

Proceptin®

Omeprazole

Capsule/IV Injection

Description

Proceptin®-20 capsule contains 20 mg of Omeprazole BP as enteric coated pellets and each Proceptin®-40 capsule contains 40 mg of Omeprazole BP as enteric coated pellets.

Proceptin®-40 IV Injection contains Omeprazole 40 mg (as lyophilized powder of Omeprazole Sodium BP) and each ampoule contains 10 ml of water for injection BP.

Clinical Pharmacology

Mechanism of Action: Omeprazole belongs to a new class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H₂-histamine antagonistic properties but that suppresses gastric acid secretion by specific inhibition of the H⁺/K⁺ ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, Omeprazole has been characterized as a gastric acid pump inhibitor in that it blocks the final step of acid production. This effect is dose related and leads to inhibition of both basal and stimulated acid secretion, irrespective of the stimulus.

Antisecretory Activity: After oral administration the onset of the antisecretory effect of Omeprazole occurs within one hour, with the maximum effect occurring within 2 hours. Inhibition of secretion is about 50% of maximum at 24 hours, and the duration of inhibition lasts up to 72 hours. The antisecretory effect thus lasts far longer than would be expected from the very short (less than one hour) plasma half-life, apparently due to prolonged binding to the parietal H⁺/K⁺ ATPase enzyme. When the drug is discontinued, secretory activity returns gradually over 3 to 5 days.

Indications

Omeprazole offers significant therapeutic gains in the treatment of acid related diseases. Healing rates are high in duodenal ulcer, gastric ulcer and erosive reflux oesophagitis; acid production is controlled effectively in Zollinger-Ellison Syndrome and symptom relief is prompt and sustained in all indications.

Less clear-cut indications where benefit might be expected but where data are limited include:

- Prevention of stress ulceration
- Prevention of the acid aspiration syndrome
- Treatment of upper gastro-intestinal bleeding

NOTE: In comparative studies, Omeprazole has been found to produce faster symptom relief and higher healing rates in a

greater percentage of patients than either Cimetidine or Ranitidine, confirming the 'therapeutic gains' achievable with Omeprazole over existing therapies.

Dosage and Administration

Proceptin® Capsule:

Duodenal Ulcer: 20 mg once daily for 4 weeks. In severe cases, 40 mg once daily for 4 weeks.

Gastric Ulcer: 20 mg once daily for 8 weeks. In severe cases, 40 mg once daily for 8 weeks.

Erosive Reflux Oesophagitis: 20 mg once daily for 4 weeks. For those not fully healed, to be continued for 4 more weeks.

Refractory Reflux Oesophagitis: 40 mg once daily for 8 weeks.

Zollinger-Ellison Syndrome: 60 mg once daily, adjusted individually and continued as long as necessary.

Most patients will be effectively controlled with 20-120 mg daily. Dosage above 80 mg should be divided and given twice daily.

Long-term maintenance treatment with Omeprazole is not recommended.

Impaired Renal or Hepatic Function: Adjustment is not required. Patients with severe liver disease should not require more than 20 mg Omeprazole daily.

Proceptin® IV Injection:

Prophylaxis of acid aspiration: Omeprazole 40 mg to be given slowly (over a period of 5 minutes) as an intravenous injection, one hour before surgery.

Duodenal ulcer, gastric ulcer or reflux oesophagitis: In patients with duodenal ulcer, gastric ulcer or reflux oesophagitis where oral medication is inappropriate, Omeprazole IV 40 mg once daily is recommended.

Zollinger- Ellison syndrome (ZES): In patients with Zollinger-Ellison Syndrome the recommended initial dose of Omeprazole given intravenously is 60 mg daily. Higher daily doses may be required and the dose should be adjusted individually. When doses exceed 60 mg daily, the dose should be divided & given twice daily.

Direction for use of IV Injection

Omeprazole lyophilized powder and water for injection is for intravenous administration only and must not be given by any other route.

Omeprazole IV injection should be given as a slow intravenous injection. The solution for IV injection is obtained by adding 10 ml water for injection to the vial containing powder. After

reconstitution the injection should be given slowly over a period of at least 2 to 5 minutes at a maximum rate of 4 ml/minute. Use only freshly prepared solution. The solution should be used within 4 hours of reconstitution.

Direction for use of IV Infusion

Omeprazole IV infusion should be given as an intravenous infusion over a period of 20-30 minutes or more. The contents of one vial must be dissolved in 100 ml saline for infusion or 100 ml 5% Dextrose for infusion. The solution should be used within 12 hours when Omeprazole is dissolved in saline and within 6 hours when dissolved in 5% Dextrose. The reconstituted solution should not be mixed or co-administered in the same infusion set with any other drug.

Contraindications

Omeprazole is contraindicated in patients with known hypersensitivity to any component of the formulation.

Use in Pregnancy and Lactation

There are no adequate or well controlled studies in this group of patients. However as with all new drugs, Omeprazole should not be given during pregnancy and lactation unless its use is considered essential.

Paediatric Use

Safety and effectiveness in children have not been established.

Adverse Effects

Side effects reported with Omeprazole in clinical studies have included nausea, diarrhoea, constipation, flatulence, abdominal colic, paresthesia, dizziness and headache but are rare. Skin rashes, leukopenia and transient elevation of plasma activation of hepatic amino-transferases have been observed occasionally in few patients and there has been no consistent relationship with treatment.

Toxicology

In two 24-months carcinogenicity studies in rats, Omeprazole at daily doses of 1.7, 3.4, 13.8, 44.0 and 140.8 mg/kg/day (approximately 4 to 352 times the human dose, based on a patient weight of 50 kg and a human dose of 20 mg) produced gastric entero-chromaffin like (ECL) cell carcinoids in a dose related manner in both male and female rats. No treatment related mucosal changes have been observed in patients treated continuously for periods upto 4 years.

Precautions

Symptomatic response to therapy with Omeprazole does not preclude the presence of gastric malignancy.

Warning

In long-term (2 years) studies in rats, Omeprazole produced a dose related increase in gastric carcinoid tumours (see

Toxicology). While available endoscopic evaluations and histologic examinations of biopsy specimens from human stomachs have not detected a risk from short-term exposure to Omeprazole, further human data on the effects of sustained hypochlorhydria and hypergastrinemia are needed to rule out the possibility of an increased risk for the development of tumours in humans receiving long-term therapy with Omeprazole.

Drug Interactions

Omeprazole can delay the elimination of Diazepam, Phenytoin and Warfarin. Monitoring of patients receiving Warfarin or Phenytoin is recommended and a reduction of Warfarin or Phenytoin dose may be necessary when Omeprazole is added to treatment. Omeprazole does not interfere with Theophylline or Propranolol metabolism.

Information to Patients

Omeprazole should be taken before meals. Patients should be cautioned that the capsules should not be opened, chewed or crushed and should be swallowed whole.

Pharmaceutical Precautions

Store in a cool and dry place. Keep out of the reach of children.

Commercial Pack

Proceptin®-20 Capsule: Box containing 60 capsules in 6x10's Alu-Alu form packs and 100 capsules in 10x10's Alu-Alu form packs. Each capsule contains Omeprazole BP 20 mg as enteric coated pellets.

Proceptin®-40 Capsule: Box containing 30 capsules in 6x5's Alu-Alu form packs. Each capsule contains Omeprazole BP 40 mg as enteric coated pellets.

Proceptin®-40 IV Injection: Each commercial box containing one vial of sterile lyophilized powder of Omeprazole Sodium BP equivalent to Omeprazole 40 mg, one ampoule of water for injection BP 10 ml and one sterile disposable syringe (10 ml).



Manufactured by

BEXIMCO PHARMACEUTICALS LTD.

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