



Indian Health Service National Pharmacy and Therapeutics Committee



Proton Pump Inhibitor Use Medication Use Evaluation

Introduction¹⁻⁶

The IHS National Pharmacy and Therapeutics Committee (NPTC) held its annual winter meeting on February 4th and 5th, in Dallas, Texas. During this meeting it was identified that proton -pump inhibitors (PPIs) remain the leading evidence-based therapy for many gastrointestinal disorders and is one of the most commonly prescribed acid suppression therapies within the Agency.

A review of the literature identifies that the low procurement cost and documented effectiveness of PPIs may lead to potential overutilization in multiple treatment arenas exposing patients to an increasing number of potential adverse effects associated with the long term use of PPIs. Overutilization is defined as utilizing a higher daily dose and/or longer duration of therapy than recommended in the prescribing information and use in patients with no documented indication.

Currently there is documentation in the literature hypothetically associating extended PPI duration of therapy and higher dosing to potential adverse effects including enteric infections with *Clostridium difficile*, bone fractures of the hip, spine, and wrist, community-acquired pneumonia, rebound acid hypersecretion and hypergastrinemia, gastric carcinoid tumor, interstitial nephritis, and nutritional deficiencies in vitamin B12, iron, and magnesium. Omeprazole also significantly decreases the metabolism of clopidogrel to its active form, thus attenuating its effects on platelet inhibition and potentially increasing cardiovascular risk which has led to the recommendation of avoiding concomitant use of Omeprazole with Clopidogrel in some of the literature. This potential drug-drug interaction has not been shown in long-term clinical trials to increase cardiovascular events, but providers are cautioned about the combination use. While the evidence of PPI adverse events is limited by the absence of randomized controlled studies, the current body of evidence points to the importance of continual review and identification of PPI overutilization. Prudent use of PPIs in patients with other risk factors for the above potential adverse events is recommended in the literature. The 2013 American College of Gastroenterology Guidelines for the treatment of GERD recommends for patients who require long-term PPI therapy, it should be administered in the lowest effective dose, including on demand or intermittent therapy. Clinical oversight can be accomplished by incorporation of a PPI overuse Medication Use Evaluation (MUE) to the facility's current quality assessment/performance improvement program. In some patients PPI step-down management of their disease may be warranted. By reducing the daily dose or eliminating the use of PPIs in appropriate patients it is hopeful potential adverse events are attenuated.

The objective of the below recommended MUE is to promote the utilization of PPIs for robust indications only, to prescribe PPIs for the appropriate duration of therapy, to use PPIs at the lowest effective dose, to exercise caution in the elderly and in patients with other risk factors for bone fractures, *Clostridium difficile* infection, pneumonia, and other potential PPI overuse associated adverse effects. The overall benefits of PPI therapy and improvement in quality of life significantly outweigh potential risks in most patients, but in patients exposed to PPI therapy without a clinical indication or are exposed to a higher dose or longer duration of therapy than needed to provide, are exposed to potential increased risks of therapy. It is important for clinicians to reassess their individual patient's need for continuation of PPI therapy long term, taking into the account of the continued value and potential adverse effects of therapy at each clinical decision point.

Proton Pump Inhibitor MUE

General Inclusion Criteria

- Identify a minimum of 30 patients using Proton Pump Inhibitors (PPIs) within the facility for a continuous length of > 16 weeks during MUE timeframe. Active outpatient prescription for PPI including Omeprazole, Esomeprazole, Lansoprazole, Dexlansoprazole, Pantoprazole, and Rabeprazole

Criterion 1

- **Is an approved indication documented for PPI?**
 - Duodenal Ulcer (maintenance & healing)
 - Eradication of *Helicobacter pylori*
 - Gastric Ulcer (maintenance & healing)
 - Gastroesophageal Reflux Disease (GERD)
 - Erosive Esophagitis (maintenance & healing)
 - Pathological Hypersecretory Conditions
 - Other (approved by P&T Committee)
- Incorrect indication for PPI
 - None of the above indications are documented
- **MUE Documentation:** Record the patient's indication on the PT Data Collection Sheet and provide a total of patients for each indication on the MUE Summary Sheet. This includes the total number of patients that do not have a documented indication

Criterion 2

- **Is the correct dose documented?**
 - Doses will vary based on PPI used
 - (see Table 1 & local current reference for dosing)
 - **MUE Documentation:** Record the current daily mg dose in the PT Data Collection Sheet
- Is the lowest PPI possible dose utilized? (review if "No")
 - Consider dose step-down therapy (see below)
 - Consider decreasing PPI dose to lowest effective dose
 - Consider utilizing on-demand therapy for Non-erosive Reflux Disease

Criterion 3

- **Is reason or indication for extended therapy documented?**
 - **Measure:** What is current duration of therapy in months?
 - **MUE Documentation:** Record total number of months a patient has been on PPI for each patient on the PT data collection sheet and average all patients duration of therapy in months and place on the MUE summary sheet
 - Duration of therapy will vary based on PPI and indication
 - Has duration of therapy been completed per manufacture Dosing guidelines or exceeded? If exceeded, then is proper Documentation in medical record provided? (review if "Yes")

Criterion 4

- **Documented ADRs to PPI (while on active PPI therapy)**
 - List all potential PPI risks documented in chart for ***past 12 months***
 - **MUE Documentation:** Record each diagnosed potential even on PT. collection sheet and give a total number for each on the summary sheet
 - Clostridium difficile – associated diarrhea
 - Bone fracture (hip, wrist, back)
 - Nutritional deficiencies listed in medical record
 - Iron
 - Magnesium
 - Vitamin B12
 - Community-acquired pneumonia

Criterion 5

- **Concomitant use of Clopidogrel and Omeprazole/Esomeprazole:**
- **MUE Documentation:** Record Yes or No on data sheet for each patient & record total number of patients currently using both medications on summary sheet
- Document the number & percent of patients on both medications

If patient is identified as a possible candidate for step-down therapy, see below. Please note Step-down plan is for GERD patients only, but may be considered for any patient the facility has identified as potentially taking a PPI dose that exceeds the FDA approved dose and length of therapy and the provider reduces the dose after consultation

Potential Step-down Therapy Consideration

- The American College of Gastroenterology guidelines published in early 2013 recommend for patients with GERD who require long-term PPI therapy, it should be administered in the lowest effective dose, including on demand or intermittent therapy in patients with non-erosive reflux disease.
- GERD Patients with documented symptoms despite PPI therapy (i.e. heartburn, regurgitation, dyspepsia), peptic stricture, extraesophageal GERD (cough, asthma, etc.), anemia, occult GI bleeding, Barrett’s esophagus, previous gastric surgery, active erosive esophagitis, open gastric/duodenal ulcer, malignant neoplasm, pregnancy or already using intermittent PPIs should be excluded from PPI step-down consideration.
 - Step-down Therapy options include:
 - Consider discontinuing PPI
 - Consider decreasing PPI dose
 - Use lowest effective continuous dose or intermittent dosing
 - Consider substituting histamine H2-receptor antagonist (H2RA)
 - Consider reducing PPI dose & adding H2RA
 - All above are used in conjunction with lifestyle modifications
 - May consider use other adjunct antacids/promotility agents as warranted
 - Maintain/Resume current PPI therapy due to worsening symptoms during step-down treatment
- **MUE Documentation:** Record on the PT Data Collection Sheet “Yes or No” whether step-down plan was performed, record the type of step-down plan initiated, and after 8 weeks the success of the plan. Provide a summary of the number of patients for each item on the MUE Summary Sheet.

References

1. Abraham NS. Proton pump inhibitors: potential adverse effects. *Curr Opin Gastroenterol*. 2012 Nov;28(6):615-20
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4. Inadomi JM, Jamal R, Murata GH, Hoffman RM, Lavezo LA, Vigil JM, Swanson KM, Sonnenberg A. Step-down management of gastroesophageal reflux disease. *Gastroenterology*. 2001 Nov;121(5):1095-100
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Table 1

Indication	Dexlansoprazole	Esomeprazole	Lansoprazole	Omeprazole	Pantoprazole	Rabeprazole
Duodenal ulcers						
Healing		–	15 mg qd X 4 wk	20 mg qd X 4 to 8 wk	40 mg qd X 2 to 4 wk (OLU) ²	20 mg qd X ≤ 4 wk
Maintain healing		–	15 mg qd	10 to 20 mg qd (OLU) ²	–	–
Eradicate <i>Helicobacter pylori</i> associated with duodenal ulcers		40 mg qd X 10 d in 3-drug regimen ^a	30 mg bid X 10 or 14 d in 3-drug regimen ^a 30 mg q8h X 14 d in 2-drug regimen ^b	20 mg bid X 10 d in 3-drug regimen ^a 40 mg qd X 14 d in 2-drug regimen ^c	40 mg bid X 10 d or 14 d in 3-drug regimen ^a (OLU) ²	20 mg bid X 7 d in 3-drug regimen ^a
Prevention of re-bleeding of high-risk duodenal ulcers		–	–	20 mg q6h or 40 mg q12h X 5 d (OLU) ²	–	–
Gastric ulcers						
Healing, non-NSAID-related		–	30 mg qd X ≤ 8 wk	40 mg qd X 4 to 8 wk	40 mg qd X 4 or 8 wk (OLU) ²	20 mg qd X 3 or 6 wk (OLU) ²
Healing, NSAID-related		20 mg qd X 4 to 8 wk (OLU) ²	30 mg qd X 8 wk	20 mg qd X 4 to 8 wk (OLU) ²	40 mg qd X 12 wk (OLU) ²	–
Reduce risk, NSAID-related		20 or 40 mg qd X ≤ 6 mo	15 mg qd X ≤ 12 wk	20 mg qd ≤ 6 mo (OLU) ²	40 mg qd X 12 wk (OLU) ²	–
Prevention of re-bleeding after acute bleeding of high-risk, gastric ulcers		–	–	20 mg q6h or 40 mg q12h X 5 d (OLU) ²	–	–
GERD						
Relieve symptoms	30 mg qd X 4 wk	20 mg qd X 4 to 8 wk	15 mg qd X ≤ 8 wk	20 mg qd X 4 wk	40 mg qd X 4 or 8 wk (OLU) ²	20 mg qd X 4 to 8 wk
Maintain symptom control in nonerosive reflux disease, on-demand therapy		20 mg qd prn (OLU) ²	–	20 mg qd prn (OLU) ²	–	–
Healing of erosive or ulcerative esophagitis	60 mg qd X 8 wk	20 or 40 mg qd X 4 to 16 wk	30 mg qd X 8 to 16 wk	20 mg qd X 4 to 8 wk	40 mg qd X 8 to 16 wk	20 mg qd X 4 to 16 wk
Maintain healing of erosive or ulcerative esophagitis	30 mg qd	20 mg qd	15 mg qd	20 mg qd	40 mg qd	20 mg qd
Maintain healing of erosive or ulcerative esophagitis, alternate-day dosing		–	30 mg qod (OLU) ²	20 to 40 mg qod (OLU) ²	–	–
Short-term treatment of GERD with history of erosive esophagitis, as an alternative to oral therapy		20 or 40 mg qd X 10 d (IV)	–	–	40 mg qd X 7 to 10 d (IV)	–
Posterior laryngitis, GERD-related		–	–	20 or 40 mg qhs X 6 to 24 wk or 20 to 40 mg bid X 4 to 12 wk (OLU) ²	–	–
Diagnosis of GERD-related noncardiac chest pain		–	30 mg qd X 4 wk (OLU) ²	20 mg bid X 14 d (OLU) ²	–	–
Other						
Reduction of risk of upper gastrointestinal bleeding in critically ill patients		–	30 mg qd (OLU) ²	40 mg initially and after 6 to 8 h, then 40 mg qd X up to 14 d (IR OME/SB powder for oral susp)	–	–
Hypersecretory conditions		40 to 240 mg/d in 1 or 2 divided doses	60-180 mg/d in 1 or 2 divided doses	60 to 360 mg/d in 1 to 3 divided doses	80 mg/d (PO) or 160 mg/d (IV) in 2 divided doses, up to 240 mg/d	60 to 120 mg/d in 1 or 2 divided doses

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Sources: (all dosages on table should be checked against a secondary source)

- All doses refer to oral administration except as indicated
- PPI monographs. Lexi-Comp Online™, Medical Lexi-Drugs Online™, Hudson, Ohio: Lexi-Comp, Inc.; updated 2014; January 26, 2014.

Legend:

- “A” refers to 3-drug regimen
 - PPI + amoxicillin 1000 mg + clarithromycin 500 mg bid X 10 to 14 d
 - PCN allergy: PPI + clarithromycin 500 mg + metronidazole 500 mg bid X 10 to 14 d or bismuth subsalicylate 525 mg + metronidazole 250 mg + tetracycline 500 mg qid X 10 to 14 d
- “B” refers to 2-drug regimen
 - PPI + amoxicillin 1000 mg tid X 14 d
- “C” refers to 2-drug regimen
 - PPI + clarithromycin 500 mg tid X 14 d
- (OLU)D refers to off label use