1.5.5.3 PROPOSED CLEAN PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ALTOSEC 20 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule of ALTOSEC 20 contains 20 mg omeprazole.

Contains sugar: Lactose anhydrous 8 mg, mannitol 142,5 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules

ALTOSEC 20 are hard gelatin capsule size '2' opaque pink body and opaque reddish brown cap, imprinted with "F5 1" on cap and body in black ink and capsule containing white to slightly beige enteric coated Omeprazole pellets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

ALTOSEC 20 is indicated for:

- The treatment of duodenal ulcer, gastric ulcer, reflux oesophagitis, and Zollinger-Ellison syndrome and for the symptomatic relief of heartburn in patients with gastro-oesophageal reflux disease.

- *H.pylori*-positive duodenal ulcers, as part of the eradication programme with appropriate antibiotics.

- The treatment of NSAID associated gastric and/or duodenal ulcer and erosions and a reduction of the risk to develop gastric and/or duodenal ulcer/erosions and a risk of reduction for relapse of a previously healed gastric and/or duodenal ulcer/erosions in patients on NSAIDs treatment.

4.2. Posology and method of administration

Posology

Adults

Duodenal ulcer

The recommended dosage is 20 mg ALTOSEC 20 once daily for two to four weeks.
In some duodenal ulcer patients refractory to other treatment regimes, 40 mg once daily may be effective.

ALTOSEC 20 is indicated for *H.pylori*-positive duodenal ulcers, as part of the eradication programme with appropriate antibiotics.

Gastric ulcer and reflux oesophagitis

The recommended dosage is 20 mg once daily for four to 8 eight weeks.
In some patients with gastric ulcer and reflux oesophagitis patients refractory to other treatment regimens, 40 mg ALTOSEC 20 once daily may be effective.
In patients with severe or symptomatic recurrent reflux oesophagitis treatment can be continued with ALTOSEC 20 at a dosage of 20 mg once daily.

Symptomatic gastro-oesophageal reflux disease (GORD)

The recommended dose is 20 mg ALTOSEC 20 mg daily.

If symptom control has not been achieved after 2 weeks of treatment with 20 mg daily further investigation is recommended.

Zollinger-Ellison Syndrome

The recommended initial dose is 60 mg ALTOSEC 20 mg once daily.

The dosage should be adjusted individually, and treatment continued as long as it is clinically indicated. Patients with severe disease and inadequate response to other therapies have been effectively controlled with more than 90 % maintained on doses of 20 mg to 120 mg daily. With doses above 80 mg daily the dose should be divided and given twice daily.

NSAID associated gastroduodenal lesions

NSAID associated gastric ulcers, duodenal ulcers or gastroduodenal erosions in patients with or without continued NSAID treatment, the recommended dosage of ALTOSEC 20 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 period.

For the prevention of NSAID associated gastric ulcers, duodenal ulcers, gastroduodenal erosions and dyspeptic symptoms, the recommended dosage of ALTOSEC 20 is 20 mg once daily.

Special populations

Elderly

No dose adjustment is necessary in the elderly.

Impaired renal function

No dose adjustment is required in patients with impaired renal function.

Impaired hepatic function

As bioavailability and plasma half-life of omeprazole are increased in patients with impaired hepatic function a daily dose of 20 mg is generally sufficient.

The long-term safety of ALTOSEC 20 in patients with renal and hepatic impairment has not been established (see section 4.3).

Paediatric population

There is no experience with ALTOSEC 20 in children.

(See section 4.4).

Method of administration

Oral administration

It is recommended to take ALTOSEC 20 capsules in the morning, preferably without food, swallowed whole with half a glass of water. The capsules must not be chewed or crushed.

For patients with swallowing difficulties who can drink or swallow semi-solid food.

The capsule can be opened, and the contents swallowed directly with half a glass of water or after mixing the contents in a slightly acidic fluid, e.g., fruit juice or applesauce, or in non-carbonated water. The dispersion should be taken immediately (or within 30 minutes). Always stir just before drinking. Rinse it down with half a glass of water. Alternatively, patients can suck the capsule and swallow the pellets with half a glass of water. Ingest without chewing the enteric coated pellets.

4.3. Contraindications

ALTOSEC 20 is contraindicated in:

- Patients with hypersensitivity to omeprazole, substituted benzimidazoles or to any excipients in ALTOSEC 20 (see section 6.1).
- Safety in pregnancy and lactation has not been established (see section 4.6).
- ALTOSEC 20 must not be used concomitantly with atazanavir and nelfinavir (see section 4.5).

4.4. Special warnings and precautions for use

ALTOSEC 20 is not indicated for mild gastrointestinal complaints such as nervous dyspepsia.

Prior to treatment the possibility of malignancy or gastric ulcer or a malignant disease of the oesophagus should be excluded as the treatment with ALTOSEC 20 may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.

Increased risk of subclinical acute or chronic interstitial nephritis associated with proton pump inhibitors (PPI's) leading to chronic renal inflammation and reduced renal function

There is an increased risk of subclinical acute or chronic interstitial nephritis associated with proton pump inhibitors (PPI's) leading to chronic renal inflammation and reduced renal function. The preferred term to describe the histological findings of tubular injury being "tubulointerstitial nephritis".

Acute tubulointerstitial nephritis is characterised by an inflammatory reaction within the tubulointerstitial space of the kidney. Acute interstitial inflammatory reactions are associated with damage to the tubulointerstitium, leading to acute kidney injury. Tubulointerstitial

nephritis may be medicine-related, infectious, systemic, autoimmune, genetic, and idiopathic with the most common cause being related to medicine exposure.
The risk of tubulointerstitial nephritis leading to chronic inflammation and reduced renal function associated with the use of proton pump inhibitors such as omeprazole, is a class effect.

Clopidogrel

Omeprazole, as in ALTOSEC 20, is a CYP2C19 inhibitor. When starting or ending treatment with ALTOSEC 20, the potential for interactions with medicines metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and ALTOSEC 20. The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of ALTOSEC 20 and clopidogrel should be avoided (see section 4.5).

Combination with other medicines

Concomitant administration of ALTOSEC 20 and atazanavir and nelfinavir is not recommended (see sections 4.3 and 4.5).

Absorption of vitamin B_{12} (Cyanocobalamin)

ALTOSEC 20 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.

Methotrexate

Use caution when administering high-dose methotrexate to patients receiving proton pump inhibitor therapy. Case reports and published population pharmacokinetic studies suggest that concomitant use of PPIs, such as omeprazole as in ALTOSEC 20, with methotrexate (primarily at high dose), may elevate and prolong serum levels of methotrexate and/or its

metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities (see section 4.5).

Clostridium difficile associated diarrhoea (CDAD)

The use of proton pump inhibitors, as in ALTOSEC 20, may be associated with an increased risk of CDAD. A diagnosis of CDAD should be considered for patients taking ALTOSEC 20 who develop diarrhoea that does not improve.

Clostridium difficile (*C. difficile*) is a bacterium that can cause diarrhoea that does not improve. Symptoms include watery stool, abdominal pain and fever, and patients may develop more serious intestinal conditions. The disease can also be spread in hospitals. Factors that may predispose an individual to developing CDAD include advanced age, certain chronic medical conditions and taking broad spectrum antibiotics. Treatment for CDAD includes the replacement of fluids and electrolytes and the use of indicated antibiotics.

Alarm symptoms

In the presence of any alarm symptoms (e.g., significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when a gastric ulcer is suspected or present, malignancy should be excluded, as treatment with ALTOSEC 20 may alleviate symptoms and delay diagnosis.

Risk of fracture

Proton pump inhibitors, such as ALTOSEC 20, 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 to

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, as in ALTOSEC 20, 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 dysrhythmia can occur, but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the omeprazole, as in ALTOSEC 20. For patients expected to be on prolonged treatment or who take ALTOSEC 20 with digoxin or medicines that may cause hypomagnesaemia (e.g., diuretics), healthcare professionals should consider measuring magnesium levels before starting ALTOSEC 20 treatment and periodically during treatment.

Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors, such as ALTOSEC 20, are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the healthcare provider should consider stopping ALTOSEC 20. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP), which can be life-

threatening or fatal, have been reported very rarely and rarely, respectively in association with omeprazole, as in ALTOSEC 20, treatment.

Interference with laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, ALTOSEC 20 treatment should be temporarily stopped five days before CgA measurements.

If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

Hepatic and renal impairment

Hepatic impairment may require a reduction in dose The long-term safety of ALTOSEC 20 in patients with renal and/or hepatic impairment has not been established.

Gastrointestinal infection

Treatment with proton pump inhibitors such as ALTOSEC 20 may lead to slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and, in hospitalised patients, possibly also *Clostridium difficile.* Decreased gastric acidity increases gastric counts of bacteria normally present in the gastrointestinal tract.

Long term treatment

When exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

Effects related to acid inhibition

During long-term treatment gastric glandular cysts have been reported in somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

Paediatric population

There is very limited experience with the use of ALTOSEC 20 in children.

Excipients:

Lactose warning

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take ALTOSEC 20.

Mannitol

ALTOSEC 20 also contains mannitol and may have a laxative effect.

4.5. Interaction with other medicines and other forms of interaction

Effects of ALTOSEC 20 on the pharmacokinetics of other active medicines:

Medicines with pH-dependent absorption

The decreased intragastric acidity during treatment with ALTOSEC 20 might increase or decrease the absorption of active medicines with a gastric pH dependent absorption.

Nelfinavir, atazanavir

The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with ALTOSEC 20. Concomitant administration of ALTOSEC 20 with atazanavir and nelfinavir is contraindicated (see sections 4.3 and 4.4). Co-administration of omeprazole (40 mg once daily) reduced mean nelfinavir exposure by ca. 40% and the mean exposure of the

pharmacologically active metabolite M8 was reduced by ca. 75 –90%. The interaction may also involve CYP2C19 inhibition.

Concomitant administration of omeprazole with atazanavir is not recommended (see section 4.4). Concomitant administration of omeprazole (40 mg once daily) and atazanavir 300 mg/ritonavir 100 mg to healthy volunteers resulted in a 75% decrease of the atazanavir exposure. Increasing the atazanavir dose to 400 mg did not compensate for the impact of omeprazole on atazanavir exposure. The co-administration of omeprazole (20 mg once daily) with atazanavir 400 mg/ritonavir 100 mg to healthy volunteers resulted in a decrease of approximately 30% in the atazanavir exposure as compared to atazanavir 300 mg/ritonavir 100 mg once daily.

Digoxin

Concomitant treatment with omeprazole (20 mg daily), as in ALTOSEC 20, and digoxin increases the bioavailability of digoxin by 10 %. Digoxin toxicity has been reported. Caution should be exercised when ALTOSEC 20 is given at high doses in elderly patients. Therapeutic medicine monitoring of digoxin should be reinforced.

Clopidogrel

Pharmacokinetic/pharmacodynamic interaction between omeprazole and clopidogrel results in a decreased exposure to the active metabolite of clopidogrel by an average of 46 % for omeprazole. This leads to a decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 16 % for omeprazole. The consequence of this would be a reduction in the antiplatelet activity of clopidogrel, which may predispose to an increase in cardiovascular events. Concomitant use of omeprazole, as in ALTOSEC 20, and clopidogrel should be avoided.

Other active medicines

The absorption of erlotinib, posaconazole, erlotinib, ketoconazole and itraconazole is significantly reduced and thus clinical efficacy may be impaired. For posaconazole and erlotinib concomitant use should be avoided.

Medicines metabolised by CYP2C19

Omeprazole, as in ALTOSEC 20 is a moderate inhibitor of CYP2C19, the major omeprazole metabolising enzyme. Thus, the metabolism of concomitant active medicines also metabolised by CYP2C19 may be decreased and the systemic exposure to these medicines increased. Examples of such medicines are warfarin and other vitamin K antagonists, cilostazol, diazepam and phenytoin.

Cilostazol

Omeprazole, as in ALTOSEC 20 given in doses of 40 mg to healthy subjects in a cross-over study, increased C_{max} and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.

Phenytoin

Monitoring phenytoin plasma concentration is recommended during the first two weeks after initiating ALTOSEC 20 treatment and, if a phenytoin dose adjustment is made, monitoring and a further dose adjustment should occur upon ending ALTOSEC 20 treatment.

Unknown mechanism

Saquinavir

Concomitant administration of ALTOSEC 20 with saquinavir/ritonavir resulted in increased plasma levels up to approximately 70 % for saquinavir associated with good tolerability in HIV-infected patients.

Tacrolimus

Concomitant administration of ALTOSEC 20 has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.

Methotrexate

When given together with proton-pump inhibitors, like ALTOSEC 20, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of ALTOSEC 20 should be considered (see section 4.4.).

Effects of other medicines on the pharmacokinetics of ALTOSEC 20

Inhibitors CYP2C19 and/or CYP3A4

Since omeprazole, as in ALTOSEC 20, is metabolised by CYP2C19 and CYP3A4, medicines known to inhibit CYP2C19 or CYP3A4 (such as clarithromycin and voriconazole) may lead to increased omeprazole serum levels by decreasing omeprazole's rate of metabolism. Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. Dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.

Inducers of CYP2C19 and/or CYP3A4

Medicines known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St John's wort) may lead to decreased omeprazole serum levels by increasing omeprazole's rate of metabolism.

Omeprazole is also partly metabolised by CYP3A4, but omeprazole does not inhibit this enzyme. Thus, ALTOSEC 20 does not affect the metabolism of medicines metabolised by CYP3A4, such as ciclosporin, lidocaine/lignocaine, quinidine, oestradiol, erythromycin, and budesonide. There is no evidence of interactions with theophylline, propranolol, metoprolol,

amoxicillin piroxicam, diclofenac, naproxen, or antacids, but there may be interactions with other medicine also metabolised via the cytochrome P450 enzyme system.

The absorption of ALTOSEC 20 is not affected by alcohol or food.

4.6. Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established (see section 4.3.)

Pregnancy

Results from three prospective epidemiological studies (more than 1000 exposed outcomes) indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child.

Breastfeeding

Omeprazole is excreted in breast milk.

Fertility

Animal studies with the racemic mixture omeprazole, given by oral administration do not indicate effects with respect to fertility.

4.7. Effects on ability to drive and use machines

ALTOSEC 20 has minor influence on ability to drive and use machines.

Since adverse reactions such as dizziness and blurred vision have been reported in patients receiving ALTOSEC 20, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that ALTOSEC 20 does not adversely affect their ability to do so (see section 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

The most frequent side effects (1 to 10 % of patients) are headache, abdominal pain, constipation, diarrhoea, flatulence, and nausea/vomiting.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP) have been reported in association with omeprazole, as in ALTOSEC 20, treatment.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (Cannot be estimated from the available data)
Infections and infestations		*Clostridium difficile* associated diarrhoea (CDAD)	
Blood and the lymphatic system disorders		Leukopenia, thrombocytopenia, agranulocytosis, pancytopenia	
Immune system disorders		Hypersensitivity reactions e.g., fever, angioedema and anaphylactic reaction/shock	
Metabolism and nutrition disorders		Hyponatraemia, hypomagnesaemia, severe hypomagnesaemia may result in hypocalcaemia, hypomagnesaemia may also be associated with hypokalaemia	
Psychiatric disorders		Insomnia, agitation, reversible mental confusion, depression, aggression, hallucinations (predominantly in severely ill patients)	
Nervous system disorders	Headache*	Dizziness*, paraesthesia,	

		somnolence, taste disturbance	
Eye disorders		Blurred vision	
Ear and labyrinth disorders		Vertigo	
Respiratory, thoracic and mediastinal disorders		Bronchospasm	
Gastrointestinal disorders	Abdominal pain, constipation, diarrhoea*, flatulence, nausea/vomiting, fundic gland polyps (benign)	Dry mouth, stomatitis, gastrointestinal candidiasis, microscopic colitis	
Hepatobiliary disorders		Increased liver enzymes, hepatitis with or without jaundice, hepatic failure, encephalopathy in patients with pre-existing liver disease	
Skin and subcutaneous tissue disorders		Dermatitis, pruritus*, rash*, urticaria*, alopecia, photosensitivity, erythema multiforme, bullous eruption, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), acute generalised exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS)	Subacute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders		Arthralgia, arthritic and myalgic symptoms*, muscular weakness, fracture of the hip, wrist or spine	
Renal and urinary disorders		Interstitial nephritis (may lead to renal failure)	
Reproductive system and breast disorders		Gynaecomastia	

General disorders and administrative site conditions		Malaise, increased sweating, peripheral oedema	

**Symptoms resolved after discontinuation of therapy*

c) Paediatric population

The safety of omeprazole has been assessed in a total of 310 children aged 0 to 16 years with acid-related disease. There are limited long-term safety data from 46 children who received maintenance therapy of omeprazole during a clinical study for severe erosive oesophagitis for up to 749 days. The adverse event profile was generally the same as for adults in short as well as in long-term treatment. There are no long-term data regarding the effects of omeprazole treatment on puberty and growth.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to: **Acino Pharma (Pty) Ltd:**

E-mail: drugsafety_ZA@acino.swiss or

SAHPRA: https://www.sahpra.org.za/health-products-vigilance/

4.9. Overdose

Symptoms

There is limited information available on the effects of overdoses of omeprazole, as in ALTOSEC 20, in humans. 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 2,400 mg omeprazole (120 times the usual recommended clinical dose).

Nausea, vomiting, dizziness, abdominal pain, headache, diarrhoea, blurred vision, confusion, diaphoresis, flushing, malaise, and tachycardia have been reported from overdosage with ALTOSEC 20. Also apathy, depression and confusion have been described in single cases.

The symptoms described in connection with omeprazole, as in ALTOSEC 20, overdosage have been transient, and no serious 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

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and class: A 11.4.3. Medicines acting on the Gastrointestinal tract. Other
Pharmacotherapeutic group: Drugs for acid-related disorders, proton pump inhibitors
ATC code: A02BC01

Mechanism of action

Omeprazole reduces gastric acid secretion. It is a specific inhibitor of the gastric proton pump in the parietal cell. It produces reversible control of gastric acid secretion with once daily dosing.

Omeprazole is a weak base and is concentrated and converted to the active form in the acid environment of intracellular canaliculi within the parietal cell, where it inhibits the enzyme H^+, K^+-ATPase–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 secretagogue.

Omeprazole has no effect on acetylcholine, histamine or gastrin receptors.

Effect on gastric acid secretion

Oral dosing with omeprazole once daily provides 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 %, 24 hours after dosing with omeprazole.

5.2. Pharmacokinetic properties

Absorption

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 to 6 hours. The systemic bioavailability of omeprazole from a single oral dose of omeprazole is approximately 35 %. After repeated once-daily administration, the bioavailability increases to about 60 %. Concomitant intake of food has no influence on the bioavailability.

Distribution

The apparent volume of distribution in healthy subjects is approximately 0,3 litres/kg and a similar value is also seen in patients with renal insufficiency. In elderly and in patients with hepatic insufficiency, the volume of distribution is slightly decreased. Concomitant intake of food has no influence on the bioavailability.

The plasma protein binding of omeprazole is about 95 %.

Biotransformation

The average half-life of the terminal phase of the 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 by the cytochrome P450 (CYP), mainly in the liver. The major part of its metabolism is dependent on the polymorphically expressed, specific isoform CYP2C19 (S-mephenytoin hydroxylase).

Identified metabolites in plasma are sulphone, sulphide and hydroxyl-omeprazole. These metabolites having no significant effect on acid secretion.

Elimination

About 80 % of the metabolites are excreted in the urine and the rest in the faeces. The two main urinary metabolites are hydroxyl-omeprazole and the corresponding carboxylic acid.

Special Populations

Renal impairment

The systemic bioavailability of omeprazole is not significantly altered in patients with reduced renal function.

Hepatic impairment

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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium hydrogen phosphate dihydrate, gelatin, hydroxypropylcellulose, hydroxypropyl methylcellulose, lactose anhydrous, magnesium stearate, mannitol, methacrylic acid copolymer Type C, microcrystalline cellulose, polyethylene glycol, red iron oxide (C.I. 77491), silicon dioxide colloidal anhydrous, sodium lauryl sulphate, titanium dioxide.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

Keep in the original packaging until required for use.

HDPE bottle, replace cap firmly after use.

6.5. Nature and contents of container

14 or 28 capsules are packed into a white high-density polyethylene bottle sealed with a white polypropylene screw cap with a safety ring together with a white low-density polyethylene desiccant capsule. The bottle is placed in an outer cardboard carton together with a leaflet.

14 or 28 capsules are packed into polyvinyl chloride blister strips sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Acino Pharma (Pty) Ltd

106 16th Road

Midrand,

1686

8. REGISTRATION NUMBER

32/11.4.3/0087

9. DATE OF FIRST AUTHORISATION

23 October 1998

10. DATE OF REVISION OF TEXT

25 February 2023

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