CEP | Providers

Managing Proton Pump Inhibitor Use in Older Adults

This tool is designed to help primary care providers assess and discuss with their patients 65 years of age or older, the potential benefits and risks of proton pump inhibitors (PPIs). This tool contains steps to support primary care providers in safely discontinuing, starting or continuing to prescribe PPIs for their older patients.

SECTION A: Potential risks and benefits of PPIs

Many common indications for PPI use require short-term treatment. However, chronic use of PPIs has become problematic and rampant.[1] PPIs are often viewed as safe and well-tolerated medications, and while the incidence of risks might be small, older adults are more susceptible due to comorbid conditions. When PPIs are inappropriately prescribed or used for too long, they can contribute to polypharmacy-related adverse reactions, medication errors, drug interactions, emergency department visits and hospitalizations.[1]

POTENTIAL RISKS FROM LONG-TERM (≥ 1 YEAR) USE^

- **Increased risk of hip fracture**[2]
  - NNH at 1 year = 4167 for women and 6667 for men[3]
- **Clostridium difficile infection**[2]
  - NNH at 1 year = 1000[3]
- **Acute interstitial nephritis**[4]
- **Community-acquired pneumonia**[2]
  - NNH at 1-6 months = 556[3]
- **Low levels of the mineral magnesium in the blood**[2]
- **Vitamin B12 deficiency**[4]
  - NNH at 1 year = 4[5]

POTENTIAL BENEFITS FROM SHORT-TERM USE[6]

- **Uninvestigated gastroesophageal reflux disease (GERD): heartburn remission**
  - PPI 72% vs. placebo 25%, NNT at 1-12 weeks = 2*
- **Prevention of NSAID-associated peptic ulcer**
  - PPI 14% vs. placebo 36%, NNT at >3 weeks = 4
- **Reflux (erosive) esophagitis**
  - Acute healing
    - PPI 83% vs. placebo 28%, NNT at 8 weeks = 2*
  - Maintenance of healed esophagus
    - PPI 78% vs. placebo 21%, NNT at 8 weeks = 2*
  - Maintenance of symptom relief
    - PPI 71% vs. placebo 24%, NNT at 8 weeks = 2*
- **Endoscopy negative reflux disease: heartburn remission**
  - PPI 38% vs. placebo 13%, NNT at 4-8 weeks = 4+
- **Functional (non-ulcer) dyspepsia: improvement in dyspepsia**
  - PPI 34% vs. placebo 25%, NNT at 2-8 weeks = 10*
- **Helicobacter pylori eradication (HPE) for peptic ulcer disease: ulcer recurrence**
  - Duodenal ulcer
    - HPE 13% vs. placebo 67%, NNT at ≤2 weeks = 2*
  - Peptic ulcer
    - HPE 16% vs. placebo 50%, NNT at 4-8 weeks = 3*

^Due to the observational nature of the evidence, harms observed may be over-represented due to potential confounding
*Quality of evidence unclear
+Moderate quality of evidence

DISCUSS WITH A PATIENT THEIR USE OF PPIs WHEN A PATIENT:

- ☐ Is ≥ 65 years of age
- ☐ Comes in for a prescription renewal or refill
- ☐ Has had a recent hospitalization
- ☐ Has had a recent medication reconciliation
- ☐ Is admitted to long-term care
- ☐ Complains of side effects (headache, nausea, diarrhea and rash, etc.)
- ☐ Is on medications that do not match their active medical concerns

Talking points

Address the patient's PPI use

"What was the initial reason that you started the PPI and does that reason still exist?"

"If you no longer have symptoms, we can consider stopping the PPI."

TIPS FOR REVIEWING PPI USE WITH PATIENTS

☑ Set EMR reminders or patient record flags to review a patient's PPI use during their next appointment.

☑ Encourage patients to talk about their PPI use at their next appointment: 1) hand out patient material to patients ages ≥ 65 or over; 2) put waiting room patient posters up; or, 3) provide screening questions while patients wait for their appointments. This type of patient material is available from the Canadian Deprescribing Network.[7]

Determine whether a PPI is appropriate or problematic[1]

Why is the patient starting/taking a PPI?

Short-term uses:
- Mild to moderate esophagitis or GERD
- Peptic ulcer disease (from NSAID; *H. pylori*)
- Upper GI symptoms without endoscopy
- Uncomplicated *H. pylori*
- ICU stress ulcer prophylaxis

Long-term uses:
- Oral corticosteroids or chronic NSAID use
- Severe esophagitis (Los Angeles grade C or D)[4]
- Barrett's esophagitis
- Pathological hypersecretory condition
- Demonstrated need for maintenance treatment (e.g. because of failure of drug discontinuation trial or H2-receptor antagonists)
- Recurrent ulcers
- Documented history of bleeding gastrointestinal ulcers[1]
- Dual antiplatelet therapy (with a prior upper GI bleed or one other risk factor)[4]

Is patient asymptomatic or has treatment duration been met/exceeded?

Yes → See Section B: Discontinuing PPIs

No → See Section C: Starting and continuing PPIs and revisit the conversation once the patient is asymptomatic or has completed the treatment duration

See Section C: Starting and continuing PPIs or consult a gastroenterologist if considering deprescribing

See Section D: Alternatives to PPIs for lifestyle changes that can reduce the risk of relapse symptoms and alternative therapies that can be used instead of PPIs

SECTION B: Discontinuing PPIs

Tapering steps

If taking a PPI is no longer appropriate for a patient, then use the following steps to help the patient taper off of the medication or taper to a lower dose.[8]

1. BEFORE STARTING A TAPER

Ensure that lifestyle changes and alternative therapies are implemented to reduce the risk of relapse symptoms during or following the taper (see Section D: Alternatives to PPIs)

Talking points

Emphasize the need to reduce polypharmacy

"I want you taking only the medications that you need. Let's see if we can take you off unnecessary medications to help you feel better."

Frame discontinuing PPIs as a trial

"Let's try taking you off the PPIs to see how you feel? If any symptoms come back, you can tell me. We can always restart the dose that you need to feel comfortable."

Reassure a patient that a PPI will be tapered instead of stopped completely

"Most patients are successful in tapering off of their PPIs. Sometimes, patients slowly decrease the dose to help their body adjust, but often, patients don't notice a recurrence of their symptoms."

2. PLAN THE TAPER

There is no evidence that one tapering approach is better than another. The tapering plan should be based on patient preference and what plan seems most tolerable.

- **Engage patients** in developing a clear plan for tapering
  - Find out when the patient's symptoms are most severe and customize their tapering plan
- **Establish the method of tapering**
  - Identify whether the Ontario Drug Benefit (ODB)[14] covers the doses you plan to use during tapering (see PPIs available in Ontario) and if not, consider alternate-day dosing or switching to another PPI [that is covered]
  - **Potential tapering methods:**
    - Reduce the dose from twice daily to once daily[8]
    - Reduce the dose from daily to every second or third day[8]
    - Stop the PPI and replace it with H2 blockers
    - Reduce the dose to PRN
  - **Include a note in the prescription** to inform the pharmacist of the tapering plan
  - **Consult the pharmacist** if pill splitting is necessary to accommodate tapering doses and to discuss packaging options for older adults (e.g. dosette or blister pack)

3. INITIATE THE TAPER AND MONITOR

- **Initiate the taper**
- **Ask the patient to call in 2-4 weeks to report any relapse symptoms**
  - Ask the patient if they are experiencing:
    - Heartburn
    - Reflux (used synonymously with heartburn)
    - Sore throat (i.e. difficulty swallowing)
    - New onset of coughing
    - Abdominal pain
  - Alternatively, if the patient is non-verbal, use a visual analogue scale (VAS) to identify pain or discomfort due to symptom relapse and look for signs of:[9]
    - Weight or appetite loss
    - Behavioural changes (e.g. agitation)
- **If the patient experiences withdrawal and/or rebound acid reflux, suggest using non-pharmacological and non-PPI pharmacological alternatives to lessen symptoms** (see Section D: Alternatives to PPIs)
  - If the patient does not tolerate the taper and the taper interferes with their normal activities, determine if the patient should return to a previous PPI dose
  - If the patient is still experiencing a recurrence of symptoms, test for *H. pylori* and contact a GI specialist for further consultation

SECTION C: Starting and continuing PPIs

For patients starting or continuing on a PPI, use the following information to ensure that the PPI is prescribed safely, considering individual patient factors.

IMPORTANT INFORMATION TO COLLECT BEFORE STARTING A PPI

☐ Preexising conditions that require a GI referral:
- **Dysphagia**[10]
- **Odynophagia**[10]
- **GI bleeding/anemia**[10]
- **Recurrent vomiting**[10]
- **Weight loss**[10]

☐ Dietary patterns and triggers (i.e. caffeine, alcohol, foods high in acid, nicotine)
☐ All prescribed and over-the-counter medications that the patient is currently taking, including supplements, vitamins and naturopathic treatments (see Medications that interact with PPIs)
☐ History of previous non-pharmacological (i.e. lifestyle changes) and pharmacological alternatives tried (see Section D: Alternatives to PPIs)
- An adequate trial of non-pharmacological and pharmacological alternatives is approximately 6-8 weeks[11]

☐ History of adverse events

TIPS FOR SAFE PPI PRESCRIBING

- Ideally, limit a prescription to 2-8 weeks (high-risk patients might need more than 8 weeks; see the section below to identify high-risk conditions)
- Discuss a tapering plan before prescribing a PPI (see Talking points)
- Consult with your local GI specialist before concomitantly administering antisecretory agents because of the marked reduction in acid inhibitory effects
  - Examples include, histamine-2 receptor antagonists (H2RAs), analogues of prostaglandin E (e.g. misoprostol) and somatostatin analogues (e.g. octreotide)[12]
- Set EMR reminders or patient record flags to prompt you to revisit PPI use at the patient's next visit and ask your patient to book a follow-up appointment within 4-8 weeks

Talking points

Provide instructions on when to take a PPI

"Take your PPI 30-60 minutes before you eat your breakfast in the morning, with a glass of water (not coffee), or before your last meal of the day."

Discuss a tapering plan before prescribing a PPI

"We will start you on the PPI and then we will slowly decrease your dose once you start feeling better."

CONTINUING PPIs

- First, it is important to determine if the chronic use of a PPI is warranted. Consider if the original indication for the PPI or ongoing risk factors for GI disease are present.

The following are high-risk conditions that may require long-term PPI use:
- **Barrett's esophagitis**[13]
- **Chronic oral corticosteroids or chronic NSAID use**[13]
- **Grade C or D esophagitis**[4]
- **Documented history of bleeding GI ulcers**[13]
- **Dual antiplatelet therapy (with a prior upper GI bleed or one other risk factor)**[4]

✓ Set annual EMR reminders or patient record flags to re-assess PPI use in patients with high-risk conditions

- Seek advice from a GI specialist for high-risk patients to assess ongoing risk factors

SECTION C: Starting and continuing PPIs (continued)

PPIs AVAILABLE IN ONTARIO					
PPI	**Type**	**Standard daily dose (healing)***	**Low daily dose (maintenance)**	**ODB coverage**	**Cost**
Dexlansoprazole* (Dexilant®)	Capsule	30[a] mg or 60[b] mg	30 mg	No**	$$$$$
Esomeprazole*+ (Nexium®)	Tablet	20[c] mg or 40[d] mg	20 mg	No**	$$$$
Lansoprazole* (Prevacid®)	Capsule	30 mg^	15 mg^	Yes • Lansoprazole is limited use[15]	$
Omeprazole*+ (Losec®)	Capsule	20 mg^	10 mg^	Yes • Some omeprazole is covered but is limited use[38] • All omeprazole magnesium is covered but is limited use[38] • 10 mg is not covered**	$
Pantoprazole* (Tecta®, Pantoloc®)	Tablet	40 mg	20 mg	Yes • Pantoprazole magnesium is covered[39] • Pantoprazole sodium is covered but is limited use[39] • 20 mg is not covered**	$
Rabeprazole* (Pariet®)	Tablet	20 mg	10 mg	Yes	$

Legend: $=<$15, $$=$15-30, $$$=$30-45, $$$$=$45-60, $$$$$=$60-75,
*= Standard dose PPI taken BID only indicated in the treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI
**= If the patient is on this PPI and needs to taper to smaller doses: stay at the higher dose but switch to alternating days OR contact the patient or their family/caregiver to see if they approve the cost of smaller doses
+= available over the counter: Esomeprazole 20 mg (Nexium 24HR capsules) and Omeprazole 20 mg (Omep Acid Reducer capsules, Heartburn Control capsules and Riva brand omeprazole)
a= Symptomatic non-erosive gastroesophageal reflux disease, b= Healing of erosive esophagitis, c=Non-erosive reflux disease, d= Reflux esophagitis, ^=Can be sprinkled on food

Note: reference to brand names does not imply endorsement of any of these products

MEDICATIONS THAT INTERACT WITH PPIs			
Medications	**Decreases absorption/ levels of PPI**	**PPI decreases efficacy/ absorption**	**PPI increases drug exposure (half-life or area under the curve [AUC])/toxicity**
Ampicillin[16]		●	
Calcium supplements[16]		●	
Carbamazepine[17]			● applies to omeprazole only
Cimetidine[16]	● applies to omeprazole only		
Clomipramine[16]		● applies to omeprazole only	
Clopidogrel[40,41]		● applies to omeprazole and esomeprazole only	
Diazepam[17]			● applies to omeprazole only
Digoxin[17]			● applies to omeprazole and rabeprazole only
Ginkgo[16]	● applies to omeprazole only		
HIV protease inhibitors[12]		●	
Iron[16]		●	
Itraconazole[16]		●	
Ketoconazole[16]		●	
Methotrexate[12]			●
Phenytoin[12]			● applies to omeprazole only
Rifampin[16]	● applies to omeprazole only		
Theophylline[12,16]			● applies to lansoprazole only
Warfarin[17]			● applies to omeprazole only

SECTION D: Alternatives to PPIs

Alternatives to managing GERD or esophagitis[8]

i. Non-pharmacological

Older adult patients can manage their GERD or esophagitis by incorporating the following lifestyle changes into their daily routines.[8]

Treatment	Level of evidence
Avoid lying down for 2-3 hours after you eat[18,21]	•
Avoid wearing tight clothing[18]	•
Elevate the head of the bed (try placing a firm pillow between the mattress and the bed frame), particularly if nocturnal or laryngeal reflux symptoms are present[18]	• • •
Modify diet: • Increase fibre intake to decrease heartburn[19] • Avoid chocolate, alcohol, caffeine, acidic citrus juices, large fatty meals, spicy food and peppermint[18] • Choose smaller quantities and eat slowly[20]	• • •
Reduce bodyweight if BMI >30 kg/m^2 or reverse recent weight gain[18]	• • •
Smoking cessation[18]	•

Talking points

"Heartburn is common. This is why we have effective over-the-counter medicine to help, which are often safer options."

"You may experience rebound symptoms, but they often go away with time and lifestyle changes. You can trial over-the-counter medication when you have rebound symptoms."

"Avoid chocolate, alcohol, caffeine, acidic citrus juices, large fatty meals, spicy food and peppermint. All of these foods can give you heartburn. Try increasing your intake of fruits, vegetables, protein and complex carbohydrates."[22]

Level of evidence: · · · · = meta-analysis or systematic review of randomized controlled trials, · · · = individual randomized controlled trial,
· · = systematic review of cohort studies, · = individual cohort study or expert opinion

SECTION D: Alternatives to PPIs (continued)

ii. Pharmacological

Medications with ODB[14] coverage can be prescribed to patients if they are concerned about the cost of obtaining them over-the-counter. When possible and appropriate, eliminate drugs that impair esophageal motility and lower esophageal sphincter tone (e.g. anticholinergic agents, beta-adrenergic agonists, calcium channel blockers, theophylline and tricyclic antidepressants).[18,31]

Treatment	Level of evidence	Dose	Notes	Side effects	ODB coverage
Antacids					
Aluminum hydroxide/ magnesium hydroxide combinations (Diovol®)[18,29]	• • • •	30 mL (regular strength) PRN after meals[18]	Avoid antacids containing magnesium or aluminum in renal dysfunction[18]	Constipation, diarrhea[18]	**No**
Alginates					
Aluminum hydroxide (Gaviscon® liquid)[18,29]	• • • •	10–20 mL PRN after meals[18]	Alginates and some antacids contain significant amounts of sodium[18]	Nausea, vomiting, belching, flatulence[18]	**No**
Magnesium carbonate (Gaviscon® tablets)[18,29]	• • • •	2–4 tablets chewed PRN after meals followed by a drink of water[18]		Nausea, vomiting, belching, flatulence[18]	**No**
Histamine H2-receptor antagonists *If creatinine clearance level is <50 mL/min then reduce dose to avoid mental status changes[27]					
Cimetidine (Tagamet®)[18,34]	• • •	400 mg twice daily[16]		Diarrhea, constipation, headache, fatigue, confusion (most likely in older adults and those with poor renal function), cardiac effects, rash Gynecomastia, impotence (rare)[18]	**Yes - generic only**
Famotidine (Pepcid AC®, Pepcid AC Maximum Strength®)[18,33]	• • •	20 mg twice daily[16]	Available without a prescription[18] Antacids may be given concomitantly if needed[18]	Diarrhea, constipation, headache, fatigue, confusion (most likely in older adults and those with poor renal function), cardiac effects, rash[18]	**Yes - generic only**
Nizatidine (Axid®)[18,32]	• • •	150 mg twice daily[16]			**Yes - only brand name available**
Ranitidine* (Zantac, Zantac Maximum Strength®)[18,35]	• • •	150 mg twice daily[16]	Available without a prescription[18]		**Yes - generic only**

Level of evidence: · · · · = meta-analysis or systematic review of randomized controlled trials, · · · = individual randomized controlled trial, · · = systematic review of cohort studies, · = individual cohort study or expert opinion.
Legend: *= Currently unavailable in Canada due to the 2019 recall and contamination. Consult Health Canada and the FDA for updates.

iii. Other alternatives

The following alternatives do not have the same efficacy as the non-pharmacological and pharmacological alternatives, but can alleviate minor symptoms of heartburn, reflux or stomach pain.

Treatment	Side effects/adverse events
Bismuth subsalicylate (Pepto Bismol®)	Salicylate toxicity, black tongue, black stool, bismuth-induced encephalopathy[28]
Calcium carbonate and magnesium hydroxide (Rolaids®)	Hypercalcemia, hypermagnesemia, milk-alkali syndrome, nephrolithiasis, abdominal pain, constipation, dehydration, diarrhea, hypercalcemia, hypercalciuria, hypomagnesemia, nausea, vomiting[26]
Calcium carbonate (Tums®)	Constipation and nausea are the most common side effects, and other possible side effects include hypercalcemia, hypercalciuria, renal calcification and renal stones There may be an increased risk of MI with high supplement doses[37]
Magnesium hydroxide (Milk of Magnesia®)	Hypermagnesemia in renal dysfunction[24]

Note: reference to brand names does not imply endorsement of any of these products.

RESOURCES

Provider resources

[i] Canadian Family Physician deprescribing proton pump inhibitors clinical practice guideline https://www.cfp.ca/content/63/5/354

[ii] Choosing Wisely Canada bye-bye, PPIs https://choosingwiselycanada.org/wpcontent/uploads/2017/07/CWC_PPI_Toolkit_v1.2_2017-07-12.pdf

[iii] Deprescribing.org webinars https://deprescribing.org/resources/deprescribing-webinars/

[iv] PPI Deprescribing.org algorithm https://www.cfp.ca/content/cfp/suppl/2017/05/05/63.5.354.DC1/Algorithm.pdf

[v] 2019 AGS Beers Criteria® list of potentially inappropriate medications in older adults published by the American Geriatrics Society https://geriatricscareonline.org/ProductAbstract/american-geriatrics-society-updated-beerscriteria-for-potentially-inappropriatemedication-use-in-older-adults/CL001

Patient resources

[i] Choosing Wisely Canada using proton-pump inhibitors (PPI) carefully https://choosingwiselycanada.org/wp-content/uploads/2017/05/GERD-EN.pdf

[ii] Deprescribing.org PPI info sheet https://www.cfp.ca/content/cfp/suppl/2017/05/05/63.5.354.DC1/PPI_InfoSheet.pdf

[iii] Mayo Clinic video on reducing heartburn, acid reflux and GERD https://www.youtube.com/watch?v=jsT1ylTz3d8

[iv] Deprescribing.org PPI patient decision aid https://deprescribing.org/wp-content/uploads/2017/10/PPI-Consult-PtDA-Oct-11-v2-wt.pdf

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[10] Canadian Association of Gastroenterology. Enhanced Primary Care Pathway: Gastroesophageal Reflux Disease (GERD). 2016. [cited 2019 September 3]. Available from https://www.cagacg. org/images/publications/GERD_Enhanced_Primary_Care_Pathway_July_2016.pdf

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[12] UpToDate. Proton pump inhibitors: Overview of use and adverse effects in the treatment of acid related disorders. 2019. [cited 2019 August 2].

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