



Proton Pump Inhibitors

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OVERVIEW

The proton pump inhibitors (PPIs) are the most potent suppressants of gastric acid secretion available and are used widely in the therapy of gastroesophageal reflux and peptic ulcer disease. PPIs are prodrugs that require gastric acid for their activation. After absorption they diffuse into the parietal cells of the stomach and accumulate in the acidic secretory canaliculi. The activated form of the PPIs binds covalently to the H⁺/K⁺-ATPase of the acid-producing parietal cell, inactivating the pump molecule that transports protons (H⁺ molecules) into the gastric lumen. While the half-life of the PPIs is measured in hours, the activated form is trapped in the parietal cell and inhibition of the proton pump generally lasts for 24 to 48 hours. Oral forms of the PPIs are rapidly absorbed and decrease gastric acidity by 80% to 95%, although peak inhibition may require several days. More rapid inhibition may be achieved by use of intravenous formulations. The PPIs are metabolized by the hepatic cytochrome P450 system (predominantly CYP 2C19 and 3A4), but are extremely well tolerated and associated with few adverse events. Liver injury due to PPIs has been reported, but is uncommon in view of the millions of individuals who take these agents.

Six PPIs are currently approved for use in the United States in various dosage forms, including enteric-coated tablets and gelatin capsules, delayed-release tablets and powdered forms for intravenous use. The initial PPI approved for use was omeprazole (1989: Prilosec) followed by lansoprazole (1995: Prevacid), rabeprazole (1999: Aciphex), pantoprazole (2000: Protonix), esomeprazole (2001: Nexium, the S-isomer of omeprazole), and dexlansoprazole (2009: Dexilant, the R-isomer of lansoprazole). Most are now available in generic forms. Omeprazole, esomeprazole and lansoprazole are also available in over-the-counter formulations.

Side effects of PPIs are uncommon, usually mild, and include nausea, abdominal discomfort, constipation, flatulence and diarrhea. Less common side effects include myopathy, arthralgias, headaches and skin rash. Rare instance of acute liver injury have been reported with most of the PPIs. In view of the wide scale use of the PPIs, clinically apparent liver injury is exceedingly rare. Each PPI is discussed separately in LiverTox, with references given after each, as the pattern of hepatic injury that occurs with their use is somewhat different, although all appear to share a tendency to cause hepatocellular liver injury with a short latency, within 4 weeks of starting, and rapid recovery on stopping.

- [Dexlansoprazole](#)
- [Esomeprazole](#)
- [Lansoprazole](#)
- [Omeprazole](#)
- [Pantoprazole](#)
- [Rabeprazole](#)

Drug Class: [Antiulcer Agents](#)