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Drug Class Update: Proton Pump Inhibitors and Histamine-2 Receptor Antagonists

Date of Review: October 2020

Date of Last Review: May 2017
Dates of Literature Search: 05/01/2017 - 05/05/2020

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:
The purpose of this update is to evaluate new evidence for proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs). Prior authorization (PA) criteria for PPIs will be reviewed to determine the need to clarify risk factors and appropriate treatment durations.

Research Questions:
1. What is the comparative effectiveness of PPIs in the treatment of peptic ulcer disease (PUD), gastrointestinal esophageal reflux disease (GERD), Zollinger-Ellison syndrome, *Helicobacter pylori (H. pylori)* eradication and non-steroidal anti-inflammatory drugs (NSAID)-induced ulcers?
2. What is the comparative effective evidence of H2RAs in the treatment of GERD?
3. What is the comparative safety of PPIs in the treatment of PUD, GERD, Zollinger-Ellison Syndrome, *H. pylori* eradication and NSAID-induced ulcers?
4. What is the comparative safety of H2RAs in the treatment of GERD?
5. What is the evidence is for the risk of gastrointestinal (GI) bleeding for aspirin, NSAIDs or anticoagulants?
6. What is the evidence for the optimal treatment duration with a PPI or H2RA?
7. Are there subpopulations in which a PPI or H2RA may be more effective or cause more harm?

Conclusions:
- One high quality guideline, two high quality systematic reviews and meta-analyses, one safety warning and one new product was identified for this drug class update.
- A high quality guideline from the National Institute for Health and Care Excellence (NICE) on the management of GERD supports current policy, including treatment durations on PPI and H2RA therapies.[1]
- In a Cochrane review of patients with functional dyspepsia, PPIs improved global symptoms of dyspepsia more than placebo (629 per 1000 patients versus 714 per 1000 patients; RR 0.88; 95% CI, 0.82 to 0.94/NNT 11 up to 8 weeks of therapy) (moderate quality evidence).[2] No difference in global symptoms of dyspepsia was demonstrated with the combination of PPIs and prokinetics (cisapride, mosapride [not available in the United States (US)]), itopride [not available in the US]) compared to prokinetics alone based on moderate evidence (RR 0.85; 95% CI, 0.68 to 1.08).[2]

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- The Food and Drug Administration has recommended that all formulations of ranitidine (ZANTAC) be removed from the market due to contaminates of N-Nitrosodimethylamine (NDMA), a carcinogen, in ranitidine products.[3]
- A new *H. pylori* triple therapy, TALICIA (omeprazole, amoxicillin and rifabutin), was approved in 2019.[4] Approval was based on one placebo-controlled trial and one active treatment trial comparing TALICIA to omeprazole and amoxicillin. There is low strength of evidence from 2 trials that TALICIA has higher eradication rates versus comparators.
- There is insufficient evidence to differentiate the need for PPI therapy to reduce the risk of GI bleeds between non-selective NSAIDs, aspirin and anticoagulants.
- There was insufficient evidence in subgroups or Medicaid-specific populations.

Recommendations:
- After clinical review no changes to the preferred drug list (PDL) are warranted.
- Modify PPI PA criteria to clarify durations of therapy.
- After review of costs in executive session famotidine (complete chew tablets), nizatidine solution, Aciphex, Dexilant, and Prevacid DR (including brand and generic formulations), Pylera capsule, and lansoprazole/amoxicillin/clarithromycin combo pack were made preferred.

Summary of Prior Reviews and Current Policy:
- Previous reviews have demonstrated no clinically significant differences in efficacy or safety between the PPIs. There is insufficient evidence of efficacy and safety differences between H2RAs.
- Coverage duration of PPI therapy for GERD is limited to 8 weeks based upon the Health Evidence Review Commission (HERC) funding of the Oregon Health Plan (OHP) prioritized list due to long-term safety concerns. PA criteria for H-pylori therapy is 2 weeks and other funded conditions for up to 1 year (**Appendix 4**).

Background:
There are many indications which necessitate the use of PPIs or H2RAs including PUD, GERD, Zollinger-Ellison syndrome, *H. pylori* eradication and NSAID-induced ulcers.[5] GERD is one of the most common GI conditions affecting one-third of adults.[6] Treatment recommendations for GERD depend upon the frequency and severity of symptoms. Eight weeks of low-dose H2RAs is recommended as initial treatment with escalation to a PPI for patients with severe symptoms or failure of twice-daily H2RAs.[7]

PPIs are the standard of care for the treatment of PUD, most often caused by the presence of *H. pylori* or NSAIDs.[8] Eradication of *H. pylori* is associated with higher healing rates of duodenal and gastric ulcers and should be treated if present.[8] First-line therapy for treatment of *H. pylori* should consider resistance patterns, prior exposure to antibiotics and patient allergies. First-line treatment options include triple therapy with clarithromycin, amoxicillin and a PPI or clarithromycin, metronidazole and a PPI. In most patients with a *H. pylori* diagnosis, a 14-day treatment of a PPI is sufficient, without maintenance therapy. Additional considerations in PUD management are the use of NSAIDs, recurrence and size of ulcer. Recommended treatment durations are presented in **Table 1.** Patients with persistent ulcers (presence of ulcers on repeat endoscopy, giant peptic ulcer [> 2 cm] and > 50 years or other comorbidities are present, history of frequent recurrent peptic ulcers [>2 documented per year], condition requiring long-term NSAID or aspirin use) and patients presenting with idiopathic ulcers (*H. pylori* negative, NSAID negative ulcer) may require maintenance PPI therapy. Patients with complicated ulcers (e.g., bleeding, perforation, penetration, or gastric outlet obstruction) may need treatment for up to 12 weeks.[8] Unless other risk factors are present, long-term prevention of a recurrent bleeding ulcer with

additional antisecretory therapy is not recommended.[9] In patients with NSAID-induced ulcers, NSAID discontinuation is recommended. If an NSAID must be used, then a cyclooxygenase-2 (COX-2)-selective NSAID, at the lowest effective dose, with a PPI is recommended. If a patient has low-dose aspirin-induced ulcer and they must continue therapy, then long-term concomitant PPI should also be given, regardless of aspirin dose.[10]

Table 1. Recommended Treatment Duration of PPI Therapy Based on Diagnosis[8,1]

Diagnosis	Duration of Therapy
Peptic Ulcer Disease (PUD)	4-8 weeks†
Duodenal Ulcer	4 weeks
Gastric Ulcer	8 weeks
H. pylori infection	14 days
Gastrointestinal Reflux Disease (GERD)	8 weeks*

Abbreviation: NSAID – non-steroidal anti-inflammatory drug
Key: * Coverage of PPI therapy for GERD is limited to 8 weeks for Fee-for-Service OHP patients. † Some patients with complicated peptic ulcer disease (ulcers with bleeding, perforation, penetration, or gastric outlet obstruction) may require up to 12 weeks of therapy.

Important treatment outcomes in the management of patients requiring treatment with PPIs and H2RAs are: healing of ulcers, reduction in symptoms of dyspepsia, eradication of *H. pylori* and quality of life.

Utilization for this class is not a substantial contributor to the overall prescription expenditures for the Oregon Health Authority (OHA). Preferred PPIs account for 90% of utilization in the Fee-for-Service (FFS) OHP population. Ninety-four percent of H2RAs are for preferred therapies. OHP policy only covers treatment of GERD up to 8 weeks.

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

Cochrane: Proton Pump Inhibitors for Functional Dyspepsia
A 2018 Cochrane review evaluated the evidence for PPI use in people with functional dyspepsia (FD) with a focus on symptom management and quality of life.[2] Functional dyspepsia was defined as persistent or recurrent epigastric pain in patients with normal upper GI findings and symptom duration for at least a month,

Rome II or III criteria (diagnosis of FD based on symptoms) or American Gastrological Association criteria for dyspepsia (dyspepsia not correlating with another diagnosis). Comparisons were between PPIs, H2RAs or prokinetics. Twenty-seven trials (only 3 trials were in the United States [US] and 5 trials were in multiple countries including the US) in patients at least 16 years of age were identified through a literature search up to May of 2017. Groups of low-dose and standard dosing of PPIs were combined since evidence suggests similar efficacy. Studies lasted from 2-8 weeks. The primary outcomes were global symptoms of dyspepsia or epigastric pain/discomfort.

Trials included in the analysis were found to be at low risk for selection, detection, reporting and publication bias. Global symptoms of dyspepsia (reporting no or minimal symptoms) were reduced with the administration of PPIs compared to placebo based on moderate-quality evidence (629 per 1000 patients versus 714 per 1000 patients, respectively; RR 0.88; 95% CI, 0.82 to 0.94/NNT 11 with up to 8 weeks of therapy).[2] There was no evidence of difference in quality of life between PPIs and placebo based on Psychological General Well-Being Index and SF-36 combined (standard mean difference [SMD] 0.01 (95% CI, 0.09 to 0.11). A small benefit, that was not statistically significant, in reduction of global symptoms of dyspepsia was reported for PPI therapy over H2RAs based on low quality of evidence (650 per 1000 patients versus 739 per 1000 patients, respectively; RR 0.88; 95% CI, 0.74 to 1.04).[2] A marginal benefit in reduction of global symptoms of dyspepsia with PPI therapy over prokinetics may exist, but evidence was of low quality (RR 0.89; 95% CI, 0.81 to 0.99/NNT 16 with treatment 2 to 4 weeks). No reduction in global symptoms of dyspepsia was found when PPIs and prokinetics were combined compared to prokinetics alone for the treatment of FD, based on moderate quality evidence (377 per 1000 patients versus 444 per 1000 patients, respectively; RR 0.85; 95% CI, 0.68 to 1.08).[2] *H. pylori* status did not change results of studied outcomes. Adverse reactions between PPIs and placebo were not statistically significantly different based on moderate quality evidence (RR 0.99; 95% CI, 0.73 to 1.33).[2] No statistically significant differences between PPIs and H2RAs for adverse events were found, based on moderate quality evidence (137 per 1000 patients vs. 144 per 1000 patients, respectively). No differences between adverse events were reported between prokinetics and PPIs based on moderate quality evidence, 113 per 1000 patients compared to 123 per 1000 patients, respectively (RR 1.09; 95% CI, 0.79 to 1.49).[2] Adverse events were decreased in patients receiving combination PPI and prokinetics compared to prokinetics alone, based on moderate quality evidence (132 per 1000 patients versus 220 per 1000 patients, respectively; RR 0.60; 95% CI, 0.39 to 0.93).

Cochrane: Pharmacological Interventions for Prevention and Treatment of Upper Gastrointestinal Bleeding in Newborn Infants

A Cochrane review evaluated pharmacological interventions studied in preterm and term neonates for the prevention of upper GI bleeding.[11] The following treatments were included: PPIs, H2RAs, antacids, sucralfate or bismuth salts. Eleven trials were included in the systematic review, which included studies published up to July of 2018. None of the identified studies were of high quality and none had a low risk of bias.[11]

Four trials evaluated H2RAs for the prevention of GI bleeding in infants in the neonatal intensive care unit. Incidence of GI bleeding was 110 per 1000 patients in those treated with an H2RA compared to 305 per 1000 patients treated in the control group (no treatment) based on moderate quality evidence (RR 0.36; 95% CI, 0.22 to 0.58).[11] No difference in mortality was found between the groups.

The treatment of infants with an upper GI bleed was studied in 7 trials using either an H2RA or PPI. There was only low or very low quality of evidence available for analysis, and therefore, no strong conclusions could be drawn.

After review, 15 systematic reviews were excluded due to poor quality (e.g, indirect network-meta analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[12–25]

New Guidelines:

NICE – 2019 Surveillance of Gastro-Esophageal Reflux Disease and Dyspepsia in Adults: Investigation and Management
National Institute for Health and Care Excellence (NICE) updated previous guidance on the management of GERD and dyspepsia in adult patients.[1] Pharmacotherapies included in the review were PPIs and H2RAs. There was limited new evidence to update long-term safety of PPIs and regimens for *H. pylori*. Evidence was not pooled due to limited number of studies. A majority of recommendations from the 2014 guideline remained unchanged (**Table 2**). For the treatment of GERD, PPI therapy of up to 8 weeks is recommended. Recommendations for the treatment of esophagitis are full-dose PPI therapy for 8 weeks. Severe esophagitis may require treatment of a standard dose PPI as maintenance therapy if symptoms persist. Peptic ulcer disease treatment ranges from 2-8 weeks based on underlying cause.[1]

Table 2. NICE Recommendations for GERD and Dyspepsia[1]

Indication	Recommendation
GERD	Full-dose PPI for 4-8 weeks Treat recurrence of symptoms with PPI at lowest dose possible to control symptoms
Severe Esophagitis	Full-dose PPI for 8 weeks
Persistent Severe Esophagitis	Full dose PPI as maintenance therapy
Peptic Ulcer Disease	PPI or H2RA therapy for 8 weeks and treat *H. pylori* if present (stop NSAID if applicable) PPI or H2RA therapy for *H. pylori* negative patients for 4 to 8 weeks
Dilation of a Esophageal Stricture	Long-term full-dose PPI therapy
Functional Dyspepsia	Low-dose PPI or H2RA for 4 weeks If symptoms continue or recur, recommend PPI or H2RA at lowest possible dose (avoid long-term therapy)
H. pylori	PPI, amoxicillin and clarithromycin or metronidazole for 7 days For penicillin allergic, recommend a PPI, clarithromycin and metronidazole for 7 days For penicillin allergic, with previous clarithromycin exposure, recommend PPI, bismuth, metronidazole and tetracycline for 7 days
H. pylori after failure of first-line treatment	PPI, amoxicillin, clarithromycin or metronidazole (whichever has not been used previously) for 7 days PPI, amoxicillin and tetracycline if patient has had previous clarithromycin and metronidazole exposure for 7 days For penicillin allergic, recommend PPI, metronidazole and levofloxacin (if not previously used) for 7 days For penicillin allergic, with previous fluoroquinolone use offer a PPI, bismuth, metronidazole, and tetracycline
Children and Young People with persistent heartburn, retrosternal or epigastric pain	PPI or H2RA for 4 weeks

Infants	PPI or H2RA for 4 weeks for overt regurgitation and at least 1 of the following: unexplained feeding difficulties (for example, refusing feeds, gagging or choking), distressed behavior and faltering growth

Abbreviations: GERD – gastrointestinal reflux disease; H2RA - histamine-2 receptor antagonist; PPI – proton pump inhibitor

There was new high quality evidence supporting the efficacy of PPIs and H2RAs from 2 new systematic reviews and meta-analyses. A review which pooled results from PPIs, H2RAs and prostaglandins (termed "gastroprotectant" drugs) demonstrated prevention and healing of ulcers and upper GI bleeding.[1] There was no significant reduction in mortality (OR 0.85; 95% CI, 0.69 to 1.04; p=0.11).[1] Symptom recurrence after initial treatment should be treated with a PPI or H2RA at the lowest possible dose.

An update to the guidance on the treatment of *H. pylori* was made to consider levofloxacin as the fluoroquinolone of choice, but reserve fluoroquinolone use for when other antibacterial treatments cannot be used:[1]

- First-line option in patients allergic to penicillin and previous exposure to both clarithromycin and metronidazole
- Second-line option in patients with previous exposure to both clarithromycin and metronidazole
- Second-line treatment in patients who are allergic to penicillin and have not had a previous exposure to a fluoroquinolone

After further review, 4 guidelines were excluded due to poor quality.[26–29,30]

New Formulations or Indications:

TALICIA (omeprazole, amoxicillin and rifabutin): The 3-drug delayed release capsule combination product was approved in 2019 and indicated for the treatment of *H. pylori* infection in adults.[4] Each capsule contains 12.5 mg of rifabutin, 10 mg omeprazole and amoxicillin 250 mg. TALICIA is given as 4 capsules every 8 hours with food for 14 days. Approval was based on two trials. The first trial was a randomized, double-blind trial comparing TALICIA to a total daily dose combination of amoxicillin 3000 mg and omeprazole 120 mg in patients testing positive for *H. pylori.* Eradication rates were 83.8% in patients treated with TALICIA and 57.7% in the control group (amoxicillin and omeprazole) (P<0.0001).[4] A second double-blind, randomized, placebo-controlled trial reported eradication rates of 76.6% with TALICIA compared to 2.4% treated with placebo.[4]

New FDA Safety Alerts:

Table 3. Description of new FDA Safety Alerts

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
Ranitidine[3]	ZANTAC	April 2020	Contaminates of N-Nitrosodimethylamine (NDMA), a carcinogen, in ranitidine products	Removal of all ranitidine products from the market

Randomized Controlled Trials:

A total of 66 citations were manually reviewed from the initial literature search. After further review, all citations were excluded because of wrong study design (eg, observational), comparator (eg, no control or placebo-controlled), or outcome studied (eg, non-clinical).

References:

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Appendix 1: Current Preferred Drug List

Histamine-2 Receptor Antagonists

Generic	Brand	Form	PDL
famotidine	ACID CONTROLLER	TABLET	Y
famotidine	ACID REDUCER	TABLET	Y
famotidine	FAMOTIDINE	TABLET	Y
famotidine	HEARTBURN RELIEF	TABLET	Y
famotidine	PEPCID	TABLET	Y
ranitidine HCl	RANITIDINE HCL	SYRUP	Y
ranitidine HCl	ZANTAC	SYRUP	Y
ranitidine HCl	ACID CONTROL	TABLET	Y
ranitidine HCl	ACID REDUCER	TABLET	Y
ranitidine HCl	HEARTBURN RELIEF 150	TABLET	Y
ranitidine HCl	RANITIDINE	TABLET	Y
ranitidine HCl	RANITIDINE HCL	TABLET	Y
ranitidine HCl	ZANTAC	TABLET	Y
cimetidine	ACID REDUCER	TABLET	N
cimetidine	CIMETIDINE	TABLET	N
cimetidine	HEARTBURN RELIEF	TABLET	N
cimetidine	TAGAMET	TABLET	N
cimetidine HCl	CIMETIDINE	SOLUTION	N
cimetidine HCl	CIMETIDINE HCL	SOLUTION	N
famotidine	FAMOTIDINE	ORAL SUSP	N
famotidine	PEPCID RPD	TAB RAPDIS	N
famotidine/Ca carb/mag hydrox	ACID REDUCER COMPLETE	TAB CHEW	N
famotidine/Ca carb/mag hydrox	COMPLETE	TAB CHEW	N
famotidine/Ca carb/mag hydrox	DUAL ACTION COMPLETE	TAB CHEW	N
nizatidine	NIZATIDINE	CAPSULE	N
nizatidine	NIZATIDINE	SOLUTION	N
ranitidine HCl	RANITIDINE HCL	CAPSULE	N

Proton Pump Inhibitors

Generic	Brand	Form	PDL
omeprazole	OMEPRAZOLE	CAPSULE DR	Y
pantoprazole sodium	PANTOPRAZOLE SODIUM	TABLET DR	Y
pantoprazole sodium	PROTONIX	TABLET DR	Y
dexlansoprazole	DEXILANT	CAP DR BP	N
esomeprazole mag/glycerin	ESOMEP-EZS	KIT CAP SP	N
esomeprazole magnesium	ESOMEPRAZOLE MAGNESIUM	CAPSULE DR	N

esomeprazole magnesium	HEARTBURN TREATMENT	CAPSULE DR	N
esomeprazole magnesium	NEXIUM	CAPSULE DR	N
esomeprazole magnesium	NEXIUM 24HR	CAPSULE DR	N
esomeprazole magnesium	ESOMEPRAZOLE MAGNESIUM	SUSPDR PKT	N
esomeprazole magnesium	NEXIUM	SUSPDR PKT	N
esomeprazole strontium	ESOMEPRAZOLE STRONTIUM	CAPSULE DR	N
lansoprazole	HEARTBURN TREATMENT 24 HOUR	CAPSULE DR	N
lansoprazole	LANSOPRAZOLE	CAPSULE DR	N
lansoprazole	PREVACID	CAPSULE DR	N
lansoprazole	PREVACID 24HR	CAPSULE DR	N
lansoprazole	LANSOPRAZOLE	TAB RAP DR	N
lansoprazole	PREVACID	TAB RAP DR	N
omeprazole	OMEPRAZOLE	TAB RAP DR	N
omeprazole	OMEPRAZOLE	TABLET DR	N
omeprazole magnesium	ACID REDUCER	CAPSULE DR	N
omeprazole magnesium	OMEPRAZOLE MAGNESIUM	CAPSULE DR	N
omeprazole magnesium	PRILOSEC	SUSPDR PKT	N
omeprazole/sodium bicarbonate	OMEPRAZOLE-SODIUM BICARBONATE	CAPSULE	N
omeprazole/sodium bicarbonate	ZEGERID	CAPSULE	N
omeprazole/sodium bicarbonate	OMEPRAZOLE-SODIUM BICARBONATE	PACKET	N
omeprazole/sodium bicarbonate	ZEGERID	PACKET	N
pantoprazole sodium	PROTONIX	GRANPKT DR	N
rabeprazole sodium	ACIPHEX SPRINKLE	CAP DR SPR	N
rabeprazole sodium	ACIPHEX	TABLET DR	N
rabeprazole sodium	RABEPRAZOLE SODIUM	TABLET DR	N

Antacids, H. Pylori

Generic	Brand	Form	PDL
omeprazole/amoxicill/rifabutin	TALICIA	CAP IR DR	N
bismuth/metronid/tetracycline	PYLERA	CAPSULE	N
lansoprazole/amoxiciln/clarith	LANSOPRAZOL-AMOXICIL-CLARITHRO	COMBO. PKG	N
omeprazole/clarith/amoxicillin	OMECLAMOX-PAK	COMBO. PKG	N

Appendix 2: Medline Search Strategy

Database(s): **Ovid MEDLINE(R) ALL** 1946 to April 17, 2020

Search Strategy:

#	Searches	Results
1	omeprazole.mp. or Omeprazole/	11353
2	pantoprazole.mp. or Pantoprazole/	2034
3	dexlansoprazole.mp. or Dexlansoprazole/	132
4	esomeprazole.mp. or Esomeprazole/	1654
5	lansoprazole.mp. or Lansoprazole/	2917
6	rabeprazole.mp. or Rabeprazole/	1361
7	bismuth.mp. or Bismuth/	12213
8	famotidine.mp. or Famotidine/	2243
9	ranitidine.mp. or Ranitidine/	7110
10	cimetidine.mp. or Cimetidine/	12587
11	nizantidine.mp.	1
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	43450
13	limit 12 to (english language and humans)	22376
14	limit 13 to yr="2017 -Current"	1310
15	limit 14 to (clinical trial, phase iii or meta analysis or practice guideline or "systematic review")	66

Appendix 3: Key Inclusion Criteria

Population	Patients with an indication for gastric acid suppression
Intervention	Proton pump inhibitor and histamine receptor antagonist therapy
Comparator	Placebo or active treatment regimen
Outcomes	Dyspepsia, ulcer healing rates, erosive esophagitis healing rates, quality of life
Timing	Symptom onset
Setting	Outpatient

Proton Pump Inhibitors (PPIs)

Goals:

- Promote PDL options
- Restrict PPI use to patients with OHP-funded conditions

Requires PA:

- Preferred PPIs beyond 68 days' duration
- Non-preferred PPIs

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/
- Individual components for treatment of *H. pylori* that are preferred products

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for a preferred PPI?	**Yes:** Go to #5	**No:** Go to #3
3. Is the treating diagnosis an OHP-funded condition (see **Table**)?	**Yes:** Go to #4	**No:** Pass to RPh; deny, not funded by OHP.
4. Will the prescriber consider changing to a preferred PPI product? Message: Preferred products are reviewed for comparative effectiveness and safety by the Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives.	**No:** Go to #5

5. Has the patient already received 68 days of PPI therapy for either of the following diagnoses: • Esophagitis or gastro-esophageal reflux disease with or without esophagitis (K20.0-K21.9); or • Current *H. pylori* infection?	**Yes:** Go to #8	**No:** Go to #6
6. Does the patient have recurrent, symptomatic erosive esophagitis that has resulted in previous emergency department visits or hospitalization?	**Yes:** Approve for 1 year	**No:** Go to #7

7. Does the patient have a history of gastrointestinal ulcer or bleed and have one or more of the following risk factors? • Age 65 years or older • Requires at least 3 months of continuous daily: i. Anticoagulant; ii. Aspirin (all doses) or non-selective NSAID; or iii. Oral corticosteroid	**Yes:** Approve for 1 year	**No:** Go to #8
8. Are the indication, daily dose and duration of therapy consistent with criteria outlined in the **Table**? Message: OHP-funded conditions are listed in the **Table**.	**Yes:** Approve for recommended duration.	**No:** Pass to RPh. Deny; medical appropriateness or not funded by OHP Message: Patient may only receive 8 weeks of continuous PPI therapy. RPh may approve a quantity limit of 30 doses (not to exceed the GERD dose in the **Table**) over 90 days if time is needed to taper off PPI. Note: No specific PPI taper regimen has proven to be superior. H2RAs may be helpful during the taper. Preferred H2RAs are available without PA.

Table. Dosing and Duration of PPI Therapy for OHP Funded Conditions.

Funded OHP Conditions*	Maximum Duration	Maximum Daily Dose
GERD: Esophageal reflux (K219) Esophagitis (K200-K210)	8 weeks* *Treatment beyond 8 weeks is not funded by OHP.	Dexlansoprazole 30 mg Dexlansoprazole Solu Tab 30 mg Esomeprazole 20 mg Lansoprazole 15 mg Omeprazole 20 mg Pantoprazole 40 mg Rabeprazole 20 mg
H. pylori Infection (B9681)	2 weeks	Dexlansoprazole 60 mg Dexlansoprazole 30 mg† Esomeprazole 40 mg Lansoprazole 60 mg Omeprazole 40 mg Pantoprazole 80 mg Rabeprazole 40 mg
Duodenal Ulcer (K260-K269)	4 weeks	
Gastric Ulcer (K250-K259)	8 weeks	
Peptic ulcer site unspecified (K270-K279)	12 weeks	
Achalasia and cardiospasm (K220) Barrett's esophagus (K22.70; K22.71x) Dyskinesia of esophagus (K224) Esophageal hemorrhage (K228) Gastritis and duodenitis (K2900-K2901; K5281) Gastroesophageal laceration-hemorrhage syndrome (K226) Gastrojejunal ulcer (K280-K289) Malignant mast cell tumors (C962) Multiple endocrine neoplasia [MEN] type I (E3121) Neoplasm of uncertain behavior of other and unspecified endocrine glands (D440; D442; D449) Perforation of Esophagus (K223) Stricture & Stenosis of Esophagus (K222) Zollinger-Ellison (E164)	1 year	

*A current list of funded conditions is available at: https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Prioritized-List.aspx

† Dexlansoprazole SoluTab 30 mg (given as 2 SoluTabs at once) are not recommended for healing of erosive esophagitis.

Implementation: *11/1/20; 6/8/16; 2/16; 10/15; 7/15; 4/15; 5/13; 5/12; 1/11; 4/10; 1/10; 9/06, 7/06, 10/04, 3/04*