# **Appropriate Use of Proton Pump Inhibitors**

Proton pump inhibitors (PPI) are among the most widely used class of medications for the prevention of gastric ulceration due to their safety profile. However, recent data suggest that the use of PPI is associated with increased risk of vitamin and mineral malabsorption, bone fractures, chronic kidney disease, pneumonia, viral gastroenteritis, and *Clostridioides difficile* infections.1-7 Because of emerging data on the potential harms associated with PPI and the frequent inappropriate use of these agents, careful review of the indications for PPI use should be performed.

The risks of upper gastrointestinal bleed (UGIB) in hospitalized patients are associated with 4 factors: acute illnesses, chronic conditions, drugs, and devices.8

PPI’s are indicated for the **treatment** of the following conditions:

* Zollinger-Ellison Syndrome
* Barrett’s esophagus
* Acute upper GI bleed
* Erosive esophagitis
* *Helicobacter pylori* treatment
* Gastric or duodenal ulcer
* Gastroesophageal reflux disease (GERD)

PPI’s are considered appropriate for the **prophylaxis** of UGIB in the following conditions:9-11

* Mechanical ventilation for greater than 48 hours
* Coagulopathy defined as platelet count <50,000/μL, INR >1.5, or PTT 2x control
* Traumatic head injuries with a [Glasgow Coma Score](https://www.mdcalc.com/glasgow-coma-scale-score-gcs) ≤10 or inability to follow simple commands
* Burns affecting >35% of total body surface area
* Major trauma with an [Injury Severity Score](https://www.mdcalc.com/injury-severity-score-iss) ≥16
* Spinal cord injury
* Partial hepatectomy
* Solid organ transplantation perioperatively in the ICU setting
* Antiplatelet therapy (usually aspirin + clopidogrel, prasugrel, or ticagrelor) in patients at high risk for GI bleeding (prior history of GI bleeding; age >60 years; concurrent use of anticoagulants, corticosteroids, or NSAID; *Helicobacter pylori* infection)
* Long-term NSAID use in patients with moderate to high risk of GI bleeding
	+ Moderate risk is defined as 1 or 2 of the following risks: age >65 years; [high dose NSAID](https://www.ncbi.nlm.nih.gov/books/NBK65641/) therapy (ibuprofen >2400 mg daily, naproxen >1000 mg daily, meloxicam >7.5 mg daily); previous history of uncomplicated ulcer; concurrent use of aspirin, corticosteroids, or anticoagulants)
	+ High risk is defined as history of complicated ulcer especially recent, or >2 risk factors outlined in the moderate risk group
* Any 2 of the following
	+ Sepsis
	+ ICU stay > 7 days
	+ Occult bleeding lasting more than 6 days
	+ High dose corticosteroids (> 250 mg/day of hydrocortisone, >50 mg/day of methylprednisolone, >60 mg/day of prednisone, >10 mg/day of dexamethasone)

Patients started on a PPI for prophylaxis of any of the conditions above should not have them continued upon discharge unless a chronic condition exists that requires their use.

Besides reviewing the indication of PPI use for appropriateness, the dose and duration of therapy should also be evaluated. As with all medications, the lowest possible dose and shortest duration of therapy should be employed. When the inciting factor (e.g., removal of the hypersecretory tumor in Zollinger-Ellison Syndrome or discontinuation of chronic NSAID) is no longer present, discontinuation of PPI should be considered.

Acid suppression and especially PPI’s are associated with increased risk of C. difficile infection (CDI) relapse.7,13 CDI patients should have PPI use evaluated closely and the agent discontinued if medically possible. If acid suppression is still necessary, consider changing to an H2-blocking agent if medically appropriate.

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**References**

1. Park HC, Kim EH, Roh YH, Kim HY, *et al*. The association between the use of proton pump inhibitors and the risk of hypomagnesemia: a systematic review and meta-analysis. PLOS One 2014 Nov 13;9(11):e112558.
2. Lam JR, Schneider JL, Zhao W, *et al*. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. JAMA 2013;310:2435-42.
3. Yang YX, Lewis JD, Epstein S, *et al*. Long-term proton pump inhibitor therapy and risk of hip fracture. JAMA 2006;296:2947-53.
4. Lazarus B, Chen Y, Wilson FP, *et al*. Proton pump inhibitor use and the risk of chronic kidney disease. JAMA Intern Med 2016;176:238-46.
5. Zirk-Sadowski J, Masoli JA, Delgado J, *et al*. Proton-pump inhibitors and long-term risk of community-acquired pneumonia in older adults. J Am Geriatr Soc 66:1332-8.
6. Vilcu AM, Sabatte L, Blanchon T, *et al*. Association between acute gastroenteritis and continuous use of proton pump inhibitors during winter periods of highest circulation of enteric viruses. JAMA Netw Open 2019 Nov 1;2(11):e1916205.
7. Arriola V, Tischendorf J, Musuuza J, *et al*. Assessing the risk of hospital-acquired *Clostridium difficile* infection with proton pump inhibitor use: a meta-analysis. Infect Control Hosp Epidemiol 2016;37:1408-17.
8. Cook D, Guyatt G. Prophylaxis against upper gastrointestinal bleeding in hospitalized patients. N Engl J Med 2018;378:2506-16.
9. American Society of Health-System Pharmacists. ASHP therapeutic guidelines on stress ulcer prophylaxis. Am J Health-Syst Pharm 1999;56:347-79.
10. Abraham NS, Hlatky MA, Antman EM, *et al*. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitros and thienopyridines: a focused update of the ACCF/ACG/AHA 2008 expert consensus document of reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. Am J Gastroenterol 2010:105:2533-49.
11. Lanza F, Chan FKL, Quigley EMM, *et al*. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol 2009;104:728-38.
12. Freedberg DE, Kim LS, Yan YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterol 2017;152:706-15.
13. Mcdonald EG, Milligan J, Frennet, et al. Continuous proton pump inhibitor therapy and the associated risk of recurrent *Clostridium difficile* infection. JAMA Int Med. 2015;175:784-91.