Clinical Policy: Proton Pump Inhibitors

Reference Number: CP.CPA.209
Effective Date: 11.16.16
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Line of Business: Medicaid – Medi-Cal

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are Proton Pump Inhibitors requiring prior authorization: rabeprazole (Aciphex/Aciphex Sprinkle®), dexlansoprazole (Dexilant®), esomeprazole Strontium (ES), esomeprazole (Nexium®), omeprazole (Prilosec® Powder), lansoprazole (Prevacid® Solutabs), omeprazole/sodium bicarbonate (Zegerid®).

FDA approved indications:

Indication	Aciphex	Dexilant	Nexium	Prilosec	Prevacid	Zegerid	Aciphex Sprinkle	ES
Duodenal ulcers	X		*	X	X	X		
Duodenal ulcers, maintenance				*	X			
Duodenal ulcers, Giant				*				
Erosive esophagitis	X	X	X	X	X	X		X
Erosive esophagitis, Maintenance	X	X	X	X	X	X		X
Gastric ulcers	*			X	X	X		
Nonsteroidal anti-inflammatory drug (NSAID)-associated gastric ulcer, risk reduction			X	*	X			X
NSAID-associated gastric ulcer, healing of				*	X			
Helicobacter pylori Triple Therapy	X		X	X	X			X
Helicobacter pylori Dual Therapy				X	X			
Helicobacter pylori Quadruple therapy	*			*	*			
Pathological hypersecretory conditions, including Zollinger-Ellison Syndrome	X		X	X	X			X
Symptomatic gastroesophageal reflux disease (GERD) (erosive/ulcerative)	X		X^	X	X^	X	X^	X

Symptomatic GERD, maintenance (erosive/ulcerative)	X							
Symptomatic GERD (non-erosive)		X	X		X			X
Indigestion	*			*				
Drug-induced GI disturbance				*				
Esophageal stricture				*				
Heartburn					*			
Reduction of risk of upper GI bleed in critically ill patients				*		X		

**Clinical trials have demonstrated the efficacy and safety for these indications, although not currently FDA-approved.*
^ *Pediatric only*

Limitation of use:
- Prevacid SoluTabs or Aciphex Sprinkle for patients less than 1 year of age

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Aciphex, Dexilant, Nexium, esomeprazole strontium, Prilosec Powder, Prevacid Solutabs, Zegerid are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. All indications (must meet all)**:**
1. Patient has one of the following:
   a. Symptomatic GERD;
   b. Esophageal- Schatzki's ring, erosive esophagitis (EE), esophageal stricture;
   c. Extra-esophageal: vocal cord damage/nodules, asthma, laryngitis and pharyngitis;
   d. Barrett's esophagus, Laryngopharyngeal reflux (LPR), or Zollinger-Ellison Syndrome (automatically qualifies for BID dosing if requested);
   e. Gastric ulcer (GU) or duodenal ulcer (DU);
   f. *H. pylori*;
   g. High-risk individuals on NSAIDs defined as ONE of the following:
      i. History of complicated Peptic Ulcer Disease (PUD);
      ii. Age > 60 years;
      iii. Concurrent anticoagulant, platelet inhibitors (e.g. warfarin, aspirin, Plavix) or oral corticosteroid (e.g. prednisone) therapy;
2. For Prevacid SoluTabs or Aciphex Sprinkle, age >1 years old;
3. For Dexilant, esomeprazole, omeprazole/sodium bicarbonate, Prevacid Solutabs, rabeprazole: failure of a minimum 4 week trial of ALL of the following preferred generic PPI at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced: omeprazole capsules, pantoprazole tablets, and lansoprazole capsules;

4. For members on Plavix and requesting Dexilant, failure of a minimum 4 week trial of pantoprazole tablets only at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. For pediatric members, Prevacid SoluTabs, Aciphex Sprinkles, or omeprazole 2 mg/mL suspension can be approved as requested;
6. For patients with a g-tube or significant dysphagia, Prevacid SoluTabs or omeprazole/sodium bicarbonate can be approved after a trial of Protonix Packets (chart note documentation may be required);
7. For two per day dosing requests of non-preferred agents, member must be titrated up from one per day;
8. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: Length of Benefit

B. Other diagnoses/indications

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DU: duodenal ulcer
EE: erosive esophagitis
ES: esomeprazole strontium
GERD: gastroesophageal reflux disease
GI: gastrointestinal

GU: gastric ulcer
H. Pylori: Helicobacter pylori
LPR: laryngopharyngeal refuls
NSAID: non-steroidal anti-inflammatory drug
PPI: proton pump inhibitor
PUD: peptic ulcer disease

Appendix B: General Information

- Dexilant 60 mg vs. Prevacid 30 mg in EE was evaluated in two studies. Non-inferiority was demonstrated in both studies, but superiority was demonstrated in only one study.
- Dexilant 90 mg was studied and did not provide additional clinical benefit over Dexilant 60 mg in EE.
- Patients with a platelet reactivity index (PRI) >50% is linked to sub-acute stent thrombosis.
- In a study by Siller-Matula JM, et al., The PRI was similar in patients on Protonix or Nexium (mean 51%; 95% CI 48-54%) and for patients on Plavix and Protonix the mean was PRI = 50% and for Plavix and Nexium the mean PRI was 54%.
- Over 90% of gastric and duodenal ulcers heal within 8 weeks of proton pump inhibitor (PPI) therapy.
- There have been models constructed to evaluate both the efficacy and cost-effectiveness of "step-up" therapy (starting with H2 antagonists and titrating to symptom control) and "step-down therapy" (starting with PPI therapy and decreasing therapy to the lowest form of acid suppression that controls symptoms). Neither method has been proven superior.
- Patients with PUD (DU or GU) should be tested for H. pylori and treated, if positive.
- For Laryngopharyngeal reflux (LPR), the American Academy of Otolaryngology recommends twice-daily dosing with PPIs for a minimum period of 6 months with the possibility of chronic treatment. BID dosing of PPIs has been shown to be superior to QD dosing in LPR.
- Zegerid is contraindicated in patients with metabolic alkalosis and hypocalcemia because of its sodium bicarbonate content.
- 2 capsules of Zegerid 20 mg are not interchangeable with 1 capsule of Zegerid 40 mg because each capsule or packet contains the same amount of sodium bicarbonate.
- Pediatric patients: The safety and efficacy of Dexilant, Zegerid and Protonix in children have not been established. The safety and efficacy of Prevacid have been established in pediatric patients 1 to 17 years of age. The safety and efficacy of omeprazole have been established in pediatric patients 1 to 16 years of age. The safety and efficacy of Nexium have been established in pediatric patients 1 to 17 years of age for up to 8 weeks. The safety and efficacy of Aciphex have been established in pediatric patients 1 year and older for up to 36 weeks.
- Safety and efficacy of proton pump inhibitors have not been established in patients less than 1 year of age. Lansoprazole was no more effective than placebo in patients 1 month to less than 1 year of age with symptomatic GERD in a multi-center, double-blind, placebo controlled study (Orenstein et al, 2009). Studies with Aciphex Sprinkle do not support its use for the treatment of GERD in pediatric patients younger than 1 year of age.

- Prevacid has a non FDA-approved, Class IIa strength recommendation for giant duodenal ulcer per Micromedex. Of 27 study patients with giant duodenal ulcer placed on Prilosec, 20 (71.4%) did not require operative intervention, and 8 (28.6%) required operation for ulcer complications.
- Prevacid has a non FDA-approved, Class IIa strength recommendation for heartburn and H. pylori quadruple therapy per Micromedex.
- Aciphex has a non FDA-approved, Class II a strength recommendation for gastric ulcers, H. pylori quadruple therapy and indigestion per Micromedex.
- Several published observational studies suggest that high-dose, defined as multiple daily doses, and longterm PPI therapy (a year or longer) may be associated with an increased risk for osteoporosis related fractures. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.
- Hypomagnesemia has been reported rarely in patients treated with PPIs for > 3 months that can lead to serious adverse events including tetany, arrhythmias, and seizures. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g.,diuretics), consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
- According to their respective package inserts, concomitant administration of either pantoprazole or dexlansoprazole with clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel-induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of Protonix or Dexilant. American Hospital Formulary Service Drug Information further states, “If concomitant proton-pump inhibitor therapy [with clopidogrel] is considered necessary, some clinicians suggest the use of pantoprazole, which appears to be the weakest inhibitor of cytochrome P450 2C19 (CYP2C19) among proton-pump inhibitors.”
- Long term daily use (longer than 3 years) of PPIs may lead to malabsorption of cyanocobalamin (vitamin B-12). PPIs can cause acute interstitial nephritis.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Prescription Proton Pump Inhibitors		
omeprazole (Prilosec®)	Adults: 20-40 mg PO QD - BID Children: (Age 1-16 yrs old) 5 to <10 kg: 5 mg PO QD 10 to <20 kg: 10 mg PO QD >20 kg: 20 mg PO QD	Doses up to 120 mg 3 times/day have been administered. Administer daily doses greater than 80 mg in divided doses.
lansoprazole (Prevacid®)	Adults: 15-30 mg PO QD - TID Pediatric: (1-11 yrs old)	Doses up to 90 mg/day PO for eradication of H.Pylori ; up to 180 mg/day PO for

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	<30 kg: 15 mg PO QD >30 kg : 30 mg PO QD (12-17 yrs old) 15-60 mg PO QD	Zollinger-Ellison syndrome.
pantoprazole (Protonix®)	Adults: 40 mg PO QD to BID Pediatric (5 years and older): ≥15 kg to <40 kg: 20 mg PO QD ≥40 kg: 40 mg PO QD	Doses up to 240 mg/day have been studied in pathological hypersecretory conditions (e.g. Zollinger-Ellison Syndrome)
High-Dose Prescription H2 Blockers		
nizatidine (Axid®, Axid® AR)	Up to 150 mg PO BID (300 mg/day)	12 weeks
famotidine (Pepcid®)	Up to 40 mg PO BID	12 weeks
cimetidine (Tagamet®, Tagamet HB®)	Up to 800 mg PO BID or 400 mg PO QID	12 weeks
ranitidine (Zantac®)	Up to 300 mg PO BID	12 weeks
Over-the-Counter (OTC) Proton Pump Inhibitors*		
Prevacid 24hr OTC® (lansoprazole) **OTC agents may not be covered	15 mg PO QD	15 mg/day for 14 days Consult MD if > 14 days
Prilosec OTC® (omeprazole) **OTC agents may not be covered	20 mg PO QD	20 mg/day for 14 days Consult MD if > 14 days
Zegerid OTC® (omeprazole/sodium bicarbonate) **OTC agents may not be covered	20 mg/1100 mg PO QD	20 mg/1100 mg/day for 14 days Consult MD if > 14 days

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose

rabeprazole (Aciphex) (Aciphex Sprinkle)	20-60 mg PO QD – BID <15 kg: 5 -10 mg PO QD ≥15 kg: 10 mg PO QD	40 mg/day (120 mg/day for Zollinger-Ellison syndrome)
esomeprazole (Nexium)	Adult: 20-40 mg PO QD to BID Pediatric: 1-11 yrs old: 10-20 mg PO QD 12-17 yrs old: 20-40 mg PO QD	80 mg/day (240 mg/day for Zollinger-Ellison syndrome)
Prilosec Granules for suspension (omeprazole magnesium)	Adults: 20-60 mg PO QD - BID Children: (Age 1-16 yrs old) 5 to <10 kg: 5 mg PO QD 10 to <20 kg: 10 mg PO QD >20 kg: 20 mg PO QD	120 mg/day (360 mg/day for Zollinger-Ellison syndrome)
Prevacid SoluTab (lansoprazole)	Adults: 15-30 mg PO QD to TID or 60mg PO QD Pediatric: (1-11 yrs old) <30 kg: 15 mg PO QD >30 kg : 30 mg PO QD (12-17 yrs old) 15-30 mg PO QD	90 mg/day (180 mg/day for Zollinger-Ellison syndrome)
omeprazole/ sodium bicarbonate (Zegerid)	20-40 mg PO QD	40 mg/day
Dexilant (dexlansoprazole)	30-60 mg PO QD	60 mg/day
esomeprazole strontium	24.65-49.3 mg PO QD to BID	80 mg/day (of esomeprazole base); 240 mg/day for Zollinger-Ellison syndrome

VI. Product Availability

Drug	Availability
Rabeprazole (Aciphex)	delayed release tablets: 20 mg delayed release sprinkle capsules: 5 mg, 10 mg
Dexlansoprazole (Dexilant)	delayed release capsule: 30 mg, 60 mg

Esomeprazole (Nexium)	delayed release capsule: 20 mg ,40 mg
Esomeprazole powder for oral suspension packets	packets: 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg
Prevacid Solutab	delayed release solutabs: 15 mg, 30 mg
Prilosec powder for oral suspension	packets: 2.5 mg, 10 mg
Zegerid Capsule	capsules: 20 mg/1100 mg, 40 mg/1100 mg
Zegerid powder for oral suspension	packets: 20 mg/1680 mg, 40 mg/1680 mg
Esomeprazole strontium	delayed release capsule: 24.65 mg (equivalent to 20 mg esomeprazole), 49.3 mg (equivalent to 40 mg esomeprazole)
Available OTC products	
Zegerid OTC	Capsule: 20 mg/1100 mg
Prevacid 24 hr OTC	Delayed release: 15 mg

VII. References

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3. Laryngopharyngeal reflux: Position statement of the Committee on Speech, Voice, and Swallowing Disorders of the American Academy of Otolaryngology-Head and Neck Surgery. *Otolaryngology-Head and Neck Surgery*. 2002;127:30-35
4. Laryngopharyngeal Reflux: Prospective Cohort Study Evaluating Optimal Dose of Proton-Pump Inhibitor Therapy and Pretherapy Predictors of Response. *Laryngoscope*. 2005; 115.
5. Lanas A. Potent gastric acid inhibition in the management of Barrett's oesophagus. *Drugs*. 2005;65 Suppl 1:75-82.
6. Spechler, S. Barrett's Esophagus. *N Engl J Med.* 2002;346:836-842.
7. Aciphex [Prescribing Information] Woodcliff Lake, NJ: Eisai, Inc; October 2016.
8. Aciphex Sprinkle [Prescribing Information] Woodcliff Lake, NJ: Eisai, Inc; April 2016.
9. Dexilant [Prescribing Information] Deerfield, IL: Takeda Pharmaceuticals; October 2016.
10. Nexium [Prescribing Information] Wilmington, DE: AstraZeneca; December 2016.
11. Prevacid [Prescribing Information] Deerfield, IL: Takeda Pharmaceuticals; December 2016.
12. Prilosec [Prescribing Information] Wilmington, DE: AstraZeneca; December 2016.
13. Zegerid [Prescribing Information] San Diego, CA: Santarus; October 2016.
14. Esomeprazole Strontium [Prescribing Information] Glasgow, KY: Amneal Pharmaceuticals; December 2014.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	06.12.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence.

Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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