APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINAL PRODUCT

TRULOC OTC gastro-resistant film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TRULOC OTC: Each tablet contains 20 mg esomeprazole equivalent to 22,26 mg esomeprazole magnesium.

Contains sugar (sucrose ± 12,31 mg and lactose monohydrate 31,875 mg per tablet).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant film coated tablet

Brick red coloured, round shape, biconvex, film coated tablets, imprinted with “20” on one side with black ink and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short-term treatment of reflux symptoms such as heartburn and regurgitation in adults.

4.2. Posology and method of administration

Posology

The recommended dose is 20 mg esomeprazole, one tablet per day. It might be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms. The duration of treatment is up to 2 weeks. Once complete relief of symptoms has occurred, treatment should be discontinued. If no symptom relief is obtained within 2 weeks of continuous treatment, the patient should consult a medical practitioner.

Special populations

Impaired renal function

Dose adjustment is not required in patients with impaired renal function. Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution (see section 5.2).

Impaired hepatic function

Dose adjustment is not required in patients with mild to moderate liver impairment. However, patients with severe liver impairment should be advised by a doctor before taking TRULOC OTC (see sections 4.4 and 5.2)

Elderly

Dose adjustment is not required in the elderly.

Paediatric population

There is no relevant use of TRULOC OTC in paediatric population below 18 years of age for the indication of “short-term treatment of reflux symptoms (e.g., heartburn and acid regurgitation)”.

Method of administration

For oral use.

The tablets should be swallowed whole with liquid and should not be chewed or crushed.

4.3 Contraindications

TRULOC OTC is contraindicated in:

- known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of TRULOC OTC
- concomitant administration of TRULOC OTC with atazanavir or nelfinavir (see section 4.5).

4.4 Special warnings and precautions for use

General

Patients should be instructed to consult a medical practitioner if:

- they have significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena and when gastric ulcer is suspected or present, malignancy should be excluded as treatment with esomeprazole may alleviate symptoms and delay diagnosis
- they have had previous gastric ulcer or gastrointestinal surgery
- they have been on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks
- they have jaundice or severe liver disease
- they are aged over 55 years with new or recently changed symptoms.

Patients with long-term recurrent symptoms of indigestion or heartburn should see their medical practitioner at regular intervals.

Patients over 55 years taking any non-prescription indigestion or heartburn remedy daily should inform their pharmacist or doctor.

Patients should not take TRULOC OTC as a long-term preventative medicinal product.

Decreased gastric acidity due to any means, including proton pump inhibitors such as TRULOC OTC tablets, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors (PPIs) may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacte*r and in hospitalized patients, also possibly *Clostridium difficile* (see section 5.1). *Clostridium difficile* is a bacterium that can cause severe debilitating diarrhoea that does not improve. Symptoms may include watery stools, abdominal pain, fever, and patients may develop more serious intestinal conditions.

Patients should consult their medical practitioners before taking this medicinal product if they are due to have an endoscopy or urea breath test.

There is an increased risk of subclinical Acute Interstitial Nephritis (AIN), associated with Proton pump inhibitors (PPIs), such as TRULOC OTC, which may progress to acute kidney injury and/or chronic renal failure. Symptoms of interstitial nephritis may persist, even when treatment with the PPI is terminated.

Combination with other medicines

Concomitant administration with TRULOC OTC and medicines such as atazanavir and nelfinavir is not recommended (see sections 4.3 and 4.5).

Therapeutic medicine monitoring is recommended during concomitant treatment with warfarin (see section 4.5).

TRULOC OTC, 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.

Concomitant administration of clopidogrel and esomeprazole resulted in decreased exposure to the active metabolite of clopidogrel by an average of 40 %. The maximum inhibition of (ADP induced) platelet aggregation decreased by an average of 14 %. Based on these data, concomitant use of TRULOC OTC and clopidogrel should be avoided.

During treatment with TRULOC OTC serum gastrin increases, in response to decreased acid secretion.

Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures.

APPROVED PROFESSIONAL INFORMATION

Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically (see Undesirable Effects 4.8).

Consider monitoring magnesium and calcium levels prior to initiation of TRULOC OTC and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism). Supplement with magnesium and/or calcium, as necessary. If hypocalcemia is refractory to treatment, consider discontinuing the PPI.

TRULOC OTC is not for long-term use, however long-term oral treatment with esomeprazole may lead to gastric glandular cysts. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign, and appear to be reversible.

Proton pump inhibitors, including TRULOC OTC, especially if used in high doses and over long durations, 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.

Proton pump inhibitors are associated with very infrequent cases of Sub-acute Cutaneous Lupus Erythematosus (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 professional should consider stopping TRULOC OTC. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Interference with laboratory tests

During treatment with antisecretory medicines, serum gastrin increases in response to the decreased acid secretion. Also, Chromogranin A (CgA) increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours. To avoid this interference, the esomeprazole treatment should be temporarily stopped 5 days before CgA measurements.

Sucrose and lactose:

TRULOC OTC tablets contain sucrose and lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with rare hereditary problems of galactose/fructose intolerance, total lactase/sucrase/isomaltase deficiency or glucose-galactose malabsorption should not take TRULOC OTC.

4.5 Interaction with other medicines and other forms of interaction

Effects of TRULOC OTC on the pharmacokinetics of other medicines:

The gastric acid suppression during treatment with TRULOC OTC, might decrease or increase the absorption of medicines with a gastric pH dependent absorption. The absorption of medicines such as ketoconazole, itraconazole and erlotinib can decrease while the absorption of medicines such as digoxin can increase during treatment with TRULOC OTC.

Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10 % (up to 30 % in 2 out of 10 subjects). Digoxin toxicity has been reported. Caution should be exercised when TRULOC OTC is given at high doses in elderly patients. Therapeutic monitoring of digoxin levels should be done.

APPROVED PROFESSIONAL INFORMATION

TRULOC OTC inhibits CYP2C19, the major TRULOC OTC metabolising enzyme. Concomitant administration of 30 mg esomeprazole resulted in a 45 % decrease in clearance of the CYP2C19 substrate diazepam. This interaction is unlikely to be of clinical relevance. Concomitant administration of 40 mg esomeprazole resulted in a 13 % increase in trough plasma levels of phenytoin in epileptic patients.

Concomitant administration of 40 mg esomeprazole to warfarin-treated patients showed that, despite elevation in the trough plasma concentration of the less potent R-isomer of warfarin, the coagulation times were within the accepted range.

From post marketed use, cases of elevated INR of clinical significance have been reported during concomitant treatment with warfarin. Close monitoring is recommended when warfarin is co-administered with TRULOC OTC at initiation of treatment, during the treatment and at ending treatment.

Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 mg p.o. daily) resulting in decreased exposure to the active metabolite of clopidogrel by an average of 40 % and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14 %. Based on these data, concomitant use of TRULOC OTC and clopidogrel should be avoided.

Omeprazole, as well as esomeprazole, act as inhibitors of CYP 2C19. Omeprazole 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 metabolites by 29 % and 69 % respectively. TRULOC OTC can be expected to have a similar effect.

Concomitant administration of 40 mg esomeprazole resulted in a 32 % increase in area under the plasma concentration-time curve (AUC) and a 31 % prolongation of elimination half-life (t½), but no significant increase in peak plasma levels of cisapride. This interaction did not alter the influence of cisapride on cardiac electrophysiology.

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

Esomeprazole, as in TRULOC OTC, has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine.

Studies evaluating concomitant administration of esomeprazole and either naproxen (nonselective NSAID) or rofecoxib (COX-2-selective NSAID) did not identify any clinically relevant interaction.

Concomitant administration of TRULOC OTC may significantly reduce the plasma levels of atazanavir.

Omeprazole has been reported to interact with some antiretroviral medicines. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral medicines. Other possible interaction mechanisms are via CYP2C19. For some antiretroviral medicines, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended.

Co-administration of esomeprazole (40 mg once daily) reduced mean nelfinavir exposure by approximately 40 % and the mean exposure of the pharmacological active metabolite was reduced by approximately 75 - 90 %. Esomeprazole, as in TRULOC OTC, substantially decreases the concentration of nelfinavir. Concomitant administration with esomeprazole and antiretroviral medicines, such as atazanavir and nelfinavir, is not recommended.

For other antiretroviral medicines, such as saquinavir, increased serum levels of 80 - 100 % have been reported. There are also some antiretroviral medicines for which unchanged serum levels have been reported when given with omeprazole. Close monitoring or dose alteration is recommended.

Tipranavir may decrease the concentration of TRULOC OTC. Co-administration is not recommended. However, if used concurrently, the dose of TRULOC OTC should be increased.

Concomitant administration of esomeprazole, as in TRULOC OTC, 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.

Effects of other medicines on the pharmacokinetics of TRULOC OTC:

TRULOC OTC is metabolised by CYP2C19 and CYP3A4. Concomitant administration of TRULOC OTC and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), resulted in a doubling of the exposure (AUC) to TRULOC OTC.

Concomitant administration of TRULOC OTC and a combined inhibitor of CYP2C-19 and CYP3A4, such as voriconazole, may result in more than tripling of the TRULOC OTC exposure.

Dose adjustment of TRULOC OTC is not required.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety during pregnancy has not been established.

Breastfeeding

Safety during lactation has not been established.

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

TRULOC OTC may cause dizziness and blurred vision, thereby affecting the ability to drive or use machinery.

APPROVED PROFESSIONAL INFORMATION

4.8 Undesirable effects

a) Summary of the safety profile

Headache, abdominal pain, diarrhoea and nausea are among those adverse reactions that have been most commonly reported in clinical trials (and also from post-marketing use). In addition, the safety profile is similar for different formulations, treatment indications, age groups and patient populations.

b) Tabulated summary of adverse reactions

Blood and lymphatic system disorders	*Less frequent* *Frequency unknown*	Leukopenia, thrombocytopenia Agranulocytosis, pancytopenia
Immune system disorders	*Less frequent*	Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/shock
Metabolism and nutrition disorders	*Less frequent*	Peripheral oedema, hyponatraemia, hypomagnesaemia, vit B_{12} malabsorption
	Frequency unknown	Severe hypomagnesaemia can correlate with hypocalcaemia. Hypomagnesaemia may also be associated with hypokalaemia

APPROVED PROFESSIONAL INFORMATION

Psychiatric disorders	*Less frequent*	Insomnia, agitation, confusion, depression, aggression, hallucination
Nervous system disorders	*Frequent*	Headache
	Less frequent	Dizziness, paraesthesia, somnolence, taste disturbance
Eye disorders	*Less frequent*	Blurred vision
Ear and labyrinth disorders	*Less frequent*	Vertigo
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Bronchospasm
Gastrointestinal disorders	*Frequent*	Abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation, fundic gland polyps (benign)
	Less frequent	Dry mouth, stomatitis, gastrointestinal candidiasis, gastrointestinal infections, microscopic colitis

APPROVED PROFESSIONAL INFORMATION

Hepatobiliary disorders	*Less frequent*	Increased liver enzymes, hepatitis with or without jaundice, hepatic encephalopathy
Skin and subcutaneous tissue disorders	*Less frequent*	Dermatitis, pruritus, urticaria, rash, alopecia, photosensitivity
	Frequency unknown	Subacute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders	*Less frequent*	Arthralgia, myalgia, muscular weakness, fracture of the hips, wrists or spine
Renal and urinary disorders	*Less frequent*	Interstitial nephritis which may progress to acute kidney injury and/or chronic renal failure, in some patient's renal failure has been reported concomitantly
Reproductive system and breast disorders	*Less frequent*	Gynaecomastia
General disorders and administration site conditions	*Less frequent*	Malaise, hyperhidrosis

Post marketing experience

Blood and lymphatic system disorders

Leukopenia, thrombocytopenia, agranulocytosis, pancytopenia

Immune system disorders

Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/shock

Metabolism and nutrition disorders

Peripheral oedema, hyponatraemia

Psychiatric disorders

Insomnia, agitation, confusion, depression, aggression, hallucination

Nervous system disorders

Headache, dizziness, paraesthesia, somnolence, taste disturbance

Eye disorders

Blurred vision

APPROVED PROFESSIONAL INFORMATION

Ear and labyrinth disorders

Vertigo

Respiratory, thoracic and mediastinal disorders

Bronchospasm

Gastrointestinal disorders

Abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation, dry mouth, stomatitis, gastrointestinal candidiasis

Hepatobiliary disorders

Increased liver enzymes, hepatitis with or without jaundice, hepatic encephalopathy, hepatic failure

Skin and subcutaneous tissue disorders

Dermatitis, pruritus, urticaria, rash, alopecia, photosensitivity, erythema multiforme, Stevens Johnson syndrome, Toxic Epidermal Necrolysis (TEN)

Musculoskeletal, connective tissue and bone disorders

Arthralgia, myalgia, muscular weakness

APPROVED PROFESSIONAL INFORMATION

Renal and urinary disorders

Interstitial nephritis, which may progress to kidney injury and/or chronic renal failure

Reproductive system and breast disorders

Gynaecomastia

General disorders and administration site conditions

Malaise, hyperhidrosis

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

APPROVED PROFESSIONAL INFORMATION

4.9 Overdose

No specific antidote is known. TRULOC OTC is extensively plasma protein bound and is therefore not readily dialysable. In any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for acid-related disorders, proton pump inhibitor.

ATC code: A02B C05

Pharmacological classification: A 11.4.3 Medicines acting on gastrointestinal tract. Other.

Mechanism of Action

Esomeprazole, the S-isomer of omeprazole, reduces gastric acid secretion through specific inhibition of the acid pump in the parietal cell, where it is concentrated and converted to the active form in the acidic environment of the secretory canaliculi and inhibits the enzyme H+K+-ATPase - the acid pump. This effect on the final step of the gastric acid secretion is dose-dependent and provides for effective inhibition of both basal and stimulated acid secretion.

APPROVED PROFESSIONAL INFORMATION

Effect on gastric acid secretion

After oral dosing with esomeprazole 20 mg and 40 mg, the onset of effect occurs within 1 hour. After repeated administration with 20 mg esomeprazole once daily for 5 days, mean peak acid output after pentagastrin stimulation is decreased by 90 % when measured 6-7 hours after dosing on day 5.

After 5 days of oral dosing with 20 mg and 40 mg of esomeprazole, intragastric pH above 4 was maintained for a mean time of 13 hours and 17 hours, respectively over 24 hours in symptomatic Gastro-oesophageal Reflux Disease (GORD) patients. The proportion of patients maintaining an intragastric pH above 4 for at least 8, 12 and 16 hours were 76 %, 54 % and 24 % respectively for esomeprazole 20 mg. Corresponding proportions for esomeprazole 40 mg were 97 %, 92 % and 56 % respectively.

Using AUC as a surrogate parameter for plasma concentration, a relationship between inhibition of acid secretion and exposure has been shown.

Food intake had no significant influence on the effect of esomeprazole on intragastric acidity.

Other effects related to acid inhibition

During long-term treatment with antisecretory medicines, gastric glandular cysts occur. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

5.2 Pharmacokinetic properties

Absorption

Esomeprazole is acid labile and is administered orally as enteric-coated granules. *In vivo* conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 89 % after repeated once-daily administration.

For 20 mg esomeprazole, the corresponding values are 50 % and 68 % respectively. Food intake both delays and decreases the absorption of esomeprazole, although this has no significant influence on the effect of esomeprazole on intragastric acidity.

Distribution

The apparent volume of distribution at steady state in healthy subjects is approximately 0,22 litres/kg body weight. Esomeprazole is 97 % plasma protein bound.

APPROVED PROFESSIONAL INFORMATION

Biotransformation

Esomeprazole is completely metabolised by the cytochrome P450 system (CYP). A major part of the metabolism of esomeprazole is dependent on the polymorphic CYP2C19, responsible for the formation of the hydroxy- and desmethyl metabolites of esomeprazole. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of esomeprazole sulphone, the main metabolite in plasma.

Elimination

The parameters below reflect mainly the pharmacokinetics in individuals with a functional CYP2C 19 enzyme (extensive metabolisers).

Total plasma clearance is about 17 litres per hour after a single dose and about 9 litres per hour after repeated administration. The plasma elimination half-life is about 1,3 hours after repeated once-daily dosing. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a non-linear dose-AUC relationship after repeated administration. This time and dose-dependency is due to a decrease of first pass metabolism and systemic clearance, probably caused by an inhibition of the CYP2C19 enzyme by esomeprazole and/or its sulphone metabolite. Esomeprazole is completely eliminated from plasma between doses, with no tendency for accumulation during once-daily administration.

The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80 % of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1 % of the parent compound is found in urine.

Special Populations

Poor Metabolisers

Approximately 2,9 ± 1,5 % of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve was approximately 100 % higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60 %. These findings have no implications for the posology of esomeprazole.

Hepatic Insufficiency

The metabolism of esomeprazole in patients with mild to moderate liver dysfunction may be impaired. The metabolic rate is decreased in patients with severe liver dysfunction resulting in a doubling of the area under the plasma concentration-time curve of esomeprazole. Therefore, a maximum of 20 mg should not be exceeded in patients with severe dysfunction. Esomeprazole or its major metabolites do not show any tendency to accumulate with once-daily dosing.

Renal Insufficiency

No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole but not for the elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.

Gender

Following a single dose of 40 mg esomeprazole, the mean area under the plasma concentration-time curve is approximately 30 % higher in females than in males. No gender difference is seen after repeated once-daily administration. These findings have no implications for the dosage of esomeprazole.

Elderly

The metabolism of esomeprazole is not significantly changed in elderly subjects (71-80 years of age).

Paediatric population

Following repeated dose administration of 20 mg and 40 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma drug concentration (t_{max}) in 12 to 18-year-olds was similar to that in adults for both esomeprazole doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Copovidone (K28)

Crospovidone (Type A)

Diethyl phthalate

Ethyl cellulose

Hypromellose

Macrogol 8000

Magnesium oxide

Magnesium stearate

Maize starch

Methacrylic acid ethyl acrylate copolymer dispersion - (consist of methacrylic acid - ethyl acrylate copolymer, sodium lauryl sulphate, polysorbate 80)

Povidone

Silica colloidal anhydrous

Silicified microcrystalline cellulose (Prosolv HD 90) (consist of cellulose microcrystalline and silica colloidal anhydrous)

Starlac (consists of lactose monohydrate and maize starch)

Sugar spheres (consist of maize, starch and sucrose)

Talc

Film coating

Hypromellose

Macrogol 8000

Talc

Titanium dioxide (E171)

Silica colloidal anhydrous

Ferric oxide red (E172)

Printing ink

Opacode S-1-17823 black ink

Ammonium hydroxide (E527)

Iron oxide black (E172)

Isopropyl alcohol

N-butyl alcohol

Propylene glycol (E1520)

Shellac Glaze

6.2 Incompatibilities

N/A

6.3 Shelf Life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

Alu/Alu blister packs containing 14 tablets each, packed in a printed outer carton.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

APPROVED PROFESSIONAL INFORMATION

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

Tel.: +27 21 707 7000

or 0860-PHARMA (742 762)

8. REGISTRATION NUMBER

57/11.4.3/0833

9. DATE OF FIRST AUTHORISATION

27 January 2026