Zoltar®

زولٹار

COMPOSITION

ZOLTAR® 20 mg Capsule
Each capsule contains:
Omeprazole USP…….20mg
as enteric coated pellets.
ZOLTAR® 40 mg Capsule
Each capsule contains:
Omeprazole USP…….40mg
as enteric coated pellets.
(USP Specs.)

DESCRIPTION

ZOLTAR® contains Omeprazole which is a substituted benzimidazole that inhibits gastric acid secretion via proton pump inhibition. It is chemically designated as 5-methoxy-2-[[(4-methoxy¬3, 5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1H benzimidazole. Its molecular formula is $C_{17}H_{19}N_3O_3S$.

CLINICAL PHARMACOLOGY

Mechanism of action
Omeprazole belongs to a class of anti-secretory 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.

Microbiology

Effect on *H. pylori*
Omeprazole and clarithromycin dual therapy and omeprazole, clarithromycin and amoxicillin triple therapy have been shown to be active against most strains of *Helicobacter pylori* in vitro and in clinical infections. *H. pylori* is associated with peptic ulcer disease, including duodenal and gastric ulcers and a major factor in the development of gastritis. *H. pylori* together with gastric acid are major factors in the development of peptic ulcer disease. *H. pylori* is a major factor in the development of atrophic gastritis which is associated with an increased risk of developing gastric cancer.
Eradication of *H. pylori* with omeprazole and antimicrobials is associated with, high rates of healing and long-term remission of peptic ulcers.

Pharmacodynamics

Antisecretory Activity
After oral administration, the onset of the antisecretory effect of omeprazole occurs within one hour, with the maximum effect occurring within two 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. The inhibitory effect of omeprazole on acid secretion increases with repeated once-daily dosing, reaching a plateau after four days. Single daily oral doses of omeprazole ranging from a dose of 10 mg to 40 mg have produced 100% inhibition of 24-hour intragastric acidity in some patients.

Serum Gastrin Effects
In studies involving more than 200 patients, serum gastrin levels increased during the first 1 to 2 weeks of once-daily administration of therapeutic doses of omeprazole in parallel with inhibition of acid secretion. No further increase in serum gastrin occurred with continued treatment. In comparison with histamine H2-receptor antagonists, the median increases produced by 20 mg doses of omeprazole were higher (1.3 to 3.6 fold vs. 1.1 to 1.8 fold increase). Gastrin values returned to pretreatment levels, usually within 1 to 2 weeks after discontinuation of therapy. Increased gastrin causes enterochromaffin-like cell hyperplasia and increased serum Chromogranin A (CgA) levels. The increased CgA levels may cause false positive results in diagnostic investigations for neuroendocrine tumors.

Enterochromaffin-like (ECL) Cell Effects
Human gastric biopsy specimens have been obtained from more than 3000 patients treated with omeprazole in long-term clinical trials. The incidence of ECL cell hyperplasia in these studies increased with time; however, no case of ECL cell carcinoids, dysplasia, or neoplasia has been found in these patients. However, these studies are of insufficient duration and size to rule out the possible influence of long-term administration of omeprazole on the development of any premalignant or malignant conditions.

Other Effects
When intragastric pH is maintained at 4.0 or above, basal pepsin output is low, and pepsin activity is decreased.
As do other agents that elevate intragastric pH, omeprazole administered for 14 days in healthy subjects produced a significant increase in the intragastric concentrations of viable bacteria. The pattern of the bacterial species was unchanged from that commonly found in saliva. All changes resolved within three days of stopping treatment.

Pharmacokinetics

Absorption
Omeprazole is acid labile so administered orally as enteric-coated pellets in capsules. Absorption is rapid, with peak plasma levels of omeprazole occurring within 0.5 to 3.5 hours. Peak plasma concentrations of omeprazole and AUC are approximately proportional to doses up to 40 mg, but because of a saturable first-pass effect, a greater than linear response in peak plasma concentration and AUC occurs with doses greater than 40 mg. Absolute bioavailability (compared with intravenous administration) is about 30-40% at doses of 20-40 mg, due in large part to pre-systemic metabolism. In healthy subjects the plasma half-life is 0.5 to 1 hour, and the total body clearance is 500-600 mL/min.

Distribution
The apparent volume of distribution in healthy subjects is approximately 0.3 l/kg body weight. Omeprazole is 97% plasma protein bound.

Metabolism
Omeprazole is completely metabolized by the cytochrome P450 system (CYP). The major part of its metabolism is dependent on the polymorphically expressed CYP2C19, responsible for the formation of hydroxyomeprazole, the major metabolite in plasma. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of omeprazole sulfone. As a consequence of high affinity of omeprazole to CYP2C19, there is a potential for competitive inhibition and metabolic drug-drug interactions with other substrates for CYP2C19. However, due to low affinity to CYP3A4, omeprazole has no potential to inhibit the metabolism of other CYP3A4 substrates. In addition, omeprazole lacks an inhibitory effect on the main CYP enzymes. Approximately 3% of the Caucasian population and 15-20% of Asian populations lack a functional CYP2C19 enzyme and are called poor metabolisers. In such individuals the metabolism of omeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 20 mg omeprazole, the mean AUC was 5 to 10 times higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were also higher, by 3 to 5 times. These findings have no implications for the dosage of omeprazole.

Excretion
The plasma elimination half-life of omeprazole is usually shorter than one hour both after single and repeated oral once-daily dosing. Omeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration. Almost 80% of an oral dose of omeprazole is excreted as metabolites in the urine, the remainder in the faeces, primarily originating from bile secretion.

INDICATIONS

Duodenal ulcer (adults)
Omeprazole is indicated for 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.
Omeprazole is also indicated in the prevention of relapse of duodenal ulcers.

Gastric ulcer (adults)
Omeprazole is indicated for short-term treatment (4-8 weeks) of active benign gastric ulcer in adults.
Omeprazole is also indicated in the prevention of relapse of gastric ulcers.

Treatment and prevention of NSAID associated gastric and duodenal ulcers (adults)
Omeprazole is indicated in the treatment of NSAID-associated gastric and duodenal ulcers and in the prevention of NSAID-associated gastric and duodenal ulcers in adult patients at risk.

Treatment of Gastroesophageal Reflux Disease (GERD) (adults and pediatric patients)

Symptomatic GERD
Omeprazole is indicated for the treatment of heartburn and other symptoms associated with GERD in pediatric patients and adults for up to 4 weeks.

Erosive Esophagitis
Omeprazole is indicated for the short-term treatment (4-8 weeks) of erosive esophagitis that has been diagnosed by endoscopy in pediatric patients and adults. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given.

Maintenance of healing of erosive esophagitis
Omeprazole is indicated to maintain healing of erosive esophagitis in pediatric patients and adults.

Note: In GERD and erosive esophagitis, Omeprazole is indicated in pediatric patients only over 1 year of age. Safety and efficacy is not established in patients less than 1 year.

Eradication of *H. pylori* in peptic ulcer disease (adults and pediatric patients)
Omeprazole in combination with clarithromycin and amoxicillin and other antimicrobial regimens, is indicated for treatment of adult and pediatric patients with H. pylori infection and peptic ulcer disease (active or up to 1-year history).

Note: Omeprazole for eradication of H.pylori is indicated in pediatric patients only above 4 years of age.Eradication of H. pylori has been shown to reduce the risk of peptic ulcer recurrence.

Pathological hyper secretory conditions (adults)
Omeprazole is indicated for the long-term treatment of pathological hyper secretory conditions (e.g. Zollinger-Ellison syndrome, multiple endocrine adenomas and systemic mastocytosis) in adults.

DOSAGE AND ADMINISTRATION

Duodenal Ulcers (adults)
The recommended adult oral dose of Zoltar® (omeprazole) for short term treatment of active duodenal ulcers is 20 mg capsule once daily. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.In patients with poorly responsive duodenal ulcers Zoltar® (Omeprazole) 40 mg capsule once daily is recommended.

For the prevention of relapse of duodenal ulcer the recommended dose is Zoltar® (Omeprazole) 20 mg capsule once daily. In case of therapy failure, the dose can be increased to 40 mg capsule once daily.

Gastric Ulcer (adults)
The recommended adult oral dose is 40 mg capsule once daily for 4-8 weeks.

For the prevention of relapse the recommended dose is 20 mg capsule once daily. If needed the dose can be increased to 40 mg capsule once daily

Treatment and prevention of NSAID associated gastric and duodenal ulcers (adults)
For the treatment of NSAID-associated gastric and duodenal ulcers in adults, the recommended dose is Zoltar® 20 mg capsule once daily. In most patients healing occurs within four weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further four weeks treatment period.

For the prevention of NSAID-associated gastric ulcers or duodenal ulcers in patients at risk (age> 60, previous history of gastric and duodenal ulcers, previous history of upper GI bleeding) the recommended dose is Zoltar®20 mg capsule once daily.

Treatment of Gastroesophageal Reflux Disease (GERD) – Adults & pediatric patients
The recommended adult oral dose for the treatment of patients with symptomatic GERD and no esophageal lesions is 20 mg capsule daily for up to 4 weeks.

The recommended adult oral dose for the treatment of patients with erosive esophagitis and accompanying symptoms due to GERD is 20 mg capsule daily for 4 to 8 weeks. In adult patients with severe esophagitis Zoltar® 40 mg capsule once daily is recommended and healing is usually achieved within eight weeks.

In pediatric patients with symptomatic GERD and erosive esophagitis omeprazole dose is weight based: 5 mg for patients 5 < 10 kg, 10 mg for patients weighing 10 < 20 kg and 20 mg for patients weighing ≥ 20 kg. For symptomatic GERD treatment duration is 2-4 weeks while for erosive esophagitis it is 4-8 weeks. Zoltar® capsule is not recommended for pediatric patients whose weight based dosing requirements are less than 20 mg. Also see Administration instructions for details

Maintenance of Healing of Erosive Esophagitis (Adults and pediatric patients)
The recommended adult oral dose of Zoltar® is 20 mg daily. It may be increased to 40 mg once daily
In pediatric patients the dose for maintenance of healing of erosive esophagitis is weight based: 5 mg for patients 5 < 10 kg, 10 mg for patients weighing 10 < 20 kg and 20 mg for patients weighing ≥ 20 kg. Zoltar® capsule is not recommended for pediatric patients whose weight based dosing requirements are less than 20 mg. Also see Administration instructions for details.

Eradication of *H. pylori* in peptic ulcer disease (adults and pediatric patients)
In adult patients Omeprazole is recommended at a dose of 20 mg – 40 mg once or twice daily as a part of multiple standard antimicrobial regimens. Some of these regimens are given below:
• ZOLTAR® 20 mg + clarithromycin 500 mg + amoxicillin 1000 mg each given twice daily for 10 days. In patients with an ulcer present at the time of initiation of therapy, an additional 18 days of ZOLTAR® 20 mg once daily is recommended for ulcer healing and symptom relief.
• ZOLTAR® 40 mg once daily + clarithromycin 500 mg three times daily for 14 days. In patients with an ulcer present at the time of initiation of therapy, an additional 14 days of ZOLTAR® 20 mg once daily is recommended for ulcer healing and symptom relief.
• ZOLTAR® 20 mg + clarithromycin 250 mg (alternatively 500 mg) + metronidazole 400 mg (or tinidazole 500 mg), each twice daily for one week
• ZOLTAR® 40 mg once daily with amoxicillin 500 mg and metronidazole 400 mg (or tinidazole 500 mg), both three times a day for one week.

In pediatric patients, treatment of peptic ulcer disease for *H. pylori* eradication with omeprazole is weight based along with other antimicrobial drugs: 10 mg for patients weighing 15-30 kg and 20 mg for patients weighing 31-40 kg or greater than 40 kg. Zoltar® capsule is not recommended for pediatric patients whose weight based dosing requirements are less than 20 mg. Also see Administration instructions for details.

Pathological Hypersecretory conditions in adults
The dosage of Zoltar® (Omeprazole) in patients with pathological hypersecretory conditions varies with the individual patient. The recommended adult oral starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Doses up to 120 mg three times daily have been administered. Daily dosages of greater than 80 mg should be administered in divided doses. Some patients with Zollinger-Ellison syndrome have been treated continuously with omeprazole for more than 5 years.

Dosing considerations in Special populations

Elderly
Dose adjustment is not needed in the elderly.

Renal impairment
Dose adjustment is not needed in patients with impaired renal function.

Hepatic impairment
In patients with impaired hepatic function a daily dose of 10–20 mg is sufficient.

Administration Instruction
For adults, it is recommended to take ZOLTAR® capsules in the morning or on an empty stomach at other time of the day, swallowed whole with half a glass of water. The capsules must not be chewed or crushed.

For pediatric patients, ZOLTAR capsules should only be used in children of specific ages who can drink fluids or follow instructions to swallow semi-solid food such as apple sauce. Open ZOLTAR® capsules and mix the contents in fruit juice or apple sauce. The mixture should be swallowed (not chewed) by the child immediately (or within 30 minutes) and always be stirred just before administration. Subsequently, plain water should be administered.
These administration requirements can also be followed for adults and elderly patients having swallowing problems. The enteric coated pellets must never be chewed.

CONTRAINDICATIONS

• Omeprazole is contraindicated in patients with known hypersensitivity to omeprazole or substituted benzimidazoles. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute interstitial nephritis, and urticaria.
• Omeprazole like other proton pump inhibitors (PPIs) must not be used concomitantly with nelfinavir.

WARNINGS AND PRECAUTIONS

Concomitant Gastric Malignancy
In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis. Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy.
Atrophic Gastritis
Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole.
Acute Interstitial Nephritis
Acute interstitial nephritis has been observed in patients taking PPIs 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

Cyanocobalamin (vitamin B-12) Deficiency
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. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.

Gastrointestinal infections and *Clostridium difficile* associated diarrhea
Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter.*
Published observational studies suggest that PPI therapy like omeprazole may also 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.

Concomitant use of omeprazole with clopidogrel
Clopidogrel is a pro-drug. 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. When using omeprazole, consider alternative anti-platelet therapy.

Bone fracture and osteoporosis
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.

Hypomagnesaemia
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.

Concomitant use of omeprazole with St. John's Wort or rifampin
Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease omeprazole concentrations. Avoid concomitant use of omeprazole with St. John's Wort or rifampin.

Interactions with Diagnostic Investigations for Neuroendocrine Tumors
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. Healthcare providers should temporarily stop omeprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g. for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Concomitant use of omeprazole with Methotrexate
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 in some patients or switching to alternative therapy with H2-receptor blockers.

Sub-acute cutaneous lupus erythematous (SCLE)
Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping omeprazole. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

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

ADVERSE REACTIONS

Blood and lymphatic system disorders
Rare: leukopenia, thrombocytopenia.
Very rare: agranulocytosis, pancytopenia.
Immune system disorders
Rare: Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock.
Metabolism and nutrition disorders
Rare: hyponatremia.
Not known: Hypomagnesaemia; severe hypomagnesaemia may result in hypocalcaemia. Hypomagnesaemia may also be associated with hypokalaemia.
Psychiatric disorders
Uncommon: insomnia
Rare: agitation, confusion, depression
Very rare: aggression, hallucinations
Nervous system disorders
Common: headache
Uncommon: dizziness, paraesthesia, somnolence
Rare: taste disturbances.
Eye disorders
Rare: blurred vision
Ear and labyrinth disorders
Uncommon: vertigo
Respiratory, thoracic and mediastinal disorders
Rare: Bronchospasm
Gastrointestinal disorders
Common: Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting.
Rare: Dry mouth, stomatitis, gastrointestinal candidiasis.
Not known: Microscopic colitis.
Hepatobiliary disorders
Uncommon: increased liver enzymes
Rare: Hepatitis with or without jaundice
Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease
Skin and subcutaneous tissue disorders
Uncommon: Dermatitis, pruritus, rash, urticaria.
Rare: Alopecia, photosensitivity
Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN)
Not known: Sub acute cutaneous lupus erythematous
Musculoskeletal and connective tissue disorders
Uncommon: Fracture of the hip, wrist or spine
Rare: Arthralgia, myalgia
Very rare: Muscular weakness
Renal and urinary disorders
Rare: interstitial nephritis
Reproductive system and breast disorders
Very rare: gynaecomastia.
General disorders and administration site conditions
Uncommon: Malaise, peripheral edema.
Rare: Increased sweating.

DRUG INTERACTIONS

Antiretroviral drugs
The decreased intragastric acidity during treatment with omeprazole might increase or decrease the absorption of active substances with a gastric pH dependent absorption.
Concomitant use of atazanavir and nelfinavir with proton pump inhibitors is not recommended. Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir and nelfinavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance. 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. Nelfinavir is contraindicated with omeprazole.
Co-administration of saquinavir with proton pump inhibitors is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction.

Drugs for which gastric pH can affect bioavailability
Due to its effects on gastric acid secretion, omeprazole can reduce the absorption of drugs where gastric pH is an important determinant of their bioavailability. The absorption of drugs such as ketoconazole, posaconazole, itraconazole, iron salts, erlotinib, and mycophenolate mofetil (MMF) can decrease.

The absorption of drugs such as digoxin can increase during treatment with omeprazole. Co-administration of digoxin with omeprazole is expected to increase the systemic exposure of digoxin. Therefore, patients may need to be monitored when digoxin is taken concomitantly with omeprazole.

Co-administration of omeprazole in healthy subjects and in transplant patients receiving MMF has been reported to reduce the exposure to the active metabolite, mycophenolic acid (MPA), possibly due to a decrease in MMF solubility at an increased gastric pH. The clinical relevance of reduced MPA exposure on organ rejection has not been established in transplant patients receiving Omeprazole and MMF. Use Omeprazole with caution in transplant patients receiving MMF.

Drugs metabolized by Cytochrome P450 pathways
Omeprazole can prolong the elimination of diazepam, warfarin and phenytoin, drugs that are metabolized by oxidation in the liver.

There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including omeprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin may need to be monitored for increases in INR and prothrombin time.

Monitoring phenytoin plasma concentration is recommended during the first two weeks after initiating omeprazole treatment.

There also have been clinical reports of interactions with cyclosporine, disulfiram, benzodiazepines. Patients should be monitored to determine if it is necessary to adjust the dosage of these drugs when taken concomitantly with Omeprazole.

Omeprazole is an inhibitor of CYP2C19 enzyme. Clopidogrel is metabolized to its active metabolite in part by CYP2C19. Concomitant use of omeprazole 80 mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant administration of Omeprazole with clopidogrel. When using, Omeprazole, consider use of alternative anti-platelet therapy

Co-administration of cilostazol with omeprazole is expected to increase concentrations of cilostazol and its active metabolite, via CYP2C19 inhibition by omeprazole. Therefore a dose reduction of cilostazol from 100 mg twice daily to 50 mg twice daily should be considered.

Drugs affecting omeprazole exposure
Since omeprazole is metabolised by CYP2C19 and CYP3A4, concomitant administration of omeprazole and voriconazole (a combined inhibitor of CYP2C19 and CYP3A4) results in more than doubling of the omeprazole exposure. Dose adjustment of omeprazole is not normally required. However, in patients with Zollinger-Ellison syndrome, who may require higher doses, patients with severe hepatic impairment or on long-term omeprazole treatment, 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. Avoid concomitant use of St. John's Wort or rifampin with omeprazole.

Tacrolimus
Concomitant administration of omeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.

Methotrexate
Concomitant administration of PPIs and methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. In high-dose methotrexate administration a temporary withdrawal of omeprazole may need to be considered or switching to alternative therapy with H2-blockers

USE IN SPECIAL POPULATIONS

Pregnancy
US FDA Pregnancy Category C: 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.

In general, omeprazole can be used during pregnancy.

Nursing mothers
Omeprazole is present in human milk. The peak concentration of omeprazole in breast milk is approximately less than 7% of the peak serum concentration. This concentration would correspond to 0.004 mg of omeprazole in 200 mL of milk. However, this is not likely to influence the child. Nevertheless, caution should be exercised when omeprazole is administered to a nursing woman.

Pediatric use
The safety and effectiveness of omeprazole has been established only in specific indications in pediatric patients. (See INDICATIONS). ZOLTAR® capsules are primarily indicated in adult patients and should be used in pediatric patients in accordance with the administration instructions set forth in DOSAGE AND ADMINISTRATION Moreover, Zoltar® capsules are not recommended for pediatric patients whose weight-based dosing requirements of omeprazole are less than 20 mg.

Geriatric use
No dosage adjustment is necessary in the elderly.

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 is sufficient.

Renal Impairment
The pharmacokinetics of omeprazole, including systemic bioavailability and elimination rate, are unchanged in patients with reduced renal function. No dosage reduction is necessary.

OVERDOSAGE
Overdoses ranged up to 2400 mg (120 times the usual recommended clinical dose). Manifestations were have been variable, but 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 over dosage is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of over dosage, treatment should be symptomatic and supportive.

PRESENTATION

Zoltar® 20mg : Pack of 14 Capsules
Zoltar® 40mg : Pack of 14 Capsules

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچّوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔
دوا کے ممکنہ منفی اثرات کے متعلق reports@pharmevo.biz
پر مطلع کریں۔

ہماری ادویات کی مزید معلومات کے لئے فارم اسسٹ کی
ہیلپ لائن نمبر 0800-82222 پر کال کریں۔
پیر تا جمعہ صبح 9:00 بجے تا شام 6:00 بجے
یا ہمیں pharmassist@pharmevo.biz پر ای میل کریں

PharmEvo®
Our dream, a healthier society
Manufactured by:
PharmEvo (Pvt.) Ltd.
Plot # A-29, North Western Industrial Zone,
Port Qasim, Karachi-75020, Pakistan
www.pharmevo.biz

DI: ZOLR 01 07/2018