Promiz Injection / Infusion / Capsule

(O m e p r a z o l e)

پرومیز انجیکشن/انفیوژن/کیپسول

(اومیپرازول)

COMPOSITION:

PROMIZ Injection 40mg

Each vial contains:

Omeprazole (as sodium) powder for reconstitution.....40mg

(Innovator's specifications)

PROMIZ Capsule 20mg

Each capsule contains:

Enteric coated pellets of Omeprazole eq. to Omperazole.....20mg

(USP specifications)

PROMIZ Capsule 40mg

Each capsule contains:

Enteric coated pellets of Omeprazole eq. to Omeprazole.....40mg

(USP specifications)

DESCRIPTION

PROMIZ (Omeprazole) IV, a substituted benzimidazole, is a proton pump inhibitor that inhibits gastric acid secretion.

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.

INDICATIONS

PROMIZ is indicated for the treatment of:

- Duodenal ulcers, benign gastric ulcers.
- Gastroesophageal reflux disease (GERD), heartburn and other symptoms associated with GERD.
- Prophylaxis of acid aspiration during general anesthesia.
- Erosive esophagitis, and long-term treatment of pathological hypersecretory conditions like Zollinger-Ellison syndrome, multiple endocrine adenomas, and systemic mastocytosis.
- Dyspepsia, prophylaxis of acid aspiration, Zollinger-Ellison syndrome.
- Eradication of helicobacter pylori infections associated with peptic ulcer disease.

DOSAGE & ADMINISTRATION

- ***For injection***

For Gastro-Esophageal Reflux Disease, Peptic Ulcer Disease, Treatment & Prophylaxis of NSAID Associated Ulcer, Duodenal Ulcer:

Promiz IV 40mg once daily for up to 5 days.

For Zollinger-Ellison Syndrome:

Initial dose of promiz IV 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 is 40 mg IV 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.

Method of Reconstitution:

- **Injection:**

For IV injection, reconstitute Promiz IV with 5ml 0.9% w/v Sodium Chloride Solution for Injection to make a 5 ml solution.

No other solvents for IV injections should be used.

After reconstitution, Promiz IV should be given as an intravenous injection slowly over a period of at least 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 Promiz IV with 5ml 0.9% w/v Sodium Chloride Solution for Injection to make 5ml solution. Than further dilute it with 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 solution for Infusion.

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.

Hepatic impaired patients:

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

- ***For capsule***

Adults

Treatment of duodenal ulcers

The recommended dose in patients with an active duodenal ulcer is Omeprazole 20mg once daily. In most patients healing occurs within two weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further two weeks' treatment period. In patients with poorly responsive duodenal ulcer Omeprazole 40mg once daily is recommended and healing is usually achieved within four weeks.

Prevention of relapse of duodenal ulcers

For the prevention of relapse of duodenal ulcer in H. pylori negative patients or when H. pylori eradication is not possible the recommended dose is Omeprazole 20mg once daily. In some patients a daily dose of 10mg may be sufficient. In case of therapy failure, the dose can be increased to 40mg.

Treatment of gastric ulcers

The recommended dose is Omeprazole 20mg 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. In patients with poorly responsive gastric ulcer Omeprazole 40mg once daily is recommended and healing is usually achieved within eight weeks.

Prevention of relapse of gastric ulcers

For the prevention of relapse in patients with poorly responsive gastric ulcer the recommended dose is Omeprazole 20mg once daily. If needed the dose can be increased to Omeprazole 40mg once daily.

H. pylori eradication in peptic ulcer disease

For the eradication of H. pylori the selection of antibiotics should consider the individual patient's drug tolerance, and should be undertaken in accordance with national, regional and local resistance patterns and treatment guidelines.

- Omeprazole 20mg + clarithromycin 500mg + amoxicillin 1,000mg, each twice daily for one week, or
- Omeprazole 20mg + clarithromycin 250mg (alternatively 500mg) + metronidazole 400mg (or 500mg or tinidazole 500mg), each twice daily for one week or
- Omeprazole 40mg once daily with amoxicillin 500mg and metronidazole 400mg (or 500mg or tinidazole 500mg), both three times a day for one week.

In each regimen, if the patient is still H. pylori positive, therapy may be repeated.

Treatment of NSAID-associated gastric and duodenal ulcers

For the treatment of NSAID-associated gastric and duodenal ulcers, the recommended dose is Omeprazole 20mg 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.

Prevention of NSAID-associated gastric and duodenal ulcers in patients at risk

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 Omeprazole 20mg once daily.

Treatment of reflux esophagitis

The recommended dose is Omeprazole 20mg 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.

In patients with severe esophagitis Omeprazole 40mg once daily is recommended and healing is usually achieved within eight weeks.

Long-term management of patients with healed reflux esophagitis

For the long-term management of patients with healed reflux esophagitis the recommended dose is Omeprazole 10mg once daily. If needed, the dose can be increased to Omeprazole 20-40mg once daily.

Treatment of symptomatic gastro-esophageal reflux disease

The recommended dose is Omeprazole 20mg daily. Patients may respond adequately to 10mg daily, and therefore individual dose adjustment should be considered.

If symptom control has not been achieved after four weeks' treatment with Omeprazole 20mg daily, further investigation is recommended.

Treatment of Zollinger-Ellison syndrome

In patients with Zollinger-Ellison syndrome the dose should be individually adjusted and treatment continued as long as clinically indicated. The recommended initial dose is Omeprazole 60mg daily. All patients with severe disease and inadequate response to other therapies have been effectively controlled and more than 90% of the patients maintained on doses of Omeprazole 20-120mg daily. When dose exceed Omeprazole 80mg daily, the dose should be divided and given twice daily.

Children

- Children over 1 year of age and ⩾ 10kg

Treatment of reflux esophagitis

Symptomatic treatment of heartburn and acid regurgitation in gastro-esophageal reflux disease.

The posology recommendations are as follows:

Age Weight Posology

⩾ 1 year of age 10–20kg 10mg once daily. The dose can be increased to 20mg once daily if needed.

⩾ 2 years of age > 20kg 20mg once daily. The dose can be increased to 40mg once daily if needed.

Reflux esophagitis: The treatment time is 4-8 weeks.

Symptomatic treatment of heartburn and acid regurgitation in gastro-esophageal reflux disease: The treatment time is 2–4 weeks. If symptom control has not been achieved after 2–4 weeks, the patient should be investigated further.

- **Children and adolescents over 4 years of age**

Treatment of duodenal ulcer caused by H. pylori.

When selecting appropriate combination therapy, consideration should be given to official national, regional and local guidance regarding bacterial resistance, duration of treatment (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents.

The treatment should be supervised by a specialist.

The dosage recommendations are as follows:

Weight	Posology
15-30kg	Combination with two antibiotics: Omeprazole 10mg, amoxicillin 25mg/kg body weight and clarithromycin 7.5mg/kg body weight are all administrated together two times daily for one week.
31-40kg	Combination with two antibiotics: Omeprazole 20mg, amoxicillin 750mg and clarithromycin 7.5mg/kg body weight are all administrated two times daily for one week.
>40kg	Combination with two antibiotics: Omeprazole 20mg, amoxicillin 1g and clarithromycin 500mg are all administrated two times daily for one week.

PHARMACOKINETICS

- **Absorption**

Omeprazole and omeprazole magnesium are acid labile and are therefore administered orally as enteric-coated granules in capsules or tablets. Absorption of omeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. Absorption of omeprazole takes place in the small intestine and is usually completed within 3-6 hours. Concomitant intake of food has no influence on the bioavailability. The systemic availability (bioavailability) from a single oral dose of omeprazole is approximately 40%. After repeated once-daily administration, the bioavailability increases to about 60%.

- **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. About 80% of the dose is excreted in the urine and the remaining 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 0.6 L/min. there is no change in half-life during treatment.

Special populations:

- **Pediatric:**

There is limited experience with omeprazole administered IV 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 bioavailability are also likely to occur in elderly patients. Dose adjustment is not required.

Renal insufficiency:

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

Hepatic insufficiency:

The volume of distribution is slightly decreased while the plasma half-life of omeprazole is increased.

PRECAUTIONS

- Should be used with caution in patients with liver or kidney disease.
- It should be used only when clearly needed during pregnancy.
- Avoid use during lactation.
- In elderly there is no problem in clinical use to data.
- 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

SIDE EFFECTS

- **Body as a Whole:**

Hypersensitivity reactions including anaphylaxis, anaphylactic, angioedema, bronchospasm, interstitial nephritis,urticaria, (see **also *Skin* below**); fever; pain; fatigue; malaise.

- **Cardiovascular:**

Chest pain or angina, tachycardia, bradycardia, palpitations, elevated blood pressure, peripheral edema

- **Endocrine:**

Gynecomastia

✓ **Gastrointestinal:**

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

Gastroduodenal carcinoids have been reported in patients with ZE syndrome on long-term treatment with PROMIZ. This finding is believed to be a manifestation of the underlying condition, which is known to be associated with such tumors.

- **Hepatic:**

Liver disease including hepatic failure (some fatal), liver necrosis(some fatal), hepatic encephalopathy hepatocellular disease, cholestatic disease, mixed hepatitis, jaundice, and elevations of liver function tests [ALT, AST, GGT, alkaline phosphatase, and bilirubin]

- **Infections and Infestations:**

Clostridium difficile associated diarrhea.

- **Metabolism and Nutritional disorders:**

Hypoglycemia, hypomagnesemia, with or without hypocalcemia and/or hypokalemia, hyponatremia, weight gain.

- **Musculoskeletal:**

Muscle weakness, myalgia, muscle cramps, joint pain, leg pain, bone fracture

- **Nervous System/Psychiatric:**

Psychiatric and sleep disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, apathy, somnolence, anxiety, and dream abnormalities; tremors, paresthesia; vertigo.

- **Respiratory:** Epistaxis, pharyngeal pain.
- **Skin:**

Severe generalized skin reactions including toxic epidermal necrolysis (some fatal), Stevens-Johnson syndrome, and erythema multiforme; photosensitivity; urticarial rash; skin inflammation; pruritus; petechiae;purpura; alopecia; dry skin; hyperhidrosis

- **Special Senses:** Tinnitus, taste perversion.
- **Ocular:**

Optic atrophy, anterior ischemic optic neuropathy, optic neuritis, dry eye syndrome, ocular irritation, blurred vision, double vision.

- **Urogenital:**

Interstitial nephritis, hematuria, proteinuria, elevated serum creatinine, microscopic pyuria, urinary tract infection, glycosuria, urinary frequency, testicular pain.

- **Hematologic:**

Agranulocytosis (some fatal), hemolytic anemia,pancytopenia, neutropenia, anemia, thrombocytopenia, leukopenia, leukocytosis

DRUG INTERACTIONS

- Some products that may interact with this drug include: cilostazol, clopidogrel, methotrexate (especially high-dose treatment), rifampin, St John's wort.
- Some products need stomach acid so that the body can absorb them properly.
- Omeprazole decreases stomach acid, so it may change how well these products work. Some affected products include atazanavir, erlotinib, nelfinavir, pazopanib, rilpivirine, certain azole antifungals (itraconazole, ketoconazole, posaconazole), among others.
- Omeprazole is metabolized by CYP2C19. Thus, when omeprazole is combined with drugs metabolized 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
- Omeprazole is very similar to esomeprazole. Do not use any medications containing esomeprazole while using omeprazole.
- 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 intra gastric pH.
- Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.
- 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 to 1.6 hours
- This medication may interfere with certain laboratory tests, possibly causing false test results.

INCOMPATIBILITIES

Infusions with low pH should not be used for diluting PROMIZ (Omeprazole) IV as fading and discoloration of solution can occur. In the event of overdose, treatment should be symptomatic and supportive.

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.

CONTRAINDICATIONS

PROMIZ is contraindicated in patients with known hypersensitivity to substituted benzimidazoles or to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic, angioedema, bronchospasm, acute interstitial nephritis, and urticaria.

STORAGE&INSTRUCTIONS

Store between 15-25°C.

Protect from heat, sunlight and moisture. Do not freeze.

Keep out of reach of children

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

HOW SUPPLIED

PROMIZ Injection 40mg

1vial + 5ml of 0.9% w/v sodium chloride solution for injection (1x5ml ampoules)

PROMIZ Capsule 20mg

14's capsules

PROMIZ Capsule 40mg

14's capsules

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:

PHARMASOL

PRIVATE LIMITED

Plot # 549,Sundar Industrial Estate,

Lahore, Pakistan.

PM-2058-00