

## Proton Pump Inhibitors (PPIs)

### Background

\*40% –70% of hospitalized residents 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<sup>+</sup> = ↓ 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.
- Residents 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)

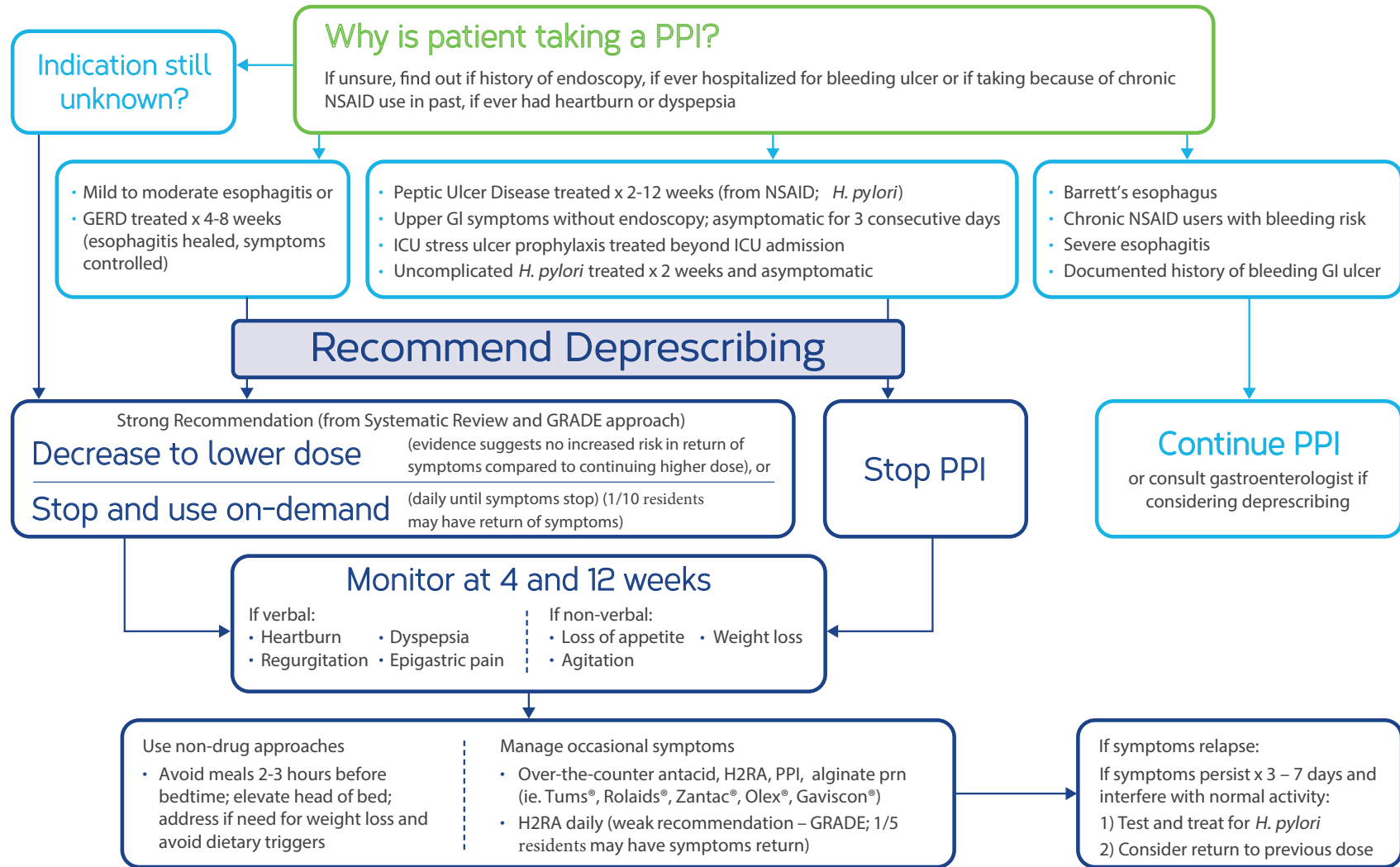
- ↓ Drug metabolism: warfarin, diazepam, cyclosporine, phenytoin, disulfiram, clopidogrel\*, etc.
  - \*Typically ↑ bioavailability and drug effects, but will work conversely for prodrugs (i.e., clopidogrel).
- ↓ Bioavailability of drugs requiring acidic environment for absorption: ampicillin, digoxin, 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 residents 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)

deprescribing.org | Proton Pump Inhibitor (PPI) Deprescribing Algorithm



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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).

Generic	Brand Names	Dosage Forms	Equivalent Dose	Labeled Indications
Dexlansoprazole	Dexilant	<b>Prescription</b> Delayed Release Capsules 30 mg, 60 mg	30 mg	<b>Erosive esophagitis</b> 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.) <b>Gastroesophageal reflux disease, symptomatic</b> 30 mg once daily for 4 weeks
Esomeprazole	Nexium	<b>Prescription</b> Delayed Release Capsules 20 mg, 40 mg Packets 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg IV 40 mg <b>OTC</b> Delayed Release Capsules/Tablets 20 mg	20 - 40 mg	<b>Erosive esophagitis</b> 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) <b>Gastroesophageal reflux disease, symptomatic</b> 20 mg once daily for 4 weeks <b>Pathological hypersecretory conditions (Zollinger-Ellison syndrome)</b> 40 mg twice daily (Doses up to 240 mg daily have been administered) <b>Peptic ulcer disease: Eradication of <i>H. pylori</i></b> 40 mg daily for 10 days (Requires combination therapy with antibiotics) <b>Heartburn (OTC labeling)</b> 20 mg once daily for 14 days (May be repeated in 4 months if needed)
Lansoprazole	Prevacid, Prevacid SoluTab	<b>Prescription</b> Delayed Release Capsules 15 mg, 30 mg Oral Disintegrating Tablet 15 mg, 30 mg <b>OTC</b> Delayed Release Capsules 15 mg	30 mg	<b>Erosive esophagitis</b> Healing: 30 mg once daily for up to 8 weeks Maintenance: 15 mg once daily (Continue until asymptomatic for 8 weeks) <b>Gastroesophageal reflux disease, symptomatic</b> 15 mg once daily for up to 8 weeks <b>Pathological hypersecretory conditions (Zollinger-Ellison syndrome)</b> 60 mg twice daily (Doses up to 90 mg twice daily have been used, administer doses >120 mg/day in divided doses) <b>Peptic ulcer disease</b> 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 <b>Heartburn (OTC labeling)</b> 15 mg once daily for 14 days (May be repeated in 4 months if needed)
Omeprazole	Prilosec	<b>Prescription</b> Delayed Release Capsules 10 mg, 20 mg, 30 mg Packets 2.5 mg, 10 mg <b>OTC</b> Delayed Release Tablets 20 mg	20 mg	<b>Erosive esophagitis</b> Healing: 20 mg to 40 mg once daily for 8 weeks once symptoms are controlled Maintenance: 20 mg once daily <b>Gastroesophageal reflux disease, symptomatic</b> 20 mg once daily for up to 8 weeks <b>Pathological hypersecretory conditions (Zollinger-Ellison syndrome)</b> 40 mg twice daily (Doses up to 180 mg daily have been used, administer doses >80 mg/day in divided doses) <b>Peptic ulcer disease</b> 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 <b>Heartburn (OTC labeling)</b> 20 mg once daily for 14 days (May be repeated in 4 months if needed)
Pantoprazole	Protonix	<b>Prescription</b> Delayed Release Tablets 20 mg, 40 mg Packets 40 mg IV 40 mg	40 mg	<b>Erosive esophagitis</b> Healing: 40 mg once daily for 8 weeks once symptoms are controlled Maintenance: 40 mg once daily <b>Pathological hypersecretory conditions (Zollinger-Ellison syndrome)</b> 80 mg twice daily (Doses up to 240 mg daily have been used in divided doses)
Rabeprazole	Aciphex	<b>Prescription</b> Delayed Release Tablets 20 mg Sprinkle Capsule 5 mg, 10 mg	20 mg	<b>Erosive esophagitis</b> Healing: 20 mg once daily for up to 8 weeks Maintenance: 20 mg once daily <b>Gastroesophageal reflux disease, symptomatic</b> 20 mg once daily for up to 4 weeks <b>Pathological hypersecretory conditions (Zollinger-Ellison syndrome)</b> 60 mg once daily (Doses up to 120 mg daily have been used in divided doses) <b>Peptic ulcer disease</b> 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