drug information perspectives

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Contents

ESOMEPRAZOLE

SYNONYM(S): S-isomer of omeprazole; S-omeprazole

TRADE NAME: Nexium

CLASSIFICATION: Gastric acid secretion suppressant; gastric acid proton pump (H+/K+ ATPase) inhibitor; PPI; benzimidazole

ACTION
- Increases intragastric pH by irreversibly blocking the hydrogen/potassium adenosine triphosphatase (H+/K+ ATPase) enzyme system (proton pump) that mediates hydrochloric acid secretion by gastric parietal cells.
- Extent of gastric acid suppression may be influenced by cytochrome P450 CYP2C19 genotype (highest in poor metabolizers; lowest in extensive metabolizers).

PHARMACOKINETICS
- ***Half-life***: 1.0 - 1.5 h.
- ***Absorption***: Oral doses rapidly absorbed; peak plasma concentration occurs in approximately 1.5-2 hours. Absolute oral bioavailability is 60-64% after single doses, 78-89% after 5 daily doses. Concomitant food intake delays and reduces absorption; AUC reduced by 43-53%.
- ***Distribution***: Plasma protein binding 97%.
- ***Metabolism***: Extensively metabolized by cytochrome P450 CYP3A4 (main enzyme) and CYP2C19 enzymes to form inactive metabolites.
- ***Elimination***: Mainly urinary; approximately 80% of oral dose excreted as metabolites and less than 1% as parent drug. Remainder excreted in feces.
- ***Special Populations***:
- ***Elderly*** (age above 71 years): AUC and Cmax modestly increased (by 25% and 18%, respectively).
- ***Hepatic impairment***: Mild to moderate hepatic impairment: Little change in drug metabolism. Severe hepatic impairment: Metabolism significantly reduced and AUC doubled.
- ***Pharmacogenetics***: Poor metabolizers of CYP2C19 (approximately 3% of Caucasians, and 13% to 20% of Asians who lack CYP2C19 activity): Metabolism decreased, resulting in AUC that is 2-3 times higher than AUC for

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extensive metabolizers. However, consensus is lacking on need for genotyping or dose adjustment; there may be increased metabolism by CYP3A4.

USES AND EFFICACY

- **Helicobacter pylori eradication and treatment of patients with H. pylori-associated duodenal ulcer**: Effective component of triple therapy with clarithromycin plus either amoxicillin (ECA) or metronidazole (ECM). ECA for 7 days produces H. pylori eradication rate ranging from 74% to 90%, and duodenal ulcer healing rate of approximately 90%.
- **Treatment and prevention of NSAID-related ulcers**: Like other PPIs, esomeprazole is effective for prevention and treatment of NSAID- or COX-2 inhibitor-associated gastrointestinal damage (including gastric and duodenal ulcers) and associated dyspeptic symptoms.
- **Gastroesophageal reflux disease (GERD):** Effective treatment for GERD with non-erosive or erosive esophagitis, and maintenance of healed erosive esophagitis.
- **Treatment of non-erosive symptomatic gastroesophageal reflux disease (NERD)(heartburn, regurgitation):** Four weeks of treatment completely resolves heartburn in 33-70% of patients.
- **Treatment of GERD with erosive esophagitis (reflux esophagitis)**: Eight weeks of treatment produces esophageal healing in 80-94% of patients.
- **Maintenance of healed erosive esophagitis**: Healing is maintained in 80-90% of patients (vs 29% with placebo). Among patients with maintained healing, more than 70% had no heartburn.
- **Zollinger-Ellison Syndrome**.

Clinical course:

- Maintains intragastric pH above 4 for 12-15 hours/day with once daily dosing of 20-40mg and for 17 hours/day with twice daily dosing of 20mg.
- Relieves gastrointestinal symptoms associated with NSAID or COX-2 inhibitor therapy in 10-11 days.
- In patients with symptomatic, non-erosive GERD, heartburn resolves after about 7 days and sustained relief is achieved after about 12 to 17 days of treatment.
- GERD with erosive esophagitis: Symptomatic relief begins in 2 days with sustained relief in 6-7 days. Symptomatic relapse usually occurs following discontinuation of PPI therapy.

Major clinical trials:

***Helicobacter pylori eradication and treatment of patients with H. pylori-associated duodenal ulcer*:** In a randomized, placebo-controlled, double-blind trial, 446 *H. pylori*-positive patients with active duodenal ulcer were randomized to receive twice daily treatment with either esomeprazole 20 mg or omeprazole 20 mg in combination with amoxicillin 1 g and clarithromycin 500 mg for 1 week, after which the omeprazole group received omeprazole monotherapy once daily and the esomeprazole group received placebo for 3 weeks. After 4 weeks, ulcer healing rates for the omeprazole/omeprazole and esomeprazole/placebo groups were 91% and 92%, and *H. pylori* eradication rates were 86% and 88%, respectively. Most common adverse events were abnormal taste and diarrhea/loose stools, which were attributed to clarithromycin and amoxicillin, respectively, and occurred with similar frequency in the esomeprazole and omeprazole groups (13% vs 12%; 9% vs 9%). These results indicate that a 7-day regimen is sufficient for duodenal ulcer healing. *Study limitation*: Failure to include esomeprazole monotherapy arm precluded evaluation of continued esomeprazole therapy on ulcer healing rate and gastrointestinal symptom relief.

Treatment of symptoms of nonsteroidal anti-inflammatory drug (NSAID)-induced gastrointestinal injury: NASA1, SPACE1: Two double-blind studies randomized 608 (NASA1) and 556 (SPACE1) patients with upper gastrointestinal symptoms associated with continuous NSAID, COX-2 inhibitor, or high-dose aspirin use to once daily treatment with esomeprazole 20 mg or 40 mg, or placebo. No patients had gastroduodenal ulcers or erosive esophagitis at baseline. After 4 weeks of treatment, both doses of esomeprazole produced statistically significant reductions in patient-reported upper gastrointestinal symptoms (pain, discomfort, or burning), significant increases in percentage of symptom-free days (27-31% vs 14-21% with placebo), significant reductions in antacid use, and significant improvement in health-related quality of life. The cumulative proportion of patients in the esomeprazole 20 mg, 40 mg, and placebo groups who achieved upper GI symptom relief were: 70%, 72%, and 58%, respectively (NASA1) and 72%, 68%, and 51%, respectively (SPACE1). Esomeprazole (both doses) was effective in maintaining symptom relief for 6 months. Gastrointestinal symptom relapse rates were 24% and 29% with esomeprazole 20 mg and 40 mg, respectively, vs 38% with placebo. *Study limitations*: Large placebo effect observed (confounds efficacy outcome). Results apply only to patients without ulcers who have upper abdominal gastrointestinal symptoms. Lack of symptoms does not mean lack of ulceration. Small benefit over placebo.

Treatment of NSAID-related gastric ulcers*: *Versus ranitidine: A double-blind study compared gastric ulcer healing efficacy of esomeprazole 40 mg or 20 mg once daily with ranitidine 150 mg twice daily in 406 patients receiving nonselective NSAIDs or COX-2 inhibitors who had at least one gastric ulcer. Patients continued to receive NSAIDs/COX-2 inhibitors. Healed gastric ulcer rates were statistically significantly higher with esomeprazole 40 mg and 20 mg than with ranitidine after 4 weeks (78%, 79%, vs 67%, respectively), and after 8 weeks (92%, 88%, vs 74%, respectively). Numerically fewer adverse events occurred with esomeprazole 40 mg and 20 mg than with ranitidine (61% and 56% vs 75%). *Limitation*: This study was too short to evaluate ulcer recurrence rate during extended treatment.

Prevention of NSAID-related gastrointestinal injury: VENUS, PLUTO (2006): In two randomized, double-blind, placebo-controlled studies, 844 (VENUS) and 585 (PLUTO) patients requiring daily NSAIDs or COX-2 inhibitor therapy received esomeprazole 20 mg or 40 mg, or placebo for 6 months. All patients had ulcer risk factors (age at least 60 years and/or ulcer in past 5 years) but were ulcer-free at baseline. At 6 months, estimated gastric or duodenal ulcer rates in VENUS and PLUTO for esomeprazole 20 mg (5%, 5%) and 40 mg (4%, 4%) groups were statistically significantly lower than rates for placebo groups (17% and 11%). Pooled analysis of data for patients receiving COX-2 inhibitors showed statistically significantly lower ulcer rates with esomeprazole 20 mg or 40 mg (0.9% and 4%) than with placebo (17%). NSAID-associated upper abdominal pain, discomfort, or burning was also significantly reduced with esomeprazole (both doses). Adverse event incidence with esomeprazole was similar to that with placebo. *Limitation*: Study does not provide information on whether the ulcer risk is lower with a PPI plus COX-2 inhibitor than with a PPI plus a nonselective NSAID.

Treatment of non-erosive symptomatic gastroesophageal reflux disease (NERD)(heartburn, regurgitation) (2004): A randomized, double-blind trial involving 1,282 patients compared esomeprazole 20 mg, esomeprazole 40 mg, and omeprazole 20 mg, given once daily. After 4 weeks, 61%, 57%, and 58% of patients in each of these regimens had complete resolution of heartburn. There were no significant differences in success rate or time to onset. *Study limitation*: Concomitant antacid or H2 receptor antagonist usage not recorded.

Treatment of GERD with erosive esophagitis (reflux esophagitis) (2000): A randomized, double-blind trial in 1,960 patients with reflux esophagitis compared esomeprazole 20 mg, esomeprazole 40 mg, and omeprazole 20 mg, given once daily. For each treatment, esophageal healing rates at week 8 were 90%, 94%, and 87%, respectively, and complete heartburn resolution rates at week 4 were 61%, 65%, and 57%. Although healing rates for both esomeprazole doses and heartburn resolution rate for esomeprazole 20 mg reached statistical significance vs omeprazole 40 mg, the differences were small. Sustained resolution of heartburn was achieved sooner with esomeprazole 40 mg (5 days) than with esomeprazole 20 mg (8 days) or omeprazole 20 mg (9 days). The three treatments were similar in tolerability and side effects, the most common being headache, abdominal pain, and diarrhea, all occurred with similar frequency. *Study limitation*: No evaluation of concomitant antacid usage.

Place in therapy
- ***Helicobacter pylori eradication and treatment of patients with H. pylori-associated duodenal ulcer***: Effective component of triple therapy for *H. pylori* eradication to treat and reduce recurrence of duodenal ulcer. Amoxicillin-based therapies are preferred because of increasing metronidazole resistance.
- ***Prevention of NSAID-related gastrointestinal injury***: PPI co-therapy recommended in patients at increased risk for NSAID (or COX-2 inhibitor)-associated gastrointestinal damage.
- ***For acute and maintenance treatment of GERD***, PPIs are drugs of first choice, except for patients with milder GERD which may be adequately controlled with over-the-counter antacids or H2 receptor antagonists.

Investigational/Unapproved Uses:
- ***Uninvestigated dyspepsia***: Canadian guidelines recommend PPI therapy for 4 to 8 weeks as first line therapy in patients aged up to 50 years with dyspepsia symptoms but without dominant heartburn who have no alarm features (eg, persistent vomiting, gastrointestinal bleeding, anemia, abdominal mass, unexplained weight loss, dysphagia) and who are H-pylori-negative, or who remain symptomatic after H. pylori eradication.

Advantages:
- Long duration of inhibition of gastric acid secretion; clinical relevance unknown.
- As effective as other PPIs at therapeutically equivalent doses.

- No dose adjustment required in elderly or renally impaired patients.
- Usually well tolerated.
- Effective with once-daily administration.

Disadvantages:
- Potential drug interactions.

Comparisons
Versus other PPI:
Clinical trial data indicate that esomeprazole's side effect profile is similar to that of other PPIs. The goal of acid suppression is to maintain the intragastric pH above 4 (the level associated with gastric healing) for a longer part of each day. Given once daily doses, esomeprazole 40 mg maintains intragastric pH above 4 for approximately 13-17 hours, which is longer than with omeprazole 20 mg or 40 mg, pantoprazole 40 mg, lansoprazole 30 mg, or rabeprazole 20 mg, and shorter than with tenatoprazole 40 mg. However, these differences do not necessarily produce a clinically significant difference in esophageal acid exposure or overall efficacy.
- ***Helicobacter pylori eradication and treatment of patients with H. pylori-associated duodenal ulcer***: At doses providing equivalent gastric acid inhibition, esomeprazole is similar in efficacy to other PPIs used in triple therapy. No significant differences among PPIs used in *H. pylori* eradication regimens; treatment failure is usually due to antibiotic resistance.
- ***For acute and maintenance treatment of GERD***: Esomeprazole 40 mg does not appear to provide a therapeutic advantage over other PPIs.
- ***Treatment of non-erosive symptomatic gastroesophageal reflux disease (NERD)(heartburn, regurgitation)***: Efficacy comparable to omeprazole 20 mg.
- ***Treatment of GERD with erosive esophagitis (reflux esophagitis):*** At equivalent doses in comparative trials, esophageal healing rates at 8 weeks were similar or only 2-5% higher with esomeprazole 40 mg than with lansoprazole 30 mg, or pantoprazole 40 mg, and only 2-10% higher than with omeprazole 20 mg.
- ***Maintenance of healed erosive esophagitis***: Esomeprazole 20 mg is only modestly more effective than lansoprazole 15 mg or pantoprazole 20 mg in maintaining healing (9-12% higher healing rate) and providing freedom from heartburn (3-7% higher rate) at 6 months.

CONTRAINDICATIONS AND PRECAUTIONS

Contraindications
- **Hypersensitivity** to esomeprazole or any other benzimidazoles (omeprazole, lansoprazole, pantoprazole, rabeprazole)

Precautions
- Prior to initiating therapy, **rule out malignancy**, especially if alarm symptoms (e.g., unexplained significant weight loss, dysphagia, hematemesis, melena, persistent vomiting) are present or gastric ulcer is suspected or present (symptom relief may mask/delay diagnosis).
- As with all PPIs, gastric enterochromaffin-like cell **hyperplasia** secondary to hypergastrinemia has occurred with esomeprazole (there is concern for potential development of gastric malignant histologic changes during long-term therapy, especially in H. pylori-positive patients and poor metabolizers).
- **Severe liver dysfunction**: Metabolism impaired, resulting in high plasma drug concentrations (potential increased side effects); limit dose.
- **Acute interstitial nephritis**: reported with esomeprazole (and other marketed PPIs). Check serum creatinine level in suspected cases.
- **Report** any unexpected or serious adverse reactions to Health Canada's adverse drug reaction monitoring program (toll free telephone 1-866-234-2345, toll free fax 1-866-678-6789).

PREGNANCY AND LACTATION
Fetal teratogenicity risk considered low, based on animal and human data for omeprazole. However, risk of birth defects following in utero exposure to omeprazole (and PPIs in general) is unclear, as both healthy offspring and those with birth defects (including anencephaly, cardiac defects, facial anomaly, hypospadias) have been reported, and other factors, such as disease severity and concomitant drugs, may have contributed to birth anomalies.

Nonsystemically absorbed drugs are first-line choices for GERD symptoms (see Omeprazole monograph). PPIs should be reserved for severe intractable symptoms or complicated GERD; may be used for aspiration prophylaxis during labor. Use during pregnancy only if benefit outweighs potential fetal risk.

The related drug omeprazole is excreted in breast milk. Use during breastfeeding not recommended because of insufficient safety data and carcinogenicity in rats. One case report of use during breastfeeding reported no adverse effects on breastfed infant.

SIDE EFFECTS
Generally well tolerated.

Cardiovascular: Rarely (<1%) hypertension, tachycardia.

CNS: Headache (3-10% vs placebo 1-7%). Rarely, dizziness, apathy, increased appetite, asthenia, confusion, aggravated depression, fatigue, hypertonia, hypesthesia, insomnia, migraine, nervousness, paresthesia, sleep disorder, somnolence, tremor, vertigo.

Dermatologic: Rarely, acne, angioedema, dermatitis, pruritus, rash, increased sweating, urticaria, Stevens-Johnson Syndrome, TEN, erytheme multiforme.

Gastrointestinal: Diarrhea (2-7% vs 1-3% with placebo); gastritis (5%); abdominal pain (2-4% vs 1% with placebo); nausea (2-4% vs 1-2% with placebo); flatulence (2-5% vs 1-2% with placebo); constipation (2% vs 1% with placebo); dry mouth (1%). Rarely (<1%) enlarged abdomen, anorexia, bowel irregularity, dyspepsia, dysphagia, epigastric pain, eructation, frequent stools, gastroenteritis, gastrointestinal dysplasia, gastrointestinal hemorrhage, tongue edema, ulcerative stomatitis, pharynx disorder. Gastric fundal polyps (case report; also reported with other PPIs; considered benign but monitoring recommended). Hypergastrinemia; enterochromaffin-like cell hyperplasia (but no dysplasia or neoplasms).

Genitourinary: Rarely, albuminuria, cystitis, dysmenorrhea, dysuria, fungal infection, genital moniliasis, glycosuria, frequency, polyuria, vaginitis, hematuria. Female loss of libido (case report associated with increased esomeprazole exposure in a patient with cytochrome P450 CYP2C19 genetic polymorphism; induction of CYP3A-mediated testosterone metabolism suspected). Acute interstitial nephritis (several cases reported with esomeprazole; also reported with other PPIs; renal function is usually restored following discontinuation of PPI, but some cases have not regained full renal function and have required long-term dialysis); case reports of acute and chronic renal failure and renal impairment. Gynecomastia (very rare, also reported rarely with omeprazole and other PPIs; variable time to onset ranging from 8 days to 4 years after start of omeprazole therapy, possible contribution from concomitant medications in some cases; most cases resolved but some did not; presumed mechanism is inhibition of CYP3A4-mediated estradiol metabolism, causing increase in estrogen).

Hematologic: Rarely, anemia, cervical lymphadenopathy, epistaxis, leukocytosis, leukopenia, thrombocytopenia.

Hepatic: Rarely, bilirubinemia, increased liver enzymes.

Metabolic: Rarely, facial, leg, peripheral or generalized edema; goiter, hyperuricemia, hyponatremia, thirst, vitamin B12 deficiency, weight gain/loss.

Neuromuscular: Rarely (<1%), arthralgia, worsening of arthritis, arthropathy, cramps, fibromyalgia syndrome, hernia, polymyalgia rheumatica, myalgia, myositis, rhabdomyolysis.

Respiratory: Respiratory infection (4-6% vs 0-3% with placebo), sinusitis (2%). Rarely, worsening of asthma, cough, dyspnea, hiccups, larynx edema, pharyngitis, rhinitis.

Other: Central fever with severe cephalalgia and myalgia (case report). Increased fractures (reported for proton pump inhibitors).

INTERACTIONS
Esomeprazole inhibits CYP2C19, 3A4 and 2C9.

DRUG	EFFECT	MECHANISM	IMPORTANCE
Atazanavir	Decreased atazanavir plasma concentration to subtherapeutic level	Unknown	Avoid; switch to fosamprenavir
Calcium Carbonate*	Decreased calcium concentrations	Decreased pH-dependent absorption	Caution; space doses
Clarithromycin	Increased esomeprazole concentrations	Decreased metabolism	Caution; monitor for increased side effects
Clopidogrel	Decreased efficacy of clopidogrel	Decreased metabolic activation	Caution
Diazepam	Potential increased sedation	Decreased diazepam metabolism (CYP2C19)	Caution; monitor; adjust dose
Digoxin*	Increased digoxin concentration	Possible increased absorption due to elevation of gastric pH	Caution; monitor for digoxin toxicity; adjust dose
Fluconazole*	Possible increased esomeprazole concentrations	Decreased metabolism	Caution; monitor for increased side effects
Fluvoxamine**	Possible increased esomeprazole concentrations	Inhibition of metabolism in extensive metabolizers of CYP2C19	Caution; monitor for increased side effects
Ginkgo biloba*	Decreased esomeprazole concentrations	Increased metabolism (CYP2C19)	Avoid or monitor for reduced efficacy; adjust dose
Itraconazole	Decreased itraconazole concentrations	Decreased absorption due to elevation of gastric pH	Consider using another antifungal

Ketoconazole	Decreased ketoconazole concentrations	Decreased absorption due to elevation of gastric pH	Consider using another antifungal
Moclobemide*	Possible increased esomeprazole and moclobemide concentration (extensive metabolizers)	Decreased metabolism by CYP2C19 in extensive metabolizers	Caution; monitor for increased side effects
St John's Wort*	Possible decreased esomeprazole concentration	Increased metabolism (CYP2C19)	Caution; monitor response
Sucralfate	Decreased esomeprazole bioavailability	Decreased absorption	Take esomeprazole at least 30 minutes before sucralfate
Tolterodine extended release*	Increased peak levels of tolterodine and its active metabolite	Faster drug release due to elevated gastric pH	Caution; space doses, monitor
Triazolam	Potential increased sedation	Decreased triazolam metabolism (CYP2C19)	Caution; monitor; adjust dose
Voriconazole	Increased esomeprazole levels	Decreased metabolism	Caution, monitor
Warfarin	Increased anticoagulant effect	Decreased warfarin metabolism	Monitor INR

* Interaction reported for omeprazole
**Interaction reported for lansoprazole

DOSAGE
Guidelines:
- Doses should be administered at least 1 hour before a meal (food decreases absorption). Tablets should be swallowed whole and not chewed or crushed.
- For patients who have difficulty swallowing whole tablets: Sachet granules: Mix contents of one sachet with 15mL water. Let thicken for a few minutes. Stir again. Drink within 30 minutes. Rinse container with water and drink that as well.

- Administration via nasogastric tube: Sachet granules: Add 1 sachet to 15mL water in a syringe. Shake. Leave to thicken a few minutes. Shake. Inject into nasogastric or gastric tube. Refill syringe with 15mL water, shake, and flush the remainder in the NG tube into the stomach.

Adults:
- ***Helicobacter pylori eradication and treatment of patients with H. pylori-associated duodenal ulcer:*** Oral: Triple Therapy: 20mg in combination with amoxicillin 1000 mg and clarithromycin 500 mg, all twice daily for 7 days. See also the AMOXICILLIN and CLARITHROMYCIN monographs.
- ***Treatment of NSAID-associated gastric ulcer***: Oral: 20mg once daily for 4-8 weeks.
- ***Prevention of NSAID-related gastric ulcer:*** Oral: 20mg once daily.
- ***Treatment of non-erosive symptomatic gastroesophageal reflux disease (NERD)(heartburn, regurgitation):*** Oral: 20mg once daily for 2 to 4 weeks. If symptoms do not resolve completely after 4 weeks, an additional 4 weeks of treatment may be considered.
- ***Maintenance of non-erosive reflux disease (NERD):*** Oral: On-demand therapy (brief course of treatment when symptoms recur) at the 20 mg dose.
- ***Treatment of GERD with erosive esophagitis (reflux esophagitis):*** Oral: 40mg once daily for 4 to 8 weeks. Healing usually occurs within 4 weeks. An additional 4 weeks of treatment is recommended if esophagitis has not healed or if symptoms persist.
- ***Maintenance of healed erosive esophagitis***: Oral: 20mg once daily. Note: controlled clinical trial data beyond 6 months is not available. Patients with erosive esophagitis should be maintained with continuous once daily doses. Intermittent and on-demand treatment (taken only when symptoms recur) is inadequate for maintaining healing. Long-term PPI therapy is required in most patients to maintain esophagitis healing and symptom control.
- ***Zollinger-Ellison Syndrome***: Oral: Initially 40mg twice a day. Adjust as needed. Rarely, up to 80mg three times daily has been used.

Elderly: No dose adjustment required.

Children 1-11 years:
Treatment of reflux esophagitis: Oral: Weight less than 20kg: 10mg once daily for 8 weeks. Weight 20kg or more: 10-20mg once daily for 8 weeks.
Treatment of non-erosive reflux disease (NERD): Oral: 10mg once daily for up to 8 weeks.

Children 12-17 years:
Treatment of reflux esophagitis: Oral: 20-40mg once daily for 4-8 weeks.
Treatment of non-erosive reflux disease (NERD): Oral: 20mg once daily for 2-4 weeks.

Renal impairment: No dose adjustment required.

Hepatic impairment: Severe hepatic function impairment: Oral: Maximum 20mg daily. Mild or moderate liver function impairment: No dose adjustment required.

Pharmacogenetics: Poor metabolizers of CYP2C19 may have higher drug levels; consensus is lacking on need for genotyping or dose adjustment (see PHARMACOKINETICS).

NURSING IMPLICATIONS
Once daily oral administration in the morning, at least 1 hour before breakfast, is adequate for most indications.

Tablets should be swallowed whole, and not chewed, crushed or split. For patients who have difficulty swallowing whole tablets, or who have a nasogastric tube, granules are available for oral suspension.

At least half of patients with symptomatic, non-erosive GERD experience complete relief of heartburn within 1 week after starting treatment.

The majority of patients with erosive GERD require 4 to 8 weeks of treatment for healing of damaged esophageal tissue to take place. Emphasize to the patient the importance of completing the full course of therapy, even though they may experience relief of gastrointestinal pain, heartburn, or other symptoms.

For treatment of peptic ulcer caused by Helicobacter pylori, esomeprazole is usually given in combination with antibiotics for a minimum period of 7 days. The patient should be made aware that the therapy must be fully completed in order to completely eliminate the bacteria.

Store in the original blister package or sachet at room temperature, protected from moisture, because the tablets and granules are sensitive to moisture.

PATIENT INSTRUCTIONS

Esomeprazole (ess-oh-MEP-ra-zole) reduces stomach acid. It is used to relieve severe heartburn or other symptoms of acid reflux (esophagitis), heal tissue damage caused by acid reflux, heal peptic ulcers, and heal and/or prevent ulcers that can be caused by nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin. In the treatment of peptic ulcers, it is often used in combination with antibiotics to get rid of the bacteria that causes ulcers.

Before taking this medication, be sure that your physician is aware if you have any of the following conditions: history of allergy or an adverse reaction to other proton pump inhibitors; liver disease; pregnancy or considering pregnancy; breast-feeding.

For the treatment of ulcers or acid reflux, this medication is usually taken once daily in the morning. Take the dose at least 1 hour before a meal.

You may take antacids as well, if needed for stomach discomfort.

The tablets must be swallowed whole with noncarbonated water. Do not crush, split or chew the tablets. If you have difficulty swallowing, the tablets can also be put in a glass of plain noncarbonated water. Do not use other liquids as they may damage the tablet contents. Stir until the tablets break up and drink the suspended tablet particles immediately or within 30 minutes. Do not chew or crush the solid pieces of the tablet; they contain the medication. To make sure you have taken all of the medication, rinse the glass thoroughly with half a glass of water and drink the contents.

For patients who have difficulty swallowing whole tablets: Sachet granules: Mix contents of one sachet with 15mL water. Let thicken for a few minutes. Stir again. Drink within 30 minutes. Rinse container with water and drink that as well.

Administration via nasogastric tube: Sachet granules: Add 1 sachet to 15mL water in a syringe. Shake. Leave to thicken a few minutes. Shake. Inject into nasogastric or gastric tube. Refill syringe with 15mL water, shake, and flush the remainder in the NG tube into the stomach.

Pain relief does not necessarily mean that ulcers have healed or gastrointestinal damage has been reversed. A full course of treatment, usually for 4 to 8 weeks, must be completed to ensure healing. You may need to continue taking the medication after initial healing in order to prevent the problem from recurring.

If you are taking this medication in combination with antibiotics, for treatment of peptic ulcer, make sure you take all of the medications for the prescribed length of time, even if you feel better. This ensures that the bacteria that cause ulcer formation have been eliminated and reduces the chance of ulcer recurrence.

If you forget to take a dose, take it as soon as you remember. However, if more than 12 hours have passed since the time for your dose, skip the missed dose and continue with your regular schedule. Do not take two doses to make up for a missed dose.

When esomeprazole is used alone, side effects occur infrequently. Headache, nausea, stomach upset, diarrhea, gas, or constipation are the more commonly reported side effects. If you are taking antibiotics with esomeprazole, they

may also cause side effects. If any unusual, bothersome, or persistent effects occur, especially weight loss or vomiting, notify your physician.

Keep the tablets in the original blister package and the granules in the sachet, until it is time for your dose, because the tablets and granules are sensitive to moisture. Store the package at room temperature, away from moisture, and out of the reach of children.

If you have experienced any unexpected or serious reactions to this drug, this can be reported to Health Canada's monitoring program (toll free telephone 1-866-234-2345, toll free fax 1-866-678-6789). Note that this is not an emergency number.

If you suspect that someone has been poisoned by this medication, call your Poison Control Centre.

PRESENTATION
Tablets, delayed release: 20, 40 mg.
Oral suspension granules: 10mg per sachet as delayed release granules.

See also the PROTON PUMP INHIBITORS and OMEPRAZOLE monographs.

References are available on request.

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