Remeprazole

ANTIULCER

Packs	
Capsules 10mg	1000
Capsules 20mg	100, 1000
Capsules 40mg	100, 1000

Composition

Each capsule contains Omeprazole enteric-coated granules.

Properties

Remeprazole is an oral antiulcer agent. Remeprazole has a long duration of action and is very potent, allowing for once-daily administration. Despite its potency, Remeprazole must be used in combination with antibiotics to be effective against *Helicobacter pylori*.

Remeprazole belongs to a new class of antisecretory agents, the substituted benzimidazoles, which suppress gastric acid secretion by inhibiting the H+/K+ ATPase enzyme system of parietal cells. Following activation in an acidic pH, Remeprazole 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. Remeprazole is characterized as a gastric acid pump inhibitor because it blocks the final step of gastric acid production. It inhibits both basal and stimulus-induced acid secretion. Remeprazole is an extremely potent drug. Intragastric pH of patients receiving Remeprazole is often higher and affected longer than during therapy with H2-antagonists. Remeprazole is also more effective than either H_2-antagonists or Sucralfate in the treatment of gastro-oesophageal reflux disease (GERD).

Remeprazole is administered orally and should be taken prior to meals, preferably in the morning. Remeprazole capsules contain enteric-coated granules, and absorption begins only after the granules have passed through the stomach. The drug is rapidly absorbed following oral administration and distributes throughout the body tissues, concentrating in the gastric parietal cells. The drug's onset of action is 1 hour, and the duration of inhibition is greater than 72 hours. Remeprazole is 95% bound to plasma proteins. Extensive hepatic metabolism occurs, and the metabolites have minimal antisecretory activity. The plasma half-life in healthy patients is 0.5-1 hour, while the half-life in patients with chronic hepatic disease is approximately 3 hours. Secretory activity returns to normal 3-5 days after therapy is discontinued. Approximately 72-80% of a dose is excreted renally, and 18-23% is excreted in the faeces.

Indications

Treatment of oesophageal reflux disease. In reflux oesophagitis the majority of patients are healed after 4 weeks. Symptom relief is rapid.

Treatment of duodenal and benign gastric ulcers including those complicating NSAID therapy.

Relief of reflux-like symptoms (e.g. heartburn) and/or ulcer-like symptoms (e.g. epigastric pain) associated with acid-related dyspepsia.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and gastroduodenal erosions in patients with a previous history of gastroduodenal lesions that require continued NSAID treatment. Relief of associated dyspeptic symptoms.

Helicobacter pylori eradication: Remeprazole should be used in combination with antibiotics for eradication of *Helicobacter pylori (Hp)* in peptic ulcer disease.

Relief of associated dyspeptic symptoms.

Prophylaxis of acid aspiration.

Zollinger-Ellison syndrome.

Dosage

Oesophageal reflux disease including reflux oesophagitis: The usual dosage is 20 mg Remeprazole once daily. The majority of patients are healed after 4 weeks. For those patients not fully healed after the initial course, healing usually occurs during a further 4-8 weeks treatment. Remeprazole can also be used at a dose of 40 mg once daily in patients with reflux oesophagitis refractory to other therapy. Healing usually occurs within 8 weeks. Patients can be continued at a dosage of 20 mg once daily.

Acid reflux disease: For long-term management Remeprazole 10 mg once daily is recommended, increasing to 20 mg if symptoms return.

Duodenal and benign gastric ulcers: The usual dose is 20 mg Remeprazole once daily. The majority of patients with duodenal ulcer are healed after 4 weeks. The majority of patients with benign gastric ulcer are healed after 8 weeks. In severe or recurrent cases the dose may be increased to 40 mg Remeprazole daily. Long-term therapy for patients with a history of recurrent duodenal ulcer is recommended at a dosage of 20 mg Remeprazole once daily.

For prevention of relapse in patients with duodenal ulcer the recommended dose is Remeprazole 10 mg, once daily, increasing to 20 mg, once daily if symptoms return.

The following groups are at risk from recurrent ulcer relapse: those with *Helicobacter pylori* infection, younger patients (<60 years), those whose symptoms persist for more than one year and smokers. These patients will require initial long-term therapy with Remeprazole 20 mg once daily, reducing to 10 mg once daily, if necessary.

Acid-related dyspepsia: The usual dosage is Remeprazole 10 mg or 20 mg once daily for 2-4 weeks depending on the severity and persistence of symptoms. Patients who do not respond after 4 weeks or who relapse shortly afterwards, should be investigated.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and gastroduodenal erosions in patients with a previous history of gastroduodenal lesions that require continued NSAID treatment: Doses of 20 mg daily are used in the treatment of ulceration associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs); a dose of 20 mg daily may also be used for prophylaxis in susceptible patients.

For the eradication of Helicobacter pylori in peptic ulceration: Remeprazole may be combined with antibacterials in dual or triple therapy. Effective triple therapy regimens include Remeprazole 40 mg daily combined with: Amoxicillin 500 mg and Metronidazole 400 mg, both three times daily; or with Clarithromycin 250 mg and Metronidazole 400 mg (or Tinidazole 500 mg) both twice daily; or with Amoxicillin 1 g and Clarithromycin 500 mg both twice daily. These regimens are given for 1 week. Dual therapy regimens such as Remeprazole 40 mg daily with Amoxicillin 750 mg or 1 g twice daily, or with Clarithromycin 500 mg three times daily, are less effective and must be given for 2 weeks.

Prophylaxis of acid aspiration: Remeprazole is also used for the prophylaxis of acid aspiration, in a dose of 40 mg the evening before surgery and a further 40 mg on the day of surgery, 2 to 6 hours before the procedure.
Zollinger-Ellison syndrome: The initial recommended dosage for patients with the Zollinger-Ellison syndrome is 60 mg by mouth once daily, but doses up to 120 mg three times daily have been administered. The majority of patients are effectively controlled by doses in the range 20 to 120 mg daily. Doses above 80 mg should be divided and given twice daily; treatment should be continued for as long as is clinically indicated.
Elderly: No dosage adjustment is required.
Impaired hepatic function: The maximum daily dose should be reduced to 20 mg in patients with impaired hepatic function
Impaired renal function: No dosage adjustment is required.
Children: In children over 2 years, doses in the range 0.7 to 1.4 mg per kg body-weight daily, up to a maximum daily dose of 40 mg, may be given for 4 to 12 weeks. For children aged 2-6 years, the capsule may be opened, see section:
"Patients with Swallowing Difficulties".
Patients with swallowing difficulties: The capsules may be opened and the contents swallowed alone or suspended in a small amount of fruit juice or yoghurt after gentle mixing. Actual capsules may be sucked and then swallowed. It is important that the contents of the capsules should not be crushed or chewed.

Side-effects

The side-effects reported most frequently with Remeprazole have been gastrointestinal disturbances, in particular diarrhoea, skin rashes, and headache; they have sometimes been severe enough to require discontinuation of treatment.
Urticaria and pruritus have been reported, usually resolving after discontinuation of treatment. In addition photosensitivity, bullous eruption, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, angioedema and alopecia have been reported in isolated cases.
Effects on the CNS, including reversible confusional states, agitation, depression, and hallucinations in severely ill patients, have occurred. Other side-effects reported rarely include arthralgia and myalgia, paraesthesia, aggression, blurred vision, taste disturbances, peripheral oedema, hyponatraemia, blood disorders including agranulocytosis, leucopenia, and thrombocytopenia, interstitial nephritis, and hepatotoxicity.
Elevated hepatic enzymes (SGPT, SGOT, alkaline phosphatase), and jaundice also have been observed.

Precautions

Remeprazole should be administered with caution to patients with hepatic disease since clearance of the drug can be prolonged. In addition, Remeprazole has been associated with hepatitis and, in rare instances, hepatic failure.
Remeprazole decreases intragastric acidity. Subsequently, the number of bacteria in gastric secretions increase. Treatment with acid-reducing drugs leads to a slightly increased risk of gastrointestinal infections such as salmonella or campylobacter.
Pregnancy:
Remeprazole should be used during pregnancy only when clearly needed.
Breast-feeding:
It is not known whether Remeprazole crosses the placenta or is excreted into breast milk. Remeprazole should be used during breast-feeding only when clearly needed.
Drug Interactions:
Remeprazole can exhibit a dose-dependent inhibition of the hepatic cytochrome P-450 enzyme system. Because of this, Remeprazole can interfere with the clearance of drugs metabolised via this pathway, resulting in increased plasma concentrations. Examples of drugs that may be affected by Remeprazole include: Alprazolam, Astemizole, Carbamazepine, Cisapride, Cyclosporine, Diazepam, Diltiazem, Erythromycin, Felodipine, Lidocaine, Lovastatin, Midazolam, Nifedipine, Quinidine, Simvastatin, Terfenadine, Triazolam, Verapamil and Phenytoin. Patients should be monitored carefully for signs of increased drug effect if Remeprazole is used with Warfarin or Phenytoin.
Remeprazole increases the pH of the stomach. This increase in intragastric pH can interfere with the absorption of Ampicillin administered in ester form, iron salts, Itraconazole, or Ketoconazole. Changes in intragastric pH can potentially alter the bioavailability of other drugs with pH-dependent absorption. It has also been shown that Remeprazole can impair absorption of Cyanocobalamin, Vitamin B_{12}.
Gastric acid pump-inhibitors may increase Digoxin bioavailability; however, the magnitude of the interaction is small. Remeprazole increases the AUC of digoxin by about 10%. Patients with digoxin serum levels at the upper end of the therapeutic range may need to be monitored for potential increases in serum digoxin levels when Remeprazole is coadministered with Digoxin.
Drug/Laboratory Test Interferences:
Antimicrobials, Lansoprazole, Remeprazole, and bismuth preparations suppress H.pylori. Ingestion of these substances within four weeks prior to performing urease or breath-tests for H. pylori detection may lead to false negative results. In the four weeks prior to performing the test, the patient must avoid the use Remeprazole and other agents, which are known to suppress H.pylori

Contra-indications

Hypersensitivity to Remeprazole. Before giving Remeprazole to patients with gastric ulcers the possibility of malignancy should be considered since Remeprazole may mask symptoms and delay diagnosis.

Overdosage

No specific antidote for Remeprazole overdosage is known. Remeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

Pharmaceutical Precautions

Storage conditions:
Remeprazole capsules should be stored below 25°C, protected from light and moisture.
Incompatibilities:
None.
Do not use beyond the expiry date stated on container.

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