**Clean Proposed Professional Information for Medicines for Human Use: GAZIGON OTC**

## SCHEDULING STATUS

S2

## 1. NAME OF THE MEDICINE

GAZIGON OTC 20 mg capsules

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Each capsule contains:**

| | |
|---|---|
| Omeprazole | 20 mg |

**Preservatives:**

| | |
|---|---|
| Methylparaben | 0,15 % *m/m* |
| Propylparaben | 0,04 % *m/m* |

Contains sugar.

Each GAZIGON OTC capsule:

Contains sucrose 165,95 mg and lactose anhydrous 2,99 mg.

Contains sweetener mannitol 55,90 mg.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Hard gelatine capsules.

Size 2 hard gelatin capsules with a dark blue body and a light blue cap, containing white to almost white uniformly rounded enteric-coated pellets. “GAZIGON OTC**”** is printed on both the shells with white ink.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

GAZIGON OTC is indicated in:

- the temporary short-term relief of heartburn and hyperacidity.

### 4.2 Posology and method of administration

**Posology**

**Short term relief of heartburn and hyperacidity**

The maximum dose is 20 mg per day and the treatment is for a maximum period of 14 days.

If no symptom relief is obtained within 2 weeks of continuous treatment, further investigation is recommended, and the patient must be advised to consult a doctor.

**Special populations**

**Elderly**

Dose reductions are not necessary in elderly patients.

The long-term safety of GAZIGON OTC in patients with renal and hepatic impairment has not been established (see sections 4.8 and 5.2).

**Impaired renal function**

Dose reductions are not necessary in renal impairment (see sections 4.4 and 5.2).

**Impaired hepatic function**

Bioavailability and plasma half-life of GAZIGON OTC are increased in patients with impaired hepatic function, therefore a daily dose of 10 – 20 mg is generally sufficient (see sections 4.4, 4.8 and 5.2).

**Paediatric population**

There is very limited experience with the use of GAZIGON OTC in children (see sections 4.4, 4.8 and 5.2).

GAZIGON OTC should not be used in children under 1 year of age or < 10 kg.

**Method of administration**

GAZIGON OTC is recommended to be given in the morning and swallowed whole with a half glass of liquid. The capsule should not be chewed or crushed.

**4.3 Contraindications**

- Hypersensitivity to omeprazole or to any of the excipients listed in section 6.1.
- Known hypersensitivity to substituted benzimidazoles.
- Safety in pregnancy and lactation has not been established (see section 4.6).
- GAZIGON OTC must not be used concomitantly with nelfinavir (see sections 4.4 and 4.5).
- Co-administration of atazanavir with GAZIGON OTC is not recommended (see sections 4.4 and 4.5).

**4.4 Special warnings and precautions for use**

**Gastric malignancy**

Prior to treatment or in the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, or melaena), the possibility of malignancy or gastric ulcer or a malignant disease of the oesophagus should be excluded as the treatment with GAZIGON OTC may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.

***Clostridium difficile*-associated diarrhoea**

Proton pump inhibitor (PPI) therapy like GAZIGON OTC may be associated with an increased risk of *Clostridium difficile-associated* diarrhoea (CDAD), especially in hospitalised patients.

This diagnosis should be considered for diarrhoea that does not improve (see section 4.8).

Patients should use the lowest dose and shortest duration of GAZIGON OTC therapy appropriate to the condition being treated.

**Acute interstitial nephritis (AIN) leading to acute kidney injury (AKI) and/or chronic kidney disease**

GAZIGON OTC may increase the risk of subclinical acute interstitial nephritis (AIN) associated with proton pump inhibitors (PPIs) leading to chronic renal inflammation and reduced renal function (tubular injury being “tubulointerstitial nephritis” also called “Acute interstitial nephritis (AIN)”) (see section 4.8).

AIN has been observed in patients taking PPIs, such as GAZIGON OTC, and may occur at any point during PPI therapy. AIN is characterised by an inflammatory reaction within the tubulointerstitial space of the kidney. Acute interstitial inflammatory reactions are associated

with damage to the tubulointerstitium and can progress to acute kidney injury (AKI) (acute renal failure).

AIN may be drug-related, infectious, systemic, autoimmune, genetic, and idiopathic with the most common cause being related to a medicine or drug exposure.

Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decrease renal function (e.g., malaise, nausea, anorexia). A delay in diagnosis and continued use of the PPI can lead to chronic renal failure.

Patients on treatment with PPIs must be frequently monitored for renal function and the urine checked for haematuria and/or proteinuria. Patients should be advised to report any decrease in urine volumes or if they suspect that there is blood in their urine. Treatment with PPIs should be discontinued in patients with AIN.

**Concomitant administration with nelfinavir and atazanavir**

The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole. Concomitant administration of proton pump inhibitors such as omeprazole as in GAZIGON OTC with nelfinavir is contraindicated and with atazanavir is not recommended (see sections 4.3 and 4.5).

If the combination of atazanavir with GAZIGON OTC is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; omeprazole 20 mg should not be exceeded.

**Hepatic and renal impairment**

The long-term safety of GAZIGON OTC in patients with renal and/or hepatic impairment has not been established.

Hepatic impairment may require a reduction in dose (see sections 4.2 and 5.2).

**Interaction with clopidogrel**

Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medicines, such as GAZIGON OTC, that interfere with CYP2C19 activity. Avoid concomitant use of clopidogrel and GAZIGON OTC. Concomitant use of clopidogrel with 80 mg omeprazole, reduced the pharmacological activity of clopidogrel even when administered 12 hours apart. When using GAZIGON OTC, consider alternative anti-platelet therapy (see section 4.5).

The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of GAZIGON OTC and clopidogrel should be discouraged.

**Subacute cutaneous lupus erythematosus (SCLE)**

Proton pump inhibitor (PPI) therapy like GAZIGON OTC is associated with very infrequent cases of SCLE (see section 4.8). 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 health care professional should consider stopping GAZIGON OTC. SCLE after previous treatment with GAZIGON OTC may increase the risk of SCLE with other proton pump inhibitors.

**Gastrointestinal infections**

Decreased gastric acidity increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with GAZIGON OTC may lead to slightly increased risk of gastrointestinal infections, such as *Salmonella* and *Campylobacter* (see section 4.8).

**Interactions with diagnostic investigations for neuroendocrine tumours**

Serum chromogranin A (CgA) levels increase secondary to medicine-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumours.

To avoid this interference, GAZIGON OTC treatment should be stopped for at least 5 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 GAZIGON OTC treatment.

**Concomitant administration with methotrexate**

Concomitant use of PPIs such as GAZIGON OTC with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of GAZIGON OTC may be considered in some patients (see section 4.5).

**Concomitant use with St John's Wort or rifampicin**

Medicines which induce CYP2C19 or CYP3A4 (such as St John's Wort or rifampicin) can substantially decrease omeprazole concentrations. Avoid concomitant use of GAZIGON OTC with St John's Wort or rifampicin.

**Excipient sucrose**

GAZIGON OTC contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

**Excipient lactose**

GAZIGON OTC contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**Excipient mannitol**

GAZIGON OTC contains mannitol which, on rare occasions, may cause hypersensitivity reactions and may have a laxative effect.

**Paediatric population**

There is very limited experience with the use of GAZIGON OTC in children.

## 4.5 Interaction with other medicines and other forms of interaction

**Effects of omeprazole on the pharmacokinetics of other active substances**

***Active substances with pH dependent absorption***

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

*Nelfinavir, atazanavir*

The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole.

Concomitant administration of omeprazole with 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 to 90 %. The interaction may also involve CYP2C19 inhibition.

Concomitant administration of omeprazole with atazanavir is not recommended (see sections 4.3 and 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 GAZIGON OTC and digoxin in healthy subjects increased the bioavailability of digoxin by 10 % as consequence of the increased intragastic pH.. Digoxin toxicity has been rarely reported. However caution should be exercised when omeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should then be reinforced.

*Other active substances*

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

***Substances metabolised by CYP2C19***

Omeprazole is a moderate inhibitor of CYP2C19, the major omeprazole metabolising enzyme. Thus, the metabolism of concomitant pro-drugs or active substances also metabolised by CYP2C19, may be decreased and the systemic exposure to these active substances decreased or increased, respectively. Examples of such an pro-drug is clopidogrel and of active substances are R-warfarin and other vitamin K antagonists, cilostazol, diazepam and phenytoin.

*Clopidogrel*

Clopidogrel is metabolised to its active metabolite in part by CYP2C19. Co-administration of clopidogrel with omeprazole, an inhibitor of CYP2C19, reduces the pharmacological activity of clopidogrel given concomitantly or 12 hours apart. Concomitant use of medicines that inhibit the activity of this enzyme may result in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in inhibition of platelet aggregation.

Results from studies in healthy subjects have shown a pharmacokinetic (PK)/pharmacodynamic (PD) interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and omeprazole (80 mg p.o. daily) resulting in a decreased exposure to the active metabolite of clopidogrel by an average of 46 % and a decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 16 %.

Inconsistent data on the clinical implications of a PK/PD interaction of omeprazole in terms of major cardiovascular events have been reported from both observational and clinical studies. As a precaution, concomitant use of omeprazole and clopidogrel should be discouraged (see section 4.4).

*Coumarin anticoagulants*

The elimination of R-warfarin and other vitamin K antagonists may be prolonged when GAZIGON OTC is given concomitantly. Monitoring of INR is recommended and dosage reductions may be necessary.

*Cilostazol*

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

*Diazepam*

The elimination of diazepam may be prolonged when GAZIGON OTC is given concomitantly.

*Phenytoin*

The elimination of phenytoin may be prolonged when GAZIGON OTC is given concomitantly.

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

***Active substances metabolised by CYP3A4***

*Tacrolimus*

Concomitant administration of omeprazole as in GAZIGON OTC has been reported to increase the serum levels of tacrolimus due to decreased CYP3A4 metabolism 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.

***Unknown mechanism***

*Saquinavir*

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

*Methotrexate*

When given together with proton-pump inhibitors, such as GAZIGON OTC methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of omeprazole may need to be considered.

**Effects of other active substances on the pharmacokinetics of omeprazole**

***Inhibitors of CYP2C19 and/or CYP3A4***

Since omeprazole is metabolised by CYP2C19 and CYP3A4, active substances 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.

*Voriconazole*

Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. As high doses of omeprazole have been well-tolerated adjustment of the omeprazole dose is not generally required. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.

*Clarithromycin*

It has been reported that use of omeprazole with clarithromycin in healthy volunteers resulted in an approximate 30 % increase in peak plasma concentrations of omeprazole, and an increase in its mean half-life from 1,2 to 1,6 hours. At the same time, plasma concentrations

of clarithromycin were also modestly increased, as were local concentrations in gastric tissue and mucus. Clarithromycin inhibits the metabolism of omeprazole mediated by the cytochrome P450 isoenzyme CYP3A4.

The interaction may contribute to the benefits of combined therapy for *Helicobacter pylori* infection.

***Inducers of CYP2C19 and/or CYP3A4***

Active substances 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.

**Other interactions**

***Concomitant administration with medicines that may cause hypomagnesaemia***

Proton pump inhibitors including, omeprazole as in GAZIGON OTC, can cause hypomagnesaemia when used for a prolonged period, and the risk may be further increased when combined with other medicines that also have this effect.

For patients expected to be on prolonged treatment or who take GAZIGON OTC with medicines that may cause hypomagnesaemia such as digoxin, tacrolimus or diuretics, measuring of magnesium levels before starting GAZIGON OTC treatment and periodically during treatment should be considered (see section 4.4).

***Alcohol or food***

The absorption of GAZIGON OTC is not affected by alcohol or food.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

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

### Breastfeeding

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

### 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

GAZIGON OTC may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Adverse drug reactions such as dizziness, visual disturbances and vertigo may occur (see section 4.8). Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

## 4.8 Undesirable effects

### a) Summary of the safety profile

It is reported that the most common side effects (1 – 10 %) are headache, abdominal pain, constipation, diarrhoea, flatulence and nausea/vomiting.

### b) Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with omeprazole.

| **System Organ Class** | **Frequency** | | |
|---|---|---|---|
| | **Frequent** | **Less Frequent** | **Not known** |
| Infections and infestations | | | *Clostridium difficile*-associated diarrhoea |
| Blood and 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,<br>confusion,<br>depression,<br>aggression,<br>hallucinations | |
| Nervous system disorders | headache,<br>dizziness,<br>paraesthesia,<br>somnolence | taste disturbance | |
| Eye disorders | | blurred vision | |

| | | | |
|---|---|---|---|
| Ear and labyrinth disorders | vertigo | | |
| Respiratory, thoracic and mediastinal disorders | | bronchospasm | |
| Gastrointestinal disorders | abdominal pain,<br>constipation,<br>diarrhoea,<br>flatulence,<br>nausea/vomiting,<br>fundic gland polyps (benign) | dry mouth,<br>stomatitis,<br>gastrointestinal candidiasis | microscopic colitis |
| Hepatobiliary disorders | increased liver enzymes | hepatitis with or without jaundice,<br>hepatic failure,<br>encephalopathy in patients with pre-existing liver disease | |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | dermatitis,<br>pruritus,<br>rash,<br>urticaria | alopecia,<br>photosensitivity,<br>erythema multiforme,<br>Stevens-Johnson syndrome,<br>toxic epidermal necrolysis (TEN) | subacute cutaneous lupus erythematosus (see section 4.4) |
| Musculoskeletal and connective tissue disorders | fracture of the hip, wrist or spine | arthralgia,<br>myalgia,<br>muscular weakness | |
| Renal and urinary disorders | | interstitial nephritis (see section 4.4) | |
| Reproductive system and breast disorders | | gynaecomastia | |
| General disorders and administration site conditions | malaise,<br>peripheral oedema | increased sweating | |

**d. Paediatric population**

The adverse event profile was generally the same in children as for adults in short- as well as in long-term treatment for acid-related disease. There are no long-term data regarding the effects of omeprazole treatment on puberty and growth. (see sections 4.2, 4.4 and 5.2).

**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 professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

### 4.9 Overdose

Blurred vision, confusion, diaphoresis, flushing, headache, malaise, nausea, and tachycardia have been reported from over-dosage with omeprazole.

There is no specific antidote for overdose with omeprazole.

TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

Due to extensive protein binding, omeprazole is not readily dialysable. Patients in whom overdose is confirmed or suspected should be referred for medical practitioner / doctor consultation.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacological classification:

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 is a proton pump inhibitor and reduces gastric acid secretion. It is a specific inhibitor of gastric proton pump in the parietal cell.

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

**Pharmacodynamic effects**

*Effect on gastric secretion*

Oral dosing with omeprazole 20 mg once daily provides inhibition of gastric acid and secretion with maximum effect being achieved within 4 days of treatment. In duodenal ulcer patients, a mean decrease of approximately 80 % in twenty-four 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.

**5.2 Pharmacokinetic properties**

**Absorption**

Omeprazole and omeprazole magnesium are acid labile and are therefore administered orally as enteric-coated granules in capsules. Absorption of omeprazole takes place in the small intestine and is usually completed within 3 - 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 %.

Orally administered omeprazole is well absorbed but to a variable extent. Absorption of omeprazole takes place in the small intestine and is usually completed within three to six hours. Concomitant intake of food has no influence on the bioavailability.

**Distribution**

The apparent volume of distribution in healthy subjects is approximately 0,3 L/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. The plasma protein binding of omeprazole is about 95 %.

**Biotransformation**

Omeprazole is entirely metabolised by the cytochrome P450 (CYP), mainly in the liver. A major part of its metabolism is dependent on the polymorphically expressed, specific isoform CYP2C19 (S-mephenytoin hydroxylase) to form hydroxy-omeprazole, and to a small extent by CYP3A4 to form omeprazole sulfone. Identified metabolites in plasma are the sulfone, the sulfide and hydroxy-omeprazole, these metabolites are inactive 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.

Clearance from the plasma is with an elimination half-life of 30 to 90 minutes.

The average half-life of the terminal phase of the plasma concentration-time curve is approximately 40 minutes. There is no change in plasma half-life during treatment. The inhibition of acid secretion is related to the area under the plasma concentration-time curve (AUC) and not to the actual plasma concentration at a given time.

**Linearity/non-linearity**

The absorption of omeprazole appears to be dose-dependent -increasing the dosage above 40 mg has been reported to increase the plasma concentrations in a non-linear fashion resulting in a non-linear dose-AUC relationship after repeated administration. In addition, bioavailability is higher after long-term use.

This time- and dose-dependency is due to a decrease of first pass hepatic metabolism due to saturation and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by omeprazole and/or its metabolites (e.g. the sulfone).

**Hepatic impairment**

The metabolism of omeprazole in patients with liver dysfunction is impaired, resulting in an increased area under the plasma concentration - time curve (AUC). Omeprazole has not shown any tendency to accumulate with once daily dosing (see section 4.2).

**Renal impairment**

The pharmacokinetics of omeprazole, including systemic bioavailability and elimination rate, are unchanged in patients with reduced renal function (see section 4.2).

**Elderly**

The metabolism rate of omeprazole is somewhat reduced in elderly subjects (75 - 79 years of age) (see section 4.2).

**Polymorphism**

The major enzyme involved in omeprazole metabolism is cytochrome P450 isoenzyme CYP2C19. This enzyme is polymorphically expressed, and individuals who are deficient in the enzyme are poor metabolisers of omeprazole. This occurs in about 3 % of

Caucasians and 15 % of Chinese, Japanese, and Koreans. These individuals have markedly higher plasma concentrations of omeprazole, and they may require dosage adjustment. Some omeprazole is metabolised by CYP3A4. and some by CYP2D6 to form desmethylomeprazole.

**Paediatric population**

Limited data from children (1 year and older), do not suggest significant differences in the pharmacokinetics of omeprazole within the recommended dosages between children and adults (see sections 4.2, 4.4 and 4.8).

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

**Content**

Sugar pellets (consisting of sucrose and purified water)

Mannitol

Lactose anhydrous

Purified talc

Sodium lauryl sulfate

Povidone/Polyvinyl pyrrolidone (PVPK-30)

Anhydrous disodium hydrogen phosphate

Sucrose (sugar)

Hypromellose phthalate/Hydroxypropyl methylcellulose phthalate (HPMCP-55)

Cetyl alcohol

Titanium dioxide

**Capsule shell**

Gelatine

Methylparaben (preservative)

Propylparaben (preservative)

***Cap - light blue***

Brilliant blue (CI 42090)

Erythrosine (CI 45430)

Quinoline yellow (CI 47005)

Titanium dioxide (CI 77891)

Carmosine (CI 14720)

***Body - dark blue***

Brilliant blue (CI 42090)

Carmosine (CI 14720)

Erythrosine (CI 45430)

Quinoline yellow (CI 47005)

Titanium dioxide (CI 77891)

**White printing ink**

Absolute alcohol

Isopropyl alcohol

Shellac dewaxed powder

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. Protect from light. Keep the aluminium strip packs in the outer carton until required for use.

**6.5 Nature and contents of container**

**14 capsules in aluminium strip pack:**

1 of these strips in one carton i.e. 14 capsules per pack

**6.6 Special precautions for disposal**

No special requirements.

**7. HOLDER OF THE CERTIFICATE OF REGISTRATION**

Dezzo Trading 392 (Pty) Ltd

Jespan Centre

Corner Garrick and Flagtail Street

Extension 8, Lenasia

1821

South Africa

**8. REGISTRATION NUMBER**

To be allocated by the Authority.

**9. DATE OF FIRST AUTHORISATION**

To be allocated by the Authority.

**10. DATE OF REVISION OF THE TEXT**

To be allocated by the Authority.