Therapeutic Class Overview
Proton Pump Inhibitors

INTRODUCTION

- The proton pump inhibitors (PPIs) are a class of antisecretory compounds that suppress gastric acid secretion and are generally considered the most potent acid suppressants available. Parietal cells line the gastric mucosa and secrete acid into the gastric lumen in response to several stimuli. Within the parietal cell, a gastric transport enzyme known as hydrogen/potassium adenosine triphosphatase is involved in the final step in acid secretion. This enzyme, commonly referred to as the proton pump, exchanges potassium ions (K^+) for hydrogen ions (H^+) resulting in a lower gastric pH. The PPIs exert their effect by covalently binding to the proton pump and irreversibly inhibiting this ion exchange, causing an increase in gastric pH. The PPIs can only inhibit proton pumps that are actively secreting acid (Wolfe et al, 2000). Approximately 70% to 80% of the proton pumps will be active following a meal (Welage, 2003). As a result, single doses of PPIs will not completely inhibit acid secretion and subsequent doses are required to inhibit previously inactive proton pumps and newly regenerated pumps. With regular dosing, maximal acid suppression occurs in three to four days (Welage, 2003; Wolfe et al, 2000).
- There are currently six PPIs available on the market in a variety of formulations. The PPIs include dexlansoprazole (DEXILANT®, DEXILANT SOLUTAB®, esomeprazole (NEXIUM®, NEXIUM IV®, NEXIUM® 24HR), esomeprazole strontium, lansoprazole (PREVACID®, PREVACID SOLUTAB®, PREVACID® 24HR), omeprazole (PRILOSEC®, PRILOSEC OTC®, ZEGERID®, ZEGERID OTC®), pantoprazole (PROTONIX®, PROTONIX IV®), and rabeprazole (ACIPHEX®, ACIPHEX® SPRINKLE™), of which certain formulations of rabeprazole, esomeprazole, lansoprazole, omeprazole, omeprazole with sodium bicarbonate, and pantoprazole are available generically. In addition, lansoprazole, esomeprazole magnesium, omeprazole, and omeprazole with sodium bicarbonate are available over-the-counter (OTC). Currently available PPI combination products include aspirin/omeprazole (YOSPRALA®) and naproxen/esomeprazole (VIMOVO®); these combination products are outside the scope of this overview and will not be reviewed.
- In August 2013, esomeprazole strontium was Food and Drug Administration (FDA)-approved without a proprietary name. Its approval was based on bioequivalence of esomeprazole strontium 24.65 mg and 49.3 mg delayed-release capsules to esomeprazole magnesium 20 and 40 mg delayed-release capsules, respectively. Shortly after its approval, the manufacturer made an authorized generic available by the same name. Both strengths of this product were discontinued for several months during 2015-2016, but reappeared on the market with a different manufacturer in September 2016.
- All of the PPIs are substituted benzimidazole derivatives and are structurally related. Omeprazole is a racemic mixture of *S*- and *R*-isomers and esomeprazole contains only the *S*-isomer of omeprazole. Following oral administration, the *S*-isomer has demonstrated higher plasma levels compared to the *R*-isomer. The PPIs primarily differ in their pharmacokinetic and pharmacodynamic properties in addition to their formulations. While some differences have been reported in head-to-head studies directly comparing the PPIs, the magnitude of these differences is generally small and the clinical significance has not been established. When administered in equivalent dosages, the PPIs have generally demonstrated comparable efficacy to one another (Dean, 2010).
  - Dexlansoprazole, the enantiomer of lansoprazole and the newest agent in the class, is the first PPI with a dual delayed-release formulation designed to provide two separate releases of medication. It contains two types of enteric-coated granules resulting in a concentration-time profile with two distinct peaks: the first peak occurs one to two hours after administration, followed by a second peak within four to five hours. In addition, it can be taken regardless of meals (DEXILANT prescribing information, 2016).
  - DEXILANT SOLUTAB, an orally disintegrating, delayed release tablet formulation of dexlansoprazole, was approved in January 2016; however, the formulation is currently not available.
- In general, all PPIs are FDA-approved for the treatment of gastroesophageal reflux disease (GERD) and for the healing and maintenance of erosive esophagitis. Some of the agents also have approval for the treatment of peptic ulcer disease, the treatment of pathological hypersecretory conditions, and *Helicobacter pylori (H. pylori)* eradication as part of combination therapy with antibiotics.
- Current national and international consensus guidelines recognize the PPIs as first-line therapy for the management of dyspepsia, GERD, peptic ulcer disease, and eradication of *H. pylori.* In addition, these agents have a role in the management of Barrett's esophagus. Currently available guidelines do not give preference to one PPI over another (American Gastroenterological Association, 2011; Chey et al, 2017; Kahrilas et al, 2008; Katz et al, 2013; Koletzko et al, 2011; Laine et al, 2012; Lanza et al, 2009; Malfertheiner et al, 2012; Shaheen et al, 2016; Talley et al, 2005; Talley, Vakil et al, 2005).

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- The agents included in this review are listed alphabetically by brand name in Table 1. Since there are multiple branded agents that contain the same generic component(s) the remaining tables in the review are organized alphabetically by generic name.

Table 1. Medications Included Within Class Review

Drug	Manufacturer	FDA Approval Date	Generic Availability
ACIPHEX (rabeprazole) delayed-release tablet	various generic	08/19/1999	√
ACIPHEX SPRINKLE (rabeprazole) delayed-release capsule	Eisai Inc.	03/26/2013	-
DEXILANT (dexlansoprazole) delayed-release capsule	Takeda Pharms	01/30/2009	-
DEXILANT SOLUTAB (dexlansoprazole) delayed-release orally disintegrating, tablet	Takeda Pharms	01/26/2016	-
esomeprazole strontium, delayed-release capsule	R2 Pharma LLC	08/06/2013	√
NEXIUM (esomeprazole magnesium) delayed-release capsule	various generic	02/20/2001	√
NEXIUM (esomeprazole magnesium) powder for delayed-release oral suspension	AstraZeneca	10/20/2006	-
NEXIUM IV (esomeprazole sodium) injection	various generic	03/31/2005	√
NEXIUM 24HR* (esomeprazole magnesium) delayed-release capsules	Pfizer Consumer Healthcare	03/28/2014	-
NEXIUM 24HR* (esomeprazole magnesium) delayed-release tablets	Pfizer Consumer Healthcare	11/23/2015	-
PREVACID (lansoprazole) delayed-release capsule	various generic	05/10/1995	√
PREVACID 24HR* (lansoprazole) delayed-release capsule	various generic	05/18/2009	√
PREVACID SOLUTAB (lansoprazole) delayed-release orally disintegrating tablet	Takeda Pharms USA	08/30/2002	-
PRILOSEC (omeprazole magnesium) delayed-release capsule	various generic	09/14/1989	√
PRILOSEC (omeprazole magnesium) powder for delayed-release oral suspension	AstraZeneca	03/20/2008	-
PRILOSEC OTC* (omeprazole magnesium) delayed-release tablet	various generic	06/20/2003	√
PROTONIX (pantoprazole) delayed-release tablet	various generic	02/02/2000	√
PROTONIX (pantoprazole) powder for delayed-release oral suspension	Wyeth Pharms Inc.	11/14/2007	-
PROTONIX IV (pantoprazole) injection, powder for solution	various generic	03/22/2001	√
ZEGERID (omeprazole with sodium bicarbonate) capsule	various generic	02/27/2006	√
ZEGERID (omeprazole with sodium bicarbonate) powder for oral suspension	various generic	06/15/2004	√
ZEGERID OTC* (omeprazole with sodium bicarbonate) capsule	various generic	12/01/2009	√
ZEGERID OTC* (omeprazole with sodium bicarbonate) powder for suspension	Bayer Healthcare	06/17/2013	-

*Available OTC.

(DRUGS@FDA.com, 2017; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2017)

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INDICATIONS

Table 2. FDA-Approved Indications

Indication	Dexlansoprazole	Esomeprazole magnesium and strontium	Esomeprazole sodium	Lansoprazole	Omeprazole magnesium	Omeprazole/ Sodium bicarbonate	Pantoprazole	Rabeprazole
GERD[e]								
Maintaining healing of erosive esophagitis	√	√		√	√	√	√	√
Treatment of erosive esophagitis	√[d]	√	√	√	√	√	√[c]	√
Treatment of symptomatic GERD	√	√		√	√	√		√
Peptic Ulcer Disease								
Healing of nonsteroidal anti-inflammatory drug (NSAID)-associated gastric ulcer				√				
H. pylori eradication to reduce the risk of duodenal ulcer recurrence		√[b]		√[b]	√[b]			√[b]
Maintenance of healing duodenal ulcers				√				
Risk reduction of NSAID-associated gastric ulcer		√		√				
Treatment of active, benign gastric ulcer				√	√	√		
Treatment of active duodenal ulcers				√	√	√		√
Other								
Risk reduction of upper gastrointestinal bleeding in critically ill patients						√		
Treatment of frequent heartburn for up to 14 days		√ (NEXIUM 24HR)		√ (PREVACID 24HR)	√ (PRILOSEC OTC)	√ (ZEGERID OTC)		
Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome		√		√	√		√[a]	√
Risk reduction of rebleeding of gastric or duodenal ulcers following therapeutic endoscopy in adults			√					

a Intravenous and oral formulation.
b As triple therapy in combination with amoxicillin and clarithromycin (esomeprazole, lansoprazole, omeprazole and rabeprazole) or dual therapy with amoxicillin (lansoprazole) or clarithromycin (omeprazole).

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c Oral formulations indicated for the short-term treatment of erosive esophagitis associated with GERD; intravenous formulation indicated for the short-term treatment of adult patients with GERD associated with a history of erosive esophagitis.
d DEXILANT SOLUTAB is not approved for healing of erosive esophagitis.
e Esomeprazole magnesium/sodium, lansoprazole, omeprazole, pantoprazole, and rabeprazole are approved for pediatric patients. Dexlansoprazole is indicated for patients 12 years of age or older. Esomeprazole strontium and omeprazole/sodium bicarbonate are approved for adult patients.

(Prescribing information: ACIPHEX, 2016; ACIPHEX SPRINKLE, 2016; DEXILANT, 2016; DEXILANT SOLUTAB, 2016; esomeprazole strontium, 2016; NEXIUM, 2016; NEXIUM IV, 2016; NEXIUM 24HR, 2016; PREVACID, 2016; PREVACID 24HR, 2016; PRILOSEC, 2016; PRILOSEC OTC, 2016; PROTONIX, 2017; PROTONIX IV, 2016; ZEGERID, 2016; ZEGERID OTC, 2016)

Information on indications, mechanism of action, pharmacokinetics, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

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CLINICAL EFFICACY SUMMARY

- Clinical trials consistently demonstrate that the PPIs are highly effective in treating, providing symptom relief, and preventing relapse in gastric acid disorders such as GERD and peptic ulcer disease (Armstrong et al, 2004; Bardhan et al, 2001; Bazzoli et al, 1998; Caro et al, 2001; Castell et al, 2002; Castell et al, 2005; Chan et al, 2010; Chey et al, 2003; Choi et al, 2007; Conrad et al, 2005; Delchier et al, 2000; Devault et al, 2006; Edwards et al, 2001; Fass et al, 2009; Fass et al, 2011; Fass et al, 2012; Felga et al, 2010; Fennerty et al, 2005; Fujimoto et al, 2011; Gisbert et al, 2003; Gisbert et al, 2004; Gisbert, Khorrami et al, 2004; Goh et al, 2007; Haddad et al, 2013; Howden et al, 2002; Howden et al, 2009; Hsu et al, 2005; Kahrilas et al, 2000; Katz et al, 2007; Khorrami et al, 2004; Kinoshita et al, 2011; Klok et al, 2003; Labenz et al, 2005[a]; Labenz et al, 2005[b]; Laine et al, 2011; Lauritsen et al, 2003; Lightdale et al, 2006; McNicholl et al, 2012; Metz et al, 2009; Mönnikes et al, 2012; Pace et al, 2005; Pilotto et al, 2007; Pouchain et al, 2012; Ramdani et al, 2002; Regula et al, 2006; Richter et al, 2001; Richter, Kahrilas, Sontag et al, 2001; Scheiman et al, 2011; Schmitt et al, 2006; Scholten et al, 2003; Sharma et al, 2001; Sharma et al, 2009; Sugano et al, 2011; Tsai et al, 2004; Ulmer et al, 2003; van Pinxteren et al, 2010; Vergara et al, 2003; Wang et al, 2006; Wu et al, 2007).
- The safety and efficacy of esomeprazole strontium have been established based on adequate and well-controlled adult studies of esomeprazole magnesium in the healing and maintenance of erosive esophagitis, symptomatic GERD, risk reduction of NSAID-associated gastric ulcer, *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence, and pathological hypersecretory conditions including Zollinger-Ellison Syndrome.
- A number of studies have compared the various PPIs to one another. While some differences have been reported, the magnitude of differences has been small and of uncertain clinical importance. In particular, the degree to which any of the reported differences would justify the selection of one versus another PPI, particularly when considering cost-effectiveness, is unclear (Wolfe, 2017).

GERD

- In meta-analyses and direct comparator trials, lansoprazole, omeprazole, pantoprazole, and rabeprazole have demonstrated comparable healing rates, maintenance of healing, and/or symptomatic relief of GERD (Bardhan et al, 2001; Caro et al, 2001; Edwards et al, 2001; Klok et al, 2003; Pace et al, 2005; Sharma et al, 2001). Furthermore, Richter et al reported that lansoprazole produced a significantly quicker and greater symptomatic relief of GERD compared to omeprazole; however, the absolute differences between the two treatments were small and the clinical impact of the difference was not measured within the clinical trial (Richter, Kahrilas, Sontag et al, 2001).
- The results of several meta-analyses and clinical trials demonstrate that esomeprazole may provide higher healing rates for erosive esophagitis and/or symptomatic relief of GERD compared to standard doses of lansoprazole, omeprazole, and pantoprazole at four and eight weeks (Castell et al, 2002; Devault et al, 2006; Edwards et al, 2001; Kahrilas et al, 2000; Klok et al, 2003; Labenz et al, 2005[a]; Labenz et al, 2005[b]; Richter et al, 2001). Subgroup analyses of two trials note higher healing rates with esomeprazole in patients with more severe disease (Labenz et al, 2005[a]; Schmitt et al, 2006).
- Close analyses of all of these trials demonstrate that the overall differences between the various PPI agents were generally small and the clinical significance is not clear. In addition, results of these trials have not been consistently demonstrated in other clinical trials, particularly in those evaluating lansoprazole and pantoprazole (Armstrong et al, 2004; Chey et al, 2003; Goh et al, 2007; Howden et al, 2002; Lightdale et al, 2006; Scholten et al, 2003).

Peptic Ulcer Diseases

- Meta-analyses and head-to-head trials comparing various PPIs for the treatment of peptic ulcer disease with *H. pylori* demonstrate comparable rates of eradication when paired with comparable antibiotic regimens (Bazzoli et al, 1998; Choi et al, 2007; Gisbert et al, 2003; Gisbert et al, 2004; Gisbert, Khorrami et al, 2004; Ulmer et al, 2003; Vergara et al, 2003; Wang et al, 2006; Wu et al, 2007).
- Results from two meta-analyses suggest that both esomeprazole- and rabeprazole-based *H. pylori* regimens are more effective with regard to eradication rates compared to traditional PPI-based regimens (lansoprazole, omeprazole, and pantoprazole) (McNicholl et al, 2012; Xin et al, 2016).

Current Guidelines

- Current consensus among various national and international treatment guidelines recommend a PPI as the first-line therapy in the treatment and maintenance of healed erosive esophagitis, symptomatic GERD, dyspepsia (patients ≤ 55 years and no alarm features), and peptic ulcer disease caused by NSAID therapy. Triple and quadruple combination therapy with antibiotics and a PPI are considered first-line therapy for peptic ulcer disease caused by *H. pylori*. None of the treatment guidelines recommend one PPI over another or one formulation of a PPI over another (American Gastroenterological Association, 2011; Chey et al, 2017; Kahrilas et al, 2008; Katz et al, 2013; Koletzko et

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al, 2011; Laine et al, 2012; Lanza et al, 2009; Malfertheiner et al, 2012; Shaheen et al, 2016; Talley et al, 2005; Talley, Vakil et al, 2005).

- According to the American Gastroenterological Association (AGA) medical position statement on the management of GERD (2008) and the American College of Gastroenterology (ACG) guideline for the diagnosis and management of GERD (2013), PPIs are considered the drug of choice in the treatment of GERD with H_2-receptor antagonists as an alternative agent that can be used for maintenance of GERD symptoms without erosive disease (AGA Institute Medical Position Panel, 2008; Katz et al, 2013). The ACG medical position notes that there are no major differences between the different PPIs (Katz et al, 2013).
- According to joint recommendations from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (2009), PPIs are recommended in older children or adolescents with chronic heartburn for four weeks in conjunction with lifestyle modifications and in infants or children with reflux esophagitis as initial treatment in conjunction with lifestyle modifications. Patients with asthma and heartburn should also be treated for heartburn (Vandenplas et al, 2009).
- According to the ACG guideline for prevention of NSAID-related ulcer complications (2009), misoprostol or high-dose PPI treatment is recommended as co-therapy with anti-inflammatory analgesics in certain patients with high- and moderate-NSAID gastrointestinal risk. In patients who require both anti-inflammatory analgesics and low-dose aspirin, naproxen with either misoprostol or a PPI are also recommended (Lanza et al, 2009).
- According to the ACG guideline on the management of *H. pylori* infection (2017), there are many first-line options for *H. pylori* treatment; a regimen should be based on patient allergies, previous macrolide exposure, and known *H. pylori* resistance rates. A PPI, clarithromycin, and amoxicillin or metronidazole (clarithromycin-based triple therapy) regimen for 14 days is recommended where *H. pylori* clarithromycin resistance is known to be < 15%. Alternately, bismuth quadruple therapy, consisting of a PPI, bismuth, tetracycline, and a nitroimidazole (metronidazole or tinidazole) for ten to 14 days should be considered as a first-line therapy option for areas of high clarithromycin resistance (Chey et al, 2017).
- High-dose PPIs are often used as primary long-term therapy in Zollinger-Ellison syndrome. PPIs are considered generally safe, even at high doses, and have demonstrated superior acid suppression, healing rates, and symptom relief compared with other antisecretory therapies (Bergsland, 2016; National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK] Web site).
- A 2015 clinical guideline by the ACG also recognized the use of PPIs in the management of Barrett's Esophagus; long-term PPI use will likely produce a net benefit for these patients (Freedberg et al, 2017; Shaheen et al, 2016).

SAFETY SUMMARY

- In general, the PPIs are well tolerated; abdominal pain, diarrhea, flatulence, headache, nausea, and vomiting are the most frequently reported adverse events.
- Long-term use of PPIs for five or more years has been associated with an increase in hip fractures (Targownik et al, 2008). When administered for seven or more years, PPIs have been associated with a significantly increased risk of an osteoporosis-related fracture. At this time, there is inadequate evidence to mandate bone density studies and calcium supplementation in patients receiving chronic PPI therapy (Freedberg et al, 2017; Kahrilas et al, 2008). Additional data are needed to determine the value of osteoporotic medications in patients receiving long-term PPI therapy (Targownik et al, 2008). The 2013 guidelines for the diagnosis and management of GERD recommend continuation of PPI therapy unless additional risk factors for osteoporosis exist (Katz et al, 2013).
- Contraindications of the PPIs include hypersensitivity to any component of their formulations. ACIPHEX, ACIPHEX SPRINKLE, DEXILANT, DEXILANT SOLUTAB, and PRILOSEC are also contraindicated in patients receiving rilpivirine-containing products.
- Warnings and precautions with the use of PPIs include acute interstitial nephritis, cyanocobalamin deficiency, *Clostridium difficile*-associated diarrhea, bone fractures, and hypomagnesemia. Concomitant use with clopidogrel, St. John's Wort, rifampin, high-dose methotrexate, and some antiretroviral medications (e.g., protease inhibitors such as atazanavir and nelfinavir) should be avoided. False positive results for diagnostic investigations of neuroendrocrine tumors may occur due to an increase in serum chromogranin A (CgA) levels. Cutaneous and systemic lupus erythematosus have been reported in patients taking PPIs; new onset events and exacerbations of existing autoimmune disease have occurred. Finally, symptomatic response to PPI therapy does not preclude the presence of gastric malignancy.
- The concomitant use of PPIs with thienopyridines such as clopidogrel was addressed in a consensus guideline from the American College of Cardiology Foundation, American College of Gastroenterology, and American Heart Association, which recommended PPI therapy be continued unless additional risk factors for cardiovascular disease exist (Abraham et al, 2010). A systematic review exploring the use of PPIs in combination with dual antiplatelet therapy that included clopidogrel showed inconclusive results for causing cardiovascular events while another

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systematic review showed an increase in cardiovascular events with pantoprazole, lansoprazole, and esomeprazole but not with omeprazole (Melloni et al, 2015; Sherwood et al, 2015). In a large, longitudinal, observational study of patients discharged after acute myocardial infarction treated with percutaneous coronary intervention, the use of clopidogrel or prasugrel in combination with a PPI was associated with statistically significantly more cardiovascular events than patients not discharged on a PPI (adjusted hazard ratio [HR], 1.38; 95% confidence interval [CI], 1.21 to 1.58). However, the authors noted that patients prescribed a concurrent PPI were more likely to be older and have more complex comorbidity profiles (Jackson et al, 2016).

- Recent research has demonstrated an association with PPIs and cardiovascular, renal, and neurological morbidity. PPI use interferes with acid production in endothelial lysosomes, leading to oxidative stress and accelerated cell death, and may contribute to the pathogenesis of the aforementioned morbidities (Yepuri et al, 2016).
  - A retrospective study using a data mining strategy identified 2.9 million patients in the general population taking PPIs for GERD. Data showed that GERD patients exposed to PPIs had a 1.16 fold increased association with myocardial infarction and a two-fold increased association with cardiovascular mortality. H_2-receptor antagonists used for GERD were not associated with any increased cardiovascular risk (Shah et al, 2015).
  - In a large cohort study, 144,032 incident users of either PPIs or H_2-antagonists were followed for five years. Patients using PPIs had an increased risk of incident chronic kidney disease (HR, 1.26; 95% CI, 1.2 to 1.33) and increased risk of estimated glomerular filtration rate decline and end-stage renal disease as compared to H_2-antagonist users (Xie et al, 2017). Similar patterns were identified in another large population-based cohort study; twice-daily PPI dosing was associated with a higher risk than once-daily dosing (Lazarus et al, 2016).
  - A prospective cohort using observational data from 73,679 patients ≥ 75 years and dementia-free at baseline were analyzed. Patients on PPIs (N = 2950) had a significantly increased risk of dementia than patients not on PPIs (HR, 1.44; 95% CI, 1.36 to 1.52, P < 0.001) (Gomm et al, 2016).

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
Dexlansoprazole	Delayed-release capsule: 30 mg 60 mg SoluTab delayed-release orally disintegrating tablets: 30 mg **Note:** Two 30 mg DEXILANT SoluTabs are not interchangeable with one 60 mg DEXILANT capsule. Both formulations are indicated for patients ≥ 12 years of age.	Treatment of symptomatic, non-erosive GERD: 30 mg daily for four weeks Treatment of erosive esophagitis: 60 mg daily for up to eight weeks Maintenance of healing of erosive esophagitis: 30 mg daily[a]	Delayed-release capsules can be taken without regard to food. Delayed-release capsules can be opened and contents sprinkled onto applesauce for immediate consumption. Delayed-release capsules can be opened and contents mixed in 20 mL of water for administration in an oral syringe for immediate consumption. Refill the oral syringe with 10 mL of water twice to ensure all of the contents are delivered. Delayed-release capsules can be opened with contents mixed in 20 mL of water and withdrawn in a catheter-tip syringe and administered by nasogastric tube. Refill the syringe with 10 mL of water twice to flush the tube. SoluTabs must be taken at least 30 minutes before a meal. SoluTabs should not be broken, chewed, or cut. Tablets should be placed on the tongue, allowed to disintegrate, and the microgranules

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
			swallowed without water. SoluTabs may also be swallowed whole with water.
Esomeprazole magnesium	Delayed-release capsule: 20 mg 40 mg Delayed-release suspension (unit-dose packets): 2.5 mg 5 mg 10 mg 20 mg 40 mg Delayed-release capsule (OTC): 22.3 mg Delayed-release tablet (OTC): 22.3 mg	Treatment of symptomatic GERD (≥ 12 years of age): 20 mg daily for four weeks[b] *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence: 40 mg daily for ten days[c] Treatment of erosive esophagitis (≥ 12 years of age): 20 mg or 40 mg daily for four to eight weeks Maintenance of healing of erosive esophagitis: 20 mg daily[a] Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome: 40 mg twice daily[d] Risk reduction of NSAID-associated gastric ulcer: 20 or 40 mg daily for up to six months[a] Treatment of frequent heartburn (OTC): 22.3 mg daily for 14 days[i] Treatment of symptomatic GERD, short-term (1 to 11 years of age)[e]: 10 mg daily for up to eight weeks Treatment of erosive esophagitis (1 to 11 years of age)[e]: Weight-based dosing Patients weighing < 20 kg: 10 mg once daily for eight weeks Patients weighing ≥ 20 kg: 10 mg or 20 mg once daily for eight weeks Treatment of erosive esophagitis due to acid-mediated GERD (1 month to < 1 year of age)[e]: Weight-based dosing Patients weighing 3 kg to 5 kg: 2.5 mg once daily for up to six	Should be taken at least one hour before meals. Capsules can be opened and contents sprinkled onto applesauce for immediate consumption. Contents can also be emptied into 60 mL catheter tipped syringe and shaken with 50 mL water for administration via nasogastric tube. Packets for delayed-release suspension should be emptied into water (5 mL for 2.5 mg or 5 mg; 15 mL for 10 mg, 20 mg, or 40 mg), stirred, left for two to three minutes to thicken, and drank within 30 minutes. Can also be emptied into catheter-tipped syringe for administration via nasogastric tube.

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		weeks Patients weighing > 5 kg to 7.5 kg: 5 mg once daily for up to six weeks Patients weighing > 7.5 kg to 12 kg: 10 mg for up to six weeks	
Esomeprazole sodium	Powder for injection: 20 mg 40 mg	Treatment of symptomatic GERD with erosive esophagitis (Adults)[f]: 20 mg or 40 mg once daily by IV injection (no less than 3 minutes) or IV infusion (10 to 30 minutes) Risk reduction of rebleeding of gastric or duodenal ulcers following therapeutic endoscopy in adults: 80 mg IV infusion over 30 minutes followed by a continuous infusion of 8 mg/h over three days (72 hours) Treatment of symptomatic GERD with erosive esophagitis (1 to 17 years of age)[f]: Weight-based dosing Patients weighing < 55 kg: 10 mg once daily Patients weighing ≥ 55 kg: 20 mg once daily Treatment of symptomatic GERD with erosive esophagitis (1 month to < 1 year)[f]: Weight-based dosing 0.5 mg/kg once daily	Should be discontinued in favor of oral therapy as soon as oral therapy is possible. No refrigeration required. Reconstituted with 0.9% sodium chloride (to be administered within 12 hours), Lactated Ringer's (within 12 hours), or 5% dextrose (within six hours). Loading dose and continuous infusion prepared by reconstitution of two 40 mg vials with 5 mL 0.9% sodium chloride each, then further diluted in 100 mL of 0.9% sodium chloride.
Esomeprazole strontium	Delayed-release capsule: 24.65 mg (equivalent to 20 mg esomeprazole) 49.3 mg (equivalent to 40 mg esomeprazole)	Treatment of erosive esophagitis in adults: 24.65 or 49.3 mg once daily for four to eight weeks Maintenance of healing of erosive esophagitis in adults: 24.65 mg once daily[a] Treatment of symptomatic GERD in adults: 24.65 mg once daily for four weeks Risk reduction of NSAID-associated gastric ulcer in adults: 24.65 or 49.3 mg once daily[a] *H. pylori* eradication (triple	Should be taken at least one hour before meals. Capsule can be swallowed whole. Do not chew or crush capsule. Capsules can be opened and contents sprinkled onto applesauce for immediate consumption. Do not chew or crush granules. Contents can also be emptied into 60 mL catheter tipped syringe and shaken with 50 mL water for administration via nasogastric tube.

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		therapy) in adults: 49.3 mg once daily for ten days[k] Pathological hypersecretory conditions in adults: 49.3 mg twice daily[d]	
Lansoprazole	Delayed-release capsule: 15 mg 30 mg Delayed-release orally disintegrating tablet: 15 mg 30 mg Delayed-release capsule (OTC): 15 mg	Treatment of symptomatic GERD and heartburn (adults): 15 mg daily for up to eight weeks *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence: 30 mg twice daily for 10 or 14 days[c] or 30 mg three times daily for 14 days[g] Treatment of active duodenal ulcers: 15 mg daily for four weeks Treatment of erosive esophagitis: 30 mg daily for up to eight weeks[h] Treatment of active, benign gastric ulcer: 30 mg daily up to eight weeks Healing of NSAID associated gastric ulcer: 30 mg daily for eight weeks Maintenance of healing duodenal ulcers: 15 mg daily Maintenance of healing of erosive esophagitis: 15 mg daily[m] Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome: 60 mg daily[d] Risk reduction of NSAID associated gastric ulcer: 15 mg daily up to 12 weeks Treatment of symptomatic GERD and erosive esophagitis (1 to 11 years of age): Weight-based dosing	Should be taken before eating and swallowed whole. Capsules (non-OTC) can be opened and contents sprinkled into applesauce, Ensure pudding, cottage cheese, yogurt, or strained pears. May be mixed in 60 mL apple juice, orange juice, or tomato juice for immediate consumption. Contents can also be mixed into 40 mL apple juice for administration via nasogastric tube, flushing with additional juice. Orally disintegrating tablets should be placed on tongue, allowed to disintegrate, and swallowed. Orally disintegrating tablets may also be mixed with water (4 mL for 15 mg tablet or 10 mL for 10 mg tablet) in an oral syringe and gently shaken for oral or nasogastric tube administration.

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		Patients weighing ≤ 30 kg: 15 mg daily for up to 12 weeks Patients weighing > 30 kg: 30 mg daily for up to 12 weeks Treatment of symptomatic nonerosive GERD (12 to 17 years of age): 15 mg once daily for up to eight weeks Treatment of symptomatic GERD with erosive esophagitis (12 to 17 years of age): 30 mg once daily for up to eight weeks Treatment of frequent heartburn (OTC): 15 mg daily for 14 days[i]	
Omeprazole magnesium	Delayed-release capsule: 10 mg 20 mg 40 mg Delayed-release suspension (unit-dose packet): 2.5 mg 10 mg Delayed-release tablet (OTC): 20 mg	Treatment of symptomatic GERD and heartburn (adults): 20 mg daily for four weeks Treatment of symptomatic GERD and erosive esophagitis due to acid-mediated GERD (1 to 16 years of age)[j]: Weight-based dosing Patients weighing 5 kg to < 10 kg: 5 mg daily Patients weighing 10 kg to < 20 kg: 10 mg daily Patients weighing ≥ 20 kg: 20 mg daily *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence (adults): 20 mg twice daily for 10 days[k] or 40 mg daily for 14 days[l] Treatment of active duodenal ulcers (adults): 20 mg daily for four weeks; some patients may require an additional four weeks Treatment of erosive esophagitis due to acid-mediated GERD (adults): 20 mg daily for four to eight weeks Treatment of erosive esophagitis due to acid-mediated GERD	Should be taken before eating. Capsules can be opened and contents sprinkled into applesauce, Ensure, pudding, cottage cheese, yogurt, strained pears, apple juice, orange juice, or tomato juice for immediate consumption. Unit-dose packets should be emptied into water (5 mL for 2.5 mg or 15 mL for 10 mg), stirred, left for two to three minutes to thicken, and drank within 30 minutes. Can also be emptied into catheter-tipped syringe for administration via nasogastric tube.

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		(1 month to < 1 year of age): Weight-based dosing Patients weighing 3 kg to < 5 kg: 2.5 mg daily for up to six weeks Patients weighing 5 kg to < 10 kg: 5 mg daily for up to six weeks Patients weighing ≥ 10 kg: 10 mg daily for up to six weeks Treatment of active, benign gastric ulcer (adults): 40 mg daily for four to eight weeks Maintenance of healing of erosive esophagitis due to acid-mediated GERD (adults): 20 mg daily[m] Maintenance of healing of erosive esophagitis due to acid-mediated GERD (1 to 16 years of age): Weight-based dosing Patients weighing 5 to < 10 kg: 5 mg daily Patients weighing 10 to < 20 kg: 10 mg daily Patients weighing ≥ 20 kg: 20 mg once daily Note: Controlled studies do not extend beyond 12 months. Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome (adults): 60 mg daily[d] Treatment of frequent heartburn (OTC): 20 mg daily for 14 days[i]	
Omeprazole/ sodium bicarbonate	Capsule: 20 mg/1,100 mg 40 mg/1,100 mg Powder for oral suspension (unit-dose packet): 20 mg/1,680 mg 40 mg/1,680 mg Capsule (OTC): 20 mg/1,100 mg	Treatment of symptomatic GERD (with no esophageal erosions): 20 mg daily for four weeks Treatment of active duodenal ulcers: 20 mg daily for four weeks; some patients may require an additional four weeks Treatment of erosive esophagitis:	Should be taken on an empty stomach at least one hour before a meal. Capsules should be swallowed intact with only water and should never be opened. Due to sodium bicarbonate content, one 40 mg unit (capsule or powder packet) is not equivalent to two 20 mg units; therefore, two 20 mg units should not be substituted for one 40 mg unit.

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
	Note: all formulations are indicated for adults only. Their safety and effectiveness in pediatric patients < 18 years of age have not been established.	20 mg daily for four to eight weeks Treatment of active, benign gastric ulcer: 40 mg daily for four to eight weeks[m] Maintenance of healing of erosive esophagitis: 20 mg daily[m] Risk reduction of upper gastrointestinal bleeding in critically ill patients: Powder for oral suspension (40 mg/1,680 mg): initial, 40 mg; followed by 40 mg six to eight hours later and 40 mg daily thereafter for 14 days[m] Treatment of frequent heartburn (OTC): 20 mg/1,100 daily for 14 days	Packets for delayed-release oral suspension should be emptied into a small cup with one to two tablespoons of water, stirred well, and drank immediately. Can also be constituted with 20 mL water in an appropriate-sized syringe for administration via nasogastric or orogastric tube. Patients receiving continuous nasogastric or orogastric tube feedings should have these feedings suspended three hours before and one hour after omeprazole/ sodium bicarbonate administration.
Pantoprazole	Delayed-release suspension (unit-dose packet): 40 mg Delayed-release tablet: 20 mg 40 mg Powder for injection: 40 mg	Treatment of erosive esophagitis: Delayed-release suspension, delayed-release tablet: 40 mg daily for up to eight weeks Maintenance of healing of erosive esophagitis: Delayed-release suspension, delayed-release tablet: 40 mg daily[m] Treatment of GERD associated with a history of erosive esophagitis: Powder for injection: 40 mg daily for seven to ten days Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome: Delayed-release suspension, delayed-release tablet: 40 mg twice daily[d] Powder for injection: 80 mg twice daily[n] Treatment of erosive esophagitis (≥ 5 years of age): Delayed-release suspension,	Powder for injection should be discontinued in favor of oral therapy as soon as oral therapy is possible. Tablets can be taken with or without food and should be swallowed whole. Delayed-release oral suspension should only be administered approximately 30 minutes prior to a meal in one teaspoonful of applesauce (eat within 10 minutes) or apple juice (drink immediately). Can also be mixed with 10 mL apple juice in a catheter-tipped 60 mL syringe for administration via nasogastric tube or gastrostomy tube. No refrigeration required. Can be reconstituted for two-minute or fifteen-minute infusion: Two-minute infusion is reconstituted with 10 mL of 0.9% sodium chloride to 4 mg/mL and must be used within 24 hours. Fifteen-minute infusion is reconstituted with 10 mL of 0.9% sodium chloride (stored up to six hours) and further

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Drug	Dosage Form: Strength	Usual Recommended Dose	Administration Considerations
		delayed-release tablet: Weight based dosing Patients weighing ≥ 15 kg to < 40 kg: 20 mg daily for eight weeks Patients weighing ≥ 40 kg: 40 mg daily for eight weeks	diluted with 100 mL of 0.9% sodium chloride, Lactated Ringer's, or 5% dextrose to a final concentration of 0.4 (GERD) or 0.8 mg/mL (pathological hypersecretory conditions). Final fifteen-minute infusion mixture must be used within 24 hours.
Rabeprazole	Delayed-release tablet: 20 mg Sprinkle delayed-release capsule: 5 and 10 mg	Treatment of symptomatic GERD: 20 mg daily for up to four weeks[b] *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence: 20 mg twice daily for seven days[c] Healing of duodenal ulcers: 20 mg daily after the morning meal for up to four weeks Healing of erosive or ulcerative GERD: 20 mg daily for four to eight weeks Maintenance of healing of erosive or ulcerative GERD: 20 mg daily[m] Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome: 60 mg daily[d] Treatment of symptomatic GERD in adolescent patients ≥ 12 years of age: 20 mg daily for up to eight weeks Treatment of GERD in pediatric patients 1 to 11 years of age (ACIPHEX SPRINKLE): Weight-based dosing Patients weighing < 15 kg: 5 mg once daily for up to 12 weeks with an option to increase to 10 mg if inadequate response Patients weighing ≥ 15 kg: 10 mg once daily for up to 12 weeks	Take 30 minutes before a meal. For *H. pylori* regimen, take with morning and evening meals. Swallow tablets whole; do not chew, crush, or split. Contents of the ACIPHEX SPRINKLE capsules may be sprinkled on a spoonful of soft food or liquid, take the full dose within 15 minutes.

GERD=gastroesophageal reflux disease; IV=intravenous; NSAID=nonsteroidal antiinflammatory drug; OTC=over-the-counter
a For dexlansoprazole, controlled studies did not extend beyond six months in adults and 16 weeks in patients 12 to 17 years of age. For esomeprazole magnesium, controlled studies did not extend beyond six months.
b If symptoms do not resolve completely after four weeks, an additional four weeks of treatment may be considered.
c As triple therapy with amoxicillin 1,000 mg twice daily plus clarithromycin 500 mg twice daily.

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d Doses in patients with pathological hypersecretory conditions vary with the individual patient. Dosage regimens should be adjusted to patient needs and continued for as long as clinically indicated.
e For 1 to 11 year olds, doses >1 mg/kg/day have not been studied. For patients 1 month to <1 year old, doses >1.33 mg/kg/day have not been studied.
f Indicated for the short-term treatment of GERD with erosive esophagitis as an alternative to oral therapy when oral esomeprazole magnesium is not possible or appropriate.
g As combination therapy with amoxicillin 1,000 mg three times daily.
h For patients who do not heal with lansoprazole for eight weeks (5 to 10%), it may be helpful to give an additional eight weeks of treatment. If there is a recurrence of erosive esophagitis, an additional eight-week course of lansoprazole may be considered.
i A 14-day course every four months may be considered if required.
j The treatment of symptomatic GERD in patients 1 to 16 years of age is once daily for up to four weeks. The treatment of erosive esophagitis due to acid-mediated GERD in patients 1 to 16 years of age is once daily for four to eight weeks. The efficacy of omeprazole used for longer than eight weeks in patients 1 to 16 years of age with erosive esophagitis has not been established. If a patient does not respond to eight weeks of treatment, an additional four weeks of treatment may be given.
k As triple therapy with amoxicillin 1,000 mg twice daily plus clarithromycin 500 mg twice daily. In patients with an ulcer present at the time of initiation of therapy, an additional 18 days of omeprazole 20 mg once daily is recommended for ulcer healing and symptom relief.
l As combination therapy with clarithromycin 500 mg three times daily. In patients with an ulcer present at the time of initiation of therapy, an additional 14 days of omeprazole 20 mg once daily is recommended for ulcer healing and symptom relief.
m Controlled studies did not extend beyond 12 months. For omeprazole magnesium only, a dosage reduction to 10 mg once daily is recommended for patients with hepatic impairment (Child-Pugh Class A, B or C) and Asian patients when used for the maintenance of healing of erosive esophagitis. patients with Zollinger-Ellison syndrome have been treated continuously with omeprazole for more than five years.
n The frequency of dosing can be adjusted to individual patient needs based on acid output measurements. Daily doses higher than 240 mg or administered more than six days have not been studied.

SPECIAL POPULATIONS

Table 4. Special Populations

Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
Dexlansoprazole	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Safety and efficacy in patients < 12 years of age have not been established.	No dosage adjustment required.	No dosage adjustment required for mild (Child-Pugh Class A) hepatic impairment. A maximum dose of 30 mg should be considered in patients with moderate (Child-Pugh Class B) hepatic impairment. Capsules and SoluTabs are not recommended in patients with severe (Child-Pugh Class C) hepatic impairment.	There are no studies with use in pregnant women to inform a drug-associated risk. Unknown whether excreted in human milk; use with caution.
Esomeprazole magnesium	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Approved for use in patients ≥ 1 month of age.	No dosage adjustment required.	No dosage adjustment required for mild-to-moderate (Child-Pugh Class A or B) liver impairment. Hepatic dose adjustment is required in patients with severe (Child-Pugh Class C) liver	There are no adequate and well-controlled studies in pregnant women; use with caution. Likely present in human milk; use with caution.

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Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
				impairment; do not exceed a dose of 20 mg.	
Esomeprazole sodium	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Approved for use in patients ≥ 1 month of age.	No dosage adjustment required.	Dose adjustments are needed in patients with liver impairment: For patients with bleeding gastric or duodenal ulcers and mild to moderate liver impairment (Child-Pugh Class A and B): Maximum continuous infusion of 6 mg/hr For patients with severe liver impairment (Child Pugh Class C): Maximum continuous infusion of 4 mg/hr	There are no adequate and well-controlled studies in pregnant women; use with caution. Likely present in human milk; use with caution.
Esomeprazole strontium	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Safety and efficacy in pediatrics have not been established.	No dosage adjustment required in patients with mild to moderate renal impairment. Due to lack of data, not recommended in patients with severe renal impairment.	No dosage adjustment required for patients with mild-to- moderate (Child-Pugh Class A or B) liver impairment. Hepatic dose adjustment is required in patients with severe (Child-Pugh Class C) liver impairment; do not exceed a dose of 24.65 mg.	Pregnancy Category C Limited published data indicate that esomeprazole and strontium are present in human milk; a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Lansoprazole	No dosage adjustment required.	Approved for use in patients > 1 year of age.	No dosage adjustment required.	Hepatic dose adjustment should be considered in severe hepatic impairment. In patients with various degrees of	Pregnancy Category B Unknown whether excreted in human milk; use with caution.

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Drug	Population and Precaution				
	Elderly	Pediatrics	Renal Dysfunction	Hepatic Dysfunction	Pregnancy* and Nursing
				chronic hepatic impairment, an increase in the mean area under the curve of up to 500% was observed at steady state compared to healthy subjects.	
Omeprazole magnesium	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Approved for use in patients > 1 month of age.	No dosage adjustment required.	Hepatic dose adjustment should be considered for the maintenance of healing of erosive esophagitis; dose reduction in Asian patients recommended for the same indication.	There are no adequate and well-controlled studies in pregnant women; use with caution. Likely present in human milk; use with caution.
Omeprazole/ sodium bicarbonate	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Safety and efficacy in patients < 18 years of age have not been established.	No dosage adjustment required.	Hepatic dose adjustment should be considered for the maintenance of healing of erosive esophagitis; dose reduction in Asian patients recommended for the same indication.	Pregnancy Category C Excreted in breast milk (< 7%) after a 20 mg dose; discontinue nursing or discontinue drug.
Pantoprazole	No evidence of overall differences in safety or efficacy observed between elderly and younger adult patients.	Approved in children ≥ 5 years of age.	No dosage adjustment required.	No dosage adjustment required.†	Pregnancy Category B Detection in human milk after a 40 mg dose; discontinue nursing or discontinue drug
Rabeprazole	No dosage adjustment required.	Approved for use in children ≥ 12 years of age (ACIPHEX) and children 1 to 11 years of age (ACIPHEX SPRINKLE).	No dosage adjustment required.	No dosage adjustment required for mild-to-moderate liver impairment. Caution is advised for patients with severe liver impairment.	No available human data on use in pregnant women to inform the drug-associated risk. Unknown whether excreted in human milk; use with caution.

†Doses > 40 mg/day have not been studied in patients with hepatic impairment.
* Pregnancy Category B = No evidence of risk in humans, but there remains a remote possibility. Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.

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Pregnancy Category C = Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

CONCLUSION

- PPIs are the most potent inhibitors of gastric acid secretion available.
- All of the PPIs are FDA-approved for the treatment and maintenance of GERD and, with the exception of dexlansoprazole and omeprazole with sodium bicarbonate, for the treatment of pathological hypersecretory conditions.
- With the exception of dexlansoprazole, esomeprazole sodium, omeprazole with sodium bicarbonate, and pantoprazole, all of the PPIs are approved for the eradication of *H. pylori* to reduce the risk of duodenal ulcer recurrence.
- Dexlansoprazole and omeprazole with sodium bicarbonate are the only PPIs that are not FDA-approved for use in children. Dexlansoprazole is indicated in patients ≥ 12 years of age, while omeprazole with sodium bicarbonate is only indicated in adults.
- All PPIs are available in delayed-release oral formulations, with the exception of esomeprazole sodium, pantoprazole IV, and omeprazole with sodium bicarbonate. All oral products can be dosed once daily.
- Dexlansoprazole is uniquely formulated to release at different time intervals, at two different sites of the small intestine. The clinical significance of this is unknown.
- Esomeprazole magnesium, omeprazole magnesium, and pantoprazole are available as granules for a delayed-release oral suspension. Omeprazole with sodium bicarbonate is available as a powder for oral suspension. Rabeprazole is available in a sprinkle delayed-release capsule formulation.
- Esomeprazole strontium was approved in August 2013 without a proprietary name. Available generically and approved based on studies of esomeprazole magnesium, esomeprazole strontium has the same indications as esomeprazole magnesium with the exception of use in pediatric patients. It is a different salt formulation available in two unique strengths: 24.65 and 49.3 mg, equivalent to esomeprazole magnesium 20 and 40 mg, respectively.
- Esomeprazole magnesium, lansoprazole, omeprazole, omeprazole magnesium, and omeprazole with sodium bicarbonate are also available in OTC formulations.
- Esomeprazole sodium and pantoprazole are available in intravenous formulations for short-term use in patients unable to take medications by mouth.
- Rabeprazole, esomeprazole magnesium, esomeprazole strontium, lansoprazole, omeprazole, omeprazole with sodium bicarbonate, and pantoprazole are all available generically, however some formulations (e.g., orally disintegrating tablets [solutabs] and oral suspensions) remain available only as brands.
- Current medical evidence demonstrates that PPI therapy is highly effective in treating, providing symptomatic relief and preventing relapse in gastric acid disorders such as erosive esophagitis and symptomatic GERD.
    - Meta-analyses and direct comparator trials demonstrate that lansoprazole, omeprazole, pantoprazole, and rabeprazole have comparable healing rates, maintenance of healing, and symptomatic relief of GERD (Bardhan et al, 2001; Caro et al, 2001; Edwards et al, 2001; Klok et al, 2003; Pace et al, 2005; Sharma et al, 2001).
    - A few trials report statistically faster and greater symptomatic relief with lansoprazole compared to omeprazole; however, the significance of these differences in clinical practice is not known (Richter, Kahrilas, Sontag et al, 2001).
    - There is evidence through meta-analyses and several clinical trials that esomeprazole provides higher healing rates for erosive esophagitis and/or symptomatic relief of GERD compared to standard doses of lansoprazole, omeprazole, and pantoprazole (Castell et al, 2002; Devault et al, 2006; Edwards et al, 2001; Kahrilas et al, 2000; Klok et al, 2003; Labenz et al, 2005[a]; Labenz et al, 2005[b]; Richter et al, 2001).
    - Subgroup analyses in two trials noted better healing rates with esomeprazole in patients with more severe disease (Labenz et al, 2005[a]; Schmitt et al, 2006).
    - Evidence suggests that there is no major difference in efficacy among the various PPIs for the short-term management of reflux esophagitis when administered in equivalent dosages.
    - Currently, there is a lack of head-to-head studies of dexlansoprazole with the other agents in this class.
- Clinical studies have demonstrated that PPIs are also highly effective in the treatment of peptic ulcer disease caused by chronic NSAID therapy or *H. pylori* infection when coupled with antibiotics.
    - Meta-analyses and head-to-head trials comparing PPIs to each other have shown comparable rates of eradication when administered at comparable doses and paired with comparable antibiotic regimens.
    - Results of meta-analyses suggest that regimens containing the new generation PPIs (esomeprazole and rabeprazole) may be more effective than the other PPIs at eradicating *H. pylori* (McNicholl et al, 2012; Xin et al, 2016).

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  - Additional studies are needed before definitive conclusions can be made regarding the use of certain PPIs in specific patient populations.
- Current consensus among various national and international treatment guidelines recommend a PPI as the first-line therapy in the treatment and maintenance of healed erosive esophagitis, symptomatic GERD, dyspepsia (patients ≤ 55 years and no alarm features), and peptic ulcer disease caused by NSAID therapy. Triple and quadruple combination therapy with antibiotics and a PPI are considered first-line therapy for peptic ulcer disease caused by *H. pylori*. No treatment guidelines recommend one PPI over another or one formulation of a PPI over another.

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