

Proton Pump Inhibitors (PPIs)

Background

40% –70% of hospitalized patients receive a PPI and as many as ½ continue post-discharge

Available PPIs: dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole

How PPIs Work: ↓ stomach acid by inhibiting the proton pump of stomach cells. ↓ H⁺ = ↓ acid!

What PPIs Treat: stomach/intestinal ulcers, GERD, H. pylori infections, esophagitis, and stress ulcers prophylaxis

Economic Impact: Short-term safety and effectiveness for these common conditions make PPIs the 3rd highest medication class sold in the US with an estimated annual spend of \$11 billion!

Risks

With PPIs so commonly prescribed it's easy to underestimate the long-term adverse drug events associated with this class of medications

Fractures

- Risk of bone fractures increases directly with dose and length of PPI treatment.
- FDA issued labeling requirement for safety info on increased risk of fractures of hip, wrist, and spine.
- Patients of advanced age and with underlying risk factors (i.e., osteoporosis) are at greatest risk.

C. difficile Infection (CDI)

- 2012 FDA Drug Safety Communication issued over ↑ risk of C. difficile-Associated Diarrhea (CDAD).
- One study concluded that PPI use during incident CDI treatment → 42% ↑ risk of CDI recurrence!

Low Magnesium

- Associated with long-term use (≥ 3 months) and typically occurs after 1 year of therapy.
- Symptoms: dizziness, muscle cramps, heart palpitations, seizures and tremors, and can be serious.

Low Vitamin B-12

- Associated with long-term use and typically occurs after ≥3 years of therapy.
- Symptoms: anemia, loss of balance, numbness or tingling in the arms and legs, and weakness.

Drug-Drug Interactions (DDI)

- ↓ Drug metabolism: warfarin, diazepam, cyclosporine, phenytoin, disulfiram, clopidogrel*, etc.
 - *Typically ↑ bioavailability and drug effects, but will work conversely for prodrugs (i.e., clopidogrel).
- ↓ Bioavailability of drugs requiring acidic environment for absorption: ampicillin, digoxin, ketoconazole, iron salts, etc
 - If PPI is absolutely necessary, administering these medications with acidic beverage (orange juice) will ↓ DDI

Clinical Pearls

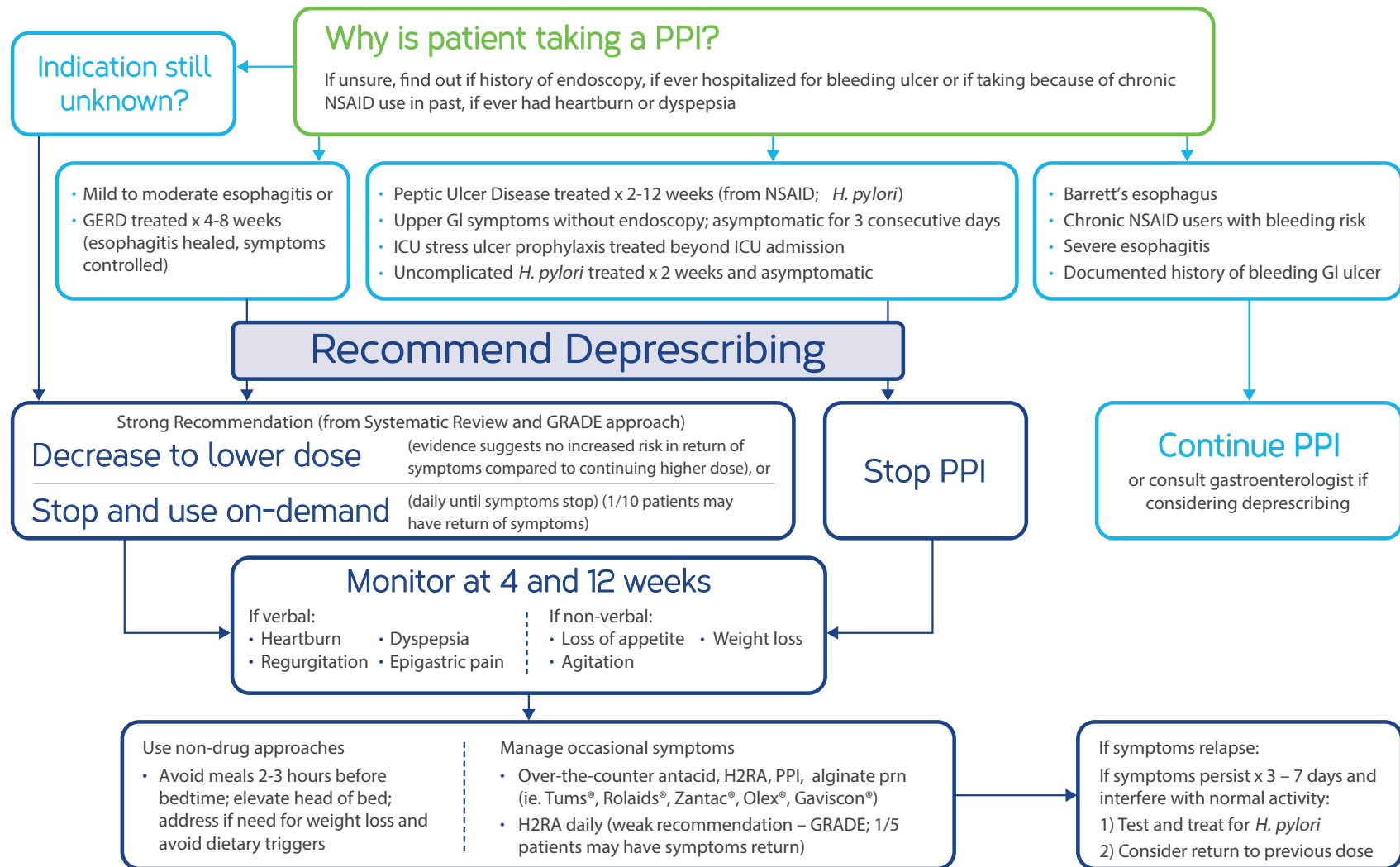
To minimize Adverse Drug Events due to unnecessary PPI exposure, consider these general recommendations

- Attempt nonpharmacologic therapies first: smoking cessation, dietary modification, elevated sleeping position, etc.
- Before initiating PPIs for intermittent reflux/GERD, trial antacids and H2RAs at maximal dosing.
- If PPI therapy is necessary, FDA recommends the lowest dose for the least amount of time required.
- **TIMING: due to mechanism of action – dose PPIs 30-60 minutes before breakfast for optimal efficacy.**
- Educate partner HCPs on eliminating PPI orders from MAR if only indicated for inpatient stress ulcer prophylaxis (SUP).
- Reserve PPIs for patients with clear indications.
- Determine duration and goals of therapy.
- Avoid broad off-label use.
- Assess PPIs for these active indications and use the accompanying algorithm to make deprescribing recommendations.
 - Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. *Deprescribing proton pump inhibitors. Evidence-based clinical practice guideline. Can Fam Physician* 2017;63:354-64 (Eng), e253-65 (Fr)





Proton Pump Inhibitor (PPI) Deprescribing Algorithm



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Generic	Brand Names	Dosage Forms	Equivalent Dose	Labeled Indications
Dexlansoprazole	Dexilant	Prescription Delayed Release Capsules 30 mg, 60 mg	30 mg	Erosive esophagitis Healing: 60 mg once daily for up to 8 weeks Maintenance: 30 mg once daily (Doses >30 mg do not provide additional benefit during maintenance phase.) Gastroesophageal reflux disease, symptomatic 30 mg once daily for 4 weeks
Esomeprazole	Nexium	Prescription Delayed Release Capsules 20 mg, 40 mg Packets 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg IV 40 mg OTC Delayed Release Capsules/Tablets 20 mg	20 - 40 mg	Erosive esophagitis Healing: 20 to 40 mg once daily for up to 8 weeks Maintenance: 20 mg once daily (Controlled studies do not extend beyond 6 months) Gastroesophageal reflux disease, symptomatic 20 mg once daily for 4 weeks Pathological hypersecretory conditions (Zollinger-Ellison syndrome) 40 mg twice daily (Doses up to 240 mg daily have been administered) Peptic ulcer disease: Eradication of <i>H. pylori</i> 40 mg daily for 10 days (Requires combination therapy with antibiotics) Heartburn (OTC labeling) 20 mg once daily for 14 days (May be repeated in 4 months if needed)
Lansoprazole	Prevacid, Prevacid SoluTab	Prescription Delayed Release Capsules 15 mg, 30 mg Oral Disintegrating Tablet 15 mg, 30 mg OTC Delayed Release Capsules 15 mg	30 mg	Erosive esophagitis Healing: 30 mg once daily for up to 8 weeks Maintenance: 15 mg once daily (Continue until asymptomatic for 8 weeks) Gastroesophageal reflux disease, symptomatic 15 mg once daily for up to 8 weeks Pathological hypersecretory conditions (Zollinger-Ellison syndrome) 60 mg twice daily (Doses up to 90 mg twice daily have been used, administer doses >120 mg/day in divided doses) Peptic ulcer disease Eradication of <i>H. pylori</i> : 30 mg two to three times daily for up to 14 days (Requires combination therapy with antibiotics) Gastric Ulcer: 30 mg once daily for up to 8 weeks Duodenal Ulcer: 15 mg once daily for up to 4 weeks Heartburn (OTC labeling) 15 mg once daily for 14 days (May be repeated in 4 months if needed)
Omeprazole	Prilosec	Prescription Delayed Release Capsules 10 mg, 20 mg, 30 mg Packets 2.5 mg, 10 mg OTC Delayed Release Tablets 20 mg	20 mg	Erosive esophagitis Healing: 20 mg to 40 mg once daily for 8 weeks once symptoms are controlled Maintenance: 20 mg once daily Gastroesophageal reflux disease, symptomatic 20 mg once daily for up to 8 weeks Pathological hypersecretory conditions (Zollinger-Ellison syndrome) 40 mg twice daily (Doses up to 180 mg daily have been used, administer doses >80 mg/day in divided doses) Peptic ulcer disease Eradication of <i>H. pylori</i> : 20 mg to 40 mg twice daily (Requires combination therapy with antibiotics) Gastric Ulcer: 20 mg to 40 mg once daily for up to 8 weeks Duodenal Ulcer: 20 mg to 40 mg once daily for up to 4 weeks Heartburn (OTC labeling) 20 mg once daily for 14 days (May be repeated in 4 months if needed)
Pantoprazole	Protonix	Prescription Delayed Release Tablets 20 mg, 40 mg Packets 40 mg IV 40 mg	40 mg	Erosive esophagitis Healing: 40 mg once daily for 8 weeks once symptoms are controlled Maintenance: 40 mg once daily Pathological hypersecretory conditions (Zollinger-Ellison syndrome) 80 mg twice daily (Doses up to 240 mg daily have been used in divided doses)
Rabeprazole	Aciphex	Prescription Delayed Release Tablets 20 mg Sprinkle Capsule 5 mg, 10 mg	20 mg	Erosive esophagitis Healing: 20 mg once daily for up to 8 weeks Maintenance: 20 mg once daily Gastroesophageal reflux disease, symptomatic 20 mg once daily for up to 4 weeks Pathological hypersecretory conditions (Zollinger-Ellison syndrome) 60 mg once daily (Doses up to 120 mg daily have been used in divided doses) Peptic ulcer disease Eradication of <i>H. pylori</i> : 20 mg twice daily for 7 days (Requires combination therapy with antibiotics) Duodenal Ulcer: 20 mg once daily for up to 4 weeks