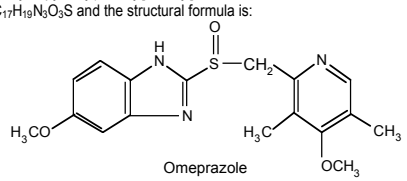
Risek® Insta

(Omeprazole + Sodium bicarbonate)
20mg+1680mg / 40mg+1680mg
Powder for Oral Suspension

DESCRIPTION

RISEK INSTA (Omeprazole + Sodium bicarbonate) is a combination of omeprazole, a proton-pump inhibitor and sodium bicarbonate, an antacid. Risek insta contains immediate-release formulation of omeprazole and sodium bicarbonate. Sodium bicarbonate raises the gastric pH and thus protect omeprazole from acid degradation.

Omeprazole is substituted benzimidazole 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

QUALITATIVE & QUANTITATIVE COMPOSITION

RISEK INSTA (Omeprazole + Sodium Bicarbonate) powder for oral suspension is available for oral administration as:

1. RISEK INSTA Powder for Oral Suspension 20mg
   Each sachet contains:
   Omeprazole USP…20mg
   Sodium Bicarbonate USP …1680mg
   (as buffer)

2. RISEK INSTA Powder for Oral Suspension 40mg
   Each sachet contains:
   Omeprazole USP…40mg
   Sodium Bicarbonate USP …1680mg
   (as buffer)

CLINICAL PHARMACOLOGY

Mechanism of Action

Omeprazole reduces gastric acid secretion through a unique mechanism of action. Omeprazole belongs to a class of anti-secretory compounds - the substituted benzimidazoles that do not exhibit anti-cholinergic or H_2 histamine antagonistic properties. It inhibits secretion of gastric acid by irreversibly blocking the enzyme system of hydrogen/potassium adenosine triphosphatase (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

Absorption:

Omeprazole is acid-labile and is administered orally on an empty stomach 1 hour prior to a meal. The absorption of omeprazole is rapid, with mean peak plasma levels being 1954ng/mL (33%) occurring at about 30 minutes (range 10 to 90 minutes) after a single dose or repeated-dose administration. Absolute bioavailability of omeprazole powder for oral suspension is about 30-40% at doses 20-40mg due in large part to presystemic metabolism. When powder for oral suspension is administered 1 hour after a meal, the omeprazole AUC is reduced by approximately 24% relative to administered 1 hour prior to meal.

Distribution:

Omeprazole is bound to plasma proteins. Protein binding is approximately 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 CYP3A4 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 (77%) was eliminated in the urine. The remainder of the dose was recoverable in the feces. The mean plasma omeprazole half-life is approximately 1 hour (ranging from 0.4 to 3.2 hours) and the total body clearance is 500-600mL/min.

Special Population

Pediatric

The pharmacokinetics of omeprazole has not been studied in patients < 18 years of age.

Geriatric

The elimination rate of omeprazole was somewhat decreased in the elderly, and bioavailability was increased. Omeprazole was 76% bioavailable when a single 40mg oral dose of omeprazole (buffered solution) was administered to healthy elderly subjects, versus 58% in young subjects given the same dose. The plasma clearance of omeprazole was 250mL/min (about half that of young subjects) and its plasma half-life averaged one hour, similar to that of young healthy subjects.

Renal Insufficiency

In patients with chronic renal impairment, whose creatinine clearance ranged between 10 and 62mL/min/1.73m^2, the disposition of omeprazole from a buffered solution was very similar to that in healthy subjects, although there was a slight increase in bioavailability. Because urinary excretion is a primary route of excretion of omeprazole metabolites, their elimination slowed in proportion to the decreased creatinine clearance.

Hepatic Insufficiency

In patients with chronic hepatic disease, the bioavailability of omeprazole from a buffered solution increased to approximately 100% and the mean plasma half-life of the drug increased to nearly 3 hours compared to the mean half-life of 1 hour in normal subjects. Plasma clearance averaged 70mL/min, compared to a value of 500-600mL/min in normal subject.

THERAPEUTIC INDICATIONS

RISEK INSTA (Omeprazole + Sodium bicartbonate) powder for oral suspension is indicated:

1. In the treatment of Gastro-Esophageal Reflux Disease (GERD):
   - For the treatment of heart burn and other symptoms associated with GERD.
   - For the treatment of erosive esophagitis which has been diagnosed by endoscopy.
2. In short term treatment of active duodenal ulcer. Some patients may require an additional therapy.
3. In short term treatment of active benign gastric ulcer.
4. For maintenance treatment of healing of erosive esophagitis.
5. For reduction treatment of risk of upper gastrointestinal bleeding in critically ill patients.

DOSAGE & ADMINISTRATION

RISEK INSTA (Omeprazole + Sodium bicarbonate) powder for oral suspension as per recommended dosing given in below table.

RISEK INSTA (Omeprazole + Sodium bicarbonate) should be taken on an empty stomach at least one hour before a meal.

Recommended doses for Adults (18 years & older)

Indication	Recommended	Dose Frequency
Short term treatment of active duodenal ulcer	20mg	Once daily for 4 weeks
Benign gastric ulcer	40mg	Once daily for 4-8 weeks
Reduction of risk of upper gastrointestinal bleeding in critically ill patients (40mg oral suspension only)	40mg	40mg initially followed by 40mg 6-8 hours later and 40mg daily thereafter for 14 days*
Gastroesophageal Reflux Disease (GERD)		
Symptomatic GERD (with no esophageal erosions)	20mg	Once daily for up to 4 weeks
Erosive esophagitis	20mg	Once daily for 4-8 weeks. **
Maintenance of healing of erosive esophagitis	20mg	Once daily

*Most patients heal within 4 weeks. Some patients may require an additional 4 weeks of therapy.

**The efficacy of RISEK INSTA (Omeprazole + Sodium bicarbonate) used for longer than 8 weeks in these patients has not been established. In the rare instance of a patient not responding to 8 weeks of treatment, it may be helpful to give upto an additional 4 weeks of treatment. If there is recurrence of erosive esophagitis or GERD, symptoms (e.g., heartburn), additional 4-8 week courses of omeprazole may be considered.

Since both 20mg and 40mg oral suspension sachets contain the same amount of sodium bicarbonate (1680mg), two sachets of RISEK INSTA (Omeprazole + Sodium bicarbonate) 20mg are not equivalent to one sachet of RISEK INSTA (Omeprazole + Sodium bicarbonate) 40mg; therefore two 20mg sachets of RISEK INSTA (Omeprazole + Sodium bicarbonate) should not be substituted for one sachet RISEK INSTA (Omeprazole + Sodium bicarbonate) 40mg.

DIRECTIONS FOR USE:
Empty the sachet contents into a small cup containing 1-2 tablespoons (15 - 30mL) of water. Stir well and drink immediately. Refill cup with water and drink. DO NOT USE OTHER LIQUIDS OR FOODS.

ADVERSE EFFECTS
The following adverse reactions were reported:
Body As a Whole
Allergic reactions, including, rarely anaphylaxis, fever, pain, fatigue, malaise and abdominal swelling.

Cardiovascular
Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema.

Gastrointestinal
Pancreatitis (sometimes fatal), anorexia, irritable colon, flatulence, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, dry mouth, stomatitis. During treatment with omeprazole, gastric fundic gland polyps have been noted rarely. These polyps are benign and appear to be reversible when treatment is discontinued.

Hepatic
Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), γ-glutamyl transpeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis, liver necrosis (sometimes fatal), hepatic failure (sometimes fatal), and hepatic encephalopathy.

Metabolic/Nutritional
Hyponatremia, hypoglycemia, and weight gain.

Musculoskeletal
Muscle cramps, myalgia, muscle weakness, joint pain, and leg pain.

Nervous System/Psychiatric
Psychic disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, tremors, apathy, somnolence, anxiety, dream abnormalities, vertigo, paresthesia and hemifacial dysesthesia.

Respiratory
Epistaxis, pharyngeal pain.

Skin
Rash and rarely, cases of severe generalized skin reactions including toxic epidermal necrolysis (TEN; sometimes fatal), Stevens-Johnson syndrome, and erythema multiforme (some severe); purpura and/or petechiae (sometimes with rechallenge); skin inflammation, urticaria, angioedema, pruritus, photosensitivity, alopecia, dry skin, and hyperhydrosis.

Special Senses
Tinnitus, taste perversion.

Ocular
Blurred vision, ocular irritation, dry eye syndrome, optic atrophy, anterior ischemic optic neuropathy, optic neuritis and double vision.

Urogenital
Interstitial nephritis (sometimes with positive rechallenge), urinary tract infection, microscopic pyuria, urinary frequency, elevated serum creatinine, proteinuria, hematuria, glycosuria, testicular pain, and gynecomastia.

Hematologic
Rare instances of pancytopenia, agranulocytosis (sometimes fatal), thrombocytopenia, neutropenia, leukopenia, anemia, leucocytosis, and hemolytic anemia have been reported.

Additional adverse reactions that could be caused by sodium bicarbonate, include metabolic alkalosis, seizures, and tetany.

CONTRAINDICATIONS
- Omeprazole is contraindicated in patients with known hypersensitivity to any component of the formulation.
- Sodium bicarbonate is contraindicated in patients with metabolic alkalosis and hypocalcemia.

PRECAUTIONS
General:
- Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy.
- Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole.
- Omeprazole powder for oral suspension contains sodium in the form of sodium bicarbonate. This should be taken into consideration for patients on a sodium-restricted diet.
- Sodium bicarbonate should be used with caution in patients with Bartter's syndrome, hypokalemia, respiratory alkalosis, and problems with acid-base balance. Long- term administration of bicarbonate with calcium or milk can cause milk-alkali syndrome.

Pregnancy:
There are no adequate and well controlled studies on the use of omeprazole in pregnant women. Omeprazole should be used during pregnancy only if the potential benefit to pregnant women justifies the potential risk to the fetus.

Nursing Mothers:
Omeprazole is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from omeprazole; a decision should be made whether, to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. In addition, sodium bicarbonate should be used with caution in nursing mothers.

Drug Interactions
- 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. Although in normal subjects no interaction with theophylline or propranolol was found, there have been clinical reports of interaction with other drugs metabolized via the cytochrome P-450 system (e.g., 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.
- Because of its profound and long-lasting inhibition of gastric acid secretion, it is theoretically possible that omeprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole, ampicillin esters, and iron salts).
- Concomitant administration of omeprazole and atazanavir has been reported to reduce the plasma levels of atazanavir.
- Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.
- Co-administration of omeprazole and clarithromycin have resulted in increases of plasma levels of omeprazole, clarithromycin, and 14-hydroxy-clarithromycin.

OVERDOSAGE
In doses ranged up to 2400mg, manifestations were 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 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. In addition, a sodium bicarbonate overdose may cause hypocalcemia, hypokalemia, hypernatremia, and seizures.

STORAGE
Store at 25°C. (Excursions permitted to 15°C - 30°C)
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
RISEK INSTA (Omeprazole + Sodium bicarbonate) 20mg+1680mg powder for oral suspension is available as sachets in packs of 10's.

RISEK INSTA (Omeprazole + Sodium bicarbonate) 40mg+1680mg powder for oral suspension is available as sachets in packs of 10's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

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

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