

New Zealand Datasheet

Name of Medicine

Dr Reddy's Omeprazole

Omeprazole 20 mg capsules

Presentation

Omeprazole capsules 20 mg: hard gelatine size 2 capsules with a light grey opaque body printed with "R158" in black ink, and a purple opaque cap printed with "Omeprazole 20 mg" in black ink. Each capsule contains omeprazole 20 mg as enteric coated pellets.

Uses

Actions

Omeprazole, a racemic mixture of two active enantiomers, reduces gastric acid secretion through a highly targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. It is rapid acting and provides control through reversible inhibition of gastric acid secretion with once daily dosing.

Site and mechanism of action

Omeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the intracellular canaliculi within the parietal cell, where it inhibits the enzyme H⁺,K⁺-ATPase, the acid pump. This effect on the final step of the gastric acid formation process is dose-dependent and provides for highly effective inhibition of both basal acid secretion and stimulated acid secretion, irrespective of the stimulus.

All pharmacodynamic effects observed can be explained by the effect of omeprazole on acid secretion.

Effect on gastric acid secretion

Oral dosing with omeprazole capsules once daily provides for rapid and effective inhibition of daytime and night-time gastric acid secretion with maximum effect being achieved within 4 days of treatment. With omeprazole capsules 20 mg, a mean decrease of at least 80% in 24-hour intragastric acidity is then maintained in duodenal ulcer patients, with the mean decrease in peak acid output after pentagastrin stimulation being about 70% twenty-four hours after dosing.

Oral dosing with omeprazole capsules 20 mg maintains an intragastric pH of ≥ 3 for a mean time of 17 hours of the 24 hour period in duodenal ulcer patients.

As a consequence of reduced acid secretion and intragastric acidity, omeprazole dose-dependently reduces/normalises acid exposure of the oesophagus in patients with gastro-oesophageal reflux disease.

The inhibition of acid secretion is related to the area under the plasma concentration-time curve (AUC) of omeprazole and not to the actual plasma concentration at a given time.

No tachyphylaxis has been observed during treatment with omeprazole.

Other effects related to acid inhibition

During long-term treatment gastric glandular cysts have been reported in a somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

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*.

Pharmacokinetics

Absorption and distribution

Omeprazole is acid labile and is therefore administered orally as enteric-coated pellets in capsules or tablets.

Absorption of omeprazole takes place in the small intestine and is usually completed within 3-6 hours. The systemic bioavailability of omeprazole from a single oral dose of omeprazole capsules is approximately 35%. After repeated once daily administration, the bioavailability increases to about 60%. The apparent volume of distribution in healthy subjects is approximately 0.3 L/kg and a similar value is also seen in patients with renal insufficiency. In elderly patients, and in patients with hepatic insufficiency, the volume of distribution is slightly decreased. Concomitant intake of food has no influence on the bioavailability. The plasma protein binding of omeprazole is about 95%.

Metabolism and excretion

After oral administration, the plasma elimination half-life of omeprazole is usually shorter than one hour and there is no change in half-life during long-term treatment. Omeprazole is completely metabolised by the cytochrome P450 system (CYP), mainly in the liver. The major part of its metabolism is dependent on the polymorphically expressed, specific isoform CYP2C19 (S-mephenytoin hydroxylase), responsible for the formation of hydroxyomeprazole, the major metabolite in plasma. In accordance with this, as a consequence of competitive inhibition, there is a potential for metabolic drug-drug interactions between omeprazole and other substrates for CYP2C19.

No metabolite has been found to have any effect on gastric acid secretion. Almost 80% of an orally given dose is excreted as metabolites in the urine, and the remainder is found in the faeces, primarily originating from bile secretion.

The systemic bioavailability and elimination of omeprazole is unchanged in patients with reduced renal function. The area under the plasma concentration-time curve, and the elimination half-life are increased in patients with impaired liver function, but omeprazole has not shown any tendency to accumulate with once daily dosing.

Children

Available data from children (1 year and older) suggests that the pharmacokinetics, within the recommended dosages (see Dosage and Administration) is similar to those reported in adults.

Indications

Dr Reddy's Omeprazole capsules are for the short-term relief of gastric reflux-like symptoms in sufferers aged 18 years and over.

Dosage and Administration

Dr Reddy's Omeprazole capsules are recommended to be given in the morning and swallowed whole with half a glass of water. The contents of the capsule should not be chewed or crushed.

For patients with swallowing difficulties the capsule can be opened and the contents swallowed directly with half a glass of liquid or after mixing the contents in a slightly acidic fluid e.g. fruit juice, yoghurt or in non carbonated water. The dispersion should be taken immediately or within 30 minutes. Alternatively patients can suck the capsule and swallow the pellets with liquid. The pellets must not be chewed or crushed.

Reflux oesophagitis

The recommended dosage is one Dr Reddy's Omeprazole capsule 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 4 weeks. The maximum daily dose should not exceed 20 milligrams.

Impaired Renal Function

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

Impaired Hepatic Function

As bioavailability and plasma half-life of omeprazole are increased in patients with impaired hepatic function a daily dose of 10 - 20 mg may be sufficient.

Elderly

Dose adjustment is not needed in the elderly.

Contraindications

Known hypersensitivity to omeprazole.

Warnings and Precautions

Dr Reddy's Omeprazole 20 mg capsules are for short-term use only, except on medical advice. Do not use the medicine for any purpose other than that specified on the pack, except on medical advice.

Do not use in those that are experiencing weight loss, persistent regurgitation of food or vomiting, difficulty swallowing or symptoms of gastro-intestinal bleeding, except on medical advice.

Consult a doctor if symptoms persist, recur or worsen or if new symptoms occur. Consult a doctor or pharmacist before use if you are pregnant or are taking any other medicines.

Use in Pregnancy and Lactation

Results from three prospective epidemiological studies indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Dr Reddy's Omeprazole capsules can be used during pregnancy.

Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used.

Effect on Ability to Drive and Use Machines

Dr Reddy's Omeprazole capsules are not likely to affect the ability to drive or use machines.

Adverse Effects

Dr Reddy's Omeprazole capsules are well tolerated and adverse reactions have generally been mild and reversible. The following events have been reported as adverse events in clinical trials or reported from routine use, but in many cases a relationship to treatment with omeprazole has not been established.

The following definitions of frequencies are used:

Common ≥1/100

Uncommon ≥1/1,000 and <1/100

Rare <1/1,000

Common	Central and peripheral nervous system:	Headache
	Gastrointestinal:	Diarrhoea, 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, dermatitis 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:	Gynaecomastia
	Gastrointestinal:	Dry mouth, stomatitis and gastrointestinal candidiasis
	Haematological:	Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia.
	Hepatic:	Encephalopathy in patients with pre-existing severe liver disease; hepatitis with or without jaundice, hepatic failure
	Musculoskeletal:	Arthralgia, muscular weakness and myalgia
	Skin:	Photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), alopecia Hypersensitivity reactions eg. angioedema, fever, bronchospasm, interstitial nephritis and anaphylactic shock.
	Other:	Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia.

Interactions

The absorption of some medicines might be altered due to the decreased intragastric acidity. The absorption of ketoconazole and itraconazole can decrease during omeprazole treatment, as it does during treatment with other acid secretion inhibitors or antacids.

No interaction with food or concomitantly administered antacids has been found. As omeprazole is metabolised in the liver through cytochrome P450 2C19 (CYP2C19), it can prolong the elimination of diazepam, phenytoin, warfarin (R-warfarin) and other vitamin K antagonists which are all in part substrates for this enzyme.

Monitoring of patients receiving phenytoin is recommended and a reduction of phenytoin dose may be necessary. However concomitant treatment with omeprazole capsules 20 mg daily did not change the blood concentration of phenytoin in patients on continuous treatment with this medicine. In patients receiving warfarin or other vitamin K antagonists, monitoring of INR is recommended and a reduction of the warfarin (or other vitamin K antagonist) dose may be necessary. Concomitant treatment with omeprazole capsules 20 mg daily did, however, not change coagulation time in patients on continuous treatment with warfarin.

Plasma concentrations of omeprazole and clarithromycin are increased during concomitant administration but there is no interaction with metronidazole or amoxicillin. These antimicrobials are used together with omeprazole for eradication of *Helicobacter pylori*.

Concomitant administration of omeprazole has been reported to reduce the plasma levels of atazanavir.

Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.

Concomitant administration of omeprazole and a CYP2C19 and CYP3A4 inhibitor, voriconazole, resulted in more than doubling of the omeprazole exposure. However, a dose adjustment of omeprazole was not required.

Results from a range of interaction studies with omeprazole capsules versus other medicines indicate that omeprazole, 20-40 mg daily, has no influence on any other relevant isoforms of CYP, as shown by the lack of metabolic interaction with substrates for CYP1A2 (caffeine, phenacetin, theophylline), CYP2C9 (S-warfarin, piroxicam, diclofenac and naproxen), CYP2D6 (metoprolol, propranolol), CYP2E1 (ethanol), and CYP3A (cyclosporin, lidocaine, quinidine, estradiol, erythromycin, budesonide).

Overdosage

Rare reports have been received of overdosage with omeprazole. 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). Nausea, vomiting, dizziness, abdominal pain, diarrhoea and headache have been reported from overdosage with omeprazole. Also apathy, depression and confusion have been described in single cases.

The symptoms described in connection to omeprazole overdosage have been transient, and no serious outcome due to omeprazole has been reported. The rate of elimination was unchanged (first order kinetics) with increased doses and no specific treatment has been needed.

Pharmaceutical Precautions

Store below 25°C.

Medicine Classification

Pharmacist Only Medicine.

Package Quantities

20 mg: Cartons of aluminium blisters containing 14 capsules.

Further Information

Each capsule contains: omeprazole 20 mg.

Excipients

Mannitol, Crospovidone, Hypromellose, Poloxamer, Meglumine, Povidone, Methacrylic acid ethyl acrylate copolymer, Triethyl citrate, Magnesium stearate, The gelatin capsules consist of Erythrosin, Patent blue V, Titanium dioxide, Gelatin, and printing ink.

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