SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Omeprazole 20 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains omeprazole 20 mg.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Capsule, hard containing gastro-resistant granules
Each capsule consists of an orange body and blue cap and contains white to beige granules marked with O20.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. Treatment of reflux oesophagitis disease. In reflux oesophagitis the majority of patients are healed after 4 weeks. Symptom relief is rapid.

2. Treatment of duodenal and benign gastric ulcers including complicating NSAID therapy.

3. Relief of reflux-like symptoms (e.g. heartburn) and/or ulcer-like symptoms (e.g. epigastric pain) associated with acid-related dyspepsia.

4. Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and gastroduodenal erosions in patients with a previous history of gastroduodenal lesions who require continued NSAID treatment.

5. Relief of associated dyspeptic symptoms.

6. *Helicobacter pylori* eradication: When used with in combination with antibiotics, Omeprazole proves effective in the eradication of *Helicobacter pylori* (*Hp*) in peptic ulcer disease.

7. Prophylaxis of acid aspiration.

8. Zollinger-Ellison syndrome.

4.2 Posology and method of administration

Oesophageal reflux disease including reflux oesophagitis:

The usual starting dose is 20 mg omeprazole taken once a day for 4 weeks. For those patients not fully healed after the initial 4 week course, healing usually occurs during a further 4-8 weeks treatment.

Omeprazole has also been used in a dose of 40mg once a day in patients with reflux oesophagitis refractory to other therapy. Healing usually occurred within 8 weeks. Continuation of therapy can be considered at a dosage of 20 mg once daily.

Acid reflux disease:

For long-term management, a dose of 10 mg once daily is recommended, increasing to 20 mg if symptoms return.

Duodenal and benign gastric ulcers:

The usual dose is 20 mg omeprazole once daily. With duodenal ulcers, the majority of patients usually are healed after 4 weeks of treatment. The majority of patients with benign gastric ulcer are healed after 8 weeks. In severe or recurrent cases the dose may be increased to 40 mg omeprazole daily. For patients with a history of recurrent duodenal ulcer, long term therapy is recommended at a dosage of 20 mg omeprazole once daily.

To prevent recurrence, in patients with duodenal ulcer, the recommended dose is omeprazole 10 mg, once daily, increasing to 20 mg, once daily if symptoms return.

The following groups of patients are at risk from recurrent ulcer relapse: those with *Helicobacter pylori* infection, younger patients (<60 years), those whose symptoms persist for more than one year and smokers. These patients will require initial long-term therapy with omeprazole 20 mg once daily, reducing to 10 mg once daily, if necessary.

Acid-related dyspepsia:

Usual dosage is 10 mg or 20 mg omeprazole once daily for 2 – 4 weeks depending on the severity and persistence of symptoms.

If the patient does not respond to treatment after 4 weeks or who relapse shortly after treatment, then the patient should be investigated.

For the treatment of NSAID-associated gastric ulcers, duodenal ulcers or gastroduodenal erosions:

The recommended dosage of omeprazole is 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 4 weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further 4 weeks treatment.

For the prophylaxis of NSAID-associated gastric ulcers, duodenal ulcers, gastroduodenal erosions and dyspeptic symptoms in patients with a previous history of gastroduodenal lesions who require continued NSAID treatment:
The recommended dosage is 20 mg omeprazole taken once a day.

Helicobacter pylori (Hp) **eradication regimens in peptic ulcer disease:**
Omeprazole is recommended at a dose of 40 mg once daily or 20 mg twice daily concomitant with antimicrobial agents as detailed below:

Triple therapy regimens in duodenal ulcer disease:
Omeprazole and the following antimicrobial combinations;

Amoxicillin 500 mg and metronidazole 400 mg both three times a day for one week.

or

Clarithromycin 250 mg and metronidazole 400 mg (or tinidazole 500 mg) both twice a day for one week.

or

Amoxicillin 1 g and clarithromycin 500 mg both twice a day for one week.

Dual therapy regimens in duodenal ulcer disease
Omeprazole and amoxicillin 750 mg to 1 g twice daily for two weeks. Alternatively, omeprazole and clarithromycin 500 mg three times a day for two weeks.

Dual therapy regimens in gastric ulcer disease:
Omeprazole and amoxicillin 750 mg to 1 g twice daily for two weeks.

In each regimen if symptoms return and the patient tests positive for *Hp*, therapy may be repeated or one of the alternative regimens can be used; if the patient is *Hp* negative then see dosage instructions for acid reflux disease.

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

Prophylaxis of acid aspiration:
For patients considered to be at risk of aspiration of the gastric contents during general anaesthesia, the recommended dosage is omeprazole 40 mg on the evening before surgery followed by a further 40 mg 2 – 6 hours prior to surgery.

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

Elderly:
Dose adjustment is not required in the elderly.

Children:
There is limited experience of the use of Omeprazole in children. In children over 2 years who present with severe ulcerating reflux oesophagitis, Omeprazole Capsules are recommended for symptomatic relief within the dose range of 0.7 – 1.4 mg/kg daily, to a maximum of 40 mg/day, for 4 – 12 weeks. Data suggest that approximately 65% of children will experience pain relief with this dose regimen.

Treatment should be initiated by a hospital based paediatrician.

For children aged 2 – 6 years, the capsule may be opened, see section: "Patients with Swallowing Difficulties."

Impaired renal function:
Dose adjustment is not required in patients with impaired renal function.

Impaired hepatic function:
As bioavailability and half-life can increase in patients with impaired hepatic function, the dose requires adjustment with a maximum daily dose of 20 mg.

Patients with swallowing difficulties:
The capsules may be opened and the contents either swallowed alone or suspended in a small amount of fruit juice or yoghurt after gentle mixing. The dispersion should be taken immediately or within 30 minutes. Actual capsules may be sucked and then swallowed. It is important that the contents of the capsules should not be crushed or chewed.

4.3 Contraindications

Known hypersensitivity to omeprazole or to any of the other constituents of the formulation.

When gastric ulcer is suspected, the possibility of malignancy should be excluded before treatment with Omeprazole 20 mg Capsules is commenced, as treatment may alleviate symptoms and delay diagnosis.

4.4 Special warnings and precautions for use

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 a slightly increased risk of gastrointestinal infections, such as *Salmonella* and *Campylobacter*.

This product contains sucrose and therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose- isomaltase insufficiency should not take this medicine.

Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10–40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Hypomagnesaemia
Severe hypomagnesaemia has been reported in patients treated with PPIs like omeprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.
For patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Omeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B_{12} (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B_{12} absorption on long-term therapy.

4.5 Interaction with other medicinal products and other forms of interaction

Due to the decreased intragastric acidity the absorption of ketoconazole or itraconazole may be reduced during omeprazole treatment as it is during treatment with other acid secretion inhibitors.

As omeprazole is metabolised in the liver through cytochrome P450, it can prolong the elimination of diazepam, phenytoin and warfarin. Monitoring of patients receiving warfarin or phenytoin is recommended and a reduction of warfarin or phenytoin dose may be required. However, concomitant treatment with Omeprazole 20 mg once daily did not change the blood concentration of phenytoin in patients on continuous treatment with phenytoin. Similarly, concomitant treatment with Omeprazole 20 mg daily did not change coagulation time in patients on continuous treatment with warfarin.

Plasma concentrations of omeprazole and clarithromycin are increased during concomitant administration. This is considered to be a useful interaction during *H. pylori* eradication. There is no interaction with metronidazole or

amoxicillin. These antimicrobials are used concomitantly with omeprazole for the eradication of *H. pylori*.

There is no evidence of an interaction with phenacetin, theophylline, caffeine, propranolol, metoprolol, ciclosporin, lidocaine, quinidine, estradiol, or antacids. The absorption of Omeprazole 20 mg Capsules is not affected by alcohol or food.

There is no evidence of an interaction with piroxicam, diclofenac or naproxen. This is considered useful when patients are required to continue these treatments.

Simultaneous treatment with omeprazole and digoxin in healthy subjects lead to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH.

4.6 Pregnancy and lactation

Results from three epidemiological studies have revealed no evidence of adverse events of omeprazole on pregnancy or on the health of the foetus / newborn child. Omeprazole 20 mg can be used during pregnancy.

Omeprazole is excreted into breast milk but is unlikely to influence the child when used in therapeutic doses.

4.7 Effects on ability to drive and use machines

No foreseen effects.

4.8 Undesirable effects

Omeprazole 20 mg Capsules are well tolerated and adverse reactions have generally been mild and reversible. The following 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 ≥ 1/1000 and < 1/100

Rare < 1/1000

Common	*Central and peripheral nervous system:* *Gastrointestinal:*	Headache Diarrhoea, constipation, abdominal pain, nausea/vomiting and flatulence
Uncommon	*Central and peripheral nervous system:*	Dizziness, paraesthesia, light headedness, feeling

		faint, somnolence, insomnia and vertigo
	Hepatic:	Increased liver enzymes
	Skin:	Rash and/or pruritus Urticaria
	Musculoskeletal disorders	Fracture of the hip, wrist or spine (see section 4.4)
	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:	Arthritic and myalgic symptoms and muscular weakness
	Reproductive system and breast disorders:	Impotence
	Skin:	Photosensitivity, bullous eruption erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia
	Other:	Hypersensitivity reactions e.g. angioedema, fever, bronchospasm, interstitial nephritis and anaphylactic shock. Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia.

Metabolism and nutritional disorders
Frequency not known: hypomagnesaemia. [*See Special warnings and precautions for use (4.4)*]

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to

report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

4.9 Overdose

Rare reports have been received of overdosage with omeprazole. Doses of up to 560 mg have been described and occasional reports have been received when single oral doses have been reached up to 2400 mg, which is 120 times the recommended clinical dose. Overdosage of omeprazole is reported to be associated with nausea, vomiting, dizziness, abdominal pain, diarrhoea and headache. Single cases of apathy, depression and confusion have been described.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: A02B C01 - Drugs for peptic ulcers and gastro-oesophageal reflux disease - Proton Pump inhibitors.

Omeprazole reduces gastric acid secretion through a unique mechanism of action. It is a specific inhibitor of the gastric proton pump in the parietal cell. It is rapidly acting and produces reversible inhibition of gastric acid secretion with once daily dosing.

An oral dose of 20 mg once a day produces a rapid and effective inhibition of gastric acid secretion with maximum effect being achieved within 4 days of treatment. In duodenal ulcer patients, a mean decrease of approximately 80% in 24-hour intragastric acidity is then maintained, with the mean decrease in peak acid output after pentagastrin stimulation being about 70%, twenty-four hours after dosing with Omeprazole 20 mg Capsules.

Clinical data for omeprazole in the prophylaxis of NSAID induced gastroduodenal lesions are derived from clinical studies of up to 6 months duration.

Helicobacter pylori (*Hp*) is associated with acid peptic disease including duodenal ulcer and gastric ulcer in which about 95% and 80% of patients respectively are infected with this bacterium. *Hp* is implicated as a major

contributing factor in the development of gastritis and ulcers in such patients. Recent evidence also suggests a causative link between *Hp* and gastric carcinoma.

Omeprazole has been shown to have a bactericidal effect on *Hp* in vitro.

Eradication of *Hp* with omeprazole and antimicrobials is associated with rapid symptom relief, high rates of healing of any mucosal lesions, and long-term remission of peptic ulcer disease thus reducing complications such as gastrointestinal bleeding as well as the need for prolonged anti-secretory treatment.

In recent clinical data in patients with acute peptic ulcer omeprazole *Hp* eradication therapy improved patients' quality of life.

During long-term treatment an increased frequency of gastric glandular cysts has been reported. These changes are a physiological consequence of pronounced inhibition of acid secretion. The cysts are benign and appear to be reversible. No other treatment related mucosal changes have been observed in patients treated continuously with omeprazole for periods up to 5 years.

Site and mechanism of action

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

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

5.2 Pharmacokinetic properties

Absorption and distribution

Omeprazole is acid labile and is administered orally as enteric-coated granules in capsules. Absorption takes place in the small intestine and is usually completed within 3 – 6 hours. The systemic bioavailability of omeprazole from a single oral dose is approximately 35%. After repeated once-daily administration, the bioavailability increases to about 60%. Concomitant intake of food has no influence on the bioavailability. The plasma protein binding of omeprazole is about 95%.

Elimination and metabolism

The average half-life of the terminal phase of the plasma concentration-time curve is approximately 40 minutes. There is no change in half-life during

treatment. 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 a given time.

Omeprazole is entirely metabolised, mainly in the liver. Identified metabolites in plasma are the sulfone, the sulfide and hydroxy-omeprazole, these metabolites have no significant effect on acid secretion. About 80% of the metabolites are excreted in the urine and the rest in the faeces. The two main urinary metabolites are hydroxy-omeprazole and the corresponding carboxylic acid.

The systemic bioavailability of omeprazole is not significantly altered in patients with reduced renal function. The area under the plasma concentration-time curve is increased in patients with impaired liver function, but no tendency to accumulation of omeprazole has been found.

Children

Available data from children (1 year and older) suggest that the pharmacokinetics within the recommended doses are similar to those reported in adults. At steady state, lower plasma levels of omeprazole were seen in some children.

5.3 Preclinical safety data

Animal toxicity:

Gastric ECL-cell hyperplasia and carcinoids, have been observed in life-long studies in rats treated with omeprazole or subjected to partial fundectomy. These changes are the result of sustained hypergastrinaemia secondary to acid inhibition, and not from a direct effect of any individual drug.

6.1 List of excipients

Sugar spheres
Sodium starch glycolate
Sodium lauryl sulfate
Povidone
Trisodium phosphate
Sodium hydroxide
Hypromellose
Methacrylic acid - ethyl acrylate (1:1)
Triethyl citrate
Titanium dioxide
Talc
Ammonia solution
Purified water

Capsule

Gelatin
Titanium dioxide (E171)
Quinoline yellow (E104)
Indigo carmine – FD&C Blue No.2 (E132)
Erythrosine – FD&C Red No.3 (E127)
Water

Printing Ink
Shellac
Dehydrated Alcohol
Isopropyl Alcohol
N-Butyl Alcohol
Propylene Glycol
Sodium Hydroxide
Povidone
Titanium Dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed.

6.5 Nature and contents of container

HDPE bottle and polypropylene cap with integral silica gel dessicant

Alu/PVC/PVDC and Polyamide/Alu/PVC blisters

Each pack contains 28 capsules

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Strandhaven Limited T/A Somex Pharma
600 High Road
Seven Kings
Ilford
Essex IG3 8BS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 15764/0029

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17/12/2007

10 DATE OF REVISION OF THE TEXT

27/04/2019