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PHARMACY & ACUTE CARE UNIVERSITY

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PPIs for the Management of Upper GI Bleed

Nonvariceal (mainly peptic ulcer) upper GI bleeding: pharmacology of 3 PPIs and key evidence. Suspected variceal bleeding: follow your institution's variceal protocol. Assess hemodynamics and resuscitate first.

72 hours
High-risk stigmata after endoscopic hemostasis: IV pantoprazole or esomeprazole 80 mg bolus, then 8 mg/h for 72 hours from endoscopy

6.7% vs 22.5%
After endoscopic hemostasis of a high-risk ulcer, high-dose PPI for 3 days cuts rebleeding versus placebo (in the landmark trial, 6.7% vs 22.5% at 30 days).

Day 14
Then oral twice daily through day 14, then once daily

Before endoscopy

- Before endoscopy, high-dose IV PPI may be considered (ESGE 2026) but must not delay endoscopy; likely reduces endoscopic treatment at index endoscopy; no proven effect on mortality, rebleeding or surgery.
- Endoscopy within 24 hours of presentation is suggested (ACG 2021); emergent (6 h or less) or urgent (12 h or less) is not recommended unless hemodynamically unstable despite adequate resuscitation (ESGE 2026).

At the scope: re-decide the PPI

- **After hemostasis of high-risk stigmata** (spurting, oozing, nonbleeding visible vessel) or adherent clot not treated endoscopically (ESGE 2021 recommends): 72 h from endoscopy.
- **Low-risk stigmata** (clean base, flat pigmented spot): no high-dose or IV PPI; do not continue a pre-endoscopy infusion for 72 hours; once-daily oral PPI.
- ESGE 2021 alternatives that can be considered: twice-daily high-dose IV bolus or oral PPI. Equivalence to the infusion is not established; best intermittent dose unknown.

The three PPIs

Drug	After hemostasis of high-risk stigmata: 72 h from endoscopy	Maintenance (oral)	Administration and interactions
Pantoprazole	Continuous: 80 mg IV bolus, then 8 mg/h. Intermittent: 80 mg IV once, then 40 mg IV every 12 h (trial regimen; not shown to be high dose). Not labelled for UGIB: safety and effectiveness not established	Low-risk: oral label has no indication for healing an active ulcer.	IV push over at least 2 min. Y-site: midazolam incompatible. Clopidogrel: no adjustment at approved IV doses; bleeding-infusion interaction not established
Esomeprazole	Continuous (labelled): 80 mg IV over 30 min, then 8 mg/h (Child-Pugh A or B: 6 mg/h; C: 4 mg/h) for 71.5 h, then oral (IV alone is not full treatment). Intermittent: none in the trials reviewed	High-risk: 40 mg twice daily, days 3 to 14, in the trial behind ICON 2019 (Rockall 6 or more). Child-Pugh C: oral maximum 20 mg daily (erosive esophagitis healing)	IV push over at least 3 min (20 or 40 mg). Bleeding regimen: dilute in 100 mL NS, give within 12 h. No other drugs through the same IV site or tubing. Avoid clopidogrel (consider another antiplatelet)
Omeprazole	IV not available in the U.S. Oral option: 40 mg PO twice daily for 72 h (trial regimen; not shown equivalent to the infusion)	Low-risk: no strength or duration for low-risk stigmata in the sources reviewed	PO: swallow whole 30 to 60 min before food. Avoid: atazanavir, clopidogrel

All three: all PPIs may raise C. difficile diarrhea risk, especially in hospitalized patients. Rilpivirine-containing products contraindicated; avoid nelfinavir; warfarin: monitor INR, PT.
Monitoring: rebleeding, most closely during the 72 hours. If recurrent, repeat endoscopy (ACG 2021 suggests; ESGE 2021 recommends, with hemostasis if indicated). Hemoglobin. Check IV site.

Key evidence

Author, year	Design (n)	Intervention	Key findings
Muñoz-Carrillo, 2026	Meta-analysis (12 RCTs, n=1,726)	Continuous vs intermittent IV bolus after hemostasis	Continuous not superior for rebleeding (RR 0.93, 95% CI 0.65 to 1.35; 11 trials, n=1,621; very low certainty); surgery and mortality: low certainty. Neither equivalence nor noninferiority established
Sriyudthsak, 2026	RCT, multicenter, single-blind (n=124)	Omeprazole 40 mg PO twice daily vs pantoprazole 8 mg/h IV, 72 h after hemostasis	72-h rebleeding 1.6% vs 4.8% (risk difference -3.1%, 95% CI -11.6% to 4.6%). Small; CI allows more rebleeding with oral
Kanno, 2022	Meta-analysis (6 RCTs, n=2,223)	PPI (oral or IV) vs placebo, H2RA or no treatment, before endoscopy	Likely reduces endoscopic treatment at index endoscopy (OR 0.68, 95% CI 0.50 to 0.93; moderate certainty). No clear effect on mortality, rebleeding, surgery or high-risk stigmata (low certainty)
Sachar, 2014	Meta-analysis (13 RCTs)	Intermittent IV or PO (40 mg IV daily to every 6 h) vs 80 mg IV, then 8 mg/h, 72 h, after endoscopic therapy	Intermittent noninferior for 7-day rebleeding (RR 0.72; upper 1-sided 95% bound 0.97); no outcome worse with intermittent
Chen, 2012	RCT (n=201)	Pantoprazole 80 mg IV, then 8 mg/h, vs standard dose 40 mg IV once daily, 72 h	30-day rebleeding 6.2% vs 5.2% (P=0.77)
Sung, 2009	RCT, multicenter (n=764)	Esomeprazole 80 mg IV, then 8 mg/h, 72 h, vs placebo after hemostasis	72-h rebleeding 5.9% vs 10.3% (P=0.026), sustained at 7 and 30 days. Surgery and mortality lower but not significant
Lau, 2007	RCT, double-blind (n=638)	Omeprazole 80 mg IV, then 8 mg/h, vs placebo before next-morning endoscopy	Less endoscopic treatment: 19.1% vs 28.4% (P=0.007). No difference in rebleeding, surgery or 30-day mortality
Lau, 2000	RCT, double-blind (n=240)	Omeprazole 80 mg IV, then 8 mg/h, 72 h, vs placebo after hemostasis of actively bleeding ulcers or nonbleeding visible vessels	30-day rebleeding 6.7% vs 22.5% (HR 3.9 for placebo vs omeprazole, 95% CI 1.7 to 9.0). Most rebleeds during the 72-h infusion

After the high-dose phase: H. pylori: test at index endoscopy; re-test if negative; treat if positive; document cure; then anti-ulcer therapy generally stops. Stop NSAIDs (if one must resume: low-dose COX-2 selective NSAID plus PPI). After the twice-daily phase, reassess need; when continued therapy is not needed, lowest dose and shortest duration appropriate.

Bottom line: re-decide the PPI at endoscopy. Give 72 hours of high-dose PPI after endoscopic hemostasis of high-risk stigmata, then oral twice daily through day 14; a clean-based or flat-spot ulcer needs no high-dose or IV PPI, only a once-daily oral PPI. Follow your institution's protocol and formulary.

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