OMEPRAZOLE-GA

PRODUCT INFORMATION

OMEPRAZOLE-GA (omeprazole) 20 mg tablets

NAME OF THE MEDICINE

Chemical name: 5-methoxy-2-[(RS)-[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]-sulphinyl]-1H-benzimidazole.

Omeprazole has the empirical formula of C_{17}H_{19}N_{3}O_{3}S, a molecular weight of 345.4 and CAS number 73590-58-6.

Structurally it is represented as:

![Chemical structure of Omeprazole]

DESCRIPTION

Omeprazole is a white or almost white powder, very slightly soluble in water, soluble in methylene chloride, sparingly soluble in alcohol and in methanol. It dissolves in dilute solutions of alkali hydroxides.

Each tablet contains 20 mg of omeprazole and the following excipients: ascorbyl palmitate, cellulose- microcrystalline, crospovidone, magnesium stearate, povidone, lactose, talc purified, hypromellose phthalate, glycerol triacetate, iron oxide red (CI77491), iron oxide black (CI77499).

PHARMACOLOGY

Omeprazole reversibly reduces gastric acid secretion by specifically inhibiting the gastric enzyme H+, K+-ATPase, the proton pump, in the acid environment of the intracellular canaliculi within the parietal cell. This effect of omeprazole on the final step of the gastric acid formation process is dose dependent and effectively inhibits both basal acid secretion and stimulated acid secretion, irrespective of the stimulus to acid production.

Omeprazole has no effect on acetylcholine or histamine receptors. No clinically significant pharmacodynamic effects, other than those explained by the effect on acid secretion, have been observed.

Effect on gastric acid secretion: Oral dosing with omeprazole 20 mg once daily provides rapid and effective reduction of gastric acid secretion. After a single dose the onset of antisecretory effect occurs within one hour and is maximal within two hours. With repeated once daily dosing the maximum effect is usually achieved within four days of commencing treatment.
A mean decrease of approximately 80% in 24 hour intragastric acidity is maintained in duodenal ulcer patients treated with an oral dose of omeprazole 20 mg. Omeprazole produces a mean decrease in peak pentagastrin stimulated acid output of approximately 70% 24 hours after dosing. When the drug is discontinued, secretory activities return to approximately 50% of maximum after 24 hours and gradually return to normal over three to five days.

**Peptic ulcer disease associated with Helicobacter pylori:** Helicobacter pylori (H. pylori) is associated with duodenal and gastric ulcer disease in about 95% and 70% of patients, respectively. H. pylori is the major factor in the development of gastritis and ulcers in such patients. Recent evidence also suggests a causative link between H. pylori and gastric carcinoma. An attempt to eradicate H. pylori is appropriate therapy in most patients with duodenal and gastric ulcer where the latter is not caused by nonsteroidal anti-inflammatory drug (NSAID) ingestion (see Dosage and Administration).

In vitro testing has shown that omeprazole has an MIC90 (minimum inhibitory concentration) of 25 microgram/mL against H. pylori. However, in vivo it only suppresses the organism without eradicating it. The combination of omeprazole and antimicrobial agents results in eradication of the organism in vivo, despite the fact that antimicrobial agents administered singly have also proved ineffective in eradicating H. pylori. The mechanism of the synergy between omeprazole and antimicrobial agents in eradicating H. pylori is not completely understood. Optimal eradication rates are achieved when omeprazole is combined with two antimicrobial agents.

Eradication of H. pylori is associated with reduced peptic ulcer recurrence.

**Other effects related to acid inhibition:** 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.

In some patients, fasting serum gastrin levels have been noted to rise two to fourfold during treatment with omeprazole. Up to 3% of patients have values exceeding 400 picogram/mL.

**Pharmacokinetics:**

**Absorption:** Omeprazole is acid labile and is administered orally as enteric coated tablets. Omeprazole is not released until the tablet is dissolved in the duodenum.

The systemic bioavailability of omeprazole from a single oral dose of omeprazole tablets is approximately 35%. After repeated once daily administration, the bioavailability increases to about 60%. Concurrent intake of food delays the absorption of omeprazole but does not influence the bioavailability.

**Distribution:** The plasma protein binding of omeprazole is approximately 95%. The inhibition of acid secretion is related to the area under the plasma concentration time curve (AUC) but not to the actual plasma concentration at any given time.

**Metabolism:** Omeprazole is entirely metabolised by the hepatic cytochrome P-450 system (CYP), mainly in the liver. Identified metabolites in plasma are the sulfone, the sulfide and hydroxyomeprazole. These metabolites have no significant effect on acid secretion. The average half-life of the terminal phase of the plasma concentration time curve following intravenous administration of omeprazole is approximately 40 minutes; the total plasma clearance is 0.3 to 0.6 L/minute.

**Excretion:** About 80% of the metabolites are excreted in urine and the remainder in faeces. The two main urinary metabolites are hydroxyomeprazole and the corresponding carboxylic acid.
CLINICAL TRIALS

Gastroesophageal reflux disease (GORD): Symptomatic GORD: Randomised controlled clinical trials (n = 1,710) were evaluated to assess the efficacy of omeprazole in the complete relief of heartburn in adult patients with symptomatic GORD after four weeks treatment comparing omeprazole 10 and 20 mg once daily with control groups of ranitidine 150 mg twice daily or placebo. The percentage of patients with complete relief of heartburn after four weeks is presented in Table 1.

Table 1
Percentage of patients with complete relief of heartburn at 4 weeks

<table>
<thead>
<tr>
<th>Study</th>
<th>Group (n)</th>
<th>Relief (% patients)</th>
<th>Group difference</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI*</td>
</tr>
<tr>
<td>Lind</td>
<td>Placebo (105)</td>
<td>13</td>
<td>Omeprazole 10 – Placebo 18</td>
</tr>
<tr>
<td></td>
<td>Omeprazole 10 (199)</td>
<td>31</td>
<td>Omeprazole 20 - Placebo 33</td>
</tr>
<tr>
<td></td>
<td>Omeprazole 20 (205)</td>
<td>46</td>
<td>Omeprazole 20 – Omeprazole 10 15</td>
</tr>
<tr>
<td>Venables</td>
<td>Ranitidine (135)</td>
<td>36</td>
<td>Omeprazole 10 - Ranitidine 0.2</td>
</tr>
<tr>
<td></td>
<td>Omeprazole 10 (126)</td>
<td>36</td>
<td>Omeprazole 20 - Ranitidine 3.7</td>
</tr>
<tr>
<td></td>
<td>Omeprazole 20 (130)</td>
<td>39</td>
<td>Omeprazole 20 – Omeprazole 10 3.5</td>
</tr>
<tr>
<td>Bate</td>
<td>Placebo (58)</td>
<td>22</td>
<td>Omeprazole 20 – Placebo 36</td>
</tr>
<tr>
<td></td>
<td>Omeprazole 20 (48)</td>
<td>58</td>
<td></td>
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</tbody>
</table>

*CI = confidence interval

Erosive oesophagitis: At the time of registration, seven randomised controlled clinical trials (n = 1,674) were evaluated to assess the efficacy of omeprazole in the prevention of relapse in patients with healed reflux oesophagitis. Omeprazole 10 and 20 mg once daily maintained endoscopic remission rates which substantially exceeded ranitidine 150 mg twice daily or placebo at six months. The difference in remission rates between omeprazole 10 and 20 mg favoured 20 mg. Three studies recorded remission rates over 12 months and an additional study continued for 18 months.

In a meta-analysis of five of the clinical trials (n = 1,154), 72 and 82% of patients remained in remission at six months on omeprazole 10 and 20 mg once daily, respectively. In a separate large study (n = 327), the remission rate following omeprazole 10 mg once daily for 18 months was 60%.

In two of the studies, patients who relapsed in the first three months of maintenance treatment were then healed and treated with a maintenance dose of omeprazole 20 mg.

The difference in the total remission rate over 6 or 12 months, while small, suggests that it may be more difficult or take longer to obtain subsequent healing and control if 10 mg rather than 20 mg had been used for initial maintenance therapy.

Gastric safety data are available from seven controlled clinical trials of up to two years duration (irrespective of indication). A full analysis of these trials was undertaken as a consequence of histological changes observed in animals (see Precautions). This involved a total of 1,128 patients with an evaluable series of biopsies; 843 patients treated continuously with omeprazole
for 6 to 12 months, 77 patients completing 18 months, and 208 patients completing two years of continuous omeprazole treatment.

Additionally, in open studies at least 109 patients were assessed by annual biopsy during continuous treatment for four years, and in this continuing study, biopsies are available for at least 14 patients treated for up to eight years. No instances of dysplasia or carcinoids of the gastric ECL cells have been reported in these studies. An association between focal hyperplasia and chronic gastritis with atrophy was found during long-term therapy. However, this finding is also observed in patients with untreated gastric ulcer disease with normal gastrin levels and is thus not a treatment related effect.

**INDICATIONS**

**Gastroesophageal reflux disease (GORD):**
*Symptomatic GORD:* The relief of heartburn and other symptoms associated with GORD.

*Erosive oesophagitis:* The treatment and prevention of relapse.

**Peptic ulcers:**
The treatment of duodenal and gastric ulcer.

Combination therapy for the treatment of peptic ulcer disease associated with *H. pylori* infection.

The treatment of gastric and duodenal ulcers and erosions associated with nonsteroidal anti-inflammatory drugs.

The prevention of gastric and duodenal ulcers and erosions associated with nonsteroidal anti-inflammatory drugs in patients assessed as being at high risk of gastroduodenal ulcer or complications of gastroduodenal ulcer.

Long-term prevention of relapse in gastric and duodenal ulceration, in patients proven to be *H. pylori* negative, or in whom eradication is inappropriate, e.g. the elderly or ineffective.

**Zollinger-Ellison syndrome:**
The treatment of Zollinger-Ellison syndrome.

**CONTRAINDICATIONS**

Hypersensitivity to omeprazole or any other ingredient.

**PRECAUTIONS**

**Undiagnosed malignancy:** As with all antisecretory agents, the presence of any alarm symptom (e.g. significant unintentional weight loss, recurring vomiting, dysphagia, hematemesis or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with omeprazole may alleviate symptoms and delay diagnosis.

**Antimicrobial resistance:** The development of antimicrobial resistance may have an adverse effect on eradication regimens. The clinical impact of this resistance on *H. pylori* has not been comprehensively studied.
**Impaired hepatic function:** Patients with impaired liver function show a markedly increased bioavailability, a reduced total plasma clearance, and up to a fourfold prolongation of the elimination half-life. However, urinary recovery over 96 hours remains unchanged indicating no accumulation of omeprazole or its metabolites. The normal dose of omeprazole 20 mg daily may be used in patients with severe liver disease (see **Dosage and Administration**).

**Carcinogenesis, mutagenesis, impairment of fertility:** In a two year carcinogenicity study in rats, omeprazole at daily doses of 13.8, 44.0 and 140.8 mg/kg/day produced gastric ECL cell hyperplasia and carcinoid tumours in a dose related manner in both male and female rats. The incidence of these effects was markedly higher in female rats.

The same effects were seen in an additional two year study in female rats at daily doses of 1.7, 3.4 and 13.8 mg/kg/day. A no effect dose was not established in female rats in the dose ranges studied.

In mice, a 78 week carcinogenicity study was performed according to relevant regulatory and scientific standards. No gastric ECL cell carcinoids were seen. However, longer term studies have not been performed in this species.

Hypergastrinaemia, ECL cell hyperplasia and gastric carcinoids have also been produced in the rat by other treatments or procedures not related to omeprazole. These include the following.

**Exogenous gastrin infusion:** Subcutaneous infusion of gastrin 17 has resulted in a significant hyperplasia of ECL cells following treatment for one month.

**H2-receptor antagonists:** In rats administered ranitidine 2 g/kg/day in their diet over 106 weeks, argyrophilic cell hyperplasia was observed in 37% of the animals and gastric carcinoids were found in 19% of the treated group.

**Surgical resection of the acid producing oxyntic mucosa:** In rats in which 75% of the stomach corpus was surgically removed, 26 of 75 animals developed ECL cell carcinoids during the 124 week study.

These findings show that the development of ECL cell carcinoids in the rat is directly related to hypergastrinaemia rather than a direct effect of omeprazole on the ECL cell.

Omeprazole may also affect other cells in the gastrointestinal tract (e.g. G cells) either directly or by inducing sustained hypochlorhydria but this possibility has not been extensively studied.

Omeprazole has been subjected to a battery of in vitro and in vivo genotoxicity tests to examine the mutagenic, clastogenic and DNA damaging potential of the drug. The in vitro assays include the Ames test, mouse lymphoma TK locus forward mutation assay and a chromosome aberration test in human lymphocytes. The in vivo tests were a chromosome aberration test in mouse bone marrow, an alkaline elution/rat liver DNA damage assay and two mouse micronucleus tests.

No evidence of significant genotoxicity was seen in these tests.

There was no evidence of an adverse effect on fertility following administration of omeprazole to male and female rats at doses up to 320 mg/kg/day orally (16-fold anticipated exposure at the clinical oral dose of 40 mg/day, based on plasma AUC) and 100 mg/kg/day intravenously (14-fold anticipated exposure at the clinical intravenous dose of 40 mg/day, based on plasma AUC). Oral administration to male rats prior to mating and to female rats prior to and throughout gestation at sevenfold clinical exposure was associated with embryofetal toxicity.
**Use in pregnancy (Category B3):** Results from three prospective epidemiological studies indicate that while there was no increase in the overall malformation rates compared with controls, the data indicated a potentially higher rate of cardiac defects in the omeprazole group.

There was no evidence of teratogenicity following administration of omeprazole to pregnant rats and rabbits during the period of organogenesis. Doses in rats were associated with systemic exposures of up to 16 and 14-fold (oral and intravenous administration, respectively) the anticipated exposure at the clinical dose of 40 mg/day (based on plasma AUC). Studies in rats did not demonstrate embryotoxicity apart from increased locomotor activity in prenatally exposed offspring at systemic exposures approximating clinical exposure, based on plasma AUC.

In rabbits, oral doses were associated with systemic exposure less than clinical exposure (plasma AUC) and intravenous doses were up to 13-fold the 40 mg/day clinical dose (on a mg/m² basis). Embryofetal toxicity and maternotoxicity occurred at doses associated with less than clinical exposures.

**Use in lactation:** Omeprazole and its metabolites are excreted in milk in rats but it is not known if this occurs in humans. In rats, reduced offspring postpartum growth rate was observed following administration of omeprazole during late gestation and throughout lactation at oral doses of 138 mg/kg/day and above (sevenfold anticipated exposure at the clinical dose of 40 mg/day, based on plasma AUC) and intravenous doses of 3.2 mg/kg/day and above (less than clinical exposure).

It is recommended that omeprazole not be used in breastfeeding mothers.

**Effect on ability to drive or operate machinery:** No effects have been observed.

**INTERACTIONS WITH OTHER MEDICINES**

**Absorption:** The decreased intragastric acidity during treatment with omeprazole might increase or decrease the absorption of drugs if the mechanism of absorption is influenced by gastric acidity.

**Theoretical interactions: ketoconazole, itraconazole:** Omeprazole produces a profound and sustained inhibition of gastric acid secretion. The absorption of compounds whose absorption depends on gastric pH, e.g. ketoconazole, itraconazole, may decrease during treatment with omeprazole.

**Metabolism: Cytochrome P450 effects:** Omeprazole is mainly metabolised via the hepatic cytochrome P450 system (CYP2C19) and may be expected to interact with the metabolism of other drugs metabolised by this enzyme.

**Clopidogrel:** Clopidogrel is metabolised to its active metabolite by CYP2C19. Inhibition of CYP2C19 by omeprazole would be expected to result in reduced drug levels of the active metabolite of clopidogrel and a reduction in its antiplatelet activity and therefore its clinical efficacy. Concomitant use of omeprazole with clopidogrel should be discouraged.

**Effects of omeprazole on other drugs:** Demonstrated interactions:

**Diazepam:** Following repeated dosing with omeprazole 40 mg once daily, the clearance of diazepam was decreased by 54% and the mean elimination half-life of diazepam was increased by 130%, with a consequent significant increase in plasma diazepam concentrations.

For omeprazole 20 mg, the clearance of diazepam was decreased by approximately 25% in the majority of the population, while no change was detected in poor metabolisers. Consideration should be given to a reduction in diazepam dosage when omeprazole tablets are coprescribed.
**Phenytoin:** Omeprazole 40 mg daily for seven days reduced plasma clearance of intravenous phenytoin by 15 to 20% and increased the elimination half-life by 27%. It is recommended that plasma concentration of phenytoin be monitored in patients co-prescribed omeprazole 40 mg and phenytoin. A reduction of the phenytoin dose may be necessary. In a study that administered omeprazole 20 mg to epileptic patients, steady-state plasma levels of phenytoin were unchanged during omeprazole treatment.

**Warfarin:** Concomitant administration of omeprazole 20 mg to patients on continuous treatment with warfarin caused a slight though statistically significant increase in the plasma concentration of the R-enantiomer of warfarin. Plasma concentrations of the more potent S-enantiomer were not affected and no change in warfarin's anticoagulant activity was observed.

It is recommended that coagulation tests be monitored closely when initiating or ceasing omeprazole tablets in patients co-prescribed warfarin or other vitamin K antagonists. A reduction of the warfarin (or other vitamin K antagonist) dose may be necessary.

**Antiretroviral drugs:**
Concomitant administration with omeprazole and drugs such as atazanavir and nelfinavir is not recommended.

Omeprazole has been reported to interact with some antiretroviral drugs. The clinical importance and the mechanisms behind these interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral drug. Other possible interaction mechanisms are via CYP2C19. For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. For other antiretroviral drugs, such as saquinavir, elevated serum levels have been reported. There are also some antiretroviral drugs of which unchanged serum levels have been reported when given with omeprazole.

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

**Potential interactions that have been excluded:** Results from a range of in vivo interaction studies with omeprazole versus other drugs indicate that omeprazole 20 to 40 mg, given repeatedly, 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, lignocaine, quinidine and oestradiol).

**Effects of other drugs on omeprazole:**

**Clarithromycin:** Plasma concentrations of omeprazole are increased during concomitant administration.

**Voriconazole:** Concomitant administration of omeprazole and CYP2C19 and CYP3A4 inhibitor, voriconazole, resulted in more than doubling of the omeprazole exposure.

**ADVERSE EFFECTS**

Omeprazole tablets are well tolerated. Most adverse reactions have been mild and transient and there has been no consistent relationship with treatment.

Adverse reactions within each body system are listed in descending order of frequency (very common: greater than or equal to 10%; common: greater than or equal to 1% and < 10%; uncommon: greater than or equal to 0.1% and < 1%; rare greater than or equal to 0.01% and < 0.1%; very rare: < 0.01%). These include the following.
**Gastrointestinal:** Common: diarrhoea, constipation, abdominal pain, nausea/vomiting, flatulence. Rare: stomatitis, gastrointestinal candidiasis and dry mouth. Very rare: dyspepsia, haemorrhagic necrotic gastritis (reported in children).

**Central and peripheral nervous system:** Common: headache. Uncommon: dizziness, paraesthesia, somnolence, insomnia, vertigo. Rare: reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients.

**Hepatic:** Uncommon: increased liver enzymes. Rare: encephalopathy in patients with pre-existing severe liver disease; hepatitis with or without jaundice, hepatic failure.

**Skin:** Uncommon: rash, urticaria and/or pruritus, dermatitis. Rare: photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), alopecia.

**Other:** Uncommon: malaise. Rare: hypersensitivity reactions, e.g. angioedema, fever, bronchospasm, interstitial nephritis, anaphylactic shock. Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia. Very rare: impaired renal function, including nephrosis, dyspnoea, weight increase and hypokalaemia (reported in children).

**Endocrine:** Rare: gynaecomastia. Very rare: impotence (although causality has not been established).

**Haematological:** Rare: leucopenia, thrombocytopenia, agranulocytosis and pancytopenia.

**Musculoskeletal:** Rare: arthralgia, muscular weakness and myalgia.

**DOSAGE AND ADMINISTRATION**

Omeprazole-GA tablets must be swallowed whole (not broken or chewed) with liquid. Omeprazole-GA is only available as 20 mg enteric coated tablets which must not be broken. For 10 mg dosing, another brand of omeprazole with a 10 mg dose strength should be used.

**Symptomatic gastroesophageal reflux disease (GORD):** Recommended dose for symptom relief: omeprazole 10 to 20 mg once daily for a maximum of four weeks.

In most patients symptom relief is rapid. If symptom control has not been achieved after four weeks treatment with omeprazole 20 mg daily, further investigation is recommended.

**Erosive oesophagitis:** Recommended healing dosage is omeprazole 20 mg once daily for four to eight weeks.

In most patients, symptomatic relief is rapid and healing is usually complete within four weeks. For those patients not fully healed on endoscopic examination during initial treatment, endoscopic healing usually occurs during a further four weeks treatment period. In patients with ulcerative reflux oesophagitis refractory to treatment, omeprazole 40 mg once daily usually produces healing within eight weeks.

**Maintenance therapy:** It is recommended that, after healing, maintenance therapy be commenced, omeprazole 10 mg once daily. If needed, this dose should be increased to omeprazole 20 mg once daily.

**Peptic ulcer disease associated with Helicobacter pylori infection:** Patients who gastric or duodenal ulceration is not associated with ingestion of non-steroidal anti-inflammatory drugs require treatment with antimicrobial agents in addition to antisecretory drugs whether on first
presentation or on recurrence. Omeprazole administered at a dose of 40 mg once daily or 20 mg twice daily in association with the following combinations has been found to achieve eradication rates of approximately 90%:

- Amoxycillin 500 mg and metronidazole 400 mg both three times a day, for two weeks; or
- Amoxycillin 1 g and clarithromycin 500mg both twice a day, for one week; or
- Clarithromycin 250 mg and metronidazole 400 mg twice a day, for one week.

Patients should be retreated if there is a return of symptoms and *H. pylori* infection. In this situation, possible resistance of the organism to the antimicrobial agents should be considered when deciding on the combination to be used.

To ensure healing in patients with active peptic ulcer disease see further dosage recommendations for duodenal and gastric ulcer.

**Duodenal ulcer: Recommended healing dosage:** Omeprazole 20 mg once daily for 4 to 8 weeks.

In most patients, symptomatic relief is rapid and healing is usually complete within 4 weeks. For those patients not fully healed during initial treatment, healing usually occurs during a further 4 weeks treatment period.

In duodenal ulcer patients refractory to treatment, omeprazole 40 mg once daily usually produces healing within 4 to 8 weeks.

*Maintenance therapy:* For the long-term prevention of relapse in patients with duodenal ulcer who are proven to be *Helicobacter pylori* negative and whose ulceration had not been associated with non-steroidal anti-inflammatory drugs (NSAIDs), the recommended dose is omeprazole 10 mg to 20 mg daily.

For nonsteroidal anti-inflammatory drug (NSAID) associated duodenal ulcers, see NSAID associated gastric or duodenal ulcers or erosions.

**Gastric ulcer:** Recommended healing dosage is omeprazole 20 mg once daily for four to eight weeks.

In most patients, symptomatic relief is rapid and healing is usually complete within four weeks. For those patients not fully healed during initial treatment, healing usually occurs during a further four weeks treatment period.

In gastric ulcer patients refractory to treatment, omeprazole 40 mg once daily usually produces healing within eight weeks.

*Maintenance therapy:* For the long-term prevention of relapse in patients with gastric ulcer who are proven to be *H. pylori* negative and whose ulceration had not been associated with nonsteroidal anti-inflammatory drugs (NSAIDs), the recommended dose is omeprazole 20 mg daily.

For nonsteroidal anti-inflammatory drug (NSAID) associated duodenal ulcers, see NSAID associated gastric or duodenal ulcers or erosions.

**NSAID associated gastric or duodenal ulcers or erosions:** In patients with or without continued NSAID treatment, the recommended dose is omeprazole 20 to 40 mg daily. Symptom resolution is rapid and healing occurs within four weeks in most patients. For those patients not
fully healed after the initial course, healing usually occurs during a further four weeks treatment period.

For the prevention of NSAID associated gastric or duodenal ulcers or erosions and dyspeptic symptoms, the recommended dose is omeprazole 20 mg once daily.

**Zollinger-Ellison syndrome:** Recommended initial dose is omeprazole 60 mg once daily. The dosage should be adjusted individually and treatment continued for as long as is clinically indicated. More than 90% of patients with severe disease and inadequate response to other therapies have been effectively controlled on doses of 20 to 120 mg daily. When doses exceed 80 mg orally daily, the dose should be divided and given twice daily.

**Use in Elderly:** No dosage adjustment of omeprazole is necessary in the elderly.

**Hepatic insufficiency:** The rate of plasma elimination of omeprazole and its metabolites is decreased in patients with liver cirrhosis. However, no accumulation has been observed during the use of the recommended dose of omeprazole 20 mg daily and no adjustment to the normal dosage regime is required (**see Precautions**).

**Renal insufficiency:** The systemic bioavailability of omeprazole is not significantly altered in patients with reduced renal function and no dosage adjustment is required.

**OVERDOSE**

**Symptoms:** 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 omeprazole 2,400 mg (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 clinical 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.

**Treatment:** In suspected cases of overdosage treatment should be supportive and symptomatic.

In cases of overdosage, it is advisable to contact the Poisons Information Centre (13 11 26) for recommendation on the management and treatment of overdosage.

**PRESENTATION AND STORAGE**

Omeprazole-GA 20 mg is a red brown, oblong, enteric coated tablet. They are available in bottles of 30 tablets and blister packs of 5*, 10* and 30 tablets.

*non-marketed

Store below 25°C.

**POISONS SCHEDULE**

S4
NAME AND ADDRESS OF THE SPONSOR
Ascent Pharma Pty Ltd
151-153 Clarendon St
South Melbourne Vic. 3205

DATE OF FIRST INCLUSION ON THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)
Bottles – 14 June 2007
Blister packs – 12 May 2009

DATE OF MOST RECENT AMENDMENT
5 March 2012