120x240mm

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Omevex

(Omeprazole)

Highnoon

COMPOSITION
Each pack contains:
Vial: Omeprazole (as Sodium) 40mg Lyophilized Powder
Ampoule: Water for injection 5mL

DESCRIPTION
Omevex (Omeprazole) is proton pump inhibitor.

MECHANISM OF ACTION
Omeprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress 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.

PHARMACOKINETICS
Omeprazole is rapidly but variably absorbed after oral doses. Absorption is not significantly affected by food. Omeprazole is acid-labile and the pharmacokinetics of various formulation developed to improve oral bioavailability may vary. The absorption of omeprazole also appears to be dose dependent; increasing the dosage above 40mg has been reported to increase the plasma concentrations in a non-linear fashion because of saturable first-pass hepatic metabolism. In addition, bioavailability is higher after long term use. Bioavailability of omeprazole may be increased in elderly patients and in patients with hepatic impairment, but is not markedly affected in patients with renal impairment. On absorption omeprazole is almost completely metabolized in the liver, mainly by the cytochrome P450 isoenzyme CYP2C19 to hydroxy omeprazole and to small extent by CYP3A4 to omeprazole sulfone. The metabolite are inactive and are excreted mostly in the urine and to lesser extent in bile. The elimination half-life from plasma is reported to be about 0.5 to 3 hours. Omeprazole is about 95% bound to plasma protein.

INDICATIONS AND USAGE
Omevex (Omeprazole) for intravenous use is indicated as an alternative to oral therapy for the following indications i.e.

Adults
- Treatment of duodenal ulcers
- Prevention of relapse of duodenal ulcers
- Treatment of gastric ulcers
- Prevention of relapse of gastric ulcers
- In combination with appropriate antibiotics, *Helicobacter pylori (H. pylori)* eradication in peptic ulcer disease
- Treatment of NSAID-associated gastric and duodenal ulcers
- Prevention of NSAID-associated gastric and duodenal ulcers in patients at risk
- Treatment of reflux esophagitis
- Long-term management of patients with healed reflux esophagitis
- Treatment of symptomatic gastro-esophageal reflux disease
- Treatment of Zollinger-Ellison syndrome

DOSAGE AND ADMINISTRATION
In patients where the use of oral medicinal products is inappropriate, Omevex (omeprazole) IV 40 mg once daily is recommended. In patients with Zollinger-Ellison Syndrome the recommended initial dose of Omevex (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 and given twice daily.
Omevex (omeprazole) is to be administered in an intravenous infusion for 20-30 minutes.

CONTRAINDICATIONS
- It is contraindicated in patients with known hypersensitivity to substituted benzimidazoles or to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis and urticaria.
- Omeprazole like other proton pump inhibitors (PPIs) should not be used concomitantly with nelfinavir.

ADVERSE REACTIONS
The reported adverse events of omeprazole are; acute interstitial nephritis, clostridium difficile-associated diarrhoea, bone fracture (hip, wrist and spine), Cutaneous and Systemic Lupus Erythematosus (SLE), hypomagnesemia, headache, abdominal pain, nausea, diarrhoea, vomiting, flatulence, Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis(TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP), hypersensitivity reactions including anaphylaxis, anaphylactic shock, angioedema, bronchospasm, taste perversion, malaise, peripheral oedema, gynecomastia, oesophageal candidiasis, microscopic colitis, stomatitis, dry mouth, gastric fundic gland polyps, liver disease including hepatic failure, liver necrosis, hepatic encephalopathy hepatocellular disease, , mixed hepatitis, jaundice, elevations of liver function tests, increased sweating, hyponatremia, muscle weakness, myalgia, arthralgia, depression, agitation, aggression, hallucinations, confusion, insomnia, somnolence, paraesthesia, vertigo, Stevens-Johnson syndrome, cutaneous lupus erythematosus and erythema multiforme, photosensitivity, urticaria, rash, skin inflammation, dermatitis, pruritus, alopecia, blurred vision, agranulocytosis, pancytopenia, thrombocytopenia, leukopenia, constipation and dizziness.
The additional reported adverse events are; cyanocobalamin (Vitamin B-12) deficiency, acid regurgitation, upper respiratory infection, rash, asthenia, back pain, cough, otitis media, fever, accidental injury, tongue discoloration, rhinitis, pharyngitis, flu-syndrome, pain, fatigue, chest pain or angina, tachycardia, bradycardia, palpitations, elevated blood pressure, pancreatitis (some fatal), anorexia, irritable colon, faecal discoloration, mucosal atrophy of the tongue, abdominal swelling, gastroduodenal carcinoids, cholestatic diseae and hypoglycaemia, weight gain, muscle cramps, joint pain, leg pain, bone fracture, sleep disturbances, nervousness, apathy, anxiety, dream abnormalities; tremors, epistaxis, pharyngeal pain, severe generalized skin reactions including toxic epidermal necrolysis, petechiae, purpura, dry skin, hyperhidrosis, optic atrophy, anterior ischemic optic neuropathy, optic neuritis, dry eye syndrome, ocular irritation, double vision, hematuria, proteinuria, elevated serum creatinine, microscopic pyuria, urinary tract infection, glycosuria, urinary frequency, testicular pain, haemolytic anaemia, neutropenia, anaemia, and leucocytosis.

DRUG INTERACTIONS
The following are drug interactions;
- Antiretroviral: Avoid concomitant use of atazanavir, nelfinavir, squinavir and rilpivirine-containing products with omeprazole. The decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir and nelfinavir) when used concomitantly with omeprazole may reduce antiviral effect and promote the development of drug resistance. The increased exposure of other antiretroviral drugs (e.g., saquinavir) when used concomitantly with omeprazole may increase toxicity. Concomitant administration of omeprazole with atazanavir is not recommended. Concomitant administration of omeprazole with nelfinavir is contraindicated
- Warfarin: Increased INR and prothrombin time in patients receiving PPIs, including omeprazole, and warfarin concomitantly. It may lead to abnormal bleeding and even death. Monitor INR and prothrombin time and adjust the dose of warfarin, if needed, to maintain target INR range.
- Methotrexate: Concomitant use of omeprazole with methotrexate (primarily at high dose) may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxy methotrexate, possibly leading to methotrexate toxicities. A temporary withdrawal of omeprazole may be considered in some patients receiving high-dose methotrexate.
- Clopidogrel: Concomitant use of omeprazole reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant use of clopidogrel with omeprazole.
- Citalopram: Increased exposure of citalopram leading to an increased risk of QT prolongation.
- Cilostazol: Increased exposure of one of the active metabolites of cilostazol (3,4-dihydro-cilostazol).
- Phenytoin: Monitor phenytoin serum concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.
- Diazepam: Monitor patients for increased sedation and reduce the dose of diazepam as needed.
- Digoxin: Monitor digoxin concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations. Therapeutics drug monitoring of digoxin should then be reinforced.
- Drugs Dependent on Gastric pH for Absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole): Omeprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity.
- Combination Therapy with Clarithromycin and Amoxicillin: Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions, including potentially fatal arrhythmias, and are contraindicated.
- Since omeprazole is metabolized by CYP2C19 and CYP3A4, active substances known to inhibit CYP2C19 or CYP3A4(such as clarithromycin and voriconazole) may lead to increased omeprazole serum levels by decreasing omeprazole's rate of metabolism. Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. As high doses of omeprazole have been well-tolerated adjustment of the omeprazole dose is not generally required. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.
- Tacrolimus: Potential for increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19. Monitor tacrolimus whole blood concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.
- Interactions with Investigations of Neuroendocrine Tumours: Serum chromogranin A (CgA) levels increase secondary to PPI-induced decrease in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumours.
- Interaction with Secretin Stimulation Test: Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma. Temporarily stop omeprazole treatment at least 14 days before assessing to allow gastrin levels to return to baseline. False Positive Urine Tests for THC: There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs. There have been clinical reports of interactions with other drugs metabolized via the cytochrome P450 system (e.g., cyclosporine, disulfiram).
- CYP2C19 or CYP3A4 Inducers: Decreased exposure of omeprazole when used concomitantly with strong inducers.
- CYP2C19 or CYP3A4 Inhibitors: Increased exposure of omeprazole when used concomitantly with strong inducers. The dose adjustment of omeprazole is not normally required in voriconazole. However, in patients with Zollinger-Ellison syndrome, who may require higher doses, dose adjustment may be considered.
- Active substances known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St John's wort) may lead to decreased omeprazole serum levels by increasing omeprazole's rate of metabolism.

WARNINGS AND PRECAUTIONS
- Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older patients, also consider an endoscopy.
- Acute tubulointerstitial nephritis (TIN) has been observed in patients taking omeprazole and may occur at any point during omeprazole therapy. Acute tubulointerstitial nephritis can progress to renal failure. Omeprazole should be discontinued in case of suspected TIN, and appropriate treatment should be promptly initiated.
- Proton pump inhibitor (PPI) therapy like omeprazole may be associated with an increased risk of Clostridium difficile-associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
- Proton pump inhibitor (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). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.
- Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs, including omeprazole. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE. The most common form of CLE reported in patients treated with PPIs was subacute CLE (SCLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving PPIs. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash; however, arthralgia and cytopenia were also reported.
- Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving Proton pump inhibitor, discontinue the drug. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g., ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.
- Avoid concomitant use of Proton pump inhibitor with clopidogrel. Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as omeprazole, that inhibit CYP2C19 activity.
- Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B-12) caused by hypo-or achlorhydria. Diagnosis should be considered if clinical symptoms consistent with cyanocobalamic deficiency are observed in patients treated with omeprazole.
- Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
- Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or Rifampicin) can substantially decrease omeprazole concentrations. Avoid concomitant use of omeprazole with St. John's Wort or Rifampicin.
- Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors.
- Omeprazole treatment should temporarily stop at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high.
- Concomitant use of PPIs with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may be considered.
- Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of PPIs. Discontinue omeprazole at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.
- In the presence of any alarm symptoms (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, hematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis.
- Co-administration of atazanavir with proton pump inhibitors is not recommended. If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g., virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; omeprazole 20 mg should not be exceeded.
- PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

USE IN SPECIFIC POPULATIONS
Pregnancy: Limited data is available with no adverse effects of omeprazole on pregnancy or on the health of foetus / newborn child. Omeprazole can be used in pregnancy.

Lactation: Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for omeprazole and any potential adverse effects on the breastfed infant from omeprazole or from the underlying maternal condition.
Paediatric Use: There is limited experience with Omeprazole for intravenous use in children.

Geriatric Use: The metabolism rate of omeprazole is somewhat reduced in elderly subjects (75-79 years of age). Dose adjustment is not needed in elderly subjects.

Impaired renal function: The pharmacokinetics of omeprazole, including systemic bioavailability and elimination rate, are unchanged in patients with reduced renal function. Dose adjustment is not needed in patients with impaired renal function.

Hepatic Impairment: The metabolism of omeprazole in patients with liver dysfunction is impaired, resulting in an increased AUC. Omeprazole has not shown any tendency to accumulate with once-daily dosing. In patients with impaired hepatic function a daily dose of 10-20 mg may be sufficient.

Effects on ability to drive and use machines
Omeprazole is not likely to affect the ability to drive or use machines. Adverse reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machinery.

Special precautions for disposal and other handling
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 05 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 6 hours of reconstitution when stored in the original vial in a cool place.

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 entire contents of each vial should be dissolved in approximately 5 ml water for injection and then immediately 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. The stability of omeprazole is influenced by the pH of the solution for infusion, which is why no other solvent or quantities should be used for dilution.
Discard the unused portion . The infusion solution should not be refrigerated.
The reconstituted and diluted solutions should not be used if it contains visible particulate matter.

OVERDOSAGE
There is limited information available on the effects of overdoses of omeprazole in humans. Symptoms of overdosage included confusion, drowsiness, blurred vision, tachycardia, nausea, vomiting, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience. No specific antidote for omeprazole overdosage is known. Omevex (Omeprazole) is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

PRESENTATION
Omevex 40mg IV Injection/Infusion: 1 vial of 40mg Omeprazole and 1 ampoule of 5mL water for injection.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30ºC. Keep in a dry place. Protect from light.

اومیویکس

(اومیپرازول)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخے کے مطابق ہی دوا فروخت اور استعمال کی جائے۔

بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔

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