Brand Names

Nexium, Nexium 24HR, Nexium 24HR Clear Minis

Indication Specific Dosing

For the treatment of symptomatic, non-erosive gastroesophageal reflux disease (GERD)

Oral dosage (esomeprazole magnesium oral capsules or suspension)

Adults

20 mg PO once daily for 4 to 8 weeks. May increase dose up to 40 mg PO twice daily in persons with partial response to once daily therapy. Continue maintenance therapy at the lowest effective dose, including on demand or intermittent therapy, in persons who continue to have symptoms after discontinuation.

Children and Adolescents 12 years and older

20 mg PO once daily for 4 weeks. Alternatively, 0.7 to 3.3 mg/kg/day PO. Do not exceed recommended adult doses (20 to 40 mg/day).

Children 1 to 11 years

10 mg PO once daily for up to 8 weeks. Alternatively, 0.7 to 3.3 mg/kg/day PO.

Infants†

Esomeprazole was not more effective than placebo in a 4-week, placebo-controlled study (data not published). Doses of 0.25 mg/kg/day and 1 mg/kg/day PO were used in a short-term pharmacokinetic study (n = 45). After 1 week of treatment, the 1 mg/kg/day dose provided similar exposure to that seen in adults receiving 20 mg/day PO; this dose also provided the most effective acid suppression. Both doses of esomeprazole were well tolerated. PPIs are not

recommended as first-line therapy for symptomatic GERD in otherwise healthy infants (1 to 11 months); non-pharmacologic measures such as diet modification and positioning strategies are preferred. Reserve pharmacologic treatment for use in infants with disease diagnosed by endoscopy (e.g., esophageal erosion).

Neonates†

Safety and efficacy have not been established; esomeprazole was not superior to placebo in 1 small randomized controlled trial. Doses of 0.5 mg/kg/day PO were used for up to 14 days in a randomized, placebo controlled study of premature and term neonates (n = 52, gestational ages 24 to 40 weeks) with symptoms of gastroesophageal reflux disease (GERD). There were no significant differences in the total number of GERD-related signs and symptoms or the total number of reflux episodes in patients receiving esomeprazole compared to those receiving placebo. Patients receiving esomeprazole did have significantly fewer acidic reflux episodes compared to patients receiving placebo. Esomeprazole was well tolerated.

For the treatment of diagnostically confirmed erosive esophagitis due to GERD

Oral dosage (esomeprazole magnesium oral capsules or suspension)

Adults

20 to 40 mg PO once daily in the morning (60 minutes before the first meal of the day) for 4 to 8 weeks. For patients who do not heal during the initial treatment course or if condition recurs, consider an additional 4 to 8 week course. Maintenance of healing: 20 mg PO once daily. Periodically reassess need for continued PPI therapy.

Children and Adolescents 12 years and older

20 mg or 40 mg PO once daily for 4 to 8 weeks. Alternatively, a dosage range of 0.7 to 3.3 mg/kg/day PO is recommended by the American Academy of Pediatrics (AAP). Do not exceed recommended adult doses (20 to 40 mg/day).

Children 1 to 11 years

0.7 to 3.3 mg/kg/day PO is recommended by the American Academy of Pediatrics (AAP). Do not exceed recommended adult doses (20 to 40 mg/day). The FDA-

approved dosage is weight based and administered PO once daily for 8 weeks as follows: 10 mg for weight less than 20 kg; 10 or 20 mg for weight 20 kg or more.

Infants

Dosing is weight based and administered PO once daily for up to 6 weeks as follows: 2.5 mg for weight 3 to 5 kg; 5 mg for weight 5.1 to 7.5 kg; and 10 mg for weight 7.6 to 12 kg. Doses more than 1.33 mg/kg/day PO have not been studied. Reserve for infants with disease diagnosed by endoscopy (e.g., esophageal erosion); nonpharmacologic measures such as diet modification and positioning strategies are recommended.

Neonates†

Safety and efficacy have not been established; esomeprazole was not superior to placebo in one small randomized controlled trial. Doses of 0.5 mg/kg/day PO were used for up to 14 days in a randomized, placebo controlled study of premature and term neonates (n = 52, gestational ages 24 to 40 weeks) with symptoms of gastroesophageal reflux disease (GERD). There were no significant differences in the total number of GERD-related signs and symptoms or the total number of reflux episodes in patients receiving esomeprazole compared to those receiving placebo. Patients receiving esomeprazole did have significantly fewer acidic reflux episodes compared to patients receiving placebo. Esomeprazole was well tolerated.

Intravenous dosage

Adults

20 mg or 40 mg IV infused once daily for up to 10 days. The IV formulation is indicated as an alternative to oral therapy for the short-term treatment of GERD when oral therapy is not possible or appropriate. Switch to oral therapy when feasible.

Children and Adolescents weighing 55 kg or more

20 mg IV once daily over 10 to 30 minutes for up to 10 days. The IV formulation is indicated as an alternative to oral therapy for the short-term treatment of GERD when oral therapy is not possible or appropriate. Switch to oral therapy when feasible.

Children and Adolescents weighing less than 55 kg

10 mg IV once daily over 10 to 30 minutes for up to 10 days. The IV formulation is indicated as an alternative to oral therapy for the short-term treatment of GERD when oral therapy is not possible or appropriate. Switch to oral therapy when feasible.

Infants

0.5 mg/kg/dose IV once daily infused over 10 to 30 minutes for up to 10 days. The IV formulation is indicated as an alternative to oral therapy for the short-term treatment of GERD when oral therapy is not possible or appropriate. Switch to oral therapy when feasible.

Neonates†

Safety and efficacy have not been established; 0.5 mg/kg/dose IV once daily infused over 10 to 30 minutes has been suggested.

For the short-term self treatment of frequent dyspepsia or pyrosis (heartburn) that occurs 2 or more times per week

Oral dosage (non-prescription esomeprazole magnesium delayed-release capsules or tablets; e.g., Nexium 24HR)

Adults

20 mg PO once daily in the morning before eating for 14 days. Full relief may take 1 to 4 days. If frequent heartburn returns, patients may repeat the course of treatment once every 4 months. Do not exceed 1 dose/day PO, treatment for 14 days, or repeat courses more frequently than every 4 months, unless directed to do so by a healthcare provider.

For the treatment of pathological hypersecretion associated with Zollinger-Ellison syndrome

Oral dosage (esomeprazole magnesium oral capsules or suspension)

Adults

Initially, 40 mg PO twice daily. Adjust dosage to attain clinical goals. Doses up to 240 mg/day PO have been administered. Patients have been treated for up to 12 months.

For Helicobacter pylori (H. pylori) eradication

As part of initial clarithromycin-based therapy in adults without previous macrolide exposure in regions where clarithromycin resistance is less than 15%

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 or 80 mg PO once daily in combination with clarithromycin and either amoxicillin or metronidazole for 14 days.

As part of initial clarithromycin-based therapy in adults with or without potential macrolide exposure or resistance†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily as part of a combination therapy as a first-line treatment option. Quadruple therapy includes a proton pump inhibitor (PPI) in combination with clarithromycin, amoxicillin, and metronidazole for 10 to 14 days. Hybrid therapy includes amoxicillin plus PPI for 7 days followed by PPI in combination with clarithromycin, amoxicillin, and metronidazole for 7 days. Sequential therapy includes PPI and amoxicillin for 5 to 7 days followed by PPI in combination with clarithromycin and metronidazole for 5 to 7 days.

As part of salvage clarithromycin-based therapy in adults who failed initial bismuth quadruple therapy†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily in combination with clarithromycin, amoxicillin, and metronidazole for 10 to 14 days. For patients with a penicillin allergy, a PPI is recommended in combination with clarithromycin and metronidazole for 14 days.

In combination with amoxicillin and metronidazole in pediatric patients†

Oral dosage (esomeprazole magnesium capsules or suspension)

Children and Adolescents weighing 35 kg or more

40 mg PO twice daily in combination with amoxicillin and metronidazole for 14 days. Triple therapy with standard-dose amoxicillin, metronidazole, and a proton pump inhibitor (PPI) is a first-line treatment option for patients infected with H. pylori strains with known susceptibility to metronidazole and resistance to clarithromycin. Triple therapy with high-dose amoxicillin, metronidazole, and a PPI is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

Children and Adolescents weighing 25 to 34 kg

30 mg PO twice daily in combination with amoxicillin and metronidazole for 14 days. Triple therapy with standard-dose amoxicillin, metronidazole, and a proton pump inhibitor (PPI) is a first-line treatment option for patients infected with H. pylori strains with known susceptibility to metronidazole and resistance to clarithromycin. Triple therapy with high-dose amoxicillin, metronidazole, and a PPI is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

Children weighing 15 to 24 kg

20 mg PO twice daily in combination with amoxicillin and metronidazole for 14 days. Triple therapy with standard-dose amoxicillin, metronidazole, and a proton pump inhibitor (PPI) is a first-line treatment option for patients infected with H. pylori strains with known susceptibility to metronidazole and resistance to clarithromycin. Triple therapy with high-dose amoxicillin, metronidazole, and a PPI is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

In combination with amoxicillin and clarithromycin in pediatric patients†

Oral dosage (esomeprazole magnesium capsules or suspension)

Children and Adolescents weighing 35 kg or more

40 mg PO twice daily in combination with amoxicillin and clarithromycin for 14 days. Triple therapy with standard-dose amoxicillin, clarithromycin, and a proton

pump inhibitor is the first-line treatment option for patients infected with fully susceptible H. pylori strains or strains susceptible to clarithromycin but resistant to metronidazole. In cases of penicillin allergy, use metronidazole in place of amoxicillin for patients infected with fully susceptible strains.

Children and Adolescents weighing 25 to 34 kg

30 mg PO twice daily in combination with amoxicillin and clarithromycin for 14 days. Triple therapy with standard-dose amoxicillin, clarithromycin, and a proton pump inhibitor is the first-line treatment option for patients infected with fully susceptible H. pylori strains or strains susceptible to clarithromycin but resistant to metronidazole. In cases of penicillin allergy, use metronidazole in place of amoxicillin for patients infected with fully susceptible strains.

Children weighing 15 to 24 kg

20 mg PO twice daily in combination with amoxicillin and clarithromycin for 14 days. Triple therapy with standard-dose amoxicillin, clarithromycin, and a proton pump inhibitor is the first-line treatment option for patients infected with fully susceptible H. pylori strains or strains susceptible to clarithromycin but resistant to metronidazole. In cases of penicillin allergy, use metronidazole in place of amoxicillin for patients infected with fully susceptible strains.

As part of a sequential therapy regimen in pediatric patients†

Oral dosage (esomeprazole magnesium capsules or suspension)

Children and Adolescents weighing 35 kg or more

40 mg PO twice daily for 10 days. Use in combination with amoxicillin for days 1 through 5, and then clarithromycin and metronidazole for days 6 through 10. Sequential therapy is a first-line treatment option for patients infected with fully susceptible H. pylori strains. Sequential therapy is not recommended if susceptibility testing is unavailable.

Children and Adolescents weighing 25 to 34 kg

30 mg PO twice daily for 10 days. Use in combination with amoxicillin for days 1 through 5, and then clarithromycin and metronidazole for days 6 through 10. Sequential therapy is a first-line treatment option for patients infected with fully susceptible H. pylori strains. Sequential therapy is not recommended if susceptibility testing is unavailable.

Children weighing 15 to 24 kg

20 mg PO twice daily for 10 days. Use in combination with amoxicillin for days 1 through 5, and then clarithromycin and metronidazole for days 6 through 10. Sequential therapy is a first-line treatment option for patients infected with fully susceptible H. pylori strains. Sequential therapy is not recommended if susceptibility testing is unavailable.

As part of a quadruple therapy regimen in pediatric patients†

Oral dosage (esomeprazole magnesium capsules or suspension)

Children and Adolescents weighing 35 kg or more

40 mg PO twice daily in combination with amoxicillin, metronidazole, and clarithromycin for 14 days. Concomitant quadruple therapy with amoxicillin, metronidazole, clarithromycin, and a proton pump inhibitor is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

Children and Adolescents weighing 25 to 34 kg

30 mg PO twice daily in combination with amoxicillin, metronidazole, and clarithromycin for 14 days. Concomitant quadruple therapy with amoxicillin, metronidazole, clarithromycin, and a proton pump inhibitor is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

Children weighing 15 to 24 kg

20 mg PO twice daily in combination with amoxicillin, metronidazole, and clarithromycin for 14 days. Concomitant quadruple therapy with amoxicillin, metronidazole, clarithromycin, and a proton pump inhibitor is a first-line treatment option for patients infected with H. pylori strains with dual resistance to clarithromycin and metronidazole or strains with unknown susceptibility.

As part of levofloxacin-based initial therapy in adults†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 or 80 mg PO once daily as part of combination therapy as a first-line treatment option. Triple therapy includes esomeprazole 40 mg PO once daily in combination with levofloxacin and amoxicillin for 10 to 14 days. Sequential

therapy includes esomeprazole 40 or 80 mg PO once daily in combination with amoxicillin for 5 to 7 days followed by esomeprazole 40 mg PO once daily in combination with levofloxacin and a nitroimidazole for 5 to 7 days. Quadruple therapy includes esomeprazole 80 mg PO once daily in combination with levofloxacin, nitazoxanide, and doxycycline for 7 to 10 days.

As part of levofloxacin-based salvage therapy in adults†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily in combination with levofloxacin and amoxicillin for 14 days. Guidelines recommend this triple therapy in patients who have failed clarithromycin-triple or bismuth-quadruple initial therapies and without previous quinolone exposure. Levofloxacin in combination with metronidazole and a PPI for 14 days could be considered for patients with a penicillin allergy who have failed prior bismuth quadruple therapy.

As part of bismuth-based initial therapy in adults†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily in combination with bismuth subcitrate or subsalicylate, metronidazole, and tetracycline for 10 to 14 days is recommended as a first-line treatment option, particularly in patients with any previous macrolide exposure or a penicillin allergy.

As part of rifabutin-based salvage therapy in adults†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily in combination with rifabutin and amoxicillin for 10 days.

As part of bismuth-based quadruple salvage therapy in adults†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

40 mg PO once daily in combination with bismuth subcitrate or subsalicylate,

tetracycline, and metronidazole for 14 days is recommended particularly in patients failing clarithromycin triple therapy. A subsequent repeat course of bismuth quadruple therapy may be considered after failed prior bismuth quadruple therapy.

For NSAID-induced ulcer prophylaxis or gastric ulcer healing†

To reduce the risk of NSAID-associated gastric ulcers in patients at risk (e.g., 60 years and older and/or documented history of gastric ulcers)

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

20 or 40 mg PO once daily. In clinical trials, the 20 and 40 mg doses showed comparable benefit in providing risk reduction. Roughly 95% of patients remained ulcer free for up to 6 months. Studies did not demonstrate significant reduction in the development of NSAID-associated duodenal ulcer due to the low incidence.

To treat an active NSAID-associated gastric ulcer in patients who continue NSAID use†

Oral dosage (esomeprazole magnesium capsules or suspension)

Adults

20 or 40 mg PO once daily. In a study, the gastric ulcer healing rates at week 8 were 85.7% (95% CI, 79.8% to 91.7%) with esomeprazole 40 mg/day and 84.8% (95% CI, 78.8% to 90.8%) with esomeprazole 20 mg/day; all patients continued to take a nonselective NSAID or a COX-2 inhibitor. In another study of patients with aspirin-related peptic ulcers, gastric ulcer healing rates at week 8 were 82.5% (95% CI, 74.2% to 90.8%) with esomeprazole 40 mg/day and 81.5% (95% CI, 73% to 90%) with esomeprazole 40 mg/day plus aspirin 100 mg/day.

For the treatment of eosinophilic esophagitis†

Oral dosage (esomeprazole magnesium)

Adults

20 to 40 mg PO twice daily for 8 to 12 weeks, then reduce dose to the lowest dose that maintains remission.

Children and Adolescents

1 mg/kg/dose (Max: 40 mg/dose) PO twice daily for 8 to 12 weeks, then reduce dose to the lowest dose that maintains remission.

For upper GI rebleeding prophylaxis of gastric or duodenal ulcers after therapeutic endoscopy

Intravenous dosage (continuous IV infusion regimen)

Adults

80 mg IV bolus infusion over 30 minutes, followed by 8 mg/hour continuous infusion for 71.5 hours after successful endoscopic hemostasis. In clinical trials, after completion of the infusion, patients received an oral PPI for 27 days. Per clinical practice guidelines, this regimen may be used in the management of active ulcer bleeding, a non-bleeding visible vessel, or visible adherent clot. Patients with ulcers that have flat pigmented spots or clean bases upon endoscopy can instead receive standard, once daily, oral proton pump inhibitor (PPI) therapy. Pre-endoscopic IV PPI therapy, may be considered in order to downstage the endoscopic lesion. If endoscopic therapy is to be delayed or cannot be performed, IV PPI therapy is recommended to reduce further bleeding. Patients with an underlying etiology for which a PPI may be beneficial (e.g., peptic ulcers, erosions) should be discharged with a prescription for standard, once daily oral PPI therapy; otherwise, discontinue the PPI before discharge.

For the treatment of gastric acid hypersecretion associated with cysteamine therapy for nephropathic cystinosis†

Oral dosage

Children 2 to 10 years†

Initial doses of 1.1 mg/kg/day PO divided twice daily were used in a small, prospective, open-label study of 12 children aged 2 to 10 years receiving cysteamine therapy. Doses were adjusted during the study based on upper GI symptoms. The mean final dose of esomeprazole was 1.7 mg/kg/day PO (range: 0.7 to 2.75 mg/kg/day PO; Max: 40 mg/day). The authors report a significant decrease in basal gastric acid output and significant improvement in symptom scores.

For stress gastritis prophylaxis† in patients unable to take oral therapy

Intravenous dosage

Adults

20 mg IV once daily. In one study, a dose of 40 mg/day IV was not superior to the 20 mg/day dosage in bleeding prevention, but was associated with complications such as pneumonia, bacterial overgrowth, and longer need for ventilation.

Children and Adolescents weighing 55 kg or more

20 mg IV once daily.

Children and Adolescents weighing less than 55 kg

10 mg IV once daily.

Infants 1 to 11 months

0.5 mg/kg/dose IV once daily.

Neonates

0.5 mg/kg/dose IV once daily.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components. Esomeprazole is also contraindicated in individuals with a history of hypersensitivity to other substituted benzimidazoles [e.g., other proton pump inhibitors (PPIs)]. Before starting therapy with esomeprazole, carefully inquire about previous hypersensitivity reactions to PPIs.

Child-Pugh class C, hepatic failure

Use caution with esomeprazole in individuals with severe hepatic impairment (Child-Pugh class C) or hepatic failure. Exposure to esomeprazole substantially increased in people with severe hepatic impairment compared to healthy subjects; dose adjustment is recommended in these individuals for the healing of erosive esophagitis, 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.

Treatment-Related Restrictions of Use

People should consult their care team prior to nonprescription (OTC) use of esomeprazole if there is a history of the following: 1) heartburn for more than 3 months, 2) frequent wheezing - particularly with heartburn, 3) unexplained weight loss, 4) nausea or vomiting, or 5) stomach or abdominal pain. Individuals should not self-medicate with esomeprazole if they have trouble swallowing (dysphagia), vomiting with blood or bloody or black stools (symptoms of GI bleeding), heartburn with lightheadedness, sweating, or dizziness and/or chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck, or shoulders; or lightheadedness (e.g., symptoms of coronary artery disease). These may be signs of a serious condition that requires medical evaluation and treatment.

General Information

In adults, symptomatic response to therapy with a proton pump inhibitor (PPI) does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adults who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older adult patients, also consider an endoscopy.

increased risk for osteoporosis

Use proton pump inhibitors (PPIs) with caution in people with an increased risk for osteoporosis. Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. People at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.

hypocalcemia, hypokalemia, hypomagnesemia, hypoparathyroidism

Use esomeprazole with caution in people with a pre-existing risk of hypocalcemia (e.g.,

hypoparathyroidism), hypokalemia, or hypomagnesemia; consider monitoring magnesium and calcium concentrations prior to initiating therapy and periodically while on treatment in at-risk patients. Supplement with magnesium and/or calcium as needed and consider discontinuing proton pump inhibitor (PPI) therapy if hypomagnesemia or hypocalcemia is refractory to treatment.

cutaneous lupus erythematosus, systemic lupus erythematosus

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in people taking proton pump inhibitors (PPIs), including esomeprazole. These events have occurred as both new onset and an exacerbation of pre-existing autoimmune disease. Avoid use of PPIs for longer than medically indicated in these patients.

geriatric

According to the Beers Criteria, proton pump inhibitors (PPIs) are considered potentially inappropriate medications (PIMs) for use in geriatric adults due to the risk of Clostridium difficile infection, pneumonia, GI malignancies, and bone loss/fractures. Avoid scheduled use for more than 8 weeks except for high-risk adults (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or a demonstrated need for maintenance treatment (e.g., due to failure of a drug discontinuation trial or inadequate response to H2-receptor blockers).

pregnancy

There are no adequate and well-controlled studies of esomeprazole use during human pregnancy. Esomeprazole is the S-isomer of omeprazole. Available epidemiologic data fail to demonstrate an increased risk of major congential malformations or other adverse pregnancy outcomes with first trimester omeprazole use. Reproduction studies in rats and rabbits resulted in dose-dependent embryo-lethality at omeprazole doses that were approximately 3.4 to 34 times an oral human dose of 40 mg (based on a body surface area for a 60 kg person). Teratogenicity was not observed in animal reproduction studies with administration of oral esomeprazole magnesium in rats and rabbits with doses about 68 times and 42 times, respectively, an oral human dose of 40 mg (based on a body surface area basis for a 60 kg person). Changes in bone morphology were observed in offspring of rats dosed through pregnancy and lactation at doses approximately 34 times or greater than an oral human dose of 40 mg. When maternal administration was confined to gestation only, there were no effects on bone physeal morphology in the offspring at any age. Esomeprazole, like omeprazole, is

known to cross the placenta to the fetus. Four epidemiological studies compared the frequency of congenital abnormalities among infants born to pregnant individuals who used omeprazole during pregnancy with the frequency of abnormalities among infants of pregnant individuals exposed to H2-receptor antagonists or other controls. Overall, slightly higher rates of congenital malformations (e.g., ventricular septal defects) and number of stillbirths have been reported for cases where exposure to omeprazole occurred in the first trimester of pregnancy and beyond. A large cohort study from Denmark did not show a significantly increased risk of birth defects in people who took proton pump inhibitors (PPIs), including omeprazole, during the first trimester. In a meta-analysis of 7 studies, there was no evidence linking PPI exposure in pregnancy to adverse outcomes such as congenital malformations, spontaneous abortions, or premature deliveries. When data was analyzed separately for omeprazole, there was no change in the results. Several studies have also reported no apparent adverse short-term infant adverse effects when single dose omeprazole (PO or IV) was administered to over 200 pregnant individuals as premedication for cesarean section under general anesthesia. Guidelines recommend a trial of lifestyle modifications as first-line therapy for heartburn, followed by antacids. For ongoing symptoms, histamine type 2-receptor antagonists (H2RAs) can be used to control heartburn symptoms in pregnancy. Proton pump inhibitors should be reserved for patients who fail H2RA therapy. Self-medication with proton pump inhibitors (OTC formulations) during pregnancy is not recommended. Pregnant patients should see their health care professional for diagnosis and treatment recommendations.

breast-feeding

Esomeprazole is compatible with breast-feeding. Esomeprazole passes into milk with a relative infant dose of 2.06%. This small amount of infant esomeprazole exposure through breast milk is unlikely to be harmful. FDA-approved labeling states there is no clinical data on the effects of esomeprazole on the breastfed infant or on milk production. Proton pump inhibitors may not be the preferred first-line agent. If heartburn or gastroesophageal reflux disease symptoms persist after delivery, antacids and sucralfate are also safe to use due to minimal breast milk passage. Histamine type 2-receptor antagonists like cimetidine and famotidine are excreted in breast milk, but are considered safe for use during lactation and may be used if symptoms persist despite antacid use.

Pregnancy And Lactation

There are no adequate and well-controlled studies of esomeprazole use during human pregnancy. Esomeprazole is the S-isomer of omeprazole. Available epidemiologic data

fail to demonstrate an increased risk of major congential malformations or other adverse pregnancy outcomes with first trimester omeprazole use. Reproduction studies in rats and rabbits resulted in dose-dependent embryo-lethality at omeprazole doses that were approximately 3.4 to 34 times an oral human dose of 40 mg (based on a body surface area for a 60 kg person). Teratogenicity was not observed in animal reproduction studies with administration of oral esomeprazole magnesium in rats and rabbits with doses about 68 times and 42 times, respectively, an oral human dose of 40 mg (based on a body surface area basis for a 60 kg person). Changes in bone morphology were observed in offspring of rats dosed through pregnancy and lactation at doses approximately 34 times or greater than an oral human dose of 40 mg. When maternal administration was confined to gestation only, there were no effects on bone physeal morphology in the offspring at any age. Esomeprazole, like omeprazole, is known to cross the placenta to the fetus. Four epidemiological studies compared the frequency of congenital abnormalities among infants born to pregnant individuals who used omeprazole during pregnancy with the frequency of abnormalities among infants of pregnant individuals exposed to H2-receptor antagonists or other controls. Overall, slightly higher rates of congenital malformations (e.g., ventricular septal defects) and number of stillbirths have been reported for cases where exposure to omeprazole occurred in the first trimester of pregnancy and beyond. A large cohort study from Denmark did not show a significantly increased risk of birth defects in people who took proton pump inhibitors (PPIs), including omeprazole, during the first trimester. In a meta-analysis of 7 studies, there was no evidence linking PPI exposure in pregnancy to adverse outcomes such as congenital malformations, spontaneous abortions, or premature deliveries. When data was analyzed separately for omeprazole, there was no change in the results. Several studies have also reported no apparent adverse short-term infant adverse effects when single dose omeprazole (PO or IV) was administered to over 200 pregnant individuals as premedication for cesarean section under general anesthesia. Guidelines recommend a trial of lifestyle modifications as first-line therapy for heartburn, followed by antacids. For ongoing symptoms, histamine type 2-receptor antagonists (H2RAs) can be used to control heartburn symptoms in pregnancy. Proton pump inhibitors should be reserved for patients who fail H2RA therapy. Self-medication with proton pump inhibitors (OTC formulations) during pregnancy is not recommended. Pregnant patients should see their health care professional for diagnosis and treatment recommendations.

Interactions

Acalabrutinib: (Major) Avoid the concomitant use of acalabrutinib capsules and proton pump inhibitors (PPI), such as esomeprazole; decreased acalabrutinib exposure may occur resulting in decreased acalabrutinib effectiveness. Consider the acalabrutinib tablet formlation or use an antacid or H2-blocker if acid suppression therapy is needed.

Separate the administration of acalabrutinib capsules and antacids by at least 2 hours; give acalabrutinib capsules 2 hours before a H2-blocker. Acalabrutinib capsule solubility decreases with increasing pH values. The AUC of acalabrutinib was decreased by 43% when acalabrutinib capsules were coadministered with another PPI for 5 days.
Adagrasib: (Moderate) Monitor for esomeprazole-related adverse effects during coadministration with adagrasib. Concurrent use may increase esomeprazole exposure. Esomeprazole is a CYP3A substrate and adagrasib is a strong CYP3A inhibitor.
Albuterol; Budesonide: (Minor) Enteric-coated budesonide granules dissolve at a pH greater than 5.5. Concomitant use of budesonide oral capsules and drugs that increase gastric pH levels can cause the coating of the granules to dissolve prematurely, possibly affecting release properties and absorption of the drug in the duodenum.
Alendronate: (Moderate) Proton pump inhibitors (PPIs) are widely used and are frequently coadministered in users of oral bisphosphonates. A national register-based, open cohort study of 38,088 elderly patients suggests that those who use proton pump inhibitors in conjunction with alendronate have a dose-dependent loss of protection against hip fracture. While causality was not investigated, the dose-response relationship noted during the study suggested that PPIs may reduce oral alendronate efficacy, perhaps through an effect on absorption or other mechanism, and therefore PPIs may not be optimal agents to control gastrointestinal complaints. It is not yet clear if all bisphosphonates would exhibit a loss of efficacy when PPIs are coadministered, but the results suggest that the interaction may occur across the class.
Alendronate; Cholecalciferol: (Moderate) Proton pump inhibitors (PPIs) are widely used and are frequently coadministered in users of oral bisphosphonates. A national register-based, open cohort study of 38,088 elderly patients suggests that those who use proton pump inhibitors in conjunction with alendronate have a dose-dependent loss of protection against hip fracture. While causality was not investigated, the dose-response relationship noted during the study suggested that PPIs may reduce oral alendronate efficacy, perhaps through an effect on absorption or other mechanism, and therefore PPIs may not be optimal agents to control gastrointestinal complaints. It is not yet clear if all bisphosphonates would exhibit a loss of efficacy when PPIs are coadministered, but the results suggest that the interaction may occur across the class.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
aMILoride; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.

Amobarbital: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Amphetamine: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Amphetamine; Dextroamphetamine Salts: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Amphetamine; Dextroamphetamine: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
Ampicillin: (Major) Proton pump inhibitors (PPIs) have long-lasting effects on the secretion of gastric acid. For enteral ampicillin, whose bioavailability is influenced by gastric pH, the concomitant administration of PPIs can exert a significant effect on ampicillin absorption.
Ampicillin; Sulbactam: (Major) Proton pump inhibitors (PPIs) have long-lasting effects on the secretion of gastric acid. For enteral ampicillin, whose bioavailability is influenced by gastric pH, the concomitant administration of PPIs can exert a significant effect on ampicillin absorption.
Apalutamide: (Major) Avoid coadministration of esomeprazole with apalutamide due to decreased esomeprazole plasma concentrations. Esomeprazole is a CYP3A4 and CYP2C19 substrate. Apalutamide is a strong CYP3A4 and CYP2C19 inducer. Coadministration with another strong inducer of CYP3A4 inducer decreased omeprazole exposure by 37.9% in CYP2C19 poor metabolizers and by 43.9% in extensive metabolizers; esomeprazole is an enantiomer of omeprazole.
Aprepitant, Fosaprepitant: (Minor) Use caution if esomeprazole and aprepitant are used concurrently and monitor for an increase in esomeprazole-related adverse effects for several days after administration of a multi-day aprepitant regimen. After administration, fosaprepitant is rapidly converted to aprepitant and shares the same drug interactions. Esomeprazole is a CYP3A4 substrate. Aprepitant, when administered as a 3-day oral regimen (125 mg/80 mg/80 mg), is a moderate CYP3A4 inhibitor and inducer; substitution of fosaprepitant 115 mg IV on day 1 of the 3-day regimen may lessen the inhibitory effects of CYP3A4. The AUC of a single dose of another CYP3A4 substrate, midazolam, increased by 2.3-fold and 3.3-fold on days 1 and 5, respectively, when coadministered with a 5-day oral aprepitant regimen. After a 3-day oral aprepitant regimen, the AUC of midazolam increased by 25% on day 4, and decreased by 19% and

4% on days 8 and 15, respectively, when given on days 1, 4, 8, and 15. As a single 40-mg oral dose, the inhibitory effect of aprepitant on CYP3A4 is weak, with the AUC of midazolam increased by 1.2-fold; the midazolam AUC increased by 1.5-fold after a single 125-mg dose of oral aprepitant. After single doses of IV fosaprepitant, the midazolam AUC increased by 1.8-fold (150 mg) and 1.6-fold (100 mg); less than a 2-fold increase in the midazolam AUC is not considered clinically important.
Aspirin, ASA; Butalbital; Caffeine: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Aspirin, ASA; Carisoprodol; Codeine: (Minor) Esomeprazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as carisoprodol. Carisoprdol is metabolized in the liver by CYP2C19 to form meprobamate. Coadministration may result in increased exposure to carisoprdol and decreased exposure of meprobamate.
Atazanavir: (Contraindicated) Coadministration of proton pump inhibitors (PPIs) with atazanavir in treatment-experienced patients is contraindicated. PPIs can be used with atazanavir in treatment-naive patients under specific administration restrictions. In treatment-naive patients >= 40 kg, the PPI dose should not exceed the equivalent of omeprazole 20 mg/day, and the PPI must be administered 12 hours before atazanavir and ritonavir; use the dosage regimen of atazanavir 300 mg boosted with ritonavir 100 mg given once daily with food. While data are insufficient to recommend atazanavir dosing in children < 40 kg receiving concomitant PPIs, the same recommendations regarding timing and maximum doses of concomitant PPIs should be followed. Closely monitor patients for antiretroviral therapeutic failure and resistance development during treatment with a PPI. A randomized, open-label, multiple-dose drug interaction study of atazanavir (300 mg) with ritonavir (100 mg) coadministered with omeprazole 40 mg found a reduction in atazanavir AUC and Cmin of 76% and 78%, respectively. Additionally, after multiple doses of omeprazole (40 mg/day) and atazanavir (400 mg/day, 2 hours after omeprazole) without ritonavir, the AUC of atazanavir was decreased by 94%, Cmax by 96%, and Cmin by 95%.
Atazanavir; Cobicistat: (Contraindicated) Coadministration of proton pump inhibitors (PPIs) with atazanavir in treatment-experienced patients is contraindicated. PPIs can be used with atazanavir in treatment-naive patients under specific administration restrictions. In treatment-naive patients >= 40 kg, the PPI dose should not exceed the equivalent of omeprazole 20 mg/day, and the PPI must be administered 12 hours before atazanavir and ritonavir; use the dosage regimen of atazanavir 300 mg boosted with ritonavir 100 mg given once daily with food. While data are insufficient to recommend atazanavir dosing in children < 40 kg receiving concomitant PPIs, the same recommendations regarding timing and maximum doses of concomitant PPIs should be

followed. Closely monitor patients for antiretroviral therapeutic failure and resistance development during treatment with a PPI. A randomized, open-label, multiple-dose drug interaction study of atazanavir (300 mg) with ritonavir (100 mg) coadministered with omeprazole 40 mg found a reduction in atazanavir AUC and Cmin of 76% and 78%, respectively. Additionally, after multiple doses of omeprazole (40 mg/day) and atazanavir (400 mg/day, 2 hours after omeprazole) without ritonavir, the AUC of atazanavir was decreased by 94%, Cmax by 96%, and Cmin by 95%. (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Atenolol; Chlorthalidone: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Atovaquone; Proguanil: (Moderate) Esomeprazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as proguanil. Monitor the patient for common proguanil side effects, such as nausea or other stomach and intestinal complaints, headache, or increased hepatic enzymes when proguanil is given chronically.
Avutometinib; Defactinib: (Major) Avoid concomitant use of defactinib and proton pump inhibitors (PPIs). Concurrent use interferes with defactinib absorption which may decrease defactinib exposure and efficacy. Concomitant use with a PPI reduced defactinib overall exposure by 79% and reduced the exposure of the M4 active metabolite by 83%.
Azilsartan; Chlorthalidone: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Barbiturates: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Belumosudil: (Major) Increase the dosage of belumosudil to 200 mg PO twice daily when coadministered with a proton pump inhibitor (PPI). Concomitant use may result in decreased belumosudil exposure and reduced belumosudil efficacy. Coadministration with other PPIs has decreased belumosudil exposure by 47% to 80% in healthy subjects.
Belzutifan: (Moderate) Monitor for anemia and hypoxia if concomitant use of esomeprazole with belzutifan is necessary due to increased plasma exposure of belzutifan which may increase the incidence and severity of adverse reactions. Reduce the dose of belzutifan as recommended if anemia or hypoxia occur. Belzutifan is a

CYP2C19 substrate and esomeprazole is a CYP2C19 inhibitor.
Benazepril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Bisacodyl: (Minor) The concomitant use of bisacodyl oral tablets with drugs that raise gastric pH like proton pump inhibitors can cause the enteric coating of the bisacodyl tablets to dissolve prematurely, leading to possible gastric irritation or dyspepsia. When taking bisacodyl tablets, it is advisable to avoid PPIs within 1 hour before or after the bisacodyl dosage.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Bosutinib: (Major) Bosutinib displays pH-dependent aqueous solubility; therefore, concomitant use of bosutinib and proton-pump inhibitors, such as esomeprazole, may result in decreased plasma exposure of bosutinib. Consider using a short-acting antacid or H2 blocker if acid suppression therapy is needed; separate the administration of bosutinib and antacids or H2-blockers by more than 2 hours.
Budesonide: (Minor) Enteric-coated budesonide granules dissolve at a pH greater than 5.5. Concomitant use of budesonide oral capsules and drugs that increase gastric pH levels can cause the coating of the granules to dissolve prematurely, possibly affecting release properties and absorption of the drug in the duodenum.
Budesonide; Formoterol: (Minor) Enteric-coated budesonide granules dissolve at a pH greater than 5.5. Concomitant use of budesonide oral capsules and drugs that increase gastric pH levels can cause the coating of the granules to dissolve prematurely, possibly affecting release properties and absorption of the drug in the duodenum.
Budesonide; Glycopyrrolate; Formoterol: (Minor) Enteric-coated budesonide granules dissolve at a pH greater than 5.5. Concomitant use of budesonide oral capsules and drugs that increase gastric pH levels can cause the coating of the granules to dissolve prematurely, possibly affecting release properties and absorption of the drug in the duodenum.
Bumetanide: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and loop diuretic use due to risk for hypomagnesemia.
Butalbital; Acetaminophen: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Butalbital; Acetaminophen; Caffeine: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4.

Barbiturates induce CYP3A4 and CYP2C19.
Butalbital; Acetaminophen; Caffeine; Codeine: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Butalbital; Aspirin; Caffeine; Codeine: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Cabotegravir; Rilpivirine: (Contraindicated) Concurrent use of proton pump inhibitors and rilpivirine is contraindicated; when these drugs are coadministered, there is a potential for treatment failure and/or the development of rilpivirine or NNRTI resistance. Proton pump inhibitors inhibit secretion of gastric acid by proton pumps thereby increasing the gastric pH; for optimal absorption, rilpivirine requires an acidic environment. Coadministration of a proton pump inhibitor and rilpivirine may result in decreased rilpivirine absorption/serum concentrations, which could cause impaired virologic response to rilpivirine.
Candesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Cannabidiol: (Moderate) Monitor for esomeprazole-related adverse effects during coadministration with cannabidiol. Concurrent use may increase esomeprazole exposure. Esomeprazole is a CYP2C19 substrate and cannabidiol is a moderate CYP2C19 inhibitor.
Captopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
carBAMazepine: (Major) Avoid concomitant use of esomeprazole and carbamazepine as esomeprazole exposure may be decreased, reducing its efficacy. Esomeprazole is a CYP3A substrate and carbamazepine is a strong CYP3A inducer.
Carisoprodol: (Minor) Esomeprazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as carisoprodol. Carisoprdol is metabolized in the liver by CYP2C19 to form meprobamate. Coadministration may result in increased exposure to carisoprdol and decreased exposure of meprobamate.
Cefpodoxime: (Moderate) Cefpodoxime proxetil requires a low gastric pH for dissolution; therefore, concurrent administration with medications that increase gastric pH, such as proton pump inhibitors (PPIs) may decrease the bioavailability of cefpodoxime. When cefpodoxime was administered with high doses of antacids and H2-blockers, peak plasma concentrations were reduced by 24% and 42% and the extent of

absorption was reduced by 27% and 32%, respectively. The rate of absorption is not affected.
Cefuroxime: (Major) Avoid the concomitant use of proton pump inhibitors (PPIs) and cefuroxime. Drugs that reduce gastric acidity, such as PPIs, can interfere with the oral absorption of cefuroxime axetil and may result in reduced antibiotic efficacy.
Chlorothiazide: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Chlorthalidone: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Cilostazol: (Major) Cilostazol is metabolized by the CYP2C19 hepatic isoenzyme and appears to have pharmacokinetic interactions with many medications that are potent inhibitors of CYP2C19, such as esomeprazole. When given concurrently with omeprazole, another CYP2C19 inhibitor, cilostazol AUC is increased by 26% and the Cmax is increased by 18%; the AUC of the active metabolite 3,4-dehydro-cilostazol is increased by 69% and the Cmax is increased by 29%. When administered concomitantly with esomeprazole, the cilostazol dosage should be reduced by 50%.
Ciprofloxacin: (Minor) Use caution when administering ciprofloxacin and esomeprazole concurrently. Ciprofloxacin is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of ciprofloxacin with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Citalopram: (Moderate) Limit the dose of citalopram to 20 mg/day if coadministered with esomeprazole. Concurrent use may increase citalopram exposure increasing the risk of QT prolongation. Citalopram is a sensitive CYP2C19 substrate; esomeprazole is a weak inhibitor of CYP2C19.
cloBAZam: (Moderate) Coadministration may increase serum concentrations of clobazam; a dosage reduction of clobazam may be necessary during coadministration of esomeprazole. Metabolism of N-desmethylclobazam, the active metabolite of clobazam, occurs primarily through CYP2C19 and esomeprazole is an inhibitor of CYP2C19. Extrapolation from pharmacogenomic data indicates that concurrent use of clobazam with moderate or potent inhibitors of CYP2C19 may result in up to a 5-fold increase in exposure to N-desmethylclobazam. Adverse effects, such as sedation, lethargy, ataxia, or insomnia may be potentiated.
clomiPRAMINE: (Minor) Esomeprazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as clomipramine.
Clopidogrel: (Major) Avoid concomitant use of clopidogrel and esomeprazole as it

significantly reduces the antiplatelet activity of clopidogrel. If necessary, consider using an alternative proton pump inhibitor such as rabeprazole, pantoprazole, lansoprazole, or dexlansoprazole. Clopidogrel requires hepatic biotransformation via 2 cytochrome dependent oxidative steps; the CYP2C19 isoenzyme is involved in both steps. Esomeprazole is an inhibitor of CYP2C19. In clinical studies, use of esomeprazole significantly reduced the antiplatelet activity of clopidogrel.
Cobicistat: (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Cysteamine: (Major) Monitor white blood cell (WBC) cystine concentration closely when administering delayed-release cysteamine (Procysbi) with proton pump inhibitors (PPIs). Drugs that increase the gastric pH may cause the premature release of cysteamine from delayed-release capsules, leading to an increase in WBC cystine concentration. Concomitant administration of omeprazole 20 mg did not alter the pharmacokinetics of delayed-release cysteamine when administered with orange juice; however, the effect of omeprazole on the pharmacokinetics of delayed-release cysteamine when administered with water have not been studied.
Dacomitinib: (Major) Avoid coadministration of esomeprazole with dacomitinib due to decreased plasma concentrations of dacomitinib which may impact efficacy. Coadministration with another proton pump inhibitor decreased the dacomitinib Cmax and AUC by 51% and 39%, respectively.
Darunavir; Cobicistat: (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Dasatinib: (Major) Avoid the concomitant use of proton pump inhibitors (PPIs) with dasatinib film-coated oral tablets, such as Sprycel. Consider using an alternative dasatinib dosage form, such as Phyrago, or antacids. Separate the administration of all dasatinib oral tablet dosage forms and antacids by at least 2 hours. PPIs alter gastric pH

and interfere with the absorption of some dasatinib dosage forms which may reduce dasatinib efficacy. The use of a PPI with Sprycel reduced dasatinib overall exposure by 43%.
Desogestrel: Ethinyl Estradiol; Ferrous Bisglycinate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Dextroamphetamine: (Moderate) Use amphetamine; dextroamphetamine and proton pump inhibitors concomitantly with caution. Gastrointestinal alkalinizing agents may increase exposure to amphetamine; dextroamphetamine and exacerbate its actions.
diazePAM: (Moderate) Monitor for an increase in diazepam-related adverse reactions, including sedation and respiratory depression, if coadministration with esomeprazole is necessary. Administration of esomeprazole with diazepam resulted in a 45% decrease in clearance of diazepam. Diazepam is a CYP2C19 substrate and esomeprazole is a CYP2C19 inhibitor.
Digoxin: (Moderate) Increased serum digoxin concentrations have been reported in patients who received digoxin and esomeprazole. Esomeprazole inhibits gastric acid secretion and increases the pH of the stomach. Changes in intragastric pH can potentially alter the bioavailability of other drugs with pH-dependent absorption, such as digoxin. Gastric acid pump-inhibitors may increase digoxin bioavailability; however, the magnitude of the interaction is small. Measure serum digoxin concentrations before initiating esomeprazole. Monitor patients for possible digoxin toxicity and reduce digoxin dose as necessary. In addition, proton pump inhibitors have been associated with hypomagnesemia. Because, low serum magnesium may lead to irregular heartbeat and increase the likelihood of serious arrhythmias, clinicians should monitor serum magnesium concentrations periodically in patients taking a PPI and digoxin concomitantly. Patients who develop hypomagnesemia may require PPI discontinuation in addition to magnesium replacement.
Dolutegravir; Rilpivirine: (Contraindicated) Concurrent use of proton pump inhibitors and rilpivirine is contraindicated; when these drugs are coadministered, there is a potential for treatment failure and/or the development of rilpivirine or NNRTI resistance. Proton pump inhibitors inhibit secretion of gastric acid by proton pumps thereby increasing the gastric pH; for optimal absorption, rilpivirine requires an acidic environment. Coadministration of a proton pump inhibitor and rilpivirine may result in decreased rilpivirine absorption/serum concentrations, which could cause impaired virologic response to rilpivirine.
Dronedarone: (Moderate) Dronedarone is metabolized by and is an inhibitor of CYP3A.

Esomeprazole is a substrate for CYP3A4. The concomitant administration of dronedarone and CYP3A substrates may result in increased exposure of the substrate and should, therefore, be undertaken with caution.
Efavirenz: (Minor) Although drug interaction studies have not been conducted, efavirenz may inhibit the metabolism of substrates for CYP2C9 or CYP2C19 such as esomeprazole. In vitro studies have shown that efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations.
Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Minor) Although drug interaction studies have not been conducted, efavirenz may inhibit the metabolism of substrates for CYP2C9 or CYP2C19 such as esomeprazole. In vitro studies have shown that efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Minor) Although drug interaction studies have not been conducted, efavirenz may inhibit the metabolism of substrates for CYP2C9 or CYP2C19 such as esomeprazole. In vitro studies have shown that efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Minor) Use caution when administering cobicistat and esomeprazole concurrently. Cobicistat is an inhibitor of CYP3A, and esomeprazole is partially metabolized by CYP3A. Coadministration of cobicistat with CYP3A substrates, such as esomeprazole, can theoretically increase esomeprazole exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Contraindicated) Concurrent use of proton pump inhibitors and rilpivirine is contraindicated; when these drugs are coadministered, there is a potential for treatment failure and/or the development of rilpivirine or NNRTI resistance. Proton pump inhibitors inhibit secretion of gastric acid by proton pumps thereby increasing the gastric pH; for optimal absorption, rilpivirine requires an acidic environment. Coadministration of a proton pump inhibitor and rilpivirine may result in decreased rilpivirine absorption/serum concentrations, which could cause impaired virologic response to rilpivirine.
Emtricitabine; Rilpivirine; Tenofovir Disoproxil Fumarate: (Contraindicated) Concurrent use of proton pump inhibitors and rilpivirine is contraindicated; when these drugs are coadministered, there is a potential for treatment failure and/or the development of

rilpivirine or NNRTI resistance. Proton pump inhibitors inhibit secretion of gastric acid by proton pumps thereby increasing the gastric pH; for optimal absorption, rilpivirine requires an acidic environment. Coadministration of a proton pump inhibitor and rilpivirine may result in decreased rilpivirine absorption/serum concentrations, which could cause impaired virologic response to rilpivirine.
Enalapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Encorafenib: (Major) Avoid concomitant use of esomeprazole and encorafenib as esomeprazole exposure may be decreased, reducing its efficacy. Esomeprazole is a CYP3A substrate and encorafenib is a strong CYP3A inducer.
Enzalutamide: (Major) Avoid coadministration of esomeprazole with enzalutamide due to decreased esomeprazole plasma concentrations. Esomeprazole is a CYP3A4 and CYP2C19 substrate. Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C19 inducer. Coadministration with another strong inducer of CYP3A4 inducer decreased omeprazole exposure by 37.9% in CYP2C19 poor metabolizers and by 43.9% in extensive metabolizers; esomeprazole is an enantiomer of omeprazole.
Erlotinib: (Major) Avoid coadministration of erlotinib with esomeprazole if possible due to decreases in erlotinib plasma concentrations. Erlotinib solubility is pH dependent and solubility decreases as pH increases. Coadministration of erlotinib with medications that increase the pH of the upper gastrointestinal tract may decrease the absorption of erlotinib. Separation of doses may not eliminate the interaction since proton pump inhibitors affect the pH of the upper GI tract for an extended period of time. Increasing the dose of erlotinib is also not likely to compensate for the loss of exposure. Coadministration with another proton pump inhibitor decreased erlotinib exposure by 46% and the erlotinib Cmax by 61%.
Escitalopram: (Moderate) Monitor for an increase in escitalopram-related adverse effects, such as QT prolongation and serotonin syndrome, if concomitant use with esomeprazole is necessary. An empiric escitalopram dosage reduction may be considered in patients with additional risk factors for adverse effects, such as age older than 60 years. Concomitant use has been observed to increase dose-adjusted escitalopram concentrations by 82%, which may increase the risk for adverse effects.
Eslicarbazepine: (Moderate) Eslicarbazepine may inhibit the CYP2C19-mediated and induce the CYP3A4-mediated metabolism of esomeprazole; both enzymes are involved in the metabolism of esomeprazole. It is unclear that the theoretical interaction would result in a net increase or decrease in PPI action. Some manufacturers recommend avoiding the coadministration of hepatic cytochrome P-450 enzyme inducers and PPIs. If eslicarbazepine and PPI must be used together, monitor the patient closely for signs and symptoms of GI bleeding or other signs and symptoms of reduced PPI efficacy, or for signs of PPI side effects.

Ethacrynic Acid: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and loop diuretic use due to risk for hypomagnesemia.
Fedratinib: (Moderate) Monitor for increased esomeprazole adverse effects as coadministration of esomeprazole and fedratinib may result in increased concentrations of esomeprazole. Although dose adjustments are not generally needed, patients with Zollinger-Ellison's syndrome who often require higher esomeprazole doses (up to 240 mg/day) may require an adjustment in esomeprazole dose. Esomeprazole is metabolized primarily by CYP2C19 and secondarily by CYP3A4; fedratinib is an inhibitor of CYP2C19 and CYP3A4.
Felbamate: (Minor) Felbamate may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
Ferric Maltol: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Fexinidazole: (Moderate) Monitor for esomeprazole-related adverse effects during coadministration with fexinidazole. Concurrent use may increase esomeprazole exposure. Esomeprazole is a CYP2C19 substrate and fexinidazole is a moderate CYP2C19 inhibitor.
Flibanserin: (Moderate) Use of esomeprazole may increase flibanserin concentrations, resulting in severe hypotension, syncope, and/or CNS depression. Monitor for flibanserin-induced adverse reactions; consider if a different PPI would be a better choice for the patient. Esomeprazole is a CYP2C19 inhibitor, and has been noted to cause clinically important drug interactions with certain CYP2C19 substrates. Flibanserin is a CYP2C19 substrate. Interactions may be especially significant for patients who are also known CYP2C19 poor metabolizers.
Fluconazole: (Minor) Fluconazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
FLUoxetine: (Minor) Fluoxetine may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
Fluvastatin: (Moderate) Concomitant administration of cimetidine, ranitidine, or omeprazole with fluvastatin can decrease fluvastatin clearance by 18 to 23%, and increase AUC by 24 to 33%. A similar interaction might be expected with esomeprazole.

fluvoxaMINE: (Minor) Fluvoxamine may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Fosphenytoin: (Moderate) Monitor phenytoin concentrations during concomitant therapy with fosphenytoin and esomeprazole due to risk for phenytoin toxicity. Concomitant use may increase phenytoin concentrations. Phenytoin is a CYP2C19 substrate and esomeprazole is a CYP2C19 inhibitor.
Furosemide: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and loop diuretic use due to risk for hypomagnesemia.
Gefitinib: (Major) Avoid coadministration of esomeprazole with gefitinib if possible due to decreased exposure to gefitinib, which may lead to reduced efficacy. If concomitant use is unavoidable, take gefitinib 12 hours after the last dose or 12 hours before the next dose of esomeprazole. Gefitinib exposure is affected by gastric pH. Coadministration with another drug to maintain gastric pH above 5 decreased gefitinib exposure by 47%.
hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
hydroCHLOROthiazide, HCTZ; Moexipril: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with esomeprazole, a CYP3A substrate, as esomeprazole toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when coadministered with idelalisib.
Imipramine: (Minor) In the hepatic oxidative system, esomeprazole is metabolized primarily by CYP2C19 and secondarily by the CYP3A4 isoenzyme. Theoretically, esomeprazole may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as imipramine.
Infigratinib: (Major) Avoid coadministration of infigratinib and gastric acid-reducing agents, such as proton pump inhibitors (PPIs). Coadministration may decrease infigratinib exposure resulting in decreased efficacy. If necessary, infigratinib may be administered two hours before or ten hours after an H2-receptor antagonist or two hours before or after a locally acting antacid. Coadministration with a PPI decreased infigratinib exposure by 45%.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration

before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Iron Salts: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Iron Salts: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Iron: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Isavuconazonium: (Moderate) Concomitant use of isavuconazonium with esomeprazole may result in increased concentrations of esomeprazole. Esomeprazole is a substrate of the hepatic isoenzyme CYP3A4; isavuconazole, the active moiety of isavuconazonium, is a moderate inhibitor of this enzyme. Caution and close monitoring are advised if these drugs are used together.
Isoniazid, INH: (Minor) Isoniazid, INH may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
Itraconazole: (Moderate) When administering proton pump inhibitors with the 100 mg itraconazole capsule and 200 mg itraconazole tablet formulations, systemic exposure to itraconazole is decreased. Conversely, exposure to itraconazole is increased when proton pump inhibitors are administered with the 65 mg itraconazole capsule. Administer proton pump inhibitors at least 2 hours before or 2 hours after the 100 mg capsule or 200 mg tablet. Monitor for increased itraconazole-related adverse effects if proton pump inhibitors are administered with itraconazole 65 mg capsules.
Ketoconazole: (Major) Avoid use of proton pump inhibitors (PPIs) with ketoconazole. Medications that increase gastric pH may impair oral ketoconazole absorption.

Ledipasvir; Sofosbuvir: (Major) Solubility of ledipasvir decreases as gastric pH increases; thus, coadministration of ledipasvir; sofosbuvir with proton pump inhibitors (PPIs) may result in lower ledipasvir plasma concentrations. Ledipasvir can be administered with PPIs if given simultaneously under fasting conditions. The PPI dose should not exceed a dose that is comparable to omeprazole 20 mg/day.
Levoketoconazole: (Major) Avoid use of proton pump inhibitors (PPIs) with ketoconazole. Medications that increase gastric pH may impair oral ketoconazole absorption.
Levonorgestrel; Ethinyl Estradiol; Ferrous Bisglycinate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Levonorgestrel; Ethinyl Estradiol; Ferrous Fumarate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Levothyroxine: (Moderate) Proton pump inhibitors (PPIs) may reduce the oral absorption of thyroid hormones and thus reduce efficacy; monitor for altered clinical response to thyroid hormone therapy if concomitant use is necessary. Alternatively, an oral liquid levothyroxine dosage form may be considered. Gastric acidity is an essential requirement for adequate absorption of levothyroxine tablets and capsules and other thyroid hormones. Gastric acidity may be less essential for the absorption of oral liquid dosage forms of levothyroxine; PPIs have been observed to have a minimal effect on the bioavailability of oral liquid levothyroxine.
Levothyroxine; Liothyronine (Porcine): (Moderate) Proton pump inhibitors (PPIs) may reduce the oral absorption of thyroid hormones and thus reduce efficacy; monitor for altered clinical response to thyroid hormone therapy if concomitant use is necessary. Alternatively, an oral liquid levothyroxine dosage form may be considered. Gastric acidity is an essential requirement for adequate absorption of levothyroxine tablets and capsules and other thyroid hormones. Gastric acidity may be less essential for the absorption of oral liquid dosage forms of levothyroxine; PPIs have been observed to have a minimal effect on the bioavailability of oral liquid levothyroxine.
Liothyronine: (Moderate) Proton pump inhibitors (PPIs) may reduce the oral absorption of thyroid hormones and thus reduce efficacy; monitor for altered clinical response to thyroid hormone therapy if concomitant use is necessary. Alternatively, an oral liquid

levothyroxine dosage form may be considered. Gastric acidity is an essential requirement for adequate absorption of levothyroxine tablets and capsules and other thyroid hormones. Gastric acidity may be less essential for the absorption of oral liquid dosage forms of levothyroxine; PPIs have been observed to have a minimal effect on the bioavailability of oral liquid levothyroxine.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Loop diuretics: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and loop diuretic use due to risk for hypomagnesemia.
Lopinavir; Ritonavir: (Moderate) Concurrent administration of esomeprazole with ritonavir may result in elevated esomeprazole plasma concentrations. Esomeprazole is metabolized by the hepatic isoenzyme CYP3A4; ritonavir is an inhibitor of this enzyme. Monitor patients for increased side effects if these drugs are administered together.
Losartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of esomeprazole by substantially decreasing its systemic exposure. If used together, an esomeprazole dosage adjustment may be necessary to obtain the desired therapeutic effect. Esomeprazole is a CYP3A4 and CYP2C19 substrate. Lumacaftor; ivacaftor is a strong inducer of CYP3A; in vitro data suggests is also has the potential to induce CYP2C19.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of esomeprazole by substantially decreasing its systemic exposure. If used together, an esomeprazole dosage adjustment may be necessary to obtain the desired therapeutic effect. Esomeprazole is a CYP3A4 and CYP2C19 substrate. Lumacaftor; ivacaftor is a strong inducer of CYP3A; in vitro data suggests is also has the potential to induce CYP2C19.
Mavacamten: (Major) Reduce the mavacamten dose by 1 level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients receiving mavacamten and starting esomeprazole therapy. Avoid initiation of esomeprazole in patients who are on stable treatment with mavacamten 2.5 mg per day because a lower dose of mavacamten is not available. Initiate mavacamten at the recommended starting dose of 5 mg PO once daily in patients who are on stable esomeprazole therapy. Concomitant use increases mavacamten exposure, which may increase the risk of adverse drug reactions. Mavacamten is a CYP2C19 substrate and esomeprazole is a weak CYP2C19 inhibitor. Concomitant use with another weak CYP2C19 inhibitor in CYP2C19 normal and rapid metabolizers increased overall mavacamten exposure by 48%.

Mefloquine: (Moderate) Proton pump inhibitors (PPIs) may increase plasma concentrations of mefloquine. Patients on chronic mefloquine therapy might be at increased risk of adverse reactions, especially patients with a neurological or psychiatric history.
Methohexital: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Methotrexate: (Major) Avoid concomitant use of methotrexate and proton pump inhibitors (PPIs) due to the risk of severe methotrexate-related adverse reactions. If concomitant use is unavoidable, closely monitor for adverse reactions; consider temporary withdrawal of the PPI in some patients receiving high-dose methotrexate. Concomitant use of methotrexate, primarily at high dose, and PPIs may increase and prolong serum concentrations of methotrexate, possibly leading to methotrexate toxicities.
metOLazone: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Mitotane: (Moderate) Use caution if mitotane and esomeprazole are used concomitantly, and monitor for decreased efficacy of esomeprazole and a possible change in dosage requirements. Mitotane is a strong CYP3A4 inducer and esomeprazole is a CYP3A4 substrate; coadministration may result in decreased plasma concentrations of esomeprazole.
Mycophenolate: (Moderate) Concomitant administration of proton pump inhibitors (PPIs) with mycophenolate mofetil (Cellcept) appears to reduce MPA exposure AUC-12h (25.8 +/- 6.4 mg/L x h with omeprazole vs. 33.3 +/- 11.5 mg//L x h without omeprazole); however, the interaction does not appear to exist with mycophenolate sodium delayed-release tablets (Myfortic). Reduced systemic exposure of MPA after mycophenolate mofetil in the presence of a PPI appears to be due to impaired absorption of mycophenolate mofetil which may occur because of incomplete dissolution of mycophenolate mofetil in the stomach at elevated pH. The clinical significance of reduced MPA exposure is unknown; however patients should be evaluated periodically if mycophenolate mofetil is administered with a PPI. Of note, MPA concentrations appear to be reduced in the initial hours after mycophenolate mofetil receipt but increase later in the dosing interval because of enterohepatic recirculation. A second peak in the concentration-time profile of MPA is observed 612 hours after dosing due to enterohepatic recirculation. For example, the 12-hour plasma concentrations of MPA

were similar among patients who received mycophenolate mofetil with or without omeprazole. The biphasic plasma concentration-time course of MPA due to extensive enterohepatic circulation hampers therapeutic drug monitoring of MPA. Drug exposure as measured by AUC-12h is the best estimator for the clinical effectiveness of mycophenolate, but measurement of full-dose interval MPA AUC-12h requires collection of multiple samples over a 12-hour period; MPA predose concentrations correlate poorly with MPA AUC-12h. The interaction does not appear to exist with Mycophenolate sodium (Myfortic).
Nelfinavir: (Major) Use of proton pump inhibitors with nelfinavir is not recommended. Coadministration may result in decreased nelfinavir exposure, subtherapeutic antiretroviral activity, and possibility resistant HIV mutations. In one study, concurrent use of nelfinavir with omeprazole resulted in decreased nelfinavir AUC, Cmax, and Cmin by 36%, 37%, and 39%, respectively.
Neratinib: (Major) Avoid concomitant use of neratinib with proton pump inhibitors due to decreased absorption and systemic exposure of neratinib; the solubility of neratinib decreases with increasing pH of the GI tract. Concomitant use with lansoprazole decreased neratinib exposure by 65%.
Nilotinib: (Major) Avoid the concomitant use of nilotinib and proton pump inhibitors (PPIs), as PPIs may cause a reduction in nilotinib bioavailability. Nilotinib displays pH-dependent solubility with decreased solubility at a higher pH. PPIs inhibit gastric acid secretion and elevate the gastric pH. Administration of a single 400-mg nilotinib dose with multiple oral doses of esomeprazole 40 mg/day reduced the nilotinib AUC by 34% in a study in healthy subjects. Increasing the dose is unlikely to compensate for the loss of nilotinib exposure; additionally, separating the administration of these agents may not eliminate the interaction as PPIs affect the pH of the upper GI tract for an extended period of time.
Nirmatrelvir; Ritonavir: (Moderate) Concurrent administration of esomeprazole with ritonavir may result in elevated esomeprazole plasma concentrations. Esomeprazole is metabolized by the hepatic isoenzyme CYP3A4; ritonavir is an inhibitor of this enzyme. Monitor patients for increased side effects if these drugs are administered together.
Nirogacestat: (Major) Avoid concomitant use of nirogacestat and proton pump inhibitors. Concurrent use may impair nirogacestat absorption which may decrease nirogacestat exposure and reduce its efficacy. Antacids may be used with nirogacestat but administration should be separated by at least 2 hours.
Norethindrone Acetate; Ethinyl Estradiol; Ferrous fumarate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus,

increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Norethindrone; Ethinyl Estradiol; Ferrous fumarate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.
Octreotide: (Moderate) Coadministration of oral octreotide with proton pump inhibitors (PPIs) may require increased doses of octreotide. Coadministration of oral octreotide with drugs that alter the pH of the upper GI tract, including PPIs, may alter the absorption of octreotide and lead to a reduction in bioavailability. This interaction has been documented with esomeprazole and can occur with the other PPIs.
OLANZapine; FLUoxetine: (Minor) Fluoxetine may inhibit the CYP2C19 isoenzyme, leading to increased plasma levels of drugs that are substrates for the CYP2C19 isoenzyme, such as esomeprazole.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Oritavancin: (Moderate) Coadministration of oritavancin and esomeprazole may result in increase in esomeprazole exposure. Esomeprazole is primarily metabolized by CYP2C19, but is also metabolized by CYP3A4. Oritavancin weakly induces CYP3A4, while weakly inhibiting CYP2C19. Coadministration of oritavancin and omeprazole resulted in a 15% increase in the ratio of omeprazole to 5-OH-omeprazole. If these drugs are administered concurrently, monitor the patient for signs of toxicity.
Paltusotine: (Moderate) Avoid the use of proton pump inhibitors (PPIs) in patients already on paltusotine 60 mg. For those on other paltusotine doses, monitor for a decrease in paltusotine efficacy during concomitant use of paltusotine and a PPI and increase the paltusotine dosage as appropriate based on response. PPIs alter gastric pH and interfere with paltusotine absorption which may reduce paltusotine exposure and efficacy. Concomitant use reduced the overall exposure of 20 mg and 60 mg of paltusotine by 21% and 42%, respectively.
PAZOPanib: (Major) Pazopanib displays pH-dependent solubility with decreased solubility at a higher pH. The concomitant use of pazopanib and proton pump inhibitors (PPIs) that elevate the gastric pH may reduce the bioavailability of pazopanib. In a study of patients with solid tumors, the AUC and Cmax of pazopanib were decreased by

approximately 40% when coadministered with esomeprazole. If a drug is needed to raise the gastric pH, consider use of a short-acting antacid; separate antacid and pazopanib dosing by several hours.
PENTobarbital: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Pexidartinib: (Major) Avoid coadministration of pexidartinib with esomeprazole as concurrent use may decrease pexidartinib exposure which may result in decreased therapeutic response. As an alternative to a proton pump inhibitor (PPI), use locally-acting antacids or H2-receptor antagonists. Coadministration of esomeprazole decreased pexidartinib exposure by 50%.
PHENobarbital: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Phenytoin: (Moderate) Monitor phenytoin concentrations during concomitant therapy with esomeprazole due to risk for phenytoin toxicity. Concomitant use may increase phenytoin concentrations. Phenytoin is a CYP2C19 substrate and esomeprazole is a CYP2C19 inhibitor.
Polyethylene Glycol; Electrolytes; Bisacodyl: (Minor) The concomitant use of bisacodyl oral tablets with drugs that raise gastric pH like proton pump inhibitors can cause the enteric coating of the bisacodyl tablets to dissolve prematurely, leading to possible gastric irritation or dyspepsia. When taking bisacodyl tablets, it is advisable to avoid PPIs within 1 hour before or after the bisacodyl dosage.
Posaconazole: (Major) The concurrent use of posaconazole immediate-release oral suspension and proton pump inhibitors (PPIs) should be avoided, if possible, due to the potential for decreased posaconazole efficacy. If used in combination, closely monitor for breakthrough fungal infections. PPIs increase gastric pH, resulting in decreased posaconazole absorption and lower posaconazole plasma concentrations. When a single 400 mg dose of posaconazole oral suspension was administered with esomeprazole (40 mg PO daily), the mean reductions in Cmax were 46% and the mean reductions in AUC were 32% for posaconazole. The pharmacokinetics of posaconazole delayed-release tablets and oral suspension are not significantly affected by PPIs. Additionally, posaconazole is a potent inhibitor of CYP3A4, an isoenzyme partially responsible for the metabolism of many PPIs (dexlansoprazole, esomeprazole, lansoprazole, omeprazole,

pantoprazole, and rabeprazole). Coadministration may result in increased plasma concentration of the PPIs.
Primidone: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Quinapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
rifAMPin: (Major) Avoid coadministration of esomeprazole with rifampin due to the risk of decreased esomeprazole plasma concentrations which may decrease efficacy. Esomeprazole is a CYP3A4 substrate and rifampin is a strong CYP3A4 inducer.
Rilpivirine: (Contraindicated) Concurrent use of proton pump inhibitors and rilpivirine is contraindicated; when these drugs are coadministered, there is a potential for treatment failure and/or the development of rilpivirine or NNRTI resistance. Proton pump inhibitors inhibit secretion of gastric acid by proton pumps thereby increasing the gastric pH; for optimal absorption, rilpivirine requires an acidic environment. Coadministration of a proton pump inhibitor and rilpivirine may result in decreased rilpivirine absorption/serum concentrations, which could cause impaired virologic response to rilpivirine.
Rilzabrutinib: (Major) Avoid concomitant use of rilzabrutinib and proton pump inhibitors (PPIs). Concurrent use may decrease rilzabrutinib exposure which may reduce its efficacy. Rilzabrutinib is pH soluble; PPIs raise gastric pH and interfere with rilzabrutinib absorption. Concomitant use with a PPI reduced rilzabrutinib overall exposure by 51%.
Risedronate: (Moderate) Use of proton pump inhibitors (PPIs) with delayed-release risedronate tablets (Atelvia) is not recommended. Co-administration of drugs that raise stomach pH increases risedronate bioavailability due to faster release of the drug from the enteric coated tablet. This interaction does not apply to risedronate immediate-release tablets. In healthy subjects who received esomeprazole for 6 days, the Cmax and AUC of a single dose of risedronate delayed-release tablets (Atelvia) increased by 60% and 22%, respectively. PPIsare widely used and are frequently coadministered in users of oral bisphosphonates. A national register-based, open cohort study of 38,088 elderly patients suggests that those who use PPIs in conjunction with alendronate have a dose-dependent loss of protection against hip fracture. While causality was not investigated, the dose-response relationship noted during the study suggested that PPIs may reduce oral alendronate efficacy, perhaps through an effect on absorption or other mechanism, and therefore PPIs may not be optimal agents to control gastrointestinal complaints. Study results suggest that the interaction may occur across the class; however, other interactions have not been confirmed and data suggest that fracture protection is not diminished when risedronate is used with PPIs. A post hoc analysis of patients who took

risedronate 5 mg daily during placebo-controlled clinical trials determined that risedronate significantly reduced the risk of new vertebral fractures compared to placebo, regardless of concomitant PPI use. PPI users (n = 240) and PPI non-users (n = 2489) experienced fracture risk reductions of 57% (p = 0.009) and 38% (p < 0.001), respectively.
Ritonavir: (Moderate) Concurrent administration of esomeprazole with ritonavir may result in elevated esomeprazole plasma concentrations. Esomeprazole is metabolized by the hepatic isoenzyme CYP3A4; ritonavir is an inhibitor of this enzyme. Monitor patients for increased side effects if these drugs are administered together.
Saquinavir: (Major) Coadministration with omeprazole results in significantly increased saquinavir concentrations. A similar interaction is expected with all proton pump inhibitors (PPIs). If saquinavir must be administered with PPIs, the patient should be closely monitored for saquinavir-related toxicities, including gastrointestinal symptoms, increased triglycerides, and deep vein thrombosis (DVT). Coadministration with omeprazole results in significantly increased saquinavir concentrations. In a small study, 18 healthy individuals received saquinavir 1000 mg (with ritonavir 100 mg) twice daily for 15 days; on days 11 through 15 omeprazole 40 mg was given once daily, which resulted in an 82% increase in the saquinavir AUC. A similar interaction is expected with all PPIs.
Secobarbital: (Major) Avoid coadministration of esomeprazole with barbiturates because it can result in decreased efficacy of esomeprazole. Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. Barbiturates induce CYP3A4 and CYP2C19.
Secretin: (Major) Discontinue proton pump inhibitors (PPIs) before performing a secretin stimulation test for gastrinoma. PPIs may cause a hyperresponse in gastrin secretion and interfere with the test's diagnostic accuracy. The time it takes gastrin concentrations to return to baseline following PPI discontinuation is highly variable.
Selpercatinib: (Major) Avoid coadministration of selpercatinib with esomeprazole due to the risk of decreased selpercatinib exposure which may reduce its efficacy. If concomitant use is unavoidable, selpercatinib must be taken with food. Coadministration under fasting conditions with another proton pump inhibitor decreased selpercatinib exposure by 69%; however, concomitant use increased selpercatinib exposure by 2% or less when it was administered with a meal.
Sodium Ferric Gluconate Complex; Ferric Pyrophosphate Citrate: (Moderate) The bioavailability of oral iron salts is influenced by gastric pH, and the concomitant administration of proton pump inhibitors can decrease iron absorption. The non-heme ferric form of iron needs an acidic intragastric pH to be reduced to ferrous and to be absorbed. Iron salts and polysaccharide-iron complex provide non-heme iron. Proton pump inhibitors have long-lasting effects on the secretion of gastric acid and thus, increase the pH of the stomach. The increase in intragastric pH can interfere with the absorption of iron salts.

Sofosbuvir; Velpatasvir: (Major) Coadministration of proton pump inhibitors (PPIs) with velpatasvir is not recommended. If it is considered medically necessary to coadminister, velpatasvir should be administered with food and taken 4 hours before omeprazole 20 mg. Other PPIs have not been studied; however, it may be prudent to separate the administration of the other PPIs similarly. Velpatasvir solubility decreases as pH increases; therefore, drugs that increase gastric pH are expected to decrease the concentrations of velpatasvir, potentially resulting in loss of antiviral efficacy.
Sofosbuvir; Velpatasvir; Voxilaprevir: (Major) Coadministration of proton pump inhibitors (PPIs) with velpatasvir is not recommended. If it is considered medically necessary to coadminister, velpatasvir should be administered with food and taken 4 hours before omeprazole 20 mg. Other PPIs have not been studied; however, it may be prudent to separate the administration of the other PPIs similarly. Velpatasvir solubility decreases as pH increases; therefore, drugs that increase gastric pH are expected to decrease the concentrations of velpatasvir, potentially resulting in loss of antiviral efficacy.
Solifenacin: (Moderate) The American College of Gastroenterology states that the effectiveness of proton pump inhibitors (PPIs) may be theoretically decreased if given with other antisecretory agents (e.g., anticholinergics). Proton pump inhibitors (PPIs) inhibit only actively secreting H+-pumps.
Sotorasib: (Major) Avoid coadministration of sotorasib and gastric acid-reducing agents, such as proton pump inhibitors (PPIs). Coadministration may decrease sotorasib exposure resulting in decreased efficacy. If necessary, sotorasib may be administered 4 hours before or 10 hours after a locally acting antacid. Coadministration with a PPI decreased sotorasib exposure by 57% under fed conditions and 42% under fasted conditions.
Sparsentan: (Major) Avoid concurrent use of sparsentan and proton pump inhibitors (PPIs) due to the risk for decreased sparsentan exposure which may reduce its efficacy. Medications that affect gastric pH may reduce sparsentan absorption.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
St. John's Wort, Hypericum perforatum: (Major) Avoid concomitant use of St. John's wort with the proton pump inhibitors (PPIs) as PPI exposure may be decreased, reducing their efficacy. PPIs are CYP3A4 and CYP2C19 substrates and St. John's wort is a strong CYP3A4 and CYP2C19 inducer. For example, coadministration of omeprazole with St. John's wort decreased omeprazole plasma concentrations by approximately 40%.
Sucralfate: (Minor) Sucralfate may delay absorption and reduce the bioavailability of lansoprazole. Lansoprazole should be taken no less than 30 minutes before sucralfate. This interaction is theoretical and is based on the interaction between sucralfate and lansoprazole; sucralfate has been shown to delay absorption and reduce the bioavailability of lansoprazole by about 17%. No information is available to determine if

a similar interaction occurs with esomeprazole.
Tacrolimus: (Moderate) Esomeprazole may increase tacrolimus whole blood trough concentrations and increase the risk of serious adverse reactions (e.g., neurotoxicity, nephrotoxicity, QT prolongation). Monitor tacrolimus whole blood trough concentrations and reduce the tacrolimus dose if needed. Tacrolimus is metabolized primarily by CYP3A4; esomeprazole inhibits CYP3A4 and thus may decrease CYP3A4-mediated metabolism of tacrolimus.
Taletrectinib: (Major) Avoid concomitant use of taletrectinib and proton pump inhibitors (PPIs). Concurrent use may decrease taletrectinib exposure, which may reduce its efficacy. Taletrectinib oral absorption is pH dependent and PPIs alter gastric pH. Concomitant use with a PPI reduced taletrectinib overall exposure by 40%.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Thiazide diuretics: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Thyroid hormones: (Moderate) Proton pump inhibitors (PPIs) may reduce the oral absorption of thyroid hormones and thus reduce efficacy; monitor for altered clinical response to thyroid hormone therapy if concomitant use is necessary. Alternatively, an oral liquid levothyroxine dosage form may be considered. Gastric acidity is an essential requirement for adequate absorption of levothyroxine tablets and capsules and other thyroid hormones. Gastric acidity may be less essential for the absorption of oral liquid dosage forms of levothyroxine; PPIs have been observed to have a minimal effect on the bioavailability of oral liquid levothyroxine.
Tipranavir: (Moderate) Some manufacturers recommend avoiding the coadministration of hepatic cytochrome P-450 enzyme inducers and proton pump inhibitors (PPIs). Tipranavir markedly induces the hepatic cytochrome P-450 enzyme CYP2C19, an enzyme responsible for the metabolism of PPIs. However, since tipranavir is not given unless it is co-prescribed with ritonavir, a known marked enzyme inhibitor, a reduction in PPI metabolism may be unlikely to occur. A reduction in PPI concentrations may increase the risk of gastrointestinal (GI) adverse events such as GI bleeding. If tipranavir and PPIs must be used together, monitor the patient closely for signs and symptoms of GI bleeding or other signs and symptoms of reduced PPI efficacy.
Tolterodine: (Moderate) The American College of Gastroenterology states that the effectiveness of proton pump inhibitors (PPIs) may be theoretically decreased if given with other antisecretory agents (e.g., anticholinergics). Proton pump inhibitors (PPIs) inhibit only actively secreting H+-pumps.
Torsemide: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and loop diuretic use due to risk for

hypomagnesemia.
Triamterene; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Trospium: (Moderate) The American College of Gastroenterology states that the effectiveness of proton pump inhibitors (PPIs) may be theoretically decreased if given with other antisecretory agents (e.g., anticholinergics). Proton pump inhibitors (PPIs) inhibit only actively secreting H+-pumps.
Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor magnesium concentration before and periodically during concomitant esomeprazole and thiazide diuretic use due to risk for hypomagnesemia.
Vemurafenib: (Moderate) Coadministration of vemurafenib and esomeprazole could lead to decreased esomeprazole concentrations and efficacy. Vemurafenib is a CYP3A4 inducer and esomeprazole is a CYP3A4 substrate. Monitor patients for efficacy.
Voriconazole: (Moderate) Monitor for increased drug toxicity as coadministration of esomeprazole and voriconazole may result in increased concentrations of both drugs. Although dose adjustments are not generally needed, patients with Zollinger-Ellison's syndrome who often require higher esomeprazole doses (up to 240mg/day) may require an adjustment in esomeprazole dose. Esomeprazole is metabolized primarily by CYP2C19 and secondarily by CYP3A4 and is also a CYP2C19 inhibitor; voriconazole is a CYP2C19 substrate and inhibitor of CYP2C19 and CYP3A4.
Warfarin: (Moderate) Monitor the INR in patients receiving warfarin with proton pump inhibitors. Increases in INR may lead to abnormal bleeding. Adjust the warfarin dose to maintain the target INR.
Xanomeline; Trospium: (Moderate) The American College of Gastroenterology states that the effectiveness of proton pump inhibitors (PPIs) may be theoretically decreased if given with other antisecretory agents (e.g., anticholinergics). Proton pump inhibitors (PPIs) inhibit only actively secreting H+-pumps.
Ziftomenib: (Major) Avoid concomitant use of ziftomenib and a proton pump inhibitor (PPI). Consider alternatives, such as an H2-blocker or antacid, if an agent that alters gastric pH is required; adjustments to timing of administration may also be necessary. Concurrent use may interfere with ziftomenib absorption which may reduce ziftomenib exposure and efficacy. Concomitant use of ziftomenib and a PPI reduced ziftomenib overall exposure by 53%.

Adverse Reaction

General Information

In general, oral esomeprazole has been well-tolerated in clinical trials (n > 10,000). Greater than 2900 patients have been evaluated in 6—12 month long studies. The types

of adverse events are similar with short or long-term use, and have been comparable to placebo rates. Additionally, the safety of esomeprazole has been studied in pediatric patients aged 1—17 years of age.

Animal and human data have demonstrated a proliferation of enterochromaffin-like cells due to hypergastrinemia, which may be associated with the development of malignant gastric carcinoma during long-term administration of proton pump inhibitors (PPIs). In over 1,000 patients treated with esomeprazole for up to 12 months, the prevalence of ECL cell hyperplasia increased with time and dose, but no patient developed ECL cell carcinoids, dysplasia, or neoplasia in the gastric mucosa. In esomeprazole clinical trials, there were dose-related increases in mean fasting gastrin levels which reached plateaus at 2 to 3 months and returned to baseline 4 weeks after drug discontinuation. According to the manufacturer of esomeprazole, < 1% of patients were reported to have hypergastrinemia or GI dysplasia. Historically, omeprazole has been given for as long as 5 years without concern for the development of gastric neoplasia. The overall risk of carcinoid tumors during therapy with PPIs is low based on cumulative safety experience; monitoring of serum gastrin levels during PPI therapy is generally not necessary.

Following completion of a comprehensive review, the FDA believes that the long-term use of omeprazole or esomeprazole is not likely to be associated with an increased risk of heart problems. Preliminary analysis of two small, long-term clinical studies raised concerns about a possible link between the long-term use of these drugs and cardiovascular events. In both studies, patients with severe gastroesophageal reflux disease (GERD) were randomized to receive drug therapy, with omeprazole or esomeprazole, or surgery to control GERD. Results from the studies appeared to show an increased risk of myocardial infarction, heart failure, and heart-related sudden death in patients who received drug therapy compared to those who received surgery. However, the results of these two studies along with results from other comparative studies of omeprazole, which did not show an increased risk of heart related adverse events, were analyzed by the FDA. The FDA did not find a correlation between the reported cardiovascular events and the use of either drug; thus, the FDA recommends that health care professionals and their patients continue to prescribe and use these two products in accordance with their labeled uses.

abdominal pain, constipation, diarrhea, dyspepsia, dysphagia, eructation, flatulence, GI bleeding, hiccups, melena, nausea, pancreatitis, stomatitis, vomiting, weight gain, weight loss, xerostomia

The most common reported adverse events associated with esomeprazole are primarily

gastrointestinal (GI) in nature. Diarrhea is among the most frequently reported adverse events (1% to 4% of esomeprazole recipients). Among patients receiving oral esomeprazole for the treatment of healing of erosive esophagitis, diarrhea was reported in 1% or more of patients; in patients receiving esomeprazole for GERD, the reported diarrhea rate was 4.3%. Diarrhea has also been reported with use of esomeprazole intravenously (IV) (3.9%). In pediatric patients, diarrhea was reported in 2.8% of patients 1 to 11 years of age, and in 2% of pediatric patients 12 to 17 years. Nausea has been reported in 1% or more of adults and 2% of adolescents taking oral esomeprazole and has been reported with esomeprazole IV (6.4%). Abdominal pain has been reported (1% to 4% oral; 5.8% esomeprazole IV). Other GI-related adverse events reported in patients receiving esomeprazole include flatulence (oral: 1% or more; IV: 10.3%), constipation (oral: 1% or more; IV: 2.5%), and xerostomia (oral: 1% or more; IV: 3.9%). Dyspepsia has also been reported in less than 1% of oral esomeprazole recipients and 6.4% with IV esomeprazole. In upper GI rebleeding prophylaxis trials, duodenal ulcer hemorrhage was reported in 4.3% of treated patients at rates similar to placebo (4.1%). Less common GI-related adverse events (less than 1% of patients) include: abdomen enlarged, bowel irregularity, dysphagia, dysplasia GI, epigastric pain, eructation, esophageal disorder, frequent stools, gastritis, gastroenteritis, GI bleeding, GI symptoms not otherwise specified, hiccups, melena, mouth disorder, pharynx disorder, rectal disorder, serum gastrin increased, tongue disorder, tongue edema, ulcerative stomatitis, weight gain, weight loss, and vomiting. During postmarketing surveillance with esomeprazole, pancreatitis, stomatitis, and taste disturbances/dysgeusia were also reported. Esomeprazole use in combination with amoxicillin and clarithromycin was associated with diarrhea (9.2%) of patients treated for H. pylori; abdominal pain (1% to 3%), nausea (2%), regurgitation (1%), and vomiting have also been reported. The use of esomeprazole in combination with amoxicillin and clarithromycin for H. pylori was associated with taste disturbance (6.6%, mostly attributed to the use of clarithromycin) and abdominal pain (3.7%).

erythema, injection site reaction, phlebitis

In GERD and erosive esophagitis trials, intravenous (IV) esomeprazole has been associated with injection site reaction (1.7%), including mild focal erythema and itching at the IV insertion site. In upper GI rebleeding prophylaxis trials, injection site reactions (4.3%) included erythema, swelling, inflammation, pruritus, phlebitis, thrombophlebitis and superficial phlebitis; with the exception of injection site reactions, IV administration was associated with a similar safety profile to that of oral administration.

agitation, anorexia, anxiety, appetite stimulation, blurred vision, confusion, depression, dizziness, drowsiness, dysgeusia, hallucinations, headache, hypertonia, hypoesthesia, insomnia, migraine, paresthesias, parosmia, tremor, vertigo, visual impairment

Headache is among the most frequently reported side effects associated with esomeprazole therapy. Among patients receiving oral esomeprazole for the treatment of healing of erosive esophagitis or GERD, headache was reported in 4% to 5.5% of patients. Headache was reported in 10.9% of patients receiving esomeprazole intravenously (IV). In pediatric patients, headache was reported in 1.9% of patients 1 to 11 years of age and in 8% of those 12 to 17 years. Dizziness (2.5%) was reported in those receiving IV esomeprazole and in less than 1% of patients receiving oral formulations. Somnolence/drowsiness was reported in less than 1% of adult patients and 1.9% of pediatric patients less than 12 years of age receiving esomeprazole for GERD. Less common (less than 1%) central nervous system adverse events possibly or probably related to esomeprazole included: anorexia, apathy, appetite stimulation, blurred vision, confusion, depression, hypertonia, nervousness (anxiety), hypoesthesia, insomnia, migraine, parosmia, paresthesias, sleep disorder, tremor, vertigo, and visual impairment. During postmarketing surveillance, aggression, agitation, depression, hallucinations, and taste disturbances (dysgeusia) have been reported. In patients treated for H. pylori, esomeprazole in combination with amoxicillin and clarithromycin was associated with dysgeusia (6.6%, determined to be mostly clarithromycin-related).

acne vulgaris, acute generalized exanthematous pustulosis (AGEP), alopecia, anaphylactic shock, anaphylactoid reactions, angioedema, diaphoresis, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), erythema multiforme, exfoliative dermatitis, hyperhidrosis, maculopapular rash, photosensitivity, pruritus, pruritus ani, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

During clinical evaluation, patients receiving IV esomeprazole reported pruritus (1.1%); pruritus has also been reported in less than 1% of patients taking oral esomeprazole. In addition, dermatological reactions occurring in less than 1% of patients judged by investigators during pre-approval trials as possibly or probably related to oral esomeprazole included: acne vulgaris, angioedema, dermatitis, pruritus ani, rash, maculopapular rash, skin inflammation, increased sweating/diaphoresis, and urticaria. During postmarketing surveillance, the following were also reported: alopecia, anaphylactic shock, anaphylactoid reactions, erythema multiforme, hyperhidrosis, photosensitivity, Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), and toxic epidermal necrolysis (some fatal). Exfoliative dermatitis has been reported with omeprazole, and could potentially occur with esomeprazole based on the similarity in dermatological reactions.

elevated hepatic enzymes, hepatic encephalopathy, hepatic failure, hepatitis, hyperbilirubinemia, jaundice

Elevated hepatic enzymes (ALT, AST, and alkaline phosphatase) and hyperbilirubinemia have been (less than 1%) reported with the use of esomeprazole. During postmarketing experience, hepatic failure, hepatitis with or without jaundice, and hepatic encephalopathy have been reported.

arthralgia, arthropathy, asthenia, back pain, bronchospasm, chest pain (unspecified), conjunctivitis, cough, dyspnea, edema, fatigue, fever, flushing, goiter, gynecomastia, hot flashes, hypertension, hyperuricemia, hyponatremia, malaise, muscle cramps, myalgia, peripheral edema, pharyngitis, polydipsia, rhinitis, sinus tachycardia, sinusitis, tinnitus, weakness

Adverse events reported in less than 1% of patients during clinical evaluation and judged by investigators as possibly or probably related to oral esomeprazole include: arthralgia, arthritis, arthropathy, asthenia, asthma, back pain, chest pain (unspecified), cough, conjunctivitis, muscle cramps, dyspnea, earache, edema, fibromyalgia syndrome, flushing, goiter, hernia, hypertension, hyperuricemia, hyponatremia, peripheral edema, hot flashes, fatigue, fever, flu-like disorder, malaise, otitis media, pain, pharyngitis, polymyalgia rheumatica, rhinitis, rigors, sinus tachycardia, thirst/polydipsia, and tinnitus. In addition, sinusitis was reported in both oral esomeprazole trials (less than 1%) and IV esomeprazole trials (1.7%). During postmarketing surveillance, muscular weakness, myalgia, gynecomastia, and bronchospasm have been reported.

infection

In clinical evaluation, a respiratory infection was reported among 1.1% of patients receiving intravenous (IV) esomeprazole. Also, increasing evidence suggests a link between acid-suppression therapy and pneumonia (community- and hospital-acquired). Several mechanisms have been proposed to account for this association. One such mechanism states that gastric pH serves as a barrier against pathogenic colonization of the gastrointestinal tract. An increase in gastric pH allows for a bacterial or viral invasion, which, in theory, can precipitate respiratory infections. Another proposed mechanism accounts for the role that gastric acid may have on stimulating the cough reflex that allows for the clearing of infectious agents from the respiratory tract. Finally, the fact that acid-suppressive therapy may impair white blood cell function, which in turn may lead to a depressed immune response to an infection, is listed among possible mechanisms. A causal relationship between the use of esomeprazole or other PPIs and pneumonia has not been established. Data from a large epidemiological trial, including individuals who developed the first occurrence of community-acquired pneumonia (CAP), suggest an increased risk of developing CAP among users of acid-suppressive

therapy compared to those who stopped therapy. After adjusting for confounders, the adjusted relative risk (RR) for CAP among PPI users compared to those who stopped therapy was 1.89 (95% CI, 1.36 to 2.62). Likewise, users of H2-blockers had an adjusted RR of 1.63 (95% CI, 1.07 to 2.48) compared to those who stopped therapy. In a second large cohort trial, acid-suppressive therapy was ordered in 52% (83% PPI and 23% H2-blocker, with some patients exposed to both) of new admissions. Hospital-acquired pneumonia occurred in 2,219 admissions (3.5%) with a higher incidence recorded among acid-suppressive therapy exposed patients compared to non-exposed patients. A subset analysis found a statistically significant association between PPI use (OR, 1.3; 95% CI, 1.1 to 1.4) and pneumonia. A non-significant association was found with H2-blockers; however, the lack of significance was attributed to the studies lack the power to detect significance for an OR of less than 1.3. Until more is known about the relationship between acid-suppression and pneumonia, clinicians are encouraged to carefully select patients before empirically initiating acid-suppressive therapy with H2-blockers or PPIs.

agranulocytosis, anemia, epistaxis, leukocytosis, leukopenia, lymphadenopathy, pancytopenia, pernicious anemia, thrombocytopenia, vitamin B12 deficiency

As with omeprazole, hematologic abnormalities have been reported rarely (less than 1%) with esomeprazole including anemia, hypochromic anemia, cervical lymphadenopathy, epistaxis, leukocytosis, leukopenia, and thrombocytopenia. Vitamin B12 deficiency has been reported in less than 1% of patients taking esomeprazole. Long-term (e.g., generally 2 to 3 years or more) treatment with acid-suppressing agents can lead to malabsorption of vitamin B12 (cyanocobalamin). In a study of healthy volunteers, it was shown that omeprazole caused a significant reduction in cyanocobalamin absorption (vitamin B12 deficiency). One large case-controlled study compared patients with and without an incident diagnosis of vitamin B12 deficiency (n = 25,956 and 184,199, respectively). A correlation was demonstrated between vitamin B12 deficiency and gastric acid-suppression therapy. Patients receiving 2 years or more of a proton pump inhibitor (PPI)(OR, 1.65 [95% CI, 1.58 to 1.73]) or 2 years or more of an H2-receptor antagonist (OR, 1.25 [95% CI, 1.17 to 1.34]) were associated with having an increased risk for vitamin B12 deficiency. A dose-dependent relationship was evident, as daily doses greater than 1.5 PPI pills/day were more strongly associated with vitamin B12 deficiency (OR, 1.95 [95% CI, 1.77 to 2.15]) compared to daily doses less than 0.75 pills/day (OR, 1.63 [95% CI, 1.48 to 1.78]; p = 0.007 for interaction). The possibility of cyanocobalamin deficiency and pernicious anemia should be considered if clinical symptoms are observed. Neurological manifestations of pernicious anemia can occur in the absence of hematologic changes. Other potentially serious, but rare, adverse events that have been reported in spontaneous postmarketing reports include agranulocytosis and pancytopenia; however, causality cannot be assessed.

cystitis, dysmenorrhea, dysuria, glycosuria, hematuria, impotence (erectile dysfunction), increased urinary frequency, interstitial nephritis, menstrual irregularity, polyuria, proteinuria

Acute tubulo-interstitial nephritis (AIN or TIN) has been observed in patients taking PPIs and may occur at any point during PPI therapy. Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g., fever, rash or arthralgia). Discontinue esomeprazole and evaluate patients with suspected acute AIN. During clinical trials, renal, endocrine, and genitourinary (GU) adverse events reported (less than 1%) in patients receiving oral esomeprazole included: abnormal urine, albuminuria (proteinuria), cystitis, dysmenorrhea, dysuria, fungal infection, glycosuria, hematuria, impotence (erectile dysfunction), menstrual irregularity, increased urinary frequency, and polyuria. Erectile dysfunction has been reported in patients receiving PPIs during postmarketing experience.

lupus-like symptoms

Cutaneous lupus erythematosus (CLE), systemic lupus erythematosus (SLE), and lupus-like symptoms have occurred in patients taking PPIs, including esomeprazole. Both exacerbation and new onset of existing autoimmune disease have been reported, with the majority of PPI-induced lupus erythematosus cases being CLE. Subacute CLE (SCLE) is the most common form of CLE reported in patients treated with PPIs, occurring within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Histological findings were usually observed without organ involvement. SLE is less commonly reported; PI associated SLE is generally milder than non-drug induced SLE. The onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from infants to the elderly. Most patients presented with rash; however, arthralgia and cytopenia were also reported. Do not administer PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE occur, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks; serological testing (ANA) may be positive, and elevated serological test results may take longer to resolve than clinical manifestations.

bone fractures

Several published observational studies suggest that proton pump inhibitor (PPI)

therapy may be associated with an increased risk for osteoporosis-related bone fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose (defined as multiple daily doses) and long-term PPI therapy (a year or longer). Use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. In patients at risk for osteoporosis-related fractures, manage according to established treatment guidelines and ensure adequate vitamin D and calcium supplementation.

hypocalcemia, hypokalemia, hypomagnesemia

Hypomagnesemia, hypocalcemia, and hypokalemia have been reported during postmarketing esomeprazole use. Cases of hypomagnesemia have been reported in association with prolonged (3 months to more than 1 year) proton pump inhibitor (PPI) use. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in patients at risk. Low serum magnesium may lead to serious adverse reactions such as muscle spasm (tetany), seizures, and irregular heartbeat (arrhythmias). Consider monitoring electrolyte concentrations and supplementing electrolytes when needed. Discontinuation of PPI therapy may be necessary.

colitis

During postmarketing surveillance of esomeprazole, microscopic colitis has been reported. A link between the onset of microscopic colitis and PPI therapy has been suggested in case reports and case series. Reports and subsequent histological confirmation of both collagenous colitis and lymphocytic colitis, two distinct forms of microscopic colitis, have been observed in patients treated with lansoprazole, another PPI. One case series included 6 patients who developed microscopic colitis after a formulary switch to lansoprazole from omeprazole; upon lansoprazole discontinuation, associated loose stools resolved. The mechanism of this rare adverse reaction is not clear; however, an idiosyncratic immune reaction is suspected. Because small changes in the structures of PPIs may elicit different immunological responses, it is difficult to predict if this adverse effect can be expected with other PPIs. Until more is known about the association between PPIs and microscopic colitis, clinicians should advise patients to report prolonged watery loose stools and should consider PPI discontinuation or substitution in these patients.

C. difficile-associated diarrhea, candidiasis, pseudomembranous colitis, superinfection, vaginitis

C. difficile-associated diarrhea (CDAD) or pseudomembranous colitis has been reported

with esomeprazole. PPI therapy, such as esomeprazole, may be associated with an increased risk of CDAD, especially in hospitalized patients. The use of gastric acid suppressive therapy, such as PPIs, may increase the risk of enteric infection or superinfection by encouraging the growth of gut microflora. If pseudomembranous colitis is suspected or confirmed, institute appropriate fluid and electrolyte management, protein supplementation, C. difficile-directed antibacterial therapy, and surgical evaluation as clinically appropriate. Other infection-related events reported in less than 1% of patients include vaginitis and candidiasis reported as gastrointestinal candidiasis, moniliasis, and genital moniliasis.

laboratory test interference

Administration of esomeprazole may result in laboratory test interference, specifically serum chromogranin A (CgA) tests for neuroendocrine tumors, urine tests for tetrahydrocannabinol (THC), secretin stimulation tests, and diagnostic tests for H. pylori. Gastric acid suppression may increase serum CgA. Increased CgA concentrations may cause false positive results in diagnostic investigations for neuroendocrine tumors. To prevent this interference, temporarily stop esomeprazole at least 14 days before assessing CgA concentrations and consider repeating the test if initial concentrations are high. If serial tests are performed, ensure the same commercial laboratory is used as reference ranges may vary. Reports have suggested use of proton pump inhibitors (PPIs) may cause false positive urine screening tests for THC. If a PPI-induced false positive urine screen is suspected, confirm the positive results using an alternative testing method. Esomeprazole may cause a hyper-response in gastrin secretion to the secretin stimulation test, falsely suggesting gastrinoma. Health care providers are advised to temporarily stop esomeprazole at least 14 days prior to performing a secretin stimulation test to allow gastrin concentrations to return to baseline. PPIs are known to suppress H. pylori; thus, ingestion of a PPI within 2 weeks of performing diagnostic tests for H. pylori may lead to false negative results. At a minimum, instruct the patient to avoid the use of esomeprazole for at least 2 weeks prior to the test.

gastric polyps

Proton pump inhibitor (PPI) use is associated with an increased risk of fundic gland gastric polyps. The risk for gastric polyps increases with long-term PPI use, especially beyond 1 year. Gastric polyps/fundic gland polyps have been reported during postmarketing surveillance with esomeprazole. Patients are usually asymptomatic, and the polyps are identified incidentally on endoscopy. Gastroduodenal carcinoids have been reported in patients with Zollinger-Ellison (ZE) syndrome receiving long-term esomeprazole; however, the ZE condition itself is known to be associated with such tumors. The overall risk of carcinoid tumors during PPI therapy is low based on

cumulative safety experience; monitoring of serum gastrin levels during PPI therapy is generally not necessary. In one trial of patients (n = 25) with H2-receptor antagonist-resistant gastroesophageal reflux disease (GERD) treated with long-term (4 years or more) esomeprazole therapy, no cases of neoplasia or dysplasia were seen in biopsies. Use the shortest duration of PPI therapy appropriate to treat the specific condition. Symptomatic response to therapy with esomeprazole does not preclude the presence of gastric cancer or other malignancy. Consider additional follow-up and diagnostic testing in adults who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older adult patients, also consider an endoscopy.

drug-induced hypergastrinemia, gastric hypersecretion

Studies suggest that long-term PPI therapy is associated with temporal gastric hypersecretion shortly following treatment discontinuation. A similar and well-established response has been noted after withdrawal of H2 blockers. Profound gastric acid suppression during PPI therapy leads to a drug-induced hypergastrinemia and subsequent rebound acid hypersecretion. In this hypersecretory state, enterochromaffin-like cell hypertrophy also results in a temporal increase in serum chromogranin A (CgA) levels. It is unclear, however, if this hypersecretory reflex results in clinically significant effects in patients on or attempting to discontinue PPI therapy. A clinically significant effect may lead to gastric acid-related symptoms upon PPI withdrawal and possible therapy dependence. Studies in healthy subjects (H. pylori negative) as well as GERD patients, present conflicting data regarding whether PPI therapy beyond 8-weeks is associated with rebound acid hypersecretion and associated dyspeptic symptoms shortly following PPI cessation. Until more consistent study results shed light on this possible effect, it is prudent to follow current treatment guidelines employing the lowest effective dose, for the shortest duration of time in symptomatic patients. For patients requiring maintenance therapy, consider on demand or intermittent PPI therapy, step down therapy to an H2 blocker, and regularly assess the need for continued gastric suppressive therapy.

Description

Esomeprazole is the S-isomer of omeprazole and is a proton pump inhibitor (PPI). Esomeprazole is approved for the healing and maintenance of erosive esophagitis, for symptomatic gastroesophageal reflux disease (GERD), for use in combination with antibiotics to eradicate Helicobacter pylori (H. pylori) in patients with active or prior duodenal ulcer disease, for risk reduction of NSAID-associated gastric ulcer, for risk reduction of upper GI rebleeding after therapeutic endoscopy, and for pathological hypersecretory conditions, including Zollinger-Ellison syndrome. A non-prescription (OTC) form is available for the short-term (14 days or less) treatment of heartburn.

Esomeprazole has a greater bioavailability compared to omeprazole, which may contribute to higher healing rates reported in studies of erosive esophagitis. Per guidelines, no clear advantage has been demonstrated for the use of one PPI over another in the treatment of GERD. Traditional delayed-release PPIs should be administered 30 to 60 minutes before a meal for optimal response. PPIs have been associated with an increased risk of C. difficile-associated diarrhea (CDAD).

Mechanism Of Action

Esomeprazole is a substituted benzimidazole proton-pump inhibitor (PPI) that suppresses gastric acid secretion by inhibiting the gastric (H+, K+)-ATPase enzyme pump. Following activation in an acidic pH, esomeprazole binds irreversibly to the H+/K+ ATPase pump on the secretory surface of the parietal cell membrane. Subsequently, the secretion of hydrogen ions into the gastric lumen is inhibited. Gastric acid pump inhibitors block the final step of gastric acid production, and inhibit both basal and stimulus-induced acid secretion. Delayed-release doses of 20 mg and 40 mg esomeprazole maintained intragastric pH > 4.0 for 12.7 hours and 16.8 hours, respectively. Significant in vitro activity against Helicobacter pylori (H. Pylori) has been demonstrated for esomeprazole. Esomeprazole monotherapy increases the clearance rate of H. pylori; however, eradication does not occur without appropriate antimicrobial therapy.

Similar to omeprazole and other PPIs, hypergastrinemia can occur during esomeprazole therapy. Although prolonged hypergastrinemia has been associated with gastric tumors in rats, long-term studies of proton pump inhibitors do not suggest the development of tumors in humans.

Pharmacokinetics

Esomeprazole is administered orally and intravenously. It is 97% bound to plasma proteins. Metabolism occurs extensively in the liver to inactive metabolites via CYP2C19 and to a lesser extent by CYP3A4. The metabolites lack antisecretory activity. Esomeprazole is a time-dependent inhibitor of CYP2C19, resulting in autoinhibition and nonlinear pharmacokinetics. The systemic exposure (AUC) increases in a more than dose proportional manner after multiple oral doses of esomeprazole. Compared to the first dose, the systemic exposure (Cmax and AUC) at steady state following once daily dosing increased by 43% and 90%, respectively, compared to after the first dose for the 20 mg dose and increased by 95% and 159%, respectively, for the 40 mg dose. The plasma elimination half-life is approximately 1.5 hours. Less than 1% of parent drug is excreted in the urine with the remainder excreted as inactive metabolites in both the

urine and feces.

Affected cytochrome P450 (CYP450) isoenzymes and drug transporters: CYP2C19, CYP3A4
Esomeprazole is metabolized by CYP2C19 and CYP3A4, and it inhibits the CYP2C19 isoenzyme. Combined inhibitors of CYP2C19 and 3A4 may raise esomeprazole exposure, while inducers of CYP2C19 or CYP3A4 may reduce esomeprazole levels and drug efficacy. Esomeprazole is a time-dependent inhibitor of CYP2C19 and can increase the systemic exposure of co-administered drugs that are CYP2C19 substrates. In addition, administration of esomeprazole increases intragastric pH and can alter the systemic exposure of certain drugs that exhibit pH-dependent solubility. In vitro and in vivo drug interaction studies note that esomeprazole is not likely to inhibit CYP3A4, CYP1A2, CYP2A6, CYP2C9, CYP2D6, or CYP2E1.

Route-Specific Pharmacokinetics

- **Oral Route**

Esomeprazole dissolves rapidly in an acidic environment and is formulated as a capsule containing enteric-coated pellets or a delayed-release tablet. Multiple dosing at 40 mg/day results in 90% bioavailability versus 64% after a single 40 mg dose. Cmax is reached within 1 to 3.5 hours. The AUC of esomeprazole (the S-isomer) is 80% higher than with omeprazole (both S- and R-isomer) due to decreased clearance and first-pass elimination of the S-isomer. Clinically this allows more esomeprazole to reach the site of action and may contribute to higher efficacy rates. Compared to the first dose, the systemic exposure (Cmax and AUC0 to 24h) of esomeprazole at steady-state following once a day dosing increased by 43% and 90%, respectively, compared to after the first dose for the 20 mg dose and increased by 95% and 159%, respectively, for the 40 mg dose. The AUC of a single 40 mg dose of esomeprazole is decreased by 33 to 53% after food intake compared to fasting conditions.

- **Intravenous Route**

The pharmacokinetics of intravenous esomeprazole were determined in healthy adult subjects following once daily administration of 20 mg and 40 mg by constant rate of infusion over 30 minutes for 5 days. The pharmacokinetic profile for the 20 mg and 40 mg dose is as follows: AUC (5.11 and 16.21 micromoles x hour/L, respectively) and Cmax (3.86 and 7.51 micromoles/L, respectively).

- **Hepatic Impairment**

Data in patients with hepatic cirrhosis showed that the mean AUC of esomeprazole was 76% higher and the half-life was 29% longer compared with GERD patients with no hepatic dysfunction. However, cirrhotic patients with mild to moderate liver dysfunction (Child-Pugh classes A and B) exhibit similar pharmacokinetic parameters to otherwise

healthy GERD patients. Cirrhotic patients with severe hepatic insufficiency (Child-Pugh class C) exhibit AUCs that are 2 to 3 times higher than those with normal liver function; dose reduction is recommended in these patients.

- **Renal Impairment**

Pharmacokinetic parameters of esomeprazole are not altered in renal insufficiency; less than 1% of an esomeprazole dose is excreted unchanged in the urine.

- **Pediatrics**

Neonates and Infants

Pharmacokinetic simulation analysis of esomeprazole showed that steady-state plasma exposure after 2.5 mg/dose PO (infant weight 3 to 5 kg), 5 mg/dose PO (infant weight 5.1 to 7.5 kg), and 10 mg/dose PO (infant weight 7.6 to 12 kg), respectively, would be similar to that seen after 10 mg/dose PO in 1 to 11 year olds and 20 mg/dose PO in 12 to 18 year olds. After repeated doses of 1 mg/kg/day PO in infants 1 to 11 months of age (n = 8), the mean half-life was 0.93 hours. Following administration of oral and intravenous esomeprazole in neonates, the geometric mean for the apparent clearance (Cl/F) was 0.55 L/hour/kg and 0.17 L/hour/kg, respectively. The apparent clearance (CL/F) increases with age in pediatric patients with GERD from 1 month to 2 years of age.

Children

A small pharmacokinetic study of esomeprazole involving 31 children ages 1 to 11 years found dose- and age-dependent properties in this population. Doses of 5 mg/day and 10 mg/day PO were examined in patients aged 1 to 5 years and 10 mg/day and 20 mg/day PO were examined in patients aged 6 to 11 years. When normalized for body weight children 5 years of age and younger demonstrated a significantly higher clearance than the older children. The study suggests that a 10 mg/day PO dose in children ages 1 to 11 years of age results in similar exposure compared to a 20 mg/day PO dose in adults. Mean daily doses were 0.71 mg/kg in the 1 to 5-year-old group and 0.34 mg/kg in the 6 to 11-year-old group. For both age groups and all doses, the mean Cmax was reached in less than 2 hours, and the elimination half-life was less than 1 hour.

Adolescents

Pharmacokinetic parameters of esomeprazole in adolescents ages 12 to 17 years were similar to those observed in adult patients with symptomatic GERD.

- **Geriatric**

The AUC and Cmax of esomeprazole were both elevated in older adults compared to younger adult patients, but dose adjustments based on age are not needed.

- **Other**

CYP2C19 Poor Metabolizers

CYP2C19, a polymorphic enzyme, is involved in the metabolism of esomeprazole. The

CYP2C19*1 allele is fully functional while the CYP2C19*2 and *3 alleles are nonfunctional. There are other alleles associated with no or reduced enzymatic function. Patients carrying 2 fully functional alleles are extensive metabolizers and those carrying 2 loss-of-function alleles are poor metabolizers. In extensive metabolizers, esomeprazole is primarily metabolized by CYP2C19. The systemic exposure to esomeprazole varies with a patient's metabolism status, with poor metabolizers having the greatest exposure and extensive metabolizers having the least exposure. Approximately 3% of Caucasians and 15 to 20% of Asians are CYP2C19 poor metabolizers. Systemic esomeprazole exposures were modestly higher (approximately 17%) in CYP2C19 intermediate metabolizers (IM; n = 6) compared to extensive metabolizers (EM; n = 17) of CYP2C19. Similar pharmacokinetic differences were noted across these genotypes in a study of Chinese healthy subjects that included 7 EMs and 11 IMs. There is very limited pharmacokinetic information for poor metabolizers (PM) from these studies. At steady state following once daily administration of esomeprazole 40 mg given intravenously, the ratio of AUC in Poor Metabolizers to AUC in the rest of the population (EMs) is approximately 1.5. This change in exposure is not considered clinically meaningful.

Administration

For storage information, see the specific product information within the How Supplied section.

Oral Administration

Administer on an empty stomach, at least 60 minutes before meals. If given once daily, administer before the first meal of the day.
May be taken during antacid therapy.

Oral Solid Formulations

Delayed-release capsules
Administer whole, do not crush or chew the delayed-release, enteric-coated granules within the capsule.
Alternatively, for patients with difficulty swallowing, the capsule contents can be sprinkled on applesauce. The applesauce should not be hot. Once sprinkled on applesauce, swallow the mixture. Do not chew. Do not store the mixture for future use. The capsule contents appear to be stable for 30 minutes when suspended in yogurt, cultured milk, apple or orange juice, or tap water. When suspending the contents of a capsule in any of these solid foods or liquids, the mixture should be swallowed without chewing; do not mix and store for future use.

Nasogastric (NG) tube Administration
The capsules can be opened and the granules emptied into a 60 mL catheter-tipped syringe and mixed with 50 mL of water. It is important to only use a catheter-tipped syringe when administering through a NG tube.
Replace the plunger and shake the syringe vigorously for 15 seconds. Hold the syringe with the tip up and check for granules remaining in the tip. Do not administer the granules if they have dissolved or disintegrated.
Attach the syringe to the NG tube and deliver the contents of the syringe through the tube into the stomach.
After administering the granules, the NG tube should be flushed with additional water.
Administer the contents of the syringe immediately; do not store.

Delayed-release capsules and tablets (non-prescription esomeprazole magnesium capsules and tablets; e.g., Nexium 24HR):
Administer whole, do not crush or chew the delayed-release capsules; administer with a glass of water in the morning before eating.

Oral Liquid Formulations

Delayed-release oral suspension granules
Do not divide the suspension packet to obtain a smaller dosage. Use the appropriate packet size for the dose to be administered.
Do not crush or chew the granules.

Administration of a 2.5-mg or 5-mg packet
Empty the contents of the packet into a container with 1 teaspoon (5 mL) of water. Stir and leave 2 to 3 minutes to thicken. Re-stir the mixture before administration; administer within 30 minutes of preparation. Flush any residual drug left in a container with more water and administer immediately.
Nasogastric (NG) or gastric tube (French size 6 or larger) administration:
Add 5 mL of water to a catheter tipped syringe and then add the contents of a 2.5mg or 5mg packet. It is important to only use a catheter-tipped syringe when administering through an NG or gastric tube.
Immediately shake the syringe and leave 2 to 3 minutes to thicken.
Upon administration, shake the syringe again, and flush the contents through the NG or gastric tube into the stomach; administer within 30 minutes of preparation.
Refill the syringe with 5 ml of water, shake to rinse and flush any remaining contents from the NG or gastric tube into the stomach.

Administration of the 10-mg, 20-mg, or 40-mg packet
Empty into a container with 1 tablespoon (15 mL) of water. Stir and leave 2 to 3 minutes to thicken. Re-stir the mixture before administration; administer within 30 minutes of

preparation. Flush any residual drug left in a container with more water and administer immediately.
Nasogastric (NG) or gastric tube (French size 6 or larger) administration:
Add 15 mL of water to a catheter tipped syringe and then add the contents of a 10mg, 20mg, or 40mg packet. It is important to only use a catheter-tipped syringe when administering through an NG or gastric tube.
Immediately shake the syringe and leave 2 to 3 minutes to thicken.
Upon administration, shake the syringe again, and flush the contents through the NG or gastric tube into the stomach; administer within 30 minutes of preparation.
Refill the syringe with 15 mL of water, shake to rinse and flush any remaining contents from the NG or gastric tube into the stomach.

Injectable Administration

For intravenous administration only.
Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.
Oral antacids may be used during treatment with intravenous esomeprazole.

Intravenous Administration

Slow IV Push
IV push administration is indicated for adults only; IV infusion administration is recommended for pediatric patients.
Reconstitute the contents of 1 vial, either 20 mg or 40 mg, with 5 mL of 0.9% Sodium Chloride for Injection (NS).
Flush the IV line with either 0.9% Sodium Chloride injection, Lactated Ringer's, or 5% Dextrose injection both prior to and after administration.
Withdraw dose from vial.
Discard any unused portion of solution remaining in the vial.
Administer slowly over no less than 3 minutes.
Do NOT administer concomitantly with any other medications through the same IV site and/or tubing.
Storage of reconstituted injection: Store at room temperature up to 30 degrees C (86 degrees F) for up to 12 hours when diluted with 0.9% Sodium Chloride injection.

Intermittent intravenous (IV) infusion
Reconstitute the contents of 1 vial with 5 mL of 0.9% Sodium Chloride injection, 5% Dextrose injection, or Lactated Ringer's.
Prior to administration, further dilute the solution with 45 mL of 0.9% Sodium Chloride injection, 5% Dextrose injection, or Lactated Ringer's to a final concentration of 0.8 mg/mL (40 mg/50 mL).

Withdraw the appropriate volume from the standard infusion preparation to prepare the desired adult or pediatric dose.
Discard any unused portion of solution remaining in the vial.
Flush the IV line with either 0.9% Sodium Chloride injection, Lactated Ringer's, or 5% Dextrose injection both prior to and after administration.
Infuse IV over 10 to 30 minutes.
Do NOT administer concomitantly with any other medications through the same IV site and/or tubing.
Storage of infusion solutions: Store at room temperature up to 30 degrees C (86 degrees F). Administer solutions diluted with 0.9% Sodium Chloride injection or Lactated Ringer's within 12 hours; administer solutions diluted with 5% Dextrose injection within 6 hours.

Continuous intravenous (IV) infusion
Reconstitute each of two 40 mg vials (80 mg total) with 5 mL of 0.9% Sodium Chloride injection; further dilute in 100 mL 0.9% Sodium Chloride injection to a final concentration of 0.8 mg/mL for preparation of both the loading dose and separate continuous infusion.
Flush the IV line with either 0.9% Sodium Chloride injection, Lactated Ringer's, or 5% Dextrose injection both prior to and after administration.
After reconstitution, give the 80 mg IV bolus as an IV infusion over a period of 30 minutes.
Follow the IV bolus with the continuous infusion at a rate of 8 mg/hour (i.e., 10 mL/hour) for 71.5 hours.
Storage of infusion solutions: Store at room temperature up to 30 degrees C (86 degrees F). Administer solutions diluted with 0.9% Sodium Chloride injection within 12 hours.

Maximum Dosage Limits

- **Adults**
  20 mg/day PO for heartburn (OTC); 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day is used off-label for H. pylori eradication; 40 mg/day IV for GERD; 80 mg IV for 1 dose, then 8 mg/hour for upper GI rebleeding prophylaxis after therapeutic endoscopy; up to 240 mg/day PO for Zollinger-Ellison syndrome.
- **Geriatric**
  20 mg/day PO for heartburn (OTC); 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day is used off-label for H. pylori eradication; 40 mg/day IV for GERD; 80 mg IV for 1 dose, then 8 mg/hour for upper GI rebleeding prophylaxis after therapeutic endoscopy; up to 240 mg/day PO for Zollinger-Ellison syndrome.
- **Adolescents**

weight 55 kg or more: 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day has been used off-label; 20 mg/day IV.
weight less than 55 kg: 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day has been used off-label; 10 mg/day IV.

- **Children**
  12 years and weight 55 kg or more: 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day has been used off-label; 20 mg/day IV.
  12 years and weight less than 55 kg: 40 mg/day PO is FDA-approved maximum; however, up to 80 mg/day has been used off-label; 10 mg/day IV.
  1 to 11 years and weight 55 kg or more: 20 mg/day PO and 20 mg/day IV are FDA-approved; however, up to 3.3 mg/kg/day PO (Max: 80 mg/day PO) has been used off-label.
  1 to 11 years and weight 20 to 54 kg: 20 mg/day PO and 10 mg/day IV are FDA-approved; however, up to 3.3 mg/kg/day PO (Max: 80 mg/day PO) has been used off-label.
  1 to 11 years and weight less than 20 kg: 10 mg/day PO and 10 mg/day IV are FDA-approved; however, up to 3.3 mg/kg/day PO (Max: 40 mg/day) has been used off-label.

- **Infants**
  In general for infants, maximum doses are 1.33 mg/kg/day PO and 0.5 mg/kg/day IV.
  weight 7.6 to 12 kg: 10 mg/day PO; 0.5 mg/kg/day IV.
  weight 5.1 to 7.5 kg: 5 mg/day PO; 0.5 mg/kg/day IV.
  weight 3 to 5 kg: 2.5 mg/day PO; 0.5 mg/kg/day IV.

- **Neonates**
  Safety and efficacy have not been established; however, 0.5 mg/kg/day PO/IV has been used off-label.

Dosage Forms

- CVS Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- CVS Esomeprazole Magnesium 24 Hour Clear Minis 20mg Delayed-Release Capsule
- Esomeprazole Magnesium 10.2mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 10mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 11.1mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 2.6mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 2.8mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 20.706mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 20mg Oral capsule, gastro-resistant pellets
- Esomeprazole Magnesium 21.8mg Powder for Oral susp/PWD

- Esomeprazole Magnesium 22.3mg Oral capsule, gastro-resistant pellets
- Esomeprazole Magnesium 22.3mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 40mg Oral capsule, gastro-resistant pellets
- Esomeprazole Magnesium 40mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 41.411mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 43.5mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 44.5mg Oral capsule, gastro-resistant pellets
- Esomeprazole Magnesium 44.5mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 5.2mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 5.6mg Powder for Oral susp/PWD
- Esomeprazole Magnesium 5mg Powder for Oral susp/PWD
- Esomeprazole Sodium 20mg Powder for solution for injection
- Esomeprazole Sodium 40mg Powder for solution for injection
- Foster & Thrive Acid Reducer 20mg Delayed-Release Capsule
- GNP Esomeprazole Magnesium 20mg Delayed-Release Capsule
- GNP Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- GNP Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- GoodSense Esomeprazole Magnesium 20mg Delayed-Release Capsule
- Kirkland Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- Leader Esomeprazole Magnesium 20mg Delayed-Release Capsule
- Leader Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- Leader Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Tablet
- Nexium 10mg Delayed-Release Powder for Suspension
- Nexium 2.5mg Delayed-Release Powder for Suspension
- Nexium 20mg Delayed-Release Capsule
- Nexium 20mg Delayed-Release Powder for Suspension
- Nexium 24HR 20mg Delayed-Release Capsule
- Nexium 24HR 20mg Delayed-Release Capsule
- Nexium 24HR 20mg Delayed-Release Tablet
- Nexium 24HR Clear Minis 20mg Delayed-Release Capsule
- Nexium 40mg Delayed-Release Capsule
- Nexium 40mg Delayed-Release Capsule
- Nexium 40mg Delayed-Release Capsule
- Nexium 40mg Delayed-Release Powder for Suspension
- Nexium 5mg Delayed-Release Powder for Suspension
- Quality Choice Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- Walgreens Esomeprazole Magnesium 20mg Delayed-Release Capsule (Cool Mint)
- Walgreens Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- Walgreens Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Capsule
- Walgreens Esomeprazole Magnesium 24 Hour 20mg Delayed-Release Tablet

Dosage Adjustment Guidelines

Hepatic Impairment

For most indications in adult patients:
Mild to moderate hepatic impairment: No dosage adjustment is recommended.
Severe hepatic insufficiency (Child-Pugh Class C): Do not exceed 20 mg/day PO or IV for most patients. For adults with severe hepatic insufficiency (Child-Pugh Class C) and pathological hypersecretory conditions including Zollinger-Ellison Syndrome, a starting dosage of 20 mg PO or IV twice daily is recommended.

For upper GI rebleeding prophylaxis after therapeutic endoscopy in adults with hepatic impairment:
No dosage adjustment of the initial 80 mg IV infusion is necessary. Do not exceed a maximum continuous infusion of esomeprazole 6 mg/hour IV for 71.5 hours in patients with mild to moderate liver impairment (Child-Pugh Classes A and B); and, do not exceed a maximum continuous infusion of 4 mg/hour IV for 71.5 hours in patients with severe liver impairment (Child-Pugh Class C).

Renal Impairment

No dosage adjustment is necessary.

Intermittent hemodialysis:
No dosage adjustment is necessary. Due to high protein binding, esomeprazole is not expected to be removed by hemodialysis.