Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT
OMEPRAZOLS 20 mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE PRODUCT

Active substance: Omeprazole (Omeprazolum).
Each Omeprazols 20 mg capsule contains 20 mg of omeprazole.
The complete list of excipients see in p. 6.1.

3. PHARMACEUTICAL FORM
Capsules.
Description: hard gelatine capsules yellow/brown containing white to slightly yellow spherical microgranules.

4. CLINICAL DESCRIPTION

4.1. Indications:

Omeprazols 20 mg Capsules is the first choice medicine in the treatment of the diseases that require gastric acid inhibition: duodenal ulcer; benign gastric ulcer; NSAID-associated duodenal or gastric ulcers and gastroduodenal erosions; duodenal ulcer associated with Helicobacter pylori; Helicobacter pylori eradication in combination with the appropriate antibacterial therapy; pathologic gastric hypersecretion in case of Zollinger-Ellison syndrome; gastric acid reduction during general anaesthesia; gastro-oesophageal reflux disease; acid reflux disease; acid related dyspepsia.

4.2. Posology and administration:

Omeprazols 20 mg Capsules should be taken before meal. Capsules should be swallowed unbroken, with plenty of liquid. Patients, who have difficulty to swallow the whole capsule, may open capsule and mix its contents with small quantity of apple or orange juice and swallow the received quantity without chewing.

Benign gastric ulcer treatment: 20 mg once a day during 8 weeks. In severe or recurrent cases dose may be raised to 40 mg once a day. In case of recurrent ulcer in anamnesis, the patients are recommended to use 20 mg once daily.
Duodenal ulcer treatment: 20 mg once a day during 4 weeks. In severe or recurrent cases dose may be raised to 40 mg once a day. Maintenance for recurrent duodenal ulcer – 20 mg once daily.

Risk of recurrent ulcer often occurs:
- in patients with Helicobacter pylori infection,
- younger patients (< 60 years),
- in patients, who maintained symptoms longer than one year,
- in smokers.

NSAID-associated duodenal or gastric ulcers and gastroduodenal erosions: 20 mg once a day for 4 weeks, followed by further 4 weeks if necessary.

Prophylaxis of gastric or duodenal ulcers and gastroduodenal lesions in patients who had gastric or duodenal ulcers or gastroduodenal lesions caused by NSAID use – 20 mg of Omeprazols 20 mg Capsules once a day, proceeding to use these NSAID.

Helicobacter pylori (HP) eradication: basic scheme - 20 mg of Omeprazols 20 mg Capsules twice daily with clarithromycin 500 mg twice daily and with amoxicillin 1000 mg twice daily, course of treatment 7 days.

For eradication of Helicobacter pylori other 3-4 preparations combination are used also, one of which is Omeprazols 20 mg Capsules, others – antimicrobials.

Zollinger-Ellison syndrome: initial dose is 60 mg once daily, usually a dose is in the range of 20-120 mg daily. If a dose is higher than 80 mg, it is recommended to divide into two single doses.

Prophylaxis of acid aspiration during general anaesthesia: 40 mg on the preceding evening and further 40 mg in the morning 2-6 hours before surgery.

Gastro-oesophageal reflux disease (GEAS) including reflux oesophagitis: the dose is 20 mg once daily during 4 weeks, if necessary the treatment continues for 4-8 weeks more. If the disease is not curable, the preparation is used at a dose of 40 mg once daily during 8 weeks; the drug can be used at a dose of 20 mg daily for a long term therapy.

Acid reflux disease: 20 mg once a day.

Acid related dyspepsia: 20 mg once a day during 2 - 4 weeks.

Children over two years in case of severe ulcerating reflux oesophagitis: 0.7-1.4 mg/kg of body weight daily for 4-12 weeks. Children with body weight 10-20 kg – the dose is 10 mg
daily, but with body weight over 20 kg – 20 mg daily. Maximal dose – 40 mg daily. The treatment is recommended to start in a hospital.

Recommended daily dose for patients with hepatic impairment should not exceed 20 mg. Elderly patients – the dose should not be adjusted. Patients with renal function impairment – the dose adjustment is not necessary.

4.3. Contra-indications

Individual hypersensitivity to omeprazole or any excipient of the preparation. It is not recommended to use concomitantly with atazanavir and cilostazol.

4.4. Special warnings and precautions for use

To avoid inappropriate treatment ulcer disease should be confirmed, a patient should undergo roentgenoscopic and endoscopic examination. Treatment may mask the possibility of gastric malignancy. Special attention should be given to the patients who have changeable symptoms of disease: decrease in body weight without any reason, observation of repeated vomiting, swallow disturbances, blood spitting, melena.

Patients with hard liver function disturbances should periodically control liver enzymes level in blood during treatment period.

After Omeprazols 20 mg Capsules administration during 14 days a considerably increase in number of living bacteria in stomach occur. Due to the reduced acidity of gastric acid, the risk to get the orally transmissive gastrointestinal infections (e.g., salmonellosis) is increased.

Lactose: Each capsule of the drug contains 8 mg of lactose. This drug should not be used by patients with rare inborn intolerability of galactose, deficit of Lapp lactase or glucose-galactose malabsorption.

Sucrose: Each capsule of the drug contains 137.43 mg of sucrose. This drug should not be used by patients with rare inborn intolerability of fructose, glucose-galactose malabsorption or sucrase-isomaltase deficiency.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of omeprazole and atazanavir is not recommended. Omeprazole sufficiently decreases atazanavir plasma concentration. Concomitant administration of omeprazole and cilostazol is not recommended. Omeprazole increases plasma concentration of cilostazol (risk of toxicity).
Omeprazole may enhance effects of warfarin, phenytoin, diazepam, and probably other drugs metabolized in the liver by oxidation. Omeprazole possibly slightly increases plasma concentration of digoxin; possibly increases plasma concentration of tacrolimus. Omeprazole increases plasma concentration of escitalopram. Omeprazole possibly reduces excretion of methotrexate (increased risk of toxicity). Omeprazole possibly reduces plasma concentration of clozapine (may decrease clozapine effect).

Since omeprazole considerably inhibits secretion of gastric acid in stomach, the absorption of the medicines, the absorption of which is affected by acidity of gastric acid (for example, ketoconazole, itraconazole, ampicillin, iron salts), may be delayed. Plasma concentration of omeprazole is increased by voriconazole (it is necessary to reduce dose of omeprazole).

Smoking and alcohol should be avoided during the therapy as it irritates gastric mucous membrane, reduces omeprazole absorption and recovery.

4.6 Pregnancy and lactation

The teratogenicity of Omeprazols is reported in experimental studies on animals. Since there are no adequate and well-controlled clinical studies on safe use of omeprazole in pregnant or breast-feeding women, Omeprazols 20 mg Capsules administration in pregnant women is not recommended. In case a mother has to take the preparation, breast-feeding should be discontinued.

4.7 Effects on ability to drive and use machines

Somnolence may occur sometimes during the drug administration that may have an effect on the ability to drive and use machines.

4.8 Undesirable effects:

Classification of undesirable effects (according to MedDRA frequency convention):

<table>
<thead>
<tr>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1/10</td>
<td>&gt; 1/100, &lt; 1/10</td>
<td>&gt; 1/1000, &lt; 1/100</td>
<td>&gt; 1/10000, &lt; 1/1000</td>
<td>&lt; 1/10000</td>
</tr>
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</table>

Like all medicines, Omeprazols 20 mg Capsules can cause undesirable effects, although not everybody gets them.
Blood and lymphatic system disorders: very rare – agranulocytosis, leucopenia, pancytopenia, thrombocytopenia.

Immune system disorders: very rare – hypersensitive reactions.

Metabolism and feeding disorders: very rare – hyponatraemia, peripheral oedema.

Psychiatric disorders: very rare – reversible confusion, agitation, hallucinations, depression and aggressiveness, mainly in seriously ill and elderly patients.

Nervous system disorders: uncommon - headache, dizziness, rare - somnolence or insomnia, paresthesia, encephalopathy (in case of severe disorder of liver function).

Gastro-intestinal tract disorders: rare - nausea, vomiting, diarrhoea or constipation, abdominal pain, flatulence, very rare – taste disturbances, stomatitis, dry mouth.

Hepatobiliary disorders: transient increase of liver enzyme activity, hepatitis with or without jaundice, liver dysfunction in patients having liver disease, pancreatitis.

Skin and subcutaneous tissue disorders: very rare – bullous eruption, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia, hypersensitivity (rash, urticaria, angioedema, bronchospasm), itch, anaphylaxis, photosensitivity.

Skeleton-muscular system: very rare - arthralgia, myalgia, muscular weakness.

Renal and urinary disorders: very rare – hematuria, proteinuria, interstitial nephritis.

Reproductive system and mammary diseases: very rare - gynaecomastia, impotence.

General disorders: very rare – sweating, fever.

4.9 Overdose:

There is lack of data regarding acute intoxication using omeprazole. Dose up to 360 mg per day is well tolerated by patients.

Procedures. In case of overdose, symptomatic and supportive treatment should be provided. Omeprazole strongly binds to plasma proteins and therefore dialyzes poorly. There are no specific antidotes.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: proton pump inhibitor.

ATC code: A02BC01
5.1. Pharmacodynamics
Omeprazole inhibits gastric acid secretion. Omeprazole specifically blocks \( \text{H}^+/\text{K}^+ \)- ATP enzyme system in the secretory surface of gastric parietal cells, blocks transport of hydrogen ions to stomach lumen and effectively inhibits both basal and stimulated gastric acid secretion. Omeprazole does not effect on receptors of acetylcholine and histamine. Omeprazole does not effect on evacuation of solid and liquid food from the stomach, inner factor secretion, and pepsin production.
Omeprazole does not have an effect directly on *Helicobacter pylori*, but it provides conditions for eradication of bacteria. Concomitant use of omeprazole with antibacterial preparations eradicates bacteria. This allows achieving the high rate of healing of mucosa и long remission, to decrease the risk of bleeding from stomach and intestine as well as decrease the period of therapy. After discontinuation of omeprazole therapy secretion is restored at the previous level within 3-4 days, but the effect of “ricochet” is not noticed.
Omeprazole does not affect CNS, cardiovascular and respiratory systems. 30-40 mg daily dose of the preparation does not cause dysfunctions of activity of thyroid gland and other organs of endocrine system. During first 2 weeks of treatment gastrin level is increased, simultaneously secretion of gastric acid is being reduced. Gastrin level does not increase further during continuation of therapy. When omeprazole treatment is interrupted, gastrin level is normalized during 1-2 weeks.

5.2. Pharmacokinetics
Absorption. Capsules of the preparation *Omeprazols 20 mg Capsules* contain coated microgranules. A capsule dissolves quickly in stomach acid medium and microgranules coated with special coating are released. They dissolve in alkaline medium in duodenum thus providing better and gradual absorption of the drug. Food uptake does not affect the absorption of the preparation.
Distribution. After peroral administration the activity of omeprazole starts within 1 hour and achieves the maximum after 2 hours, but inhibition of secretion continues for 24 hours. Inhibition of secretion depends on the dose. Maximal pharmacological effect is achieved within 4 days. The preparation decreases the secretion of gastric juice not less than for 80 %
during 24 hours. Administration of omeprazole keeps internal gastric pH>3 approximately during 17 hours.

95 % of omeprazole binds with plasma proteins. Omeprazole is extensively metabolized in the liver forming inactive metabolites. Half-life elimination time is apr.0.5-3 hours. Bioavailability of the drug increases in elderly patients and patients with liver dysfunction; renal impairment does not influence it.

Excretion. 72 – 80 % of omeprazole are excreted from organism in the urine and 20 % - in the bile.

5.3 Preclinical safety data

Carcinogenicity. In two 24 -month studies in rats, omeprazole, given in doses 1.7; 3.4; 13.8; 44.0 and 140.8 mg/kg of body weight (corresponding to 4 to 352 times the human dose, given to a patient having 50 kg of body weight in a dose of 20 mg of omeprazole daily) caused end-life gastric carcinoid tumors and enterochromaffin-like (ECL) cell hyperplasia in a dose-related manner in both male and female animals. Incidence was markedly higher in female rats, which had higher blood levels of omeprazole. Gastric carcinoids seldom occur in the untreated rat. Additionally, ECL cell hyperplasia was present in all treated groups of both sexes. In one of the studies, female rats were treated with 13.8 mg/kg/daily of omeprazole (about 35 times the human dose) for one year, and then the rats were observed for an additional year without the drug. No carcinoids were seen in these rats. An increased incidence of treatment-related ECL cell hyperplasia was observed at the end of one year (94 % of treated rats against 10 % of rats in the control group). By the second year, the difference between treated rats and rats of control group was much smaller (46 % against 26 %), but still showed more hyperplasia in the treated group.

Mutagenicity. Omeprazole was not mutagenic in vitro tests, and in an in vivo rat liver DNA damage assay.

Reproduction. Doses 13.8 up to 138 mg/kg/daily are not toxic or deleterious to the reproductive performance of animals.

Teratogenicity. Teratogenic studies in pregnant rats at doses 138 mg/kg/daily (345 times the human dose) in rabbits at doses till 69 mg/kg/daily (172 times the human dose) did not show omeprazole to have any teratogenic potential. Omeprazole produced dose-related increases in
embryo-lethality, fetal resorptions, and pregnancy disruptions in rabbits receiving omeprazole at doses 6.9 – 69.9 mg/kg/daily (about 17 to 172 times the human dose). In rats, dose-related embryo/fetal toxicity and postnatal developmental toxicity were observed in offspring resulting from parents treated with omeprazole at doses 13.8-138 mg/kg/daily (about 35 to 345 times the human dose). There are no adequate and well-controlled studies in pregnant women.

6. PHARMACEUTICAL INFORMATION

6.1 List of excipients: sucrose (137.43), maize starch, lactose (8 mg), hydroxypropylmethylcellulose, sodium laurilsulphate, hydroxypropylcellulose, dibasic sodium phosphate, hydroxypropylmethylcellulose phthalate, diethylphthalate.

Hard gelatine capsules composition: titanium dioxide (E 171), yellow, red and black iron oxide (E 172).

6.2 Incompatibilities

Not known.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Protect from moisture and light.

6.5. Nature and contents of container

10 capsules in blister from PVC film and lacquered aluminium foil, 3 blisters (30 tablets) and package leaflet in the carton pack.

6.6. Instructions for use and handling

Unused product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

JSC "Olainfarm".

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8. MARKETING AUTHORISATION NUMBER IN LATVIA: 97-0072.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION:

09.04.1997/10.05.2002/30.07.2007
OMEPRAZOLS 20 mg capsules

Summary of Product Characteristics

10. LAST REVISION OF SMPC: May, 2007

Translated by RGD sen. engineer

L. Želnina

The translation conforms to the original document.

Head of Regulatory Affairs, PhD (Biochem.)

A. Lece

Approved:

R.Lūse (signature) 23.05.2007.

L. Cudechkis, MD 24.05.2007.