV [package insert]. Wilmington DE: AstraZeneca LP; November 2020.
6. Prevacid [package insert]. Warren, NJ: Takeda Pharmaceuticals America, Inc.; November 2020.
7. Prilosec [package insert]. Wilmington DE: AstraZeneca LP.; December 2016.
8. Protonix [package insert]. Philadelphia, PA: Pfizer Inc.; June 2018.
9. Protonix IV [package insert]. Philadelphia, PA: Pfizer Inc.; June 2018.
10. Zegerid [package insert]. San Diego, CA: Santarus, Inc.; November 2020.

Policy History

Date	Action
September 2004	In order to be consistent with current benefit design, Zegerid was included in the overall current upfront PPI 90 quantity allowance per year
January 2009	Removal of Prilosec/omeprazole from the FEP PA Program (all strengths). Prescription Prilosec/omeprazole 20mg will be covered by the plan.
February 2009	Addition of Kapidex to PA process
March 2009	Removal of Prevacid Naprapac due to discontinuation by the manufacturer in December of 2008
March 2010	Kapidex name change to Dexilant due to dispensing errors

June 2010	Line extension, addition of Vimovo, a FDA approved fixed-dose combination of delayed-release enteric-coated naproxen, a non-steroidal anti-inflammatory drug (NSAID), and immediate-release esomeprazole, a stomach acid-reducing proton pump inhibitor (PPI), approved for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers
November 2011	Addition of short bowel syndrome as an approvable diagnosis with 2-year approval
December 2012	Annual editorial review and reference update
March 2013	Annual editorial review and reference update
April 2013	Removal of Vimovo into separate criteria. Line-extension First-Lansoprazole
September 2013	Line-extension addition of Esomeprazole Strontium
June 2014	Annual editorial review and reference update
March 2015	Annual editorial review and reference update. Removal of non-supported diagnoses
March 2016	Addition of Dexilant Solutabs Policy number change from 5.09.01 to 5.50.01
June 2016	Annual review
September 2016	Annual editorial review and reference update Esomeprazole Strontium removed due to product discontinuation.
March 2017	Annual editorial review and reference update
February 2018	Esomeprazole Strontium products currently available on the market, added back into criteria
March 2018	Annual editorial review and reference update
June 2018	Annual review and reference update
March 2019	Annual review and reference update
September 2019	Changed approval duration from lifetime to 2 years for Barrett's, Erosive, and Sclerodermal esophagitis; and hypersecretory disease (Zollinger-Ellison Syndrome)
December 2019	Annual review. Moved Zegerid to MFE with PA only. Revised First-Lansoprazole PA quantity from 10,800 mL/365 to 2,700 mL/90
March 2020	Annual review
December 2020	Aciphex, Aciphex Sprinkle (rabeprazole), First-Lansoprazole, Nexium, Prevacid, Prevacid Solutab, and Protonix: certain formulations require formulary exception + PA
March 2021	Annual review and reference update
September 2022	Annual review
June 2023	Annual review

February 2024	Addition of First-Pantoprazole to policy as product requiring formulary exception + PA
March 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.