Omeprazole

Omepron®

40 mg/ 10 mL Powder for IV Injection

PROTON PUMP INHIBITOR

FORMULATION
Each IV Injection combination pack contains:

Vial containing:
Omeprazole sodium……..42.6 mg
(equivalent to 40mg Omeprazole)

Ampule of solvent containing:
Polyethylene glycol 400……..4000 mg
Citric acid monohydrate……6 mg
Water for Injection……q.s. 10 mL

PRODUCT DESCRIPTION
Omeprazole (Omepron®) 40 mg Lyophilized Powder for Injection is a white to off-white lyophilized powder in a colorless, clear vial. The powder dissolves completely and appears as a clear, colorless solution after reconstitution.

PHARMACODYNAMICS
Omeprazole is a proton pump inhibitor that belongs to a class of antisecretory compounds, the substituted benzimidazoles. It 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.

PHARMACOKINETICS
Omeprazole's apparent volume of distribution is approximately 0.3 L/kg in healthy subjects and in patients with renal insufficiency. The volume of distribution is slightly decreased in elderly patients and in patients with hepatic insufficiency. Omeprazole is highly protein bound with about 95% bound to plasma proteins.
Omeprazole is completely metabolized mainly in the liver via the cytochrome P450 system (CYP). A major part of its metabolism is dependent on CYP2C19 (S-mephenytoin hydroxylase) which is responsible for the formation of hydroxyomeprazole, its major metabolite in the plasma. The average half-life after IV administration is approximately 40 minutes and total plasma clearance is 0.3 to 0.6 L/min.

About 80% of the metabolites are excreted in the urine and the remaining metabolites are seen in the feces. Patients with impaired liver function have increased elimination half-life; however, omeprazole has not shown any accumulation with once daily oral dosing.

USES/INDICATIONS
- For the short term treatment of the following conditions when oral medication is not feasible:
  - Duodenal ulcer
  - Gastric ulcer
  - Ulcerative esophagitis
  - Zollinger-Ellison Syndrome
  - Gastroesophageal Reflux Disease (GERD)

DOSAGE AND ADMINISTRATION
Omeprazole (Omepron®) should be administered only by slow intravenous (IV) injection (not less than 2.5 minutes) at a rate of no greater than 4 mL/minute.
Omeprazole (Omepron®) IV injection is **NOT** intended for use as IV infusion.
Recommended Dose: 40 mg once daily.
Patients with Zollinger-Ellison Syndrome may require a higher dose and/or several doses.
Individual dosage adjustment is necessary in these patients.

- Parenteral omeprazole should be shifted to oral omeprazole as soon as feasible. Usual treatment period for intravenous omeprazole is 2-3 days.
- Inspect the solution for particulate matter and discoloration before administration.
- If intravenous therapy is necessary for more than three days, dosage must be adjusted and reduced to 10-20 mg per day based on patient's response.

Preparation of Dosage Form
Reconstitute powder with 10 mL of the solvent provided. No other should be used.

Stability
Omeprazole should be used within 4 hours after reconstitution.

CONTRAINDICATIONS
- Hypersensitivity to omeprazole, other proton pump inhibitors or any component of the product.

WARNINGS and PRECAUTIONS
- Gastric malignancy should be excluded at initiation of treatment and at follow-up of gastric ulcer therapy.
- Gastritis has been reported occasionally in gastric corpus biopsies from patients on long-term omeprazole therapy.
- The use of acid-suppressants such as omeprazole may increase a patient's risk of community-acquired pneumonia.

DRUG INTERACTIONS
- Omeprazole is metabolized via the hepatic cytochrome P-450 2C19 enzyme and may inhibit the metabolism of some drugs metabolized by this system.
- Omeprazole may prolong the elimination of warfarin, phenytoin, diazepam, and other vitamin K antagonists.
- Concomitant administration may increase plasma concentrations of omeprazole and clarithromycin but no interaction is found with metronidazole and amoxicillin when used for the eradication of H. pylori.
- Conflicting data suggest a dose-dependent reduction in cyanocobalamin absorption with concomitant use of omeprazole.
- Omeprazole may affect the bioavailability of pH-dependent drugs such as ketoconazole, itraconazole, ampicillin esters, or iron salts.
- Concomitant administration with omeprazole may reduce plasma levels of atazanavir.
- Serum levels of tacrolimus may increase when taken together with omeprazole.
- Concomitant administration with voriconazole resulted in more than doubling of omeprazole exposure. However, dosage adjustment of omeprazole was not necessary.

HIGH RISK GROUPS

Use in Pregnancy
Omeprazole may be used in pregnant women. Epidemiological studies on omeprazole have shown no adverse effects on pregnancy or on the health of the fetus/baby.

Use in Breastfeeding Mothers
Omeprazole is excreted in human milk. In rats, omeprazole has been shown to be excreted in milk at low concentrations. Decision should be made whether to discontinue omeprazole or breastfeeding since omeprazole may cause potential serious adverse effects to the baby.

Use in the Elderly
There is no difference in efficacy and safety observed between geriatric and younger patients. However, some elderly patients may exhibit increased sensitivity to the drug and may be at risk for potential side effects.

Use in Children
There is limited experience with the use of omeprazole IV in children.

Use in Patients with Impaired Hepatic Function
Consider dose adjustment in patients with hepatic impairment especially in those requiring prolonged use since plasma half-life is increased in these patients.

Use in Patients with Impaired Renal Function
No dosage adjustment is necessary in patients with impaired kidney function.

Use in Asian Population
Consider dose reduction in Asian patients receiving long-term omeprazole therapy for maintenance of healing of erosive esophagitis. The bioavailability of omeprazole appears to be increased in these patients.

UNDESIRABLE EFFECTS
Omeprazole is generally well-tolerated and most adverse reactions have been mild and transient.

Nervous System Effects: Headache, vertigo, dizziness, weakness (asthenia) pain, fatigue, malaise, paresthesia, hemifacial dysesthesia, and psychic disturbances (e.g., depression, aggression, confusion, anxiety, agitation, insomnia, nervousness, tremors, apathy, dream abnormalities, somnolence, and hallucinations) have been reported but not directly attributable to the drug in many cases.

Gastrointestinal Effects: Constipation and diarrhea, nausea, vomiting, abdominal pain, flatulence, and acid regurgitation. Occasionally, dysphagia, abdominal swelling, irritable colon, fecal discoloration, pancreatitis (sometimes fatal), esophageal candidiasis, mucosal atrophy of the tongue, anorexia, dry mouth, dysgeusia, and tongue discoloration have been reported.

Musculoskeletal: Back pain, muscle cramps, myalgia, muscle weakness, arthralgia, joint pain, and leg pain have been occasionally reported with the use of omeprazole.

Dermatologic and Sensitivity Reactions: Rash, severe generalized reactions (e.g., toxic epidermal necrolysis), Stevens-Johnson Syndrome, erythema multiforme, exfoliative dermatitis, and lichenoid eruptions. Other effects include skin inflammation, urticaria, purpura and/or petechiae, bullous eruption, angioedema, pruritus, alopecia, dry skin, and hyperhydrosis. Allergic reactions, including rare cases of anaphylaxis have also been reported.

Genitourinary Effects: Acute interstitial nephritis and sexual disturbances such as priaprism have been occasionally reported with the use of omeprazole. Urinary tract infection, microscopic pyuria, urinary frequency, elevated serum creatinine concentration, proteinuria, hematuria, glycosuria, and testicular pain have also been reported but in many cases not attributed to omeprazole.

Hepatic Effects: mild and rare reports of increased serum aminotransferases (transaminases) (AST) and (ALT), γ-glutamyltransferase (GGT, γ-glutamyltranspeptidase, GGTP), alkaline phosphatase and bilirubin concentrations have been reported. Symptomatic liver disease including hepatocellular, cholestatic, or mixed hepatitis, jaundice, liver necrosis, hepatic failure, and hepatic encephalopathy have occurred rarely.

Respiratory Effects: Upper respiratory tract infections and cough. Epistaxis and pharyngeal pain have been reported occasionally. Other effects that were reported with combined omeprazole and clarithromycin therapy were rhinitis, pharyngitis and flu syndrome.
The use of proton pump inhibitors has been associated with an increased risk for developing certain infections such as community-acquired pneumonia. These drugs should only be used when clearly needed using the lowest effective dose in patients with severe community-acquired pneumonia.

Cardiovascular Effects: Chest pain, angina pectoris, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema have been reported occasionally.

Hematologic Effects: Leukocytosis, neutropenia, pancytopenia, agranulocytosis, anemia, hemolytic anemia, and thrombocytopenia have been reported rarely.

Other Adverse Effects: Cough, fever, tinnitus, gynecomastia, acute gout, photosensitivity, blurred vision, alopecia, sweating, taste disturbances, and otitis media.

OVERDOSAGE AND TREATMENT
Two cases of omeprazole overdose were characterized by drowsiness, headache (possibly due to a metabolite) and tachycardia. Both patients recovered without specific treatment.
Intravenous doses of 270 mg given in a day and up to 650 mg over a three-day period in clinical trials did not show any dose-related adverse reactions. As in all cases where overdosing is suspected, treatment should be symptomatic and supportive.

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

STORAGE
Store at temperatures not exceeding 25°C. Protect from light, heat and moisture.

AVAILABILITY
Omeprazole (Omepron®) 40 mg Powder for IV Injection, in box of 1 Vial

ADVERSE DRUG REACTION REPORTING STATEMENT
For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

Manufactured by STANDARD CHEM. & PHARM. CO., LTD.
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