Omeprazole

Risek®

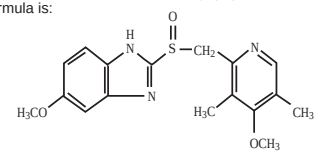
40mg/vial

Lyophilized Powder for Intravenous Injection and Infusion

Proton Pump Inhibitor

DESCRIPTION

Omeprazole (Risek®) IV, a substituted benzimidazole, is a proton pump inhibitor that inhibits gastric acid secretion. Chemically omeprazole is 5-methoxy-2-[[(4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl] sulfinyl]-1Hbenzimidazole. The molecular formula is $C_{17}H_{19}N_3O_3S$ and the structural formula is:



Omeprazole

FORMULATION

Omeprazole (Risek®) IV 40mg
Each vial contains:
Omeprazole sodium equivalent to omeprazole...40mg
(suitably buffered)

CLINICAL PHARMACOLOGY

Mechanism of Action

Omeprazole reduces gastric acid secretion through a unique mechanism of action. Omeprazole belongs to a new class of anti-secretory compounds, the substituted benzimidazoles that do not exhibit anti-cholinergic or histamine antagonistic properties. It inhibits secretion of gastric acid by irreversibly blocking the enzyme system of hydrogen/potassium adenosine triphosphate (H+/K+ ATPase), the proton pump of the gastric parietal cell. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

Pharmacokinetics

Distribution

The apparent volume of distribution in healthy subjects is approximately 0.3L/kg. The plasma protein binding of omeprazole is about 95%.

Metabolism & Excretion

Following absorption, omeprazole is almost completely metabolized in the liver, primarily by the cytochrome P450 isoenzyme CYP2C19 to form hydroxy-omeprazole and to a small extent by CYP3A to form omeprazole sulfone. These metabolites are inactive and excreted mostly in the urine and to a lesser extent in the bile. The majority of the dose (80%) is eliminated in the urine and the remainder is recoverable in the feces. The elimination half-life from plasma following IV administration of omeprazole is approximately 40 minutes. The total plasma clearance is 0.3 to 0.6L/min. There is no change in half-life during treatment.

Special Populations

Pediatric

There is limited experience with omeprazole administered intravenously in children.

Geriatric

In elderly patients the volume of distribution is slightly decreased as compared to healthy patients. A slight decrease in elimination rate and an increase in bioavailablity are also likely to occur in elderly patients. Dose adjustment is not needed in the elderly.

Renal Insufficiency

The distribution volume in patients with reduced renal function is similar to that seen in healthy patients. Dose adjustment is not needed in patients with impaired renal function.

Hepatic Insufficiency

In patients with impaired liver function the volume of distribution is slightly decreased, while the plasma half-life of omeprazole is increased.

THERAPEUTIC INDICATIONS

Omeprazole (Risek®) IV should be administered intravenously only either as an infusion or injection and should not be given by any other route.
Omeprazole (Risek®) IV is indicated for patients who are unable to take oral therapy for the short-term (upto 5 days) treatment of:

1. Gastro-oesophageal reflux disease.
2. Peptic ulcer disease.
3. Treatment and prophylaxis of NSAID-associated ulceration.
4. Duodenal ulcer.
5. Zollinger-Ellison syndrome.
6. Prophylaxis of acid aspiration.

DOSAGE & ADMINISTRATION

Indication	Dosage
1. Gastro-oesophageal reflux disease. 2. Peptic ulcer disease. 3. Treatment and prophylaxis of NSAID-associated ulceration. 4. Duodenal ulcer.	Omeprazole (Risek®) IV 40mg once daily for upto 5 days
Zollinger-Ellison syndrome.	Initial dose of Omeprazole (Risek®) IV given intravenously is 60mg daily. Higher daily doses may be required and the dose should be adjusted individually. Dose greater than 60mg should be given twice daily.
Prophylaxis of acid aspiration during general anesthesia.	Recommended dose of Omeprazole (Risek®) IV is 40mg to be given slowly (over a period of 5 minutes) as an intravenous injection, in the evening before surgery and a further 40mg one hour before surgery.

Hepatic Impaired Patients

For patients with impaired hepatic function a daily dose of 10-20mg may be sufficient.

Direction for reconstitution

Injection:

For IV injection, reconstitute Omeprazole (Risek®) IV with 10mL sterile water for injection to make a 10mL solution containing 4mg/mL omeprazole approximately.
No other solvents for IV injection should be used.
After reconstitution, Omeprazole (Risek®) IV should be given as intravenous injection, slowly over a period of atleast 2.5 minutes at a maximum rate of 4mL/min. The reconstituted solution is stable for approximately 8 hours when stored in the original vial in a cool place.

Infusion:

For IV infusion, reconstitute Omeprazole (Risek®) IV with 10mL sterile water for injection to make a 10mL solution containing 4mg/mL omeprazole approximately. Next add the 10mL reconstituted solution to 90mL of 0.9% w/v of sodium chloride solution for injection, 5% w/v of dextrose solution for injection or 5% w/v of mannitol to make 100mL solution containing 0.4mg/mL of omeprazole approximately. *No other solution should be used for infusion.*
The reconstituted infusion should be given intravenously over a period of 20-30 minutes.
The prepared infusion solution should be used within 3 hours of preparation and any unused portion should be discarded.
The infusion solution should not be refrigerated.
The diluted infusion solution is approximately stable for upto 18 hours when stored in a cool place and protected from sunlight.

The reconstituted and diluted solutions should not be used if it contains visible particulate matter.

ADVERSE EFFECTS

Omeprazole is well tolerated and the adverse reactions have generally been mild and reversible.

Common

Central and peripheral nervous system: Headache.

Gastrointestinal: Diarrhea, constipation, abdominal pain, nausea/vomiting and flatulence.

Uncommon
Central and peripheral nervous system: Dizziness, paraesthesia, somnolence, insomnia and vertigo.
Hepatic: Increased liver enzymes.
Skin: Rash and/or pruritis, urticaria.
Other: Malaise.

Rare
Central and peripheral nervous system: Reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients.
Endocrine: Gynecomastia.
Gastrointestinal: Dry mouth, stomatitis and gastrointestinal candidiasis.
Hematological: Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia.
Hepatic: Encephalopathy in patients with pre-existing severe liver disease, hepatitis with or without jaundice, hepatic failure, increased liver enzymes.
Musculoskeletal: Arthritic and myalgic symptoms and muscular weakness.
Reproductive system: Impotence, breast disorders.
Skin: Photosensitivity, bullous eruption erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia.
Others: Hypersensitivity reactions e.g., angioedema, fever, bronchospasm, interstitial nephritis and anaphylactic shock. Increased sweating, peripheral edema, blurred vision, taste disturbance and hyponatremia.
Isolated cases of irreversible visual impairment have been reported in critically ill patients particularly at high doses, however no casual relationship has been established. Gastro-duodenal carcinoids have been reported in patients with Zollinger-Ellison syndrome on long-term treatment with omeprazole.

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

PRECAUTIONS
General:
- When gastric ulcer is suspected, the possibility of malignancy should be excluded as treatment may alleviate symptoms and delay diagnosis.
- 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 a slightly increased risk of gastrointestinal infections, such as *Salmonella* and *Campylobacter*.

Pregnancy:
There is no evidence of adverse events of omeprazole on pregnancy or on the health of the fetus/newborn child when omeprazole was given to pregnant women. However, administration should be done under caution.

Nursing Mothers:
Omeprazole is excreted in breast milk. Thus a decision should be taken to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Drug Interactions
- In common with the use of other inhibitors of acid secretion or antacids, the absorption of ketoconazole and itraconazole can decrease during treatment with omeprazole due to decreased intragastric acidity during treatment with omeprazole. With voriconazole, the plasma concentration of both drugs may be increased and a reduced dose of omeprazole is recommended.
- Omeprazole is metabolised by CYP2C19. Thus, when omeprazole is combined with drugs metabolised by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin and warfarin, the plasma concentrations of these drugs may be increased and a dose reduction could be needed.
- Simultaneous treatment with omeprazole and digoxin in healthy subjects lead to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH.
- Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.
- Omeprazole like other PPIs should not be co-administered with atazanavir.
- Use of omeprazole and clarithromycin results in an approximate 30% increase in peak plasma concentrations of omeprazole and an increase in its mean half-life from 1.2 hours to 1.6 hours.

INCOMPATIBILITIES
Infusions with low pH should not be used for diluting Omeprazole (Risek®) IV as fading and discoloration of solution can occur.

OVERDOSAGE
Symptoms were transient and no serious clinical outcome has been reported with omeprazole overdose. No specific antidote for omeprazole overdose is known. Omeprazole is extensively bound to plasma proteins and is therefore, not readily dialyzable. In the event of overdose, treatment should be symptomatic and supportive.

STORAGE CONDITIONS
Store at temperatures not exceeding 25°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

AVAILABILITY
Omeprazole (Risek®) IV 40mg lyophilized powder for injection is available as USP type I amber glass vial + 10mL clear glass ampoule.

Keep out of reach of children.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
For suspected adverse drug reaction, report to FDA: www.fda.gov.ph

REGISTRATION NUMBER: DR-XY31530

DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION:
Initial: 7 March, 2006 (Lemery, Mexico)
Initial: 18 November, 2010 (Getz Pharma)
Renewal: 8 April, 2016

DATE OF REVISION OF PACKAGING INSERT: 26 October, 2017.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Getz pharma (PVT) LIMITED
www.getzpharma.com
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