omeprazole

**Powder for solution for infusion**

Composition
1 vial of dry substance contains: Omeprazole sodium equivalent to omeprazole 40 mg.
For excipients see “List of excipients”.

**Pharmaceutical Form**
Powder for solution for infusion

**Indications**
Duodenal ulcer, gastric ulcer and reflux oesophagitis. Zollinger-Ellison syndrome.

**Posology and method of administration**
Duodenal ulcer, gastric ulcer and reflux oesophagitis: Patients who cannot be given oral medication can be treated parenterally with 40 mg once daily. The usual treatment period before transfer to oral treatment is 2-3 days.
In Zollinger-Ellison syndrome the dose should be adjusted individually. Higher doses and/or several doses daily may be required.
Intravenous treatment can be given as an infusion over a period of 20-30 minutes. After reconstitution start the infusion immediately.

**Impaired renal function**
A dose adjustment is not necessary for patients with impaired renal function.

**Impaired liver function**
In patients with impaired liver function clearance is greatly reduced.

**Elderly patients**
A dose adjustment is not necessary in elderly patients.

**Children**
There is only limited experience of treatment in children.

**Contraindications**
Known hypersensitivity to omeprazole

**Special warnings and special precautions for use**
Suspected ulcer disease must be verified objectively at an early stage by means of X-ray or endoscopy in order to avoid inadequate treatment.
When gastric ulcer is present or suspected or in the presence of any of the following alarm symptoms: significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena, malignancy should be excluded as treatment may alleviate symptoms and delay diagnosis.

**Interactions**
Effects of omeprazole on the pharmacokinetics of other drugs
The following combinations with Losec powder for solution for infusion should be avoided: ketoconazole and itraconazole.
Omeprazole might influence the absorption of other drugs due to its effect on the gastric pH.
The dissolution of ketoconazole tablets in the stomach is adversely affected if the pH of the gastric juice increases as a result of drug treatment (antacids, secretion-inhibiting agents, sucralfate). This leads to ineffective plasma concentrations of ketoconazole. During concomitant administration of omeprazole and itraconazole the plasma concentration and AUC of itraconazole are reduced by approximately 65%, probably as a result of poorer absorption, which is dependent on pH.
Omeprazole inhibits the enzyme CYP2C19 and therefore increased plasma levels of other drugs (diazepam, warfarin, phenytoin) metabolised via this enzyme might be expected. A dose reduction of these drugs may be necessary.
During concomitant administration of clarithromycin or erythromycin and omeprazole the plasma concentrations of omeprazole were increased. The plasma concentrations of omeprazole are not influenced during concomitant administration with amoxicillin or metronidazole.
In concomitant administration of omeprazole and atazanavir, reduced plasma levels of atazanavir have been reported. Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.

**Effects of other drugs on the pharmacokinetics of omeprazole**

Drugs inhibiting the enzymes CYP2C19 or CYP3A (HIV protease inhibitors, ketoconazole, itraconazole) might increase the plasma concentrations of omeprazole.

No interactions between omeprazole and antacids, theophylline, caffeine, quinidine, lidocaine, propranolol, metoprolol or ethanol have been detected.

**Pregnancy and lactation**

Pregnancy. Well-conducted epidemiological studies indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Omeprazole can be used during pregnancy.

Lactation. Omeprazole is excreted in breast milk. Influence, if any, on the child is unknown.

**Effects on ability to drive and use machines**

Losec is not likely to affect the ability to drive or use machines.

**Undesirable effects**

The most common symptoms that have been reported in clinical trials with Losec have been gastrointestinal, such as diarrhoea, nausea and constipation, and also headache, each one in 1-3 % of cases.

<table>
<thead>
<tr>
<th>Common (&gt;1/100, &lt;1/10)</th>
<th>Less common (&gt;1/1000, &lt;1/100)</th>
<th>Rare (&gt;1/10000, &lt;1/1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General:</td>
<td>General:</td>
<td>General:</td>
</tr>
<tr>
<td>Headache.</td>
<td>Fatigue.</td>
<td>Increased sweating, peripheral oedema, hyponatraemia. Hypersensitivity reactions such as angioedema, fever and anaphylactic shock.</td>
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<tr>
<td>Gastrointestinal:</td>
<td>Rash, pruritus, urticaria.</td>
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</tr>
<tr>
<td>Diarrhoea, nausea/vomiting, constipation, abdominal pain, flatulence.</td>
<td>Changes in liver function tests.</td>
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<tr>
<td>Liver:</td>
<td>Neurological:</td>
<td></td>
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<tr>
<td>Changes in liver function tests.</td>
<td>Paraesthesia, dizziness, drowsiness.</td>
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<tr>
<td>Skin:</td>
<td>Psychiatric:</td>
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<td></td>
<td>Sleep disturbance.</td>
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<td></td>
<td>Genitourinary:</td>
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<td></td>
<td>Interstitial nephritis.</td>
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<td></td>
<td>Eyes:</td>
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<td></td>
<td>Blurred vision.</td>
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</tbody>
</table>

Isolated cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported, but a relationship with omeprazole could not be established. In severely ill patients, in isolated cases irreversible visual disturbances have been reported in connection with treatment with high doses of omeprazole given as intravenous injection. However, no causal relationship with omeprazole could be established.

**Overdose**

Intravenous doses up to 270 mg in a day and up to 650 mg over a three-day period have been studied in clinical trials without any dose-related adverse reactions.

Symptoms: Dizziness, apathy, headache, tachycardia. Nausea, vomiting, flatulence, diarrhoea. See also Undesirable effects.

**Pharmacodynamic properties**

ATC code: A02B C01
Acid-inhibiting agents - proton pump inhibitors.

Omeprazole is a substituted benzimidazole. Omeprazole is a racemate of two active enantiomers. The secretion of hydrochloric acid in the stomach is inhibited by omeprazole through its specific effect on the proton pump in the parietal cells. The effect on acid secretion is reversible. Omeprazole is a weak base, which is concentrated and converted into active form in the acidic environment in the
parietal cell, where it inhibits H+, K+-ATPase, i.e. the final step in the production of the gastric acid. The inhibition is dose-dependent, and affects both basal and stimulated acid secretion, irrespective of the type of stimulation. Omeprazole does not affect cholinergic or histaminergic receptors. Like treatment with H2-receptor blockers, treatment with omeprazole results in reduced acidity in the stomach and thus an increase in gastrin in proportion to the reduction in acidity. The gastrin increase is reversible. During long-term treatment the frequency of glandular cysts in the stomach may increase. These changes are physiological and a consequence of the inhibition of acid secretion. They are benign and reversible.

Decreased gastric acidity with proton pump inhibitors or other acid-inhibiting agents, increases the amount of bacteria normally present in the gastrointestinal tract, why such treatment may lead to a slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

No pharmacodynamic effects of clinical significance other than those due to the effect of omeprazole on acid secretion have been found. The effect on acid secretion is directly correlated to the area under the plasma concentration curve (AUC), but not to the actual plasma concentration of omeprazole.

Intravenous administration of Losec 40 mg results in an immediate reduction of hydrochloric acid secretion. A single dose of 40 mg intravenously has approximately the same effect on the acidity of the gastric juice for 24 hours as a single oral dose of 80 mg or repeated oral administration of 20 mg once daily.

**Pharmacokinetic properties**

**Absorption**

Binding to plasma proteins is approximately 95% and the volume of distribution is 0.3 L/kg.

**Metabolism**

Omeprazole is metabolised completely, mainly in the liver. Mainly the enzymes CYP2C19 and CYP3A4 catalyse the metabolism. Identified metabolites are the sulphone, the sulphide and hydroxy-omeprazole, which have no significant effect on the acid secretion. Total plasma clearance is 0.3-0.6 L/min.

**Elimination**

The half-life in plasma in the elimination phase is approximately 40 minutes (30-90 minutes) after multiple doses.Approximately 80% of the metabolites are excreted via the urine and the remainder in the faeces.

**Patient factors**

Clearance is greatly reduced in patients with impaired liver function.

**List of excipients**

Vial of active substance: Disodium edetate 1.5 mg, sodium hydroxide for pH adjustment.

**Incompatibilities**

No known incompatibility when recommended instructions are followed.

**Shelf Life**

Please refer to the expiry date on the outer carton.

**Pack size**

Please refer to the outer carton for pack size.

**Special precautions for storage**

Do not store above 25°C. Store in the outer carton. Sensitive to light.

Vials that have been taken out of their outer pack can be kept in normal indoor light for up to 24 hours.

**Instructions for use and handling**

Solution for infusion is obtained by dissolving powder for solution for infusion in 100 ml sodium chloride 9 mg/ml or in 100 ml glucose 50 mg/ml. The stability of omeprazole is influenced by the pH of the solution for infusion, why no other solvents or quantities should be used for dilution.

Reconstituted solution for infusion must be used within 12 hours after reconstitution with sodium chloride 9 mg/ml.

Reconstituted solution for infusion must be used within 6 hours after reconstitution with glucose 50 mg/ml.

**Preparation**

1. With a syringe draw 5 ml of infusion solution from the infusion bottle or bag.
2. Add the infusion solution to the vial with the freeze-dried omeprazole, mix thoroughly making sure all omeprazole is dissolved.
3. Draw the omeprazole solution back into the syringe.
4. Transfer the solution into the infusion bottle or bag.
5. Repeat 1-4 to make sure all omeprazole is transferred from the vial into the infusion bottle or bag.

**Alternative preparation for infusions in flexible containers.**
1. Use a double ended transfer needle and attach to the injection membrane of the infusion bag. Connect the other needle-end to the vial with freeze dried omeprazole.
2. Dissolve the omeprazole substance by pumping the infusion solution back and forward between the infusion bag and the vial.
3. Make sure all omeprazole is dissolved and remove the empty vial and needle from the bag.

**Date of revision of text**
October 2005