# Peptic ulcer disease: Treatment and secondary prevention

**AUTHOR:** Nimish B Vakil, MD, AGAF, FACP, FACG, FASGE
**SECTION EDITOR:** Mark Feldman, MD, MACP, AGAF, FACG
**DEPUTY EDITOR:** Shilpa Grover, MD, MPH, AGAF

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## INTRODUCTION

A peptic ulcer is a defect in the gastric or duodenal wall that extends through the muscularis mucosa into the deeper layers of the wall. The management of patients with peptic ulcer disease is based on the etiology, ulcer characteristics, and anticipated natural history. This topic will review the initial management of peptic ulcer disease. The management of recurrent peptic ulcer disease, the complications of peptic ulcer disease, surgical management of peptic ulcer disease, and the clinical manifestations and diagnosis of peptic ulcer disease are discussed separately. (See "Approach to refractory peptic ulcer disease" and "Overview of complications of peptic ulcer disease" and "Surgical management of peptic ulcer disease" and "Peptic ulcer disease: Clinical manifestations and diagnosis".)

## INITIAL MANAGEMENT

### Treat the underlying etiology

**Eradication of Helicobacter pylori (H. pylori)** — Patients with peptic ulcers should be tested for infection with *H. pylori* and treated accordingly ( algorithm 1) [1-4]. Eradication of *H. pylori* in patients with peptic ulcer disease is associated with higher healing rates in patients with duodenal and gastric ulcers. A meta-analysis of 24 randomized trials that included 2102

patients with peptic ulcer disease revealed that the 12-month ulcer remission rates for gastric and duodenal ulcers were significantly higher in patients successfully eradicated of *H. pylori* infection as compared with those with a persistent infection (97 and 98 percent versus 61 and 65 percent, respectively) [5]. In addition, eradication of *H. pylori* infection is associated with lower ulcer recurrence rates in patients with gastric and duodenal ulcers who are not placed on maintenance antisecretory therapy [6]. Treatment regimens for *H. pylori* are discussed in detail, separately. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults" and "Treatment regimens for Helicobacter pylori in adults".)

**Discontinue nonsteroidal anti-inflammatory drugs (NSAIDs)** — Patients with peptic ulcers should be advised to avoid NSAIDs. NSAIDs, including aspirin, increase the risk of peptic ulcer disease and are associated with an increased risk of complications from a peptic ulcer.

**Rare or unclear cause** — Rare causes of ulcer disease (eg, infections, Crohn disease, ischemia) should be addressed and treated. In patients with peptic ulcer disease of unclear etiology, additional evaluation is needed to exclude other rare causes of peptic ulcer disease (see "Unusual causes of peptic ulcer disease"). Gastrointestinal bleeding is a complication of severe coronavirus infections and peptic ulcer disease is the most common cause. In one study of consecutive patients in Northern Italy, the prevalence was 0.5 percent and the mortality rate was 21 percent, primarily due to pulmonary complications [7].

**Initial antisecretory therapy**

**Choice of therapy** — All patients with peptic ulcers should receive antisecretory therapy with a proton pump inhibitor (PPI; eg, omeprazole 20 to 40 mg daily or equivalent) to facilitate ulcer healing ( algorithm 1 and table 1). PPI use results in faster control of peptic ulcer disease symptoms and higher ulcer healing rates as compared with H2RA as a consequence of stronger acid suppression. PPIs also heal NSAID-related ulcers more effectively as compared with H2RAs [8]. (See "Antiulcer medications: Mechanism of action, pharmacology, and side effects", section on 'Indications and comparative efficacy' and "Proton pump inhibitors: Overview of use and adverse effects in the treatment of acid related disorders", section on 'Pharmacology'.)

Combining PPIs and H2RAs adds to cost without enhancing healing. Although antacids and sucralfate can heal duodenal ulcers, they are not routinely recommended to treat peptic ulcers as PPIs heal ulcers more rapidly and to a greater extent.

**Duration** — The duration of initial antisecretory therapy varies based on the ulcer characteristics, the underlying etiology (*H. pylori*, NSAID use) and the presence of ulcer complications (eg, bleeding, perforation, penetration, or gastric outlet obstruction) [9]. (See "Overview of complications of peptic ulcer disease" and 'Prevention of recurrence' below.)

**Complicated ulcer** — All patients with complicated peptic ulcers (ulcers with bleeding, perforation, penetration, or gastric outlet obstruction) should initially receive high-dose acid suppressive therapy. The treatment of bleeding peptic ulcers is discussed in detail separately. (See "Approach to acute upper gastrointestinal bleeding in adults", section on 'Acid suppression'.)

In patients with peptic-ulcer-related complications **other than bleeding** (gastric outlet obstruction, penetration, perforation), high-dose twice-daily PPI treatment is reasonable to enhance healing (eg, oral omeprazole 40 mg twice daily), but dosing should generally be reduced to once daily after four weeks. In patients with complicated duodenal ulcers, we suggest antisecretory treatment for four to eight weeks. In patients with complicated gastric ulcers, we suggest antisecretory therapy for a total duration of 8 to 12 weeks. In patients with gastric ulcers, we discontinue antisecretory therapy only after ulcer healing has been confirmed by upper endoscopy. (See "Overview of complications of peptic ulcer disease", section on 'Acid suppressive therapy' and 'Gastric ulcers' below.)

**Uncomplicated ulcer**

**H. pylori-positive ulcer** — In patients with uncomplicated ulcers, PPI (eg, omeprazole 20 mg twice daily) given for 14 days, along with the antibiotic regimen to treat *H. pylori*, is usually adequate to induce healing. Additional antisecretory therapy is not needed in the absence of persistent or recurrent symptoms following therapy or other indications for maintenance antisecretory therapy [10,11]. Eradication *of H. pylori* even without concurrent acid suppression therapy heals >90 percent of duodenal ulcers [12,13]. (See 'Prevention of recurrence' below.)

**NSAID-induced ulcer** — Patients with NSAID-associated ulcers should be treated with a PPI (eg, omeprazole 20 to 40 mg daily) for four to eight to weeks based on the size of the ulcer ( table 1). In patients with peptic ulcers who need to remain on NSAIDs or aspirin, maintenance antisecretory therapy with a PPI (eg, omeprazole 20 mg daily) can reduce the risk of ulcer complications or recurrence [14]. (See 'Prevention of recurrence' below and "NSAIDs (including aspirin): Treatment and secondary prevention of gastroduodenal toxicity".)

**Non-H. pylori, non-NSAID ulcer** — In patients with *H. pylori*-negative ulcers that are not associated with NSAID use, we suggest initial PPI therapy for four weeks for uncomplicated duodenal ulcers, and eight weeks for a gastric ulcer or any complicated ulcer before repeat endoscopic evaluation to assess for ulcer healing. Although the natural history of these ulcers is unclear, it is important to review the patient's history for the adequacy of *H. pylori* testing and for a history of NSAID use. Limited data on the natural history of these ulcers suggest that they may be more difficult to heal and have a higher rate of recurrence. In the absence of *H. pylori*

and NSAID use, we continue long-term acid inhibitory therapy with PPIs [15]. (See 'Prevention of recurrence' below and 'Repeat upper endoscopy in selected patients' below.)

**Other general measures** — Underlying risk factors for peptic ulcer disease should be addressed and treated. Given the many benefits of smoking cessation, we advise patients to stop smoking and advise them to limit alcohol intake to one alcoholic beverage a day [16]. Evidence to support the use of a bland diet or dietary restrictions in patients with peptic ulcer disease is lacking. (See "Peptic ulcer disease: Epidemiology, etiology, and pathogenesis", section on 'Risk factors'.)

## SUBSEQUENT MANAGEMENT

### Repeat upper endoscopy in selected patients

**Duodenal ulcers** — Given the low risk of malignancy in patients with duodenal ulcers, a repeat upper endoscopy is not routinely recommended, but may be performed in selected patients four weeks after initial treatment unless symptoms persist or recur ( algorithm 1). Endoscopy should be repeated in patients with signs of ongoing bleeding [17]. The decision to perform a repeat upper endoscopy in patients with duodenal ulcers of unclear etiology should be individualized. (See "Unusual causes of peptic ulcer disease".)

**Gastric ulcers** — We suggest a surveillance endoscopy (with biopsies of the ulcer if still present) be performed after 8 to 12 weeks in patients with gastric ulcers and any one of the following ( algorithm 1):

- Symptoms persist despite medical therapy.
- Unclear etiology.
- Giant ulcer (>2 cm).
- Biopsies not performed or inadequate sampling on the index upper endoscopy. To adequately sample a gastric ulcer, we suggest a minimum of four biopsies should be obtained, with at least one from each of the four quadrants of the ulcer. Additional biopsies of the edges should be taken with jumbo forceps if there are endoscopic features of a malignant gastric ulcer.
- Ulcer appears suspicious for malignancy on index upper endoscopy (mass lesion, elevated irregular ulcer borders, or abnormal adjacent mucosal folds). Surveillance endoscopy should be considered in patients whose gastric ulcer appears endoscopically suspicious

for malignancy, even if biopsy samples from the index endoscopy are benign. False-negative biopsy specimen results have been reported to occur in 2 percent to 5 percent of malignant ulcers.

- Patients with bleeding ulcers at initial presentation who show signs of continued bleeding [17].

- Risks factors for gastric cancer (eg, age >50 years*, Helicobacter pylori*, immigrants from a region with high prevalence of gastric cancer [eg, Japan, Korea, Taiwan, Costa Rica], family history of gastric cancer, the presence of gastric atrophy, adenoma, dysplasia, intestinal metaplasi*a*).

Our approach is not to perform an upper endoscopy for surveillance in patients with small benign-appearing antral gastric ulcers due to nonsteroidal anti-inflammatory drug use that have been adequately biopsied and have no evidence of dysplasia or malignancy if the patient has no risk factors for gastric cancer [18-20].

There are limited prospective outcome data to guide which patients with peptic ulcers should undergo surveillance endoscopy. Our recommendations are consistent with the 2010 guidelines by the American Society for Gastrointestinal Endoscopy [17]. The incidence of gastric cancer on follow-up endoscopy of an apparently benign gastric ulcer ranges from 0.8 to 4.3 percent. The rationale behind endoscopic follow-up of a patient with a gastric ulcer is that the absence of symptoms does not reliably exclude malignancy, and surveillance endoscopy may identify patients with gastric cancer at an early stage [21,22]. However, it is unclear if endoscopic surveillance is cost-effective or improves survival [21,23].

**Refractory ulcers** — A refractory peptic ulcer is defined as an endoscopically proven ulcer greater than 5 mm in diameter that does not heal after 8 to 12 weeks of treatment with a proton pump inhibitor (PPI). Approximately 5 to 10 percent of ulcers are refractory to initial PPI therapy. The evaluation and management of refractory ulcers is discussed elsewhere. (See "Approach to refractory peptic ulcer disease".)

## PREVENTION OF RECURRENCE

**Aspirin/nonsteroidal anti-inflammatory drug (NSAID) avoidance** — The need for aspirin and NSAIDs should be carefully assessed in patients with a history of peptic ulcer disease. NSAIDs, including aspirin, increase the risk of bleeding in patients with prior peptic ulcer disease. For patients who must continue aspirin or NSAIDs, or both, we recommend treatment with a proton pump inhibitor (PPI) for as long as the NSAID and/or aspirin is used. This is particularly

important in patients who need continued NSAIDs and have additional risk factors for gastroduodenal toxicity (age >65 years, complicated peptic ulcer disease, high-dose NSAID use, NSAID use with other medications associated with peptic ulcer disease [eg, SSRIs, low-dose aspirin]). (See "NSAIDs (including aspirin): Treatment and secondary prevention of gastroduodenal toxicity".)

**H. pylori eradication** — In addition, *H. pylori* infection should be eradicated, if known to be present. For patients with *H. pylori* infection who cannot discontinue NSAIDs, rebleeding rates are reduced with eradication of *H. pylori* infection in combination with long-term PPI therapy. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Confirm eradication in all patients'.)

In patients treated for *H. pylori,* eradication of infection should be confirmed four or more weeks after the completion of therapy [4]. The choice of test depends on the need for an upper endoscopy (eg, follow-up of bleeding peptic ulcer). (See 'Repeat upper endoscopy in selected patients' above and "Indications and diagnostic tests for Helicobacter pylori infection in adults".)

PPIs should be held for one to two weeks prior to testing to reduce false-negative results. Serologic testing should not be performed to confirm eradication as patients may continue to have antibodies after eradication. Diagnostic evaluation and treatment of *H. pylori* are discussed in detail, separately. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Medications that should be discontinued prior to testing'.)

**Maintenance antisecretory therapy** — The decision to continue maintenance antisecretory therapy varies based on the patient and ulcer characteristics and risk factors for recurrent peptic ulcer disease [9]. While PPIs, H2 receptor antagonists, and prostaglandin analogs have been used as maintenance therapy to prevent recurrent ulcers, PPIs are the most effective agents in preventing recurrent ulcers and recurrent ulcer bleeding [24].

We continue maintenance antisecretory therapy with a PPI (eg, omeprazole 20 mg daily) in the following patients with peptic ulcer disease ( table 1) [25-31]:

- Giant (>2 cm) peptic ulcer and age >50 years or multiple co-morbidities
- *H. pylori*-negative, NSAID-negative ulcer disease
- Failure to eradicate *H. pylori* (including salvage therapy)
- Frequently recurrent peptic ulcers (>2 documented recurrences a year)
- Continued NSAID use

The prevention of recurrent gastroduodenal toxicity associated with NSAID, low-dose aspirin or both therapies (secondary prevention) is discussed in detail, separately. (See "Overview of the

treatment of bleeding peptic ulcers", section on 'Resumption of anticoagulants and antiplatelet agents' and "NSAIDs (including aspirin): Treatment and secondary prevention of gastroduodenal toxicity".)

## TREATMENT DURING PREGNANCY AND LACTATION

When peptic ulcer disease is diagnosed in a woman who is pregnant, the focus of treatment is typically acid suppression with a proton pump inhibitor (PPI) [32]. If *Helicobacter pylori* (*H. pylori*) is present, antimicrobial treatment is typically deferred until after delivery. However, there is some evidence that *H. pylori* can cause severe nausea/vomiting in pregnancy, including hyperemesis gravidarum [33,34]. Thus, if indicated, *H. pylori* treatment can be considered in pregnancy. A meta-analysis of safety studies showed no significant adverse outcomes with PPI use in pregnant women [35-37]. The available evidence based on clinical studies in pregnancy supports the safety of older proton pump inhibitors such as omeprazole and pantoprazole with little data available on the newer proton pump inhibitors. Similarly, limited data with omeprazole and pantoprazole suggest that excretion in breast milk does occur but the levels are low [38-40]. (See "Medical management of gastroesophageal reflux disease in adults", section on 'Pregnancy and lactation' and "Prenatal care: Patient education, health promotion, and safety of commonly used drugs", section on 'Antibiotics'.)

## DISEASE COURSE

Approximately 60 percent of peptic ulcers heal spontaneously but with eradication of *Helicobacter pylori* (*H. pylori*) infection, ulcer healing rates are >90 percent [5,41-44]. Approximately 5 to 10 percent of ulcers are refractory to antisecretory therapy with a proton pump inhibitor (PPI). The risk of complications in patients with chronic peptic ulcer disease is 2 to 3 percent per year. (See "Approach to refractory peptic ulcer disease".)

Even with continued PPI use, approximately 5 to 30 percent of peptic ulcers recur within the first year based on whether *H. pylori* has been successfully eradicated [45,46]. Recurrent ulcers are usually due to *H. pylori* infection or nonsteroidal anti-inflammatory drug use but in rare cases may be due to other etiologies ( table 2).

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Peptic ulcer disease".)

## INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Peptic ulcers (The Basics)" and "Patient education: H. pylori infection (The Basics)" and "Patient education: Gastritis (The Basics)")
- Beyond the Basics topics (see "Patient education: Peptic ulcer disease (Beyond the Basics)" and "Patient education: Helicobacter pylori infection and treatment (Beyond the Basics)")

## SUMMARY AND RECOMMENDATIONS

- **Treatment of the underlying etiology**
  - Patients with peptic ulcer disease should be tested for *Helicobacter pylori* (*H. pylori*). Patients with *H. pylori* should be treated with a goal of eradication of *H. pylori* infection. In patients treated for *H. pylori,* eradication of infection should be confirmed four or more weeks after the completion of eradication therapy. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults".)
  - Patients with peptic ulcers should be advised to avoid nonsteroidal anti-inflammatory drugs (NSAIDs). Contributing factors should be addressed and treated (eg, treating medical comorbidities, poor nutritional status, ischemia). (See 'Rare or unclear cause' above and "Unusual causes of peptic ulcer disease", section on 'Etiology' and "Unusual causes of peptic ulcer disease", section on 'Evaluation of H. pylori and NSAID negative ulcers'.)

- **Antisecretory therapy** – All patients with peptic ulcer disease should receive antisecretory therapy with a proton pump inhibitor (PPI) to facilitate ulcer healing ( algorithm 1). The choice and duration of therapy varies based on the etiology, ulcer location (eg, gastric or duodenal), and the presence of ulcer complications (eg, bleeding, perforation, penetration, or gastric outlet obstruction). (See 'Initial antisecretory therapy' above.)

- **Indications for surveillance endoscopy**

  - Patients with duodenal ulcers who have been treated do not need further endoscopy unless symptoms persist at four weeks or recur. (See 'Duodenal ulcers' above.)

  - In patients with gastric ulcers, the decision to perform surveillance endoscopy should be individualized. We suggest surveillance endoscopy (with biopsies of the ulcer if still present) be performed after 8 to 12 weeks of antisecretory therapy in patients with gastric ulcers and any one of the following (see 'Repeat upper endoscopy in selected patients' above):

    - Symptoms despite medical therapy
    - Unclear etiology
    - Giant gastric ulcer (>2 cm)
    - Biopsies not performed or inadequate sampling on the index upper endoscopy
    - Ulcer appears suspicious for malignancy on index upper endoscopy (mass lesion, elevated irregular ulcer borders, or abnormal adjacent mucosal folds)
    - Patients with bleeding ulcers at initial presentation who show signs of continued bleeding
    - Risks factors for gastric cancer

- **Prevention of recurrence**

  - The need for aspirin and NSAIDs should be carefully assessed in patients with a history of peptic ulcer disease. NSAIDs, including aspirin, increase the risk of bleeding in patients with prior peptic ulcer disease. In patients treated for *H. pylori,* eradication of infection should be confirmed four or more weeks after the completion of therapy.

  - Maintenance antisecretory therapy should be limited to high-risk subgroups of patients with peptic ulcer disease. These include individuals with any one of the following (see 'Prevention of recurrence' above):

    - Refractory peptic ulcer
    - *H. pylori*-negative, NSAID-negative ulcer disease

- Giant (>2 cm) ulcer and age >50 years or multiple comorbidities
- Failure of *H. pylori* eradication, including rescue therapies
- Frequently recurrent peptic ulcers (>2 documented recurrences a year)
- Continued NSAID use

- **Disease course** – Approximately 60 percent of peptic ulcers heal spontaneously but with eradication of *H. pylori* infection, ulcer healing rates are >90 percent. Even with continued proton pump inhibitor (PPI) use, approximately 5 to 30 percent of peptic ulcers recur within the first year based on whether *H. pylori* has been successfully eradicated. Approximately 5 to 10 percent of ulcers are refractory to antisecretory therapy with a PPI. The risk of complications in patients with chronic peptic ulcer disease is 2 to 3 percent per year. (See 'Disease course' above and "Approach to refractory peptic ulcer disease" and "Overview of complications of peptic ulcer disease".)

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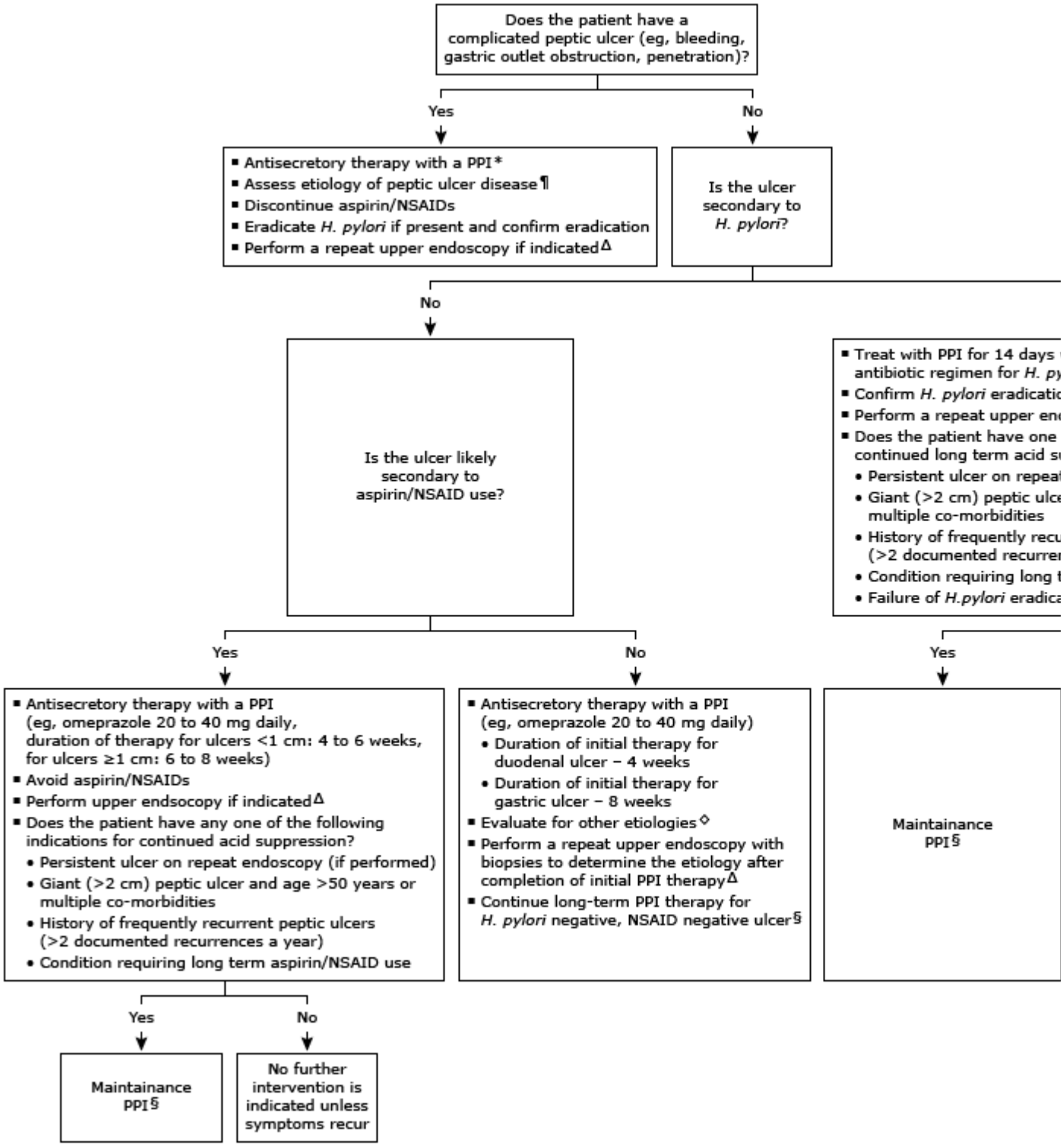
Topic 25 Version 34.0

## GRAPHICS

### Overview of the management of the adult patient with peptic ulcer disease




PPI: proton pump inhibitor; *H. pylori: Helicobacter pylori*; NSAID: non steroidal anti-inflammatory drug; IV: intravenous.

* Patients with complicated peptic ulcers should receive initial acid suppressive therapy with an IV PPI. In general, once patients are tolerating oral medications, they should be switched to an oral PPI. However, in patients with bleeding peptic ulcers the duration of IV PPI and timing of transition to oral PPI is based on the risk of rebleeding. Refer to UpToDate text on treatment of bleeding peptic ulcers.

¶ In patients with bleeding duodenal or gastric ulcer on upper endoscopy, we perform a gastric mucosal biopsy at the time of the initial endoscopy unless it is impractical or difficult, such as with a blood-filled stomach. A negative biopsy result does not exclude *H. pylori* in the setting of an active upper gastrointestinal bleed, and another test for active *H. pylori* infection should be performed to confirm a negative result.

Δ A repeat upper endoscopy is indicated in patients with any one of the following:

- Persistent symptoms or recurrent symptoms after discontinuation of PPI therapy
- Complicated ulcer (bleeding) with evidence of ongoing bleeding
- Giant gastric ulcer (>2 cm)
- Ulcer with features of malignancy at index endoscopy
- Gastric ulcer that was not biopsied or inadequately sampled on the index upper endoscopy (for adequate sampling we suggest 4 biopsies obtained from four quadrants of the ulcer and additional biopsies of the edges with jumbo forceps if there are endoscopic features of a malignant gastric ulcer)
- Gastric ulcers in a patient with risk factors for gastric cancer (Refer to UpToDate text on the management of peptic ulcer disease)
- Gastric ulcer of unclear etiology

◇ Refer to UpToDate text on rare causes of peptic ulcer disease.

§ Examples of typical maintenance doses for PPI include omeprazole 20 mg daily, lansoprazole 30 mg daily, esomeprazole 20 mg daily, and pantoprazole 40 mg daily.

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Graphic 126285 Version 1.0

## Recommendations for PPI doses in active therapy of uncomplicated gastroduodenal ulcers*

| Drug | Dose (adult) |
|---|---|
| Dexlansoprazole | 30 to 60 mg |
| Esomeprazole | 20 to 40 mg |
| Lansoprazole | 30 mg |
| Omeprazole | 20 to 40 mg |
| Pantoprazole | 40 mg |
| Rabeprazole | 20 mg |
| **All administered by mouth daily before breakfast** | |

PPI: proton pump inhibitor.

* As a general rule, active duodenal ulcers should be treated for four to six weeks and gastric ulcers for six to eight weeks.

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*Adapted from: Wolfe MM, Sachs G. Acid suppression: Optimizing therapy for gastroduodenal ulcer healing, gastroesophageal reflux disease, and stress-related erosive syndrome. Gastroenterology 2000; 118:S9.*

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Graphic 81079 Version 5.0

## Causes of recurrent peptic ulcer disease

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|---|
| **Persisting *H. pylori* infection** |
| Poor compliance with treatment |
| Resistant organism |
| Inadequate *H. pylori* regimen |
| Unrecognized *H. pylori* infection: |
| False negative *H. pylori* testing |
| Skipped or inadequate testing |
| **Ulcers related to nonsteroidal anti-inflammatory drugs (NSAIDs)** |
| Continued NSAID use |
| Undiscovered NSAID use |
| Poor response to co-therapy with a proton pump inhibitor (PPI) or histamine 2 receptor antagonist (H2RA) |
| **Other mechanisms** |
| Hypersecretory states: |
| Gastrinoma |
| Antral G cell hyperfunction |
| Idiopathic hypersecretory duodenal ulcer |
| Co-therapies: |
| Glucocorticoids (especially when given with NSAIDs) |
| Cytotoxic drugs |
| Other drugs, such as methamphetamine or cocaine use |
| Uncommon causes: |
| Cancer |
| Crohn disease |
| Infections other than *H. pylori* |
| Eosinophilic, inflammatory, infiltrative conditions |

*H. pylori*: *Helicobacter pylori*.

Graphic 101181 Version 2.0