Omsta®

(Omeprazole)

Highnoon

COMPOSITION

Omsta 20mg Capsule: Each capsule contains: Omeprazole (as enteric-coated pellets) 20mg

Omsta 40mg Capsule: Each capsule contains: Omeprazole (as enteric-coated pellets) 40mg

DESCRIPTION

Omsta (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

It is indicated in the following conditions;

- short-term treatment of active duodenal ulcer in adults. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.
- helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence.
- short-term treatment (4 to 8 weeks) of active benign gastric ulcer in adults.
- treatment of heartburn and other symptoms associated with GERD for up to 4 weeks in patients 1 year of age and older.
- paediatric patients 1 year of age to adults for the short-term treatment (4 to 8 weeks) of Erosive Esophagitis (EE) due to acid-mediated GERD that has been diagnosed by endoscopy in patients 1 year of age and older.
- in paediatric patients 1 month to less than 1 year of age for the short-term treatment (up to 6 weeks) of EE due to acid-mediated GERD in pediatric patients 1 month to less than 1 year of age.
- for the maintenance healing of EE due to acid-mediated GERD in patients 1 year of age and older.
- indicated for the long-term treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome, multiple endocrine adenomas and systemic mastocytosis) in adults.

DOSAGE AND ADMINISTRATION

The recommended adult dosage regimen is:

- Active duodenal ulcer: A dose of 20 mg capsule once daily for 4 weeks
- Helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence:
  - In triple therapy treatment Omsta (omeprazole) 20 mg capsule in combination with amoxicillin 1000 mg and Clarithromycin 500 mg. Take all three drugs twice daily for 10 days in patients with an ulcer present at the time of initiation of therapy, continue Omsta (omeprazole) 20 mg once daily for an additional 18 days for ulcer healing and symptom relief. It may be given as, Omsta (omeprazole) 20 mg capsule twice daily or 40 mg once daily combined with amoxicillin 500 mg and metronidazole 400mg, both three times daily. It may also be given as, Omsta (omeprazole) 20 mg capsule twice daily or 40 mg once daily combined with clarithromycin 250mg and metronidazole 400mg (or tinidazole 500mg), both twice daily.
  - In dual therapy treatment Omsta (omeprazole) 40 mg capsule once daily in combination with Clarithromycin 500 mg three times 14 days In patients with an ulcer present at the time of initiation of therapy, an additional 14 days of Omsta (omeprazole) 20 mg once daily is recommended for ulcer healing and symptom relief.
- *Active benign gastric ulcer:* A dose of 40 mg capsule once daily for 4 to 8 weeks
- *Treatment of symptomatic GERD:* A dose of 20 mg capsule once daily for 4 weeks
- *Treatment of EE due to Acid-Mediated GERD:* A dose of 20 mg capsule once daily for 4 to 8 weeks
- *Maintenance of healing of EE due to Acid-Mediated GERD:* A dose of 20mg capsule once daily for up to 12 months
- *Pathological hypersecretory conditions:* The starting dose is 60 mg once daily; adjust to patient needs, daily dosage of greater than 80 mg should be administered in divided doses. Dosages up to 120 mg three times daily have been administered, as long as indicated. Some patients with Zollinger-Ellison syndrome have been treated continuously for more than 5 years.

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.
- Proton pump inhibitors (PPIs), including omeprazole, are contraindicated in patients receiving nelfinavir and rilpivirine-containing products.

ADVERSE REACTIONS

The reported adverse events of omeprazole are; acute interstitial nephritis, clostridium difficile-associated diarrhea, bone fracture, Cutaneous and Systemic Lupus Erythematosus (SLE), cyanocobalamin (Vitamin B-12) deficiency, hypomagnesemia, headache, abdominal pain, nausea, diarrhea, vomiting, flatulence, acid regurgitation, upper respiratory infection, constipation, dizziness, rash, asthenia, back pain, cough, otitis media, fever, accidental injury, tongue discoloration, rhinitis, pharyngitis, flu-syndrome, and taste perversion.

The additional reported adverse events are; hypersensitivity reactions including anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, urticaria, pain, fatigue, malaise, chest pain or angina, tachycardia, bradycardia, palpitations, elevated blood pressure, peripheral edema, gynecomastia, pancreatitis (some fatal), anorexia, irritable colon, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, stomatitis, abdominal swelling, dry mouth, microscopic colitis, gastric fundic gland polyps, gastroduodenal carcinoids, liver disease including hepatic failure, liver necrosis, hepatic encephalopathy hepatocellular disease, cholestatic disease, mixed hepatitis, jaundice, and elevations of liver function tests, hypoglycemia, hyponatremia, weight gain, muscle weakness, myalgia, muscle cramps, joint pain, leg pain, bone fracture, sleep disturbances, depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, apathy, somnolence, anxiety, dream abnormalities, tremors, paresthesia, vertigo, epistaxis, pharyngeal pain, severe generalized skin reactions including toxic epidermal necrolysis, Stevens-Johnson syndrome, cutaneous lupus erythematosus and erythema multiforme, photosensitivity, urticaria, rash, skin inflammation, pruritus, petechiae, purpura, alopecia, dry skin, hyperhidrosis, optic atrophy, anterior ischemic optic neuropathy, optic neuritis, dry eye syndrome, ocular irritation, blurred vision, double vision, interstitial nephritis, hematuria, proteinuria, elevated serum creatinine, microscopic pyuria, urinary tract infection, glycosuria, urinary frequency, testicular pain, agranulocytosis, hemolytic anemia, pancytopenia, neutropenia, anemia, thrombocytopenia, leukopenia and leukocytosis.

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.
- 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 hydroxymethotrexate, 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.
- 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.
- 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 Tumors: 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 tumors.
- 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.

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 interstitial nephritis has been observed in patients taking Proton pump inhibitor (PPI) including omeprazole. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue omeprazole if acute interstitial nephritis develops.
- 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 cyanocobalamin 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 Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic syndrome symptom (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in associate with the use of PPIs. Discontinue omeprazole as first sign and symptom of severe cutaneous adverse reaction or other signs of hypersensitivity and consider further evaluation.
- PPI use is associated with an increased risk of fundic gland polyps that increase 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: There are no adequate and well-controlled studies with omeprazole in pregnant women. Available epidemiologic data fail to demonstrate an increased risk of major congenital malformations or other adverse pregnancy outcomes with first trimester omeprazole use.

Lactation: Limited data suggest omeprazole may be present in human milk. There are no clinical data on the effects of omeprazole on the breastfed infant or on milk production. 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.

Pediatric Use: The safety and effectiveness of omeprazole have not been established in patients less than 1 year of age for treatment of symptomatic GERD, maintenance of healing of EE due to acid-mediated GERD, treatment of active duodenal ulcer, H. pylori eradication to reduce the risk of duodenal ulcer recurrence, treatment of active benign gastric ulcer, pathological hypersecretory conditions and for patients less than 1 month of age for any indication.

Geriatric Use: There were no differences in safety and effectiveness between the elderly and younger subjects.

Hepatic Impairment: In patients with hepatic impairment (Child-Pugh Class A, B, or C) exposure to omeprazole substantially increased compared to healthy subjects. Dosage reduction of omeprazole to 10 mg once daily is recommended for patients with hepatic impairment for maintenance of healing of EE.

OVERDOSAGE

There is limited information available on the effects of overdoses of omeprazole in humans. In the literature, doses of up to 560 mg have been described, and occasional reports have been received when single oral doses have reached up to 2,400 mg omeprazole (120 times the usual recommended clinical dose).

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. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

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 30°C. Keep in a dry place. Protect from light.

PRESENTATION

Omsta 20mg Capsules: Alu. Alu. Blister Pack of 2 x 7's.

Omsta 40mg Capsules: Alu. Alu. Blister Pack of 2 x 7's.

اومسٹا®

(اومیپرازول)

خوراک و ہدایات:

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

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

خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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