

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Lomex-T 20 mg acid-resistant tablet.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 20 mg of the active substance omeprazole.

Excipients: See section 6.1.

3. PHARMACEUTICAL FORM

Acid-resistant tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ulcer disease of the duodenum and stomach. Inflammation of the esophagus due to reflux esophagitis. Eradication of helicobacter pylori in ulcer disease (along with antibiotics). Ulcer disease or an erosion in the duodenum and stomach caused by treatment with non-steroidal anti-inflammatory drugs (NSAID). Preventive measure in treatment with non-steroidal anti-inflammatory drugs due to an increased risk of problems, such as ulcer disease of the stomach, esophagus or duodenum, erosion in the stomach and/or the duodenum or dyspepsia. Symptomatic treatment of heartburn and water brash due to gastro-esophageal reflux disease. Zollinger-Ellison syndrome.

The drug is also intended for long-term treatment of inflammation of the esophagus caused by reflux and of recurring ulcers in the stomach and duodenum, provided that satisfactory results have not been achieved with 10 mg per day of an equivalent drug, and at that time the dose may be raised to 20-40 mg of omeprazole (1-2 Lomex-T 20 mg acid resistant tablets) once a day.

4.2 Posology and method of administration

It is recommended that the tablets be taken in the morning. They should be swallowed whole with ½ a glass of water. The tablets may neither be chewed nor ground.

Dosage

Duodenal ulcer: The recommended dose for patients with an active duodenal ulcer is 20 mg once a day. Symptoms disappear rapidly and for most patients the ulcer heals within two weeks. For patients with an ulcer that does not fully heal in that time, the ulcer usually heals with two additional weeks of therapy. For patients with a duodenal ulcer that responds poorly to treatment, it is recommended to administer 40 mg once a day, and the ulcer usually heals within four weeks.

As prophylaxis against recurring duodenal ulcers a dose of 10 mg omeprazole once a day is recommended. As Lomex-T acid-resistant tablets contain 20 mg of omeprazole it is recommended to initiate treatment with an equivalent medicine of lower strength. If need be the dose may be increased to 20-40 mg omeprazole (1-2 Lomex-T 20 mg acid-resistant tablets) once a day.

For duodenal ulcers caused by treatment with non-steroidal anti-inflammatory drugs (NSAID), see the section on *Ulcers or erosion caused by treatment with non-steroidal anti-inflammatory drugs (NSAID)*

Eradication of *Helicobacter pylori*, see the section on *Eradication of Helicobacter pylori in ulcer disease*.

Gastric ulcer: The recommended dose is 20 mg once a day. Symptoms disappear rapidly and for most patients the ulcer heals within four weeks. For patients with an ulcer that does not fully heal in that time, the ulcer usually heals with four additional weeks of therapy.

For patients with a gastric ulcer that responds poorly to treatment, it is recommended to administer 40 mg once a day, and the ulcer usually heals within 8 weeks.

As prophylaxis against recurring gastric ulcers that have responded poorly to treatment, a dose of 20 mg of omeprazole once a day is recommended. If required, the dose may be increased to 40 mg once a day.

For gastric ulcers caused by treatment with anti-inflammatory antirheumatics (NSAID), see the section on *Ulcers or erosion caused by treatment with non-steroidal anti-inflammatory drugs (NSAID)*.

For eradication of *Helicobacter pylori*, see the section on *Eradication of Helicobacter pylori in ulcer disease*.

Ulcer disease or erosion caused by treatment with non-steroidal anti-inflammatory drugs (NSAID): The recommended dose for patients with gastric ulcer, duodenal ulcer or erosion in the stomach and/or duodenum caused by treatment with anti-inflammatory antirheumatics, whether the treatment is long-term or not, is 20 mg of omeprazole once a day. The symptoms disappear quickly and for most patients ulcers

will heal within four weeks. For patients with an ulcer that does not fully heal in that time, the ulcer usually heals with four additional weeks of therapy.

The recommended dose to prevent gastric ulcer, duodenal ulcer or erosion in the stomach and/or the duodenum, and dyspepsia, is 20 mg once a day.

Eradication of Helicobacter pylori in ulcer disease.

Three-drug treatment: Omeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg, all administered twice a day for one week

or

omeprazole 20 mg, clarithromycin 250 mg and metronidazole 400 mg (or tinidazole 500 mg) all administered twice a day for one week

or

omeprazole 40 mg once a day along with amoxicillin 500 mg and metronidazole 400 mg, both administered three times a day for one week.

Two-drug treatment: Omeprazole 40-80 mg daily along with amoxicillin 1.5 g daily, administered in divided doses for two weeks. Clinical trials have used 1.5-3 g daily doses of amoxicillin

or

omeprazole 40 mg once a day along with clarithromycin 500 mg three times a day for 2 weeks.

To ensure that lesions will heal for patients with active ulcer disease, see further on the dosage of the product for gastric and duodenal ulcers.

Each treatment may be repeated if the patient still tests positive for *Helicobacter pylori*.

Esophageal inflammation caused by reflux: Recommended dose is 20 mg once a day.

Symptoms disappear rapidly and for most patients healing is achieved within four weeks. For patients that do not fully heal in that time, healing usually occurs with four additional weeks of therapy. For patients with serious inflammation of the esophagus caused by reflux, the recommended dose is 40 mg once a day, and healing is usually achieved within 8 weeks.

For long-term treatment of patients with esophageal inflammation caused by reflux, the recommended dose is 10 mg once a day. As Lomex-T acid-resistant tablets contain 20 mg of omeprazole, it is recommended to initiate treatment with an equivalent medicine of lower

strength. If required, the dose may be increased to 20-40 mg of omeprazole (1-2 Lomex-T 20 mg acid-resistant tablets) once a day.

Serious esophageal inflammation for children, one year of age or older:

For children over 20 kg the recommended dose is 20 mg omeprazole (one Lomex-T 20 mg acid-resistant tablet) once a day; if required the dose may be doubled. It is not recommended to initiate treatment of children under 20 kg with Lomex-T 20 mg acid-resistant tablets, as the recommended dose for these children (10-20 kg) is 10 mg omeprazole once a day; if required, however, the dose may be increased to 20 mg of omeprazole once a day.

Treatment of symptoms due to reflux disease : The recommended dose is 20 mg daily.

Symptoms disappear rapidly. If symptomatic treatment is not successful after 4 weeks of treatment with 20 mg daily, further investigations are indicated.

Zollinger-Ellison syndrome: For patients with Zollinger-Ellison syndrome the dose is individually decided, and treatment should be continued as long as required by the clinical condition. The recommended initial dose is 60 mg daily. All patients with a serious disease that has not responded to other treatment, have received satisfactory results from the product; more than 90% of the patients were given maintenance doses of 20-120 mg daily. Should the daily dose exceed 80 mg, it must be divided into two.

Impaired renal function: Doses for patients with impaired renal function need not be changed.

Impaired hepatic function: As the bioavailability and half-life of omeprazole in plasma is increased in the event of impaired hepatic function, it might be sufficient to administer lower doses (10-20 mg daily doses).

The elderly: The dosage need not be altered for the elderly.

4.3 Contraindications

The medicine should not be administered to patients with known hypersensitivity to omeprazole or other ingredients of the drug.

4.4 Special warnings and special precautions for use

When gastric ulcer is suspected, a malignant disease should be excluded, as treatment with omeprazole may reduce symptoms and delay diagnosis.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of some drugs may increase due to increased acidity in the stomach. Thus, it might be expected that the absorption of ketoconazole would decrease with simultaneous omeprazole treatment, as will happen when other drugs that reduce acid secretion or are acid-binding are administered.

No interaction with food or simultaneous taking of acid-binding drugs has been reported.

As omeprazole is metabolized in the liver by cytochrome P450 2C19 (CYP2C19), this may delay the elimination of diazepam, R-warfarin and phenytoin. It is advisable to observe patients who are given warfarin and phenytoin, and it may prove necessary to reduce the dose.

Nonetheless, simultaneous treatment with 20 mg per day has not altered the concentration of phenytoin in blood of patients undergoing continuous treatment with the drug. In the same manner, simultaneous treatment with 20 mg per day did not alter the clotting time of patients undergoing long-time treatment with warfarin.

While the blood concentration of omeprazole and clarithromycin is increased with simultaneous treatment with these drugs, no interaction is reported with metronidazole and amoxicillin. These antibiotics are administered simultaneously with omeprazole to eradicate *Helicobacter pylori*. The results of numerous studies of the interaction of omeprazole with other drugs indicate that repeated oral administration of omeprazole 20-40 mg has no effect on other important isoform CYPs, as has been shown that an interaction does not occur with the substrates for CYP1A2

(caffeine, phenacetin and theophylline), CYP2C9 (S-warfarin, pyroxicam, diclophenac and naproxen), CYP2D6 (methoprolol and propranolol), CYP2E1 (ethanol), and CYP3A (cyclosporin, lidocaine, chinidine, estradiol, erythromycin, and budesonide).

4.6 Pregnancy and lactation

As applies to most drugs, omeprazole should not be administered to pregnant or lactating women unless there are cogent reasons. Omeprazole, administered to women during childbirth, in doses up to 80 mg within a 24-hour period has not caused adverse effects in the baby. Animal experiments have not revealed any risk due to treatment with the drug during pregnancy and lactation, and there is no evidence of toxic effects or fetus-damaging effects.

4.7 Effects on ability to drive and use machines

It is unlikely that the drug has any effect on the ability to drive or use machines.

4.8 Undesirable effects

The medicine is well tolerated, and undesirable effects have usually been mild and have subsided. The following symptoms have been observed in clinical studies, or reported during normal use. In many instances, their connection to treatment with omeprazole has not been proved.

During short-term clinical studies, undesirable effects caused by the administration of omeprazole acid-resistant tablets have been similar to undesirable effects that have been reported with the administration of omeprazole acid-resistant capsules.

Common (>1%):

Central and peripheral nervous system: Headache.

Digestive tract: Diarrhea, constipation, stomach ache, nausea/vomiting, and increased flatulence.

Rare (0.-1-1%):

Central and peripheral nervous system: Dizziness, altered cutaneous sensation, drowsiness, insomnia, and vertigo.

Liver: Increase in liver enzymes.

Skin: Rash and/or pruritus. Urticaria.

Other: Malaise.

Very rare (<0,1%):

Central and peripheral nervous system: Temporary confusion, agitation, aggressiveness, depression and hallucinations, especially for very ill patients.

Endocrine glands: Gynecomastia in men.

Digestive tract: Xerostomia, stomatitis, and candida infection in the digestive tract.

Blood: Reduction in the number of leucocytes, reduction in the number of blood platelets, agranulocytosis, and pancytopenia.

Liver: Encephalopathy in patients with a history of serious liver disease, hepatitis with or without jaundice, and liver failure.

Musculo-skeletal system: Arthralgia, muscular hypotonia, and myalgia.

Skin: Increased photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), and hair loss.

Other: Hypersensitivity, e.g. angioedema, fever, bronchospasms, interstitial nephritis, and allergic shock. Increased perspiration, edema of the extremities, visual disturbance, altered sense of taste, and hyponatremia.

4.9 Overdose

A single dose, up to 400 mg, of omeprazole capsules with enteric coating has not caused any serious symptoms. Elimination speed remained unaltered (linear pharmacokinetic reaction) with increased doses, and no special treatment has been required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic effects

ATC category: A 02 B C 01

Omeprazole is a racemic of two active enantiomers. Omeprazole reduces acid secretion, and its effect is very specific. It specifically reduces the activity of the proton pump within parietal cells. The drug is fast-acting and effects reversible control of acid secretion when administered once a day.

Effective targets and effective mode Omeprazole is a weak base, and its concentration and metabolism into an active substance increases in the highly acid canaliculi of parietal cells where it acts as a inhibitor on the H⁺, K⁺, -ATPase acid pump. This function in the final phases of gastric secretion is dose-related and highly inhibitory for both production at rest and production caused by any kind of stimulation, independent of the stimulant. All pharmacological effects that appear may be explained by the effect of omeprazole on acid secretion.

Effect on gastric secretion: The drug, administered orally once a day, causes rapid and active inhibition of gastric secretion 24 hours a day, and a maximum effect is reached after four days of treatment. The quantity of acid in the gastric juice, measured for 24 hours for patients with duodenal ulcers, generally fell by 80% upon the administration of 20 mg, and the average reduction of maximum acid secretion after pentagastrin stimulation was about 70% in 24 hours after the dose was administered.

After the administration of 20 mg of the drug, the average acidity of the gastric juice is above pH 3 for 17 hours during a 24-hour period for patients with duodenal ulcers.

Due to lower acid secretion, and the higher pH of the gastric juice, omeprazole causes dose-related effects in such manner that a lower quantity of acid is delivered into the esophagus in patients with esophagitis caused by reflux. Inhibition of gastric secretion is related to the AUC of omeprazole blood concentration, not the actual blood concentration of the drug at a certain point in time.

The effect of omeprazole is not reduced with long-term use (tachyphylaxis).

Effect on Helicobacter pylori: Helicobacter pylori is associated with ulcer disease of the digestive tract, including gastric and duodenal ulcers. About 95% of patients of patients with gastric ulcer, and about 70% of patients with duodenal ulcer are infected with the bacterium. Helicobacter pylori is one of the chief causal factors in gastritis. Helicobacter pylori, along with gastric acid, is the chief cause of ulcers in the esophagus, stomach and duodenum. It has been shown that Helicobacter pylori plays a part in the formation of gastric carcinoma.

Omeprazole has bacteriocidal effect on Helicobacter pylori *in vitro*.

Eradication of Helicobacter pylori with omeprazole and antibiotics results in symptoms disappearing rapidly, mucosal ulcers heal rapidly, and there is a long remission of the ulcer disease. This decreases problems such as bleeding from the digestive tract, as well as the need for long-term treatment of acid secretion.

Other effects connected to acid inhibition: During long-term treatment, cysts have been detected in gastric glands. Such changes result from lowered acid secretion; they are benign and subside when treatment is discontinued.

5.2 Pharmacokinetic properties

Absorption and distribution: Omeprazole is absorbed in the small intestine, and absorption is, in general, completed within 3-6 hours. The bioavailability of omeprazole after one single dose is about 35%. After repeated administration once a day the bioavailability rises gradually to 60%. The distribution volume for healthy individuals is about 0.3 l/kg, and similar values are also reported for patients with impaired renal function. For the elderly, and patients with impaired renal function, the distribution volume is slightly smaller. The simultaneous taking of food has no effect on bioavailability. The protein binding of omeprazole in blood is about 95%.

Metabolism and excretion: The half life of omeprazole in blood is, in general, less than 1 hour, and no change in the half life is seen during long-term treatment.

Omeprazole is completely metabolized by the cytochrome P450 (CYP) system, mostly in the liver. The metabolism of the drug is dependent on a specific isoform CYP2C19 (S-mephenytoin hydroxylase); this results in the production of hydroxyomeprazole which is the chief metabolite in blood.

No metabolites which affect gastric secretion have been detected.

About 80% of an orally-administered dose is excreted in urine in metabolized form; the remainder is found in faeces, mostly from biliary secretion.

Impaired renal and hepatic function:

Bioavailability and excretion of omeprazole remain unchanged in patients with impaired renal function. While the AUC is larger for patients with impaired liver function, nothing indicates that there is accumulation of omeprazole when it is administered once a day.

Children: Available data on children (1-years and older) indicate that pharmacokinetic properties are similar to those of adults when recommended doses are administered.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The following excipients are used: β -cyclodextrin, lactose, maize starch, sodium starch glycolate, magnesium stearate, hypromellose thalate, acetylated monoglyceride, and the colouring agent titan dioxide (white) and black iron oxide.

6.2 Incompatibilities

Not known.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at room temperature (<25°C).

Lomex-T acid-resistant tablets are sensitive to moisture and should be stored in a dry location.

6.5 Nature and contents of container

Brown-coloured glass tablet containers with a white sealed plastic cap.

Each container contains 14, 28, 56 or 100 Lomex-T 20 mg acid-resistant tablets.

The tablet containers contain a desiccant capsule that must not be removed.

6.6 Instructions for use, handling and disposal

No special instructions

7. MARKETING AUTHORIZATION HOLDER

Actavis hf.

Reykjavíkurvegi 76-78

220 Hafnarfjörður

Iceland

8. MARKETING AUTHORIZATION NUMBER

Lomex-T 20 mg acid-resistant tablets: IS/1/02/110/01

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Lomex-T 20 mg acid-resistant tablets: Market authorization first granted 10th May 2002.

10. DATE OF REVISION OF THE TEXT

13 July 2004