

CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review



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DESCRIPTION: Proton pump inhibitors (PPIs) are among the most commonly used medications in the world. Developed for the treatment and prevention of acid-mediated upper gastrointestinal conditions, these agents are being used increasingly for indications where their benefits are less certain. PPI over-prescription imposes an economic cost and contributes to polypharmacy. In addition, PPI use has been increasingly linked to a number of adverse events (PPI-associated adverse events [PAAEs]). Therefore, de-prescribing of PPIs is an important strategy to lower pill burden while reducing real costs and theoretical risks. The purpose of this clinical update was to provide Best Practice Advice (BPA) statements about how to approach PPI de-prescribing in ambulatory patients. **METHODS:** Our guiding principle was that, although PPIs are generally safe, patients should not use any medication when there is not a reasonable expectation of benefit based on scientific evidence or prior treatment response. Prescribers are responsible for determining whether PPI use is absolutely or conditionally indicated and, when uncertainty exists, to incorporate patient perspectives into PPI decision making. We collaboratively outlined a high-level “process map” of the conceptual approach to de-prescribing PPIs in a clinical setting. We identified the following 3 key domains that required BPA guidance: documentation of PPI indication; identifying suitable candidates for consideration of de-prescribing; and optimizing successful de-prescribing. Co-authors drafted 1 or more potential BPAs, supported by literature review, for each domain. All co-authors reviewed, edited, and selected or rejected draft BPAs for inclusion in the final list submitted to the American Gastroenterological Association Governing Board. Because this was not a systematic review, we did not carry out a formal rating of the quality of evidence or strength of the presented considerations.

BEST PRACTICE ADVICE STATEMENTS

BEST PRACTICE ADVICE 1: All patients taking a PPI should have a regular review of the ongoing indications for use and documentation of that indication. This review should be the responsibility of the patient's primary care provider. **BEST PRACTICE ADVICE 2:** All patients without a definitive indication for chronic PPI should be considered for trial of de-prescribing. **BEST PRACTICE ADVICE 3:** Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI. **BEST PRACTICE ADVICE 4:** Patients with complicated gastroesophageal reflux disease, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.

BEST PRACTICE ADVICE 5: Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing. **BEST PRACTICE ADVICE 6:** PPI users should be assessed for upper gastrointestinal bleeding risk using an evidence-based strategy before de-prescribing. **BEST PRACTICE ADVICE 7:** Patients at high risk for upper gastrointestinal bleeding should not be considered for PPI de-prescribing. **BEST PRACTICE ADVICE 8:** Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper gastrointestinal symptoms due to rebound acid hypersecretion. **BEST PRACTICE ADVICE 9:** When de-prescribing PPIs, either dose tapering or abrupt discontinuation can be considered. **BEST PRACTICE ADVICE 10:** The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PAAEs. The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

Proton pump inhibitors (PPIs) are among the most commonly used medications in the United States, if not the world. Observational studies have demonstrated that PPI use has increased over time and that 7%–15% of patients use these medications at any time, with the prevalence increasing to 40% for patients 70 years or older.^{1–4} Approximately one-quarter of all patients who receive a PPI will continue to use them for at least 1 year.⁵ Although PPIs are the treatment of choice for the management of acid-mediated upper gastrointestinal (GI) conditions, such as erosive esophagitis and peptic ulcer disease,^{6–9} these agents are being used increasingly for less clear indications and for indeterminate durations. In a large observational study examining ambulatory visits of PPI users, nearly two-thirds had no clear indication for PPI use.¹⁰ In this context, multiple national gastroenterology organizations have called for

Abbreviations used in this paper: BPA, Best Practice Advice; GERD, gastroesophageal reflux disease; GI, gastrointestinal; PAAE, proton pump inhibitor-associated adverse event; PCP, primary care provider; PPI, proton pump inhibitor; RAHS, rebound acid hypersecretion; RCT, randomized controlled trial.



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limiting PPI use.^{11–13} In addition, PPIs have been available over-the-counter in the United States since 2003; therefore, physicians may not be involved in a patient's decision to initiate therapy.¹⁴

As PPI use has become more common, the emerging literature has identified several adverse effects potentially linked to these drugs,^{15,16} from chronic kidney disease to fracture to dementia and, most recently, COVID-19.^{17–21} All studies to date reporting these specific associations have been observational and therefore cannot establish causality.²² In contrast, randomized controlled trials (RCTs) comparing PPIs with placebo have not shown a higher rate of any adverse event among PPI users.²³ Nonetheless, this body of literature has raised concerns among prescribers and patients about the long-term safety of PPIs. This concern may promote inappropriate discontinuation of PPIs when a strong indication for use exists.²⁴ In this context, we developed a set of Best Practice Advice (BPA) statements about how to approach PPI de-prescribing—"the clinically supervised process of stopping or reducing the dose of medications when they cause harm or no longer provide benefit"—in ambulatory patients.²⁵

Best Practice Advice 1: All patients taking a PPI should have a regular review of the ongoing indications for use and documentation of that indication. This review should be the responsibility of the patient's primary care provider (PCP).

To determine whether a PPI's potential benefits outweigh the potential harms, it is essential to know why the PPI was prescribed and the indications for continuing use. Without an ongoing indication or evidence of benefit for the prescribing indication, the PPI can only incur harm. These harms include pill burden, medication-related costs, and potential adverse effects related to long-term use. Therefore, clinicians should clearly document an acceptable indication for the drug and that the indication is ongoing. In the absence of an appropriate ongoing indication, the medication should be considered for de-prescribing.

Currently, most PPIs are prescribed by PCPs.²⁶ Although gastroenterologists may be consulted, they do not generally provide long-term follow-up for patients using PPIs for common indications (eg, uncomplicated gastroesophageal reflux disease [GERD] and dyspepsia). PCPs are also likely the first physician point of contact for patients using over-the-counter PPIs. Therefore, we suggest that the PCP should be primarily responsible for reviewing the presence of ongoing indications for PPI use, and identifying candidates for de-prescribing. When a gastroenterologist is involved in the patient's care, we encourage documentation, as applicable, of indications for prolonged PPI use and clinical end points that signify PPI discontinuation. In health care settings with the infrastructure to review medication use, misuse, or overuse more broadly, a pharmacist- or nurse-specialist-centered multidisciplinary approach may facilitate systematic identification of inappropriate PPI use and de-prescribing.²⁷

Best Practice Advice 2: All patients without a definite indication for chronic PPI should be considered for trial of de-prescribing.

Definite and conditional indications for long-term and short-term PPI use are shown in Table 1. Multiple studies

have found that patients often take PPIs in the absence of a continuing indication.^{28–31} The vast majority of trials demonstrating efficacy have tested durations of 4–12 weeks,³² or no more than 6–12 months for maintenance therapy.³³ Chronic PPI use may be unintended. For example, a PPI initiated in the hospital for an acute indication (eg, stress ulcer prophylaxis) may be continued at discharge without the review of indication and ongoing need suggested in BPA 1.³⁴ In addition, PPIs are frequently initiated without a definite indication, notably for empiric treatment of laryngopharyngeal symptoms of cough, throat clearing, globus, and voice hoarseness. Because an RCT has definitively demonstrated that PPIs have no benefit in the empiric management of these symptoms,³⁵ these patients should be considered for de-prescribing.

Best Practice Advice 3: Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.

Double-dose PPIs (standard dose twice daily or a double-strength dose once daily) have not been studied in any RCT and are not US Food and Drug Administration-approved. Nonetheless, up to 15% of PPI users are on a higher-than-standard dose.³⁶ Higher-dose PPIs increase the costs of care and have been more strongly associated with certain complications, including community-acquired pneumonia, hip fracture, and *Clostridium difficile* infection; although there is no direct evidence of a causal relationship between PPI use and these adverse events.^{37–39} There is evidence to support the use of higher doses of oral PPIs over standard dosing in the acute setting to prevent rebleeding from peptic ulcer disease.⁴⁰ However, there is minimal evidence to support their use for the maintenance of healed esophagitis or prevention of complications of peptic ulcer disease.

High-dose PPIs are often recommended in patients with suspected laryngopharyngeal reflux or Barrett's esophagus.^{41,42} No study of Barrett's esophagus specifically demonstrates that double-dose PPIs are superior to standard-dose PPIs to prevent extension or progression to dysplasia or cancer. In addition, PPIs at any dose are ineffective in managing laryngopharyngeal symptoms.³⁵ High-dose PPIs are indicated for Zollinger-Ellison syndrome, which is exceedingly rare (1/1,000,000).^{43,44} Therefore, most high-dose PPI users should be considered for stepping down to standard dosing.

In a trial of 117 patients using higher-than-standard doses of PPIs for GERD, 80% successfully stepped down to standard doses of PPI without significant recurrence of symptoms or the need to again increase the PPI dose.⁴⁵ Therefore, PPI dose de-escalation for GERD can be effective for the majority of users. It is unknown whether this success rate for de-escalation can be duplicated across other indications.

Best Practice Advice 4: Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.

Most patients with GERD have nonerosive disease.⁴⁶ However, approximately 20% of patients with untreated

Table 1. Indications for Proton Pump Inhibitor Use

Indications					
Definitely indicated for long-term use (>8 wk)	Conditionally indicated for long-term use	Not indicated for long-term use	Definitely indicated for acute/short-term use (≤8 wk)	Conditionally indicated for acute/short-term use	Not indicated for acute/short-term use
Barrett's esophagus	PPI-responsive endoscopy-negative reflux disease, with recurrence on PPI cessation	Symptoms of nonerosive reflux disease with no sustained response to high-dose PPI therapy	<i>Helicobacter pylori</i> eradication	Initial or on-demand treatment of endoscopy-negative reflux disease	Empiric treatment of laryngopharyngeal symptomatology
Clinically significant (LA Classification grade C/D) erosive esophagitis	PPI-responsive functional dyspepsia, with recurrence on PPI cessation	Functional dyspepsia with no sustained response to PPI therapy	Stress ulcer prophylaxis for ICU patients with risk factors	Initial treatment of functional dyspepsia	Acute undifferentiated abdominal pain
Esophageal strictures from GERD (ie, peptic strictures)	PPI-responsive upper airway symptoms ascribed to laryngopharyngeal reflux, with recurrence on PPI cessation	Steroid therapy in the absence of ASA/nonsteroidal anti-inflammatory drug therapy	Uninvestigated GERD/dyspepsia	Uninvestigated dyspepsia	Acute nausea and vomiting not believed to be related to GERD/esophagitis
Zollinger-Ellison syndrome	Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement	Prevention of recurrent upper GI bleeding from causes other than: Peptic ulcer disease, including gastric and duodenal erosions	Treatment of NSAID-related gastric and duodenal peptic ulcers	Ulcer prevention after sclerotherapy or band ligation treatment of esophageal varices	Any isolated lower GI symptomatology
Eosinophilic esophagitis	Secondary prevention of gastric and duodenal peptic ulcers with no concomitant antiplatelet drugs	Erosive esophagitis		Prevention of rebleeding from Mallory-Weiss tears	
Gastroprotection in users of ASA/nonsteroidal anti-inflammatory drug at high risk for GI bleeding					
Prevention of progression of idiopathic pulmonary fibrosis					

ASA, aspirin; ICU, intensive care unit; LA, Los Angeles.

GERD have erosive esophagitis.⁴⁷ Erosive esophagitis can lead to GERD-related complications, such as GI bleeding or stricture formation. PPIs have been shown to be effective in healing erosive esophagitis and in preventing the development and recurrence of complications of GERD in long-term users.⁴⁸ A history of erosive esophagitis is also more common among persons who are found to have Barrett's esophagus.⁴⁹ In addition, recurrence of esophagitis is common after withdrawal of treatment, particularly in those with more clinically significant disease (eg, symptomatic Los Angeles Classification grade C or D).⁵⁰

Therefore, in patients with a known history of more severe erosive esophagitis (Los Angeles Classification grade C/D) or those with GERD-related complications, PPIs should generally not be considered for discontinuation unless the benefits and harms have been weighed and discussed with the patient. Because many patients with GERD are treated empirically, and even severe erosive esophagitis generally heals with PPI use without long-term sequelae, it may not be known whether a PPI user has had severe erosive esophagitis, or has a predisposition to developing more severe erosive esophagitis in the absence of ongoing PPI use. In these patients, de-prescribing can be considered, but PPI use should be quickly re-initiated in those who develop symptoms or signs suggestive of the emergence of complicated GERD, with consideration of upper endoscopy to confirm the presence of severe erosive esophagitis.

Best Practice Advice 5: Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.

There are several conditions in which a trial of de-prescribing has the potential to cause greater harm than benefit and should therefore not be pursued. First, one key long-term complication of GERD is esophageal adenocarcinoma.⁵¹ In patients with its known precursor lesion, Barrett's esophagus, there is evidence from both observational studies and RCTs that PPIs reduce the risk of esophageal adenocarcinoma.^{52,53} Thus, patients with known Barrett's esophagus should not be considered for a trial of de-prescribing.

In patients with eosinophilic esophagitis, PPIs are often the first-line pharmacologic therapy.^{54–56} With PPI therapy, clinical response and histologic remission have been observed in 61% and 51% of patients with symptomatic esophageal eosinophilia, respectively.⁵⁶ But not every patient with eosinophilic esophagitis requires a PPI, especially those who respond to other pharmacologic therapy (topical steroids) or to nonpharmacologic therapy.^{57,58} However, de-prescribing the PPI in a patient who has previously responded may result in a high rate of symptomatic and histologic recurrence. The long-term consequences of untreated eosinophilic esophagitis are not well characterized, although some patients may develop fibrotic strictures, likely influenced by uncontrolled eosinophilic inflammation.⁵⁹

In idiopathic pulmonary fibrosis, low-quality evidence suggests that PPIs reduce the likelihood of disease

progression.^{60–62} Until evidence comes to light that definitively demonstrates PPIs are ineffective in preventing idiopathic pulmonary fibrosis progression, we believe it is reasonable to not target these patients for PPI de-prescribing.

Best Practice Advice 6: PPI users should be assessed for upper GI bleeding risk using an evidence-based strategy before de-prescribing.

Best Practice Advice 7: Patients at high risk for upper GI bleeding should not be considered for PPI de-prescribing.

One of the key benefits of PPIs is that they markedly reduce the likelihood of upper GI bleeding.^{63,64} Because risk factors for upper GI bleeding (such as concomitant over-the-counter aspirin use) are often “hidden,” it is imperative that, before de-prescribing, patients be carefully assessed for such risk factors and overall upper GI bleeding risk to avoid adverse outcomes.^{65–67}

The benefit of PPIs in ambulatory patients at elevated GI bleeding risk has been demonstrated in both RCTs and well-designed observational studies.^{24,68–72} Despite these data, precisely which patients are at sufficiently increased risk for upper GI bleeding to warrant PPI co-therapy remains uncertain. Clearly, individuals with hypersecretory states, such as Zollinger-Ellison syndrome, should not be de-prescribed. But for others, multiple guidance statements offer varying recommendations, as shown in Table 2.^{73–77}

Although these guidance statements differ, they generally indicate that patients are at high risk for upper GI bleeding if they have a history of upper GI bleeding, are taking multiple antithrombotics (including both anticoagulants and antiplatelets agents), or are taking aspirin or a nonsteroidal anti-inflammatory drug with an additional risk factor for upper GI bleeding (eg, older than 60 years, severe medical comorbidity, using second nonsteroidal anti-inflammatory drug or aspirin, taking an antithrombotic, or taking an oral corticosteroid). In such patients, the PPI should not be de-prescribed due to the sufficiently increased likelihood of future upper GI bleeding events.

Best Practice Advice 8: Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper GI symptoms due to rebound acid hypersecretion.

Rebound acid hypersecretion (RAHS) is a physiologic phenomenon that can occur with discontinuation of prolonged PPI therapy.^{80,81} PPIs inhibit gastric acid production, resulting in an increase in intragastric pH. At high pH levels, serum gastrin levels rise, as inhibition of gastric secretion normally only occurs in the presence of gastric acid.⁸² Hypergastrinemia, in turn, promotes the proliferation of parietal cells and enterochromaffin-like cells; this, in turn, increases the capacity of the stomach to produce acid. As long as PPIs are continued, gastric acid secretion is held in check. However, once PPIs are discontinued, the acid-generating potential of the increased parietal cell mass is unleashed, potentially causing a profound decline in gastric acidity, which may promote the development of upper GI symptoms.^{83–85} In a double-blinded RCT enrolling persons

Table 2. Examples of Guidance Recommendations for Proton Pump Inhibitor Gastroprotection

Group	Year	Clinical focus	Populations for whom PPI gastroprotection is recommended
ACG ⁷⁵	2009	NSAIDs	Patients using NSAIDs who are at moderate or high risk of upper GI bleeding (1 or more risk factors, including prior ulcer, older than 65 years, high-dose NSAID therapy, concurrent use of aspirin (including low-dose), corticosteroids, or anticoagulants).
ACP ^{77,78}	2010, updated in 2019	Prior upper GI bleeding	Patients with prior ulcer bleeding who require an NSAID (the NSAID should preferably be a COX-2 inhibitor).
ACCF/ACG/AHA ⁷³	2010	Antiplatelet therapy	Patients with a history of upper GI bleeding or with multiple risk factors for GI bleeding who require antiplatelet therapy. Risk factors include advanced age; concurrent use of anticoagulants, steroids, or NSAIDs, including aspirin; and <i>Helicobacter pylori</i> infection.
ESC/EACTS ⁷⁴	2017	Dual antiplatelet therapy	Patients using dual antiplatelet therapy.
ACCP ⁷⁹	2018	Atrial fibrillation	Patients using aspirin and an oral anticoagulant.
ACC ⁷⁶	2020	Antithrombotics	Patients on 2 or more antithrombotic agents.

ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACCP, American College of Chest Physicians; ACG, American College of Gastroenterology; ACP, American College of Physicians; AHA, American Heart Association; ESC, European Society of Cardiology; EACTS, European Association for Cardio-Thoracic Surgery.

without a history of upper GI symptoms, Reimer et al⁸⁴ demonstrated that PPI withdrawal after an 8-week course of PPI led to a higher incidence of upper GI symptoms compared with patients in whom PPI was continued. Although intragastric pH was not measured in this study, the findings are consistent with a role for RAHS in post-PPI withdrawal symptoms. The anticipated duration of RAHS after PPI withdrawal is not well characterized, although physiologic studies have suggested that enterochromaffin-like cells and parietal cell mass can still be present 8 weeks after PPI withdrawal, although they have usually regressed by 6 months after withdrawal.⁸⁰

Inadomi et al⁸⁶ found that although approximately one-half of all patients with uncomplicated GERD who discontinued PPI were able to remain off PPIs 6 months later, three-quarters of those who successfully discontinued PPIs were using H₂-receptor antagonists or over-the-counter antacids for symptom control. Therefore, we suggest that the use of as-needed H₂-receptor antagonists and/or contact antacids for treatment of upper GI symptoms after PPI withdrawal would be reasonable. Similarly, using PPIs on demand in place of continuous PPIs provides effective symptom control, and could also be considered as a partial de-prescribing strategy.⁸⁷ A recent RCT also demonstrated that persons who do not have evidence of abnormal esophageal acid exposure (acid exposure time >4.0%) in the first 7 days after PPI withdrawal on ambulatory pH testing are much more likely to not require PPI re-initiation.³⁵ However, the feasibility of ambulatory pH testing before any attempt at discontinuation is unclear.

Therefore, patients who discontinue PPIs should be advised that they may experience upper GI symptoms at least in the short term, and that this does not necessarily mean they have to immediately return to using continuous

PPIs. The use of on-demand PPIs, histamine type-2 receptor antagonists, or neutralizing antacids on an as-needed basis may be helpful for controlling symptoms in the short term without committing to continuous PPI therapy. Severe persistent symptoms lasting more than 2 months after PPI discontinuation may suggest the presence of a continuing indication for PPI therapy on a non-acid-mediated cause of symptoms.

Best Practice Advice 9: When de-prescribing PPIs, either dose tapering or abrupt discontinuation can be considered.

Because of concerns that symptoms occurring as a consequence of RAHS may be a barrier against successful discontinuation of PPI therapy, some have proposed using a tapering regimen in order to gradually decrease the profundity of acid inhibition, thus allowing for gradual regression of parietal cell hyperplasia while still affording some degree of control over acid secretion. There is 1 published trial that compared abrupt discontinuation of PPIs with a tapered dosing regimen over 3 weeks (PPI daily to PPI every other day for 3 weeks, then discontinuing), which showed no significant difference between the 2 study arms in the likelihood of remaining off PPIs and symptom free at 6 months (31% vs 22% for tapered vs abrupt discontinuation).⁸⁸ However, given that the regression of parietal and enterochromaffin-like cell hyperplasia may take 2–6 months to complete, it is possible that this tapering regimen was too rapid to be effective.

At this time, we suggest that tapering or abrupt discontinuation are reasonable; in either case, patients should be advised to be mindful of developing recurrent upper GI symptoms as a consequence of RAHS, and should try to manage with lower-potency options for symptom control.

Best Practice Advice 10: The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PPI-associated adverse events (PAAEs). The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

Much of the increasing concern about PPI overuse and the need for de-prescribing has been driven by concern about PAAEs, including some associated with significant morbidity or mortality.^{18,20,39,89–91} Much of the evidence linking PPI use to PAAEs has emerged from retrospective studies. However, these associations are not necessarily causal, and they can potentially be explained by residual confounding and other analytic biases.^{22,92} Many of these associations between PPI use and PAAEs lack a plausible mechanism of action. Moreover, no RCT has yet demonstrated that PPI users have an increased incidence of any of the PAAEs.²³

In spite of this, studies have shown that concern among patients about PPI-related complications is common, with nearly 40% having made an attempt at discontinuing PPIs, of whom 83% did so without being advised to by a physician.⁹³ Patients who reported “extreme concern” about PPI-related adverse effects were 20 times more likely to have tried to discontinue PPIs. More concerning, three-quarters of physicians reported that they have altered treatment plans because of concerns about PPIs, and approximately 80% state that they would discontinue PPIs after being presented with a clinical scenario of a patient at high risk of upper GI bleeding.⁹⁴ The discontinuation of PPIs in patients with definite indications on the basis of concern about the unproven risk may lead to both recurrent symptoms and serious complications in those with definite indications for PPI therapy. Therefore, physicians should not use concern about unproven complications of PPI use as a justification for PPI de-prescribing if there remain ongoing valid indications for PPI use.

Discussion

The decisions about PPI discontinuation are complex and nuanced, and consequences for inappropriate or poorly considered discontinuation can be significant. Conversely, the unchecked use of PPIs in situations when indications are absent or murky is a major contributor to health care costs, and even a small risk of medical harm is significant in the complete absence of benefit. We also recognize that PPI discontinuation requires a systematic approach, and that patients and their PCPs may not have the tools or resources to undertake this task in the face of competing medical concerns. We are hopeful that these BPA statements will be valuable to the clinician and patient in providing guidance for approach and decision making about this issue. We also encourage physicians to partner with pharmacists to implement these BPAs in their clinical settings.

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Author contributions

All authors provided equal contribution to the writing of this manuscript.

Conflicts of interest

These authors disclose the following: Dr Fisher received funding from Exact Sciences for research, consulting, and Advisory Board participation; Guardant Health for Advisory Board participation; Freenome for research; and Takeda for research. Dr Fisher is currently employed by Eli Lilly and Company. None of these activities are related to proton pump inhibitors or medication de-prescribing. Dr Targownik has received investigator-initiated funding from Janssen Canada and served on advisory boards for AbbVie Canada, Takeda Canada, Merck Canada, Pfizer Canada, Janssen Canada, Roche Canada, and Sandoz Canada. She is the lead on an IBD Registry supported by AbbVie Canada, Takeda Canada, Merck Canada, Pfizer Canada, Amgen Canada, Roche Canada, and Sandoz Canada. The remaining author discloses no conflicts.

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