PROFESSIONAL INFORMATION

PEPLOC RANGE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

PEPLOC 20 mg, tablets.

PEPLOC 40 mg, tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each PEPLOC 20 mg tablet contains pantoprazole sodium sesquihydrate equivalent to 20 mg pantoprazole.

Each PEPLOC 40 mg tablet contains pantoprazole sodium sesquihydrate equivalent to 40 mg pantoprazole.

PEPLOC 20 mg contains sugar (sugar alcohol — mannitol 70,50 mg/tablet).

PEPLOC 40 mg contains sugar (sugar alcohol — mannitol 141,0 mg/tablet).

PEPLOC is essentially ‘sodium free’.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant tablets.

PEPLOC 20 mg: Orangish, biconvex and oval gastro-resistant tablet.

Diameter 4,7 mm x 9,0 mm.

PEPLOC 40 mg: Orangish, biconvex and oval gastro-resistant tablet.

Diameter: 6,1 mm x 11,7 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PEPLOC 40 mg is indicated for the short-term treatment of duodenal ulcers, gastric ulcers and reflux oesophagitis.

If the duodenal ulcer has been demonstrated to be associated with *Helicobacter pylori* infection, PEPLOC 40 mg used in combination with appropriate antibiotics may be useful.

PEPLOC 40 mg is indicated for the treatment of Zollinger-Ellison syndrome.

PEPLOC 20 mg is indicated for the symptomatic improvement (e.g. heartburn, acid regurgitation, pain on swallowing) and healing of mild gastro-oesophageal reflux disease (GORD).

In patients with healed reflux disease, recurring symptoms can be controlled using an on-demand regimen of PEPLOC 20 mg once daily when required. PEPLOC 20 mg is indicated for long-term management and prevention of relapse in gastro-oesophageal reflux disease (GORD).

PEPLOC 20 mg is indicated for the prevention of gastroduodenal lesions and dyspeptic symptoms induced by nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) in patients at risk, and with a need for continuous NSAID treatment.

4.2 Posology and method of administration

Posology

Duodenal ulcer

The recommended oral dose is 40 mg of PEPLOC once daily. The total treatment with intravenous and oral pantoprazole should be 2 - 4 weeks. If the duodenal ulcer has been demonstrated to be associated with *Helicobacter pylori* infection, 40 mg of PEPLOC used in combination with appropriate antibiotics may be useful.

Gastric ulcer

The recommended oral dose is 40 mg of PEPLOC once daily for 4 - 8 weeks. In the case of a suspected gastric ulcer, malignancy of the gastric ulcer should be excluded, as treatment could conceal the symptoms and may delay diagnosis.

Reflux oesophagitis

The recommended oral dose is 40 mg of PEPLOC once daily in the morning for 4 - 8 weeks.

Zollinger-Ellison syndrome

For the management of Zollinger-Ellison syndrome patients should start their treatment with a daily dose of 80 mg of PEPLOC. Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion as a guide. With doses above 80 mg daily, the dose should be divided and given twice daily.

Mild Gastro-oesophageal reflux disease (GORD)

The recommended oral dose is 20 mg of PEPLOC per day. A 4-week period is usually required for healing of mild GORD. If this is not sufficient, healing will usually be achieved within a further 4 weeks. In patients with healed reflux disease, reoccurring symptoms can be controlled using an on-demand regimen of 20 mg once daily when required.

Long-term management and prevention of relapse in GORD

For long-term management a maintenance dose of one 20 mg PEPLOC tablet per day is recommended, increasing to 40 mg PEPLOC per day if a relapse occurs. After healing of the relapse, the dose can be reduced to 20 mg of PEPLOC. Experience with long-term administration is limited.
For prevention of gastro-duodenal lesions and dyspeptic symptoms induced by nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) in patients at risk and with a need for continuous NSAID treatment, the recommended oral dose is 20 mg of PEPLOC per day.

Special populations

Elderly patients

No dosage adjustment is necessary in the elderly.

Impaired renal and liver function

No dosage adjustment is required in the presence of impaired renal function. A daily dose of 20 mg PEPLOC should not be exceeded in patients with mild to moderately severe liver impairment (see sections 4.4 and 5.2).

Paediatric population

Safety and efficacy in children has not been established (see section 4.3).

Method of administration

Oral use.

The recommended once daily dose of PEPLOC should be taken in the morning. PEPLOC should be swallowed whole with a little water either before or during breakfast.

4.3 Contraindications

- hypersensitivity to pantoprazole or to any of the ingredients of PEPLOC (see section 6.1)
- safety and efficacy in children has not been established
- severely impaired liver function
- co-administration with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use

The daily dose of PEPLOC 40 mg should not be exceeded in elderly patients or those with impaired renal function.

Co-administration with anticoagulants

The response to anticoagulants such as warfarin may be affected by any concomitant medication. It is therefore good practice to monitor the patient with additional PT (prothrombin time)/INR (international normalised ratio) determinations when PEPLOC is initiated, discontinued or taken irregularly.
Changes in absorption should be observed when medicines whose absorption is pH-dependent, e.g. ketoconazole, are taken concomitantly.

Gastric malignancy

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

Diagnosis of reflux oesophagitis

Diagnosis of reflux oesophagitis should be confirmed by endoscopy.

Clostridium difficile associated diarrhoea (CDAD)

PEPLOC may be associated with an increased risk of *Clostridium difficile* associated diarrhoea (CDAD). A diagnosis of CDAD should be considered for patients taking PEPLOC who develop diarrhoea that does not improve. Patients should use the lowest dose and shortest duration of PEPLOC therapy appropriate to the condition being treated.

Gastrointestinal infections caused by bacteria

Proton pump inhibitors (PPIs), such as PEPLOC might be expected to increase the counts of bacteria normally present in the upper gastrointestinal tract and may therefore lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as *Salmonella* and *Campylobacter*.

Hypomagnesaemia

Severe hypomagnesaemia has been rarely reported in patients treated with proton pump inhibitors (PPIs) like PEPLOC 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. Hypomagnesaemia may lead to hypocalcaemia and/or hypokalaemia (see section 4.8). In most affected patients, hypomagnesaemia (and hypomagnesaemia associated hypocalcaemia and/or hypokalaemia) improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicines that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Bone fractures

The use of PEPLOC may be associated with an increased risk of bone fractures in the hip, wrist or spine. This effect has been reported mostly in people taking high doses, on long-term treatment, and in those who were 50 years and older.

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.

Hepatic impairment

In patients with severe liver impairment, the liver enzymes should be monitored regularly during treatment with PEPLOC. In the case of a rise of the liver enzymes, PEPLOC should be discontinued.

Mild gastro-intestinal complaints

PEPLOC should not be used for mild gastro-intestinal complaints such as nervous dyspepsia.

Vitamin B_{12} absorption

PEPLOC over a long period of time (e.g. longer than 3 years) in patients with Zollinger-Ellison

syndrome and other pathological hyper secretory conditions may lead to malabsorption of vitamin B_{12} caused by hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B_{12} absorption or if respective clinical symptoms are observed.

Co-administration with NSAIDs

Use of PEPLOC 20 mg as a preventative of gastroduodenal ulcers, induced by nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), should be restricted to patients who require continued NSAID treatment and have an increased risk to develop gastrointestinal complications.

Combination therapy

In the case of combination therapy, the summaries of product characteristics of the respective medicines should be observed.

Co-administration with HIV protease inhibitors

Co-administration of PEPLOC is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH, such as atazanavir, due to significant reduction in their bioavailability (see section 4.5).

Long-term treatment

In long-term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of subacute 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 provider should consider stopping PEPLOC. SCLE, after previous treatment with a proton pump inhibitor, may increase the risk of SCLE with other proton pump inhibitors.

Interference with laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, PEPLOC treatment should be stopped for at least 5 days before CgA measurements (see section 5.1). 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.

Acute Interstitial Nephritis

Acute interstitial nephritis has been observed in patients taking proton pump inhibitors (PPIs) including PEPLOC. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction and is associated with damage to the tubulointerstitium, leading to acute kidney injury. Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decreased renal function (e.g. malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g. fever, rash or arthralgia). Interstitial nephritis may lead to renal failure. Discontinue PEPLOC if acute interstitial nephritis develops (see section 4.8).

Sodium

PEPLOC contains sodium.

PEPLOC contains less than 1 mmol sodium (0,023 g) per dose, that is to say essentially ‘sodium free’.

4.5 Interaction with other medicines and other forms of interaction

Concomitant intake of food has no influence on the bioavailability.

Coumarin anticoagulants (phenprocoumon or warfarin)

However, the response to anticoagulants such as warfarin, phenprocoumon and acenocoumarol may be affected by any concomitant medicine. It is therefore good practice to monitor the patient with

additional PT (prothrombin time)/INR (international normalised ratio) determinations when PEPLOC is initiated, discontinued or taken irregularly.

Medicines with pH-dependent absorption pharmacokinetics

PEPLOC may reduce or increase the absorption of medicines which bioavailability is pH-dependent, e.g. ketoconazole, itraconazole, posaconazole and other medicines like erlotinib.

HIV protease inhibitors

It has been shown that co-administration of atazanivir 300 mg/ritonavir 100 mg with proton pump inhibitors (PPI) such as PEPLOC resulted in a substantial reduction in the bioavailability of atazanivir. The absorption of atazanavir is pH-dependent. Therefore, PPIs, including PEPLOC, should not be co-administered with atazanavir. (see section 4.3).

If the combination of HIV protease inhibitors with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended. A PEPLOC dose of 20 mg per day should not be exceeded. Dosage of the HIV protease inhibitor may need to be adjusted.

Methotrexate

Concomitant use of PPIs, including PEPLOC, with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities.

Inhibitors of CYP2C19

Inhibitors of CYP2C19, such as fluvoxamine, could increase the systemic exposure of pantoprazole. A dose reduction may be considered for patients treated long-term with high doses of PEPLOC, or those with hepatic impairment.

Enzyme inducers affecting CYP2C19 and CYP3A4

Enzyme inducers affecting CYP2C19 and CYP3A4, such as rifampicin and St John´s wort

(*Hypericum perforatum*), may reduce the plasma concentrations of PPIs that are metabolized through these enzyme systems.

Other interactions studies:

The active ingredient of PEPLOC is metabolised in the liver via the cytochrome P450 enzyme system. An interaction of PEPLOC with other medicines or compounds which are metabolised using the same enzyme system cannot be excluded.

However, no clinically significant interactions were observed when used concomitantly with caffeine, carbamazepine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline, warfarin and oral contraceptives.

However, the response to anticoagulants such as warfarin, phenprocoumon and acenocoumarol may be affected by any concomitant medicine. It is therefore good practice to monitor the patient with additional PT (prothrombin time)/INR (international normalised ratio) determinations when PEPLOC is initiated, discontinued or taken irregularly.

There were no interactions with concomitantly administered antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy and during lactation has not been established.

Animal studies have shown reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of PEPLOC during pregnancy.

Breastfeeding

There is insufficient information on the excretion of pantoprazole in human milk but excretion into human milk has been reported. A risk to the newborns/infants cannot be excluded. Therefore, breastfeeding while on PEPLOC is not recommended.

Fertility

There was no evidence of impaired fertility following the administration of pantoprazole in animal studies. There is no data on fertility in humans with PEPLOC.

4.7 Effects on ability to drive and use machines

PEPLOC has no or negligible influence on the ability to drive and use machines.

PEPLOC may affect the ability to drive in that adverse effects, such as dizziness and visual disturbances may occur (see section 4.8). If affected, patients should not drive or operate machines.

4.8 Undesirable effects

a. Summary of the safety profile

Approximately 5 % of patients can be expected to experience adverse drug reactions (ADRs).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

b. Tabulated list of adverse effects

System Organ Class	**Frequency**	**Side effects**
Infections and Infestations	Frequency unknown	*Clostridium difficile*-associated diarrhoea*
Blood and lymphatic system disorders	Less frequent	Leukopenia, thrombocytopenia, pancytopenia, agranulocytosis
Immune system disorders	Less frequent	Anaphylactic reactions including anaphylactic shock and angioedema

Metabolism and nutrition disorders	Less frequent	Increased bilirubin, elevated triglycerides and increased body temperature, lipid increases, hypocalcaemia**, hyperlipidaemia, weight changes
Psychiatric disorders	Less frequent Frequency unknown	Mental depression, sleep disorders, depression, disorientation Hallucination*, confusion*
Nervous system disorders	Frequent Less frequent Frequency unknown	Headache Dizziness, taste disorders Paraesthesia
Eye disorders	Less frequent	Disturbances in vision (blurred vision)
Gastrointestinal disorders	Frequent Less frequent Frequency unknown	Gastrointestinal complaints such as upper abdominal pain, diarrhoea, constipation or flatulence Nausea, vomiting, dry mouth, abdominal distension and bloating, abdominal pain and discomfort Microscopic colitis*

Hepatobiliary disorders	Less frequent Frequency unknown	Increased bilirubin Severe hepatocellular damage* leading to jaundice* with or without hepatic failure* and increased liver enzymes (transaminases, γ-GT)
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Allergic reactions such as pruritus and skin rash, urticaria Severe skin reactions such as Stevens-Johnson syndrome*, erythema multiforme*, toxic epidermal necrolysis* (Lyell syndrome) and photosensitivity*, drug reaction with eosinophilia and systemic symptoms (DRESS)*, subacute cutaneous lupus erythematosus*
Musculoskeletal, connective tissue and bone disorders	Less frequent Frequency unknown	Arthralgia, myalgia, fracture of the hip, wrist or spine Hyponatraemia, hypomagnesaemia, hypocalcaemia in association with hypomagnesaemia, muscle spasm as a consequence of electrolyte disturbance*

Renal and urinary disorders	Frequency unknown	Interstitial nephritis* (in some patients renal failure has been reported concomitantly) (see section 4.4)
Reproductive system and breast disorders	Less frequent	Gynaecomastia
General disorders and administrative site conditions	Less frequent	Asthenia, fatigue, malaise, and peripheral oedema, body temperature increased

*Post-marketing reports.

**Hypocalcaemia in association with hypomagnesaemia.

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 online service for adverse drug reaction reporting by using either of the following the links: https://www.sahpra.org.za/Publications/Index/8 or https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

The described side effects may be exacerbated.

There are no known symptoms of overdose in humans.

Systemic exposure with up to 240 mg administered intravenously over 2 minutes was well tolerated.

Management of overdose:

As pantoprazole is extensively protein bound, it is not readily dialysable.

No specific therapeutic recommendation can be made in cases of overdosage with clinical signs of intoxication.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors

ATC code: A02BC02

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

Mechanism of action

Pantoprazole is a proton pump inhibitor, i.e. it inhibits specifically and dose-proportionally H^+, K^+-ATPase, the enzyme which is responsible for gastric acid secretion in the parietal cells of the stomach.

Pantoprazole is a substituted benzimidazole which accumulates in the acidic compartment of the parietal cells after absorption. In the parietal cell, it is protonated and chemically re-arranged to the active inhibitor, a cyclic sulphonamide, which binds to the H^+, K^+-ATPase, thus inhibiting the proton pump and causing suppression of stimulated and basal gastric acid secretion after single and multiple intravenous and oral pantoprazole dosing. Because pantoprazole acts distal to the receptor level, it can influence gastric acid secretion irrespective of the nature of the stimulus.

Pantoprazole exerts its full effect in a strongly acidic environment (pH < 3) and remains mostly inactive at higher pH values, which explains its selectivity for the acid secreting parietal cells of the stomach. Therefore, the complete pharmacological and therapeutic effect for pantoprazole can only

be achieved in the acid-secreting parietal cells. By means of a feedback mechanism this effect is diminished at the same rate as acid secretion is inhibited.

Effect on gastric acid secretion

Although pantoprazole has a half-life of approximately 1 hour, the antisecretory effect increases during repeated once daily administration, demonstrating that the duration of action markedly exceeds the serum elimination half-life.

5.2 Pharmacokinetic properties

Absorption:

Pantoprazole is unstable in acid and is administered orally in the form of an enteric coated tablet. Absorption takes place in the small intestine. On average, the maximum serum/plasma concentrations are approximately 2 - 3 microgram/mL about 2½ hours after administration of 40 mg pantoprazole daily, as a single or multiple doses in healthy volunteers. The absolute systemic bioavailability of pantoprazole from single and multiple oral doses of pantoprazole is approximately 77 %. Concomitant intake of food had no influence on AUC, maximum serum concentration and thus bioavailability. Only the variability of the lag-time will be increased by concomitant food intake.

Distribution:

Pantoprazole's serum protein binding is about 98 %. Volume of distribution is about 0.15 L/kg.

Biotransformation:

Pantoprazole is almost exclusively metabolised in the liver. The main metabolite is desmethylpantoprazole, which is conjugated with sulphate other metabolic pathway includes oxidation by CYP3A4.

Elimination:

Renal elimination represents the most important route of excretion (approximately 80 %) for the

metabolites of pantoprazole. The balance is excreted with the faeces. The half-life of the main metabolite is approximately 1½ hours, which is slightly longer than that of pantoprazole.

Linearity/non-linearity:

The plasma kinetics for pantoprazole administration are linear over the dose range of 10 - 80 mg.

Pharmacokinetics in special patient groups

Pharmacokinetic profile in patients with impaired liver or renal function

For patients with mild to moderately severe hepatic cirrhosis, the elimination half-life values increase from 1 hour to between 7 - 9 hours. The AUC values increase by a factor of 6 - 8, while the maximum serum concentration only increases by a factor of 1,5 in comparison with healthy subjects.

In patients with renal impairment, the half-life of the main metabolite is moderately increased but there is no accumulation at therapeutic doses. The half-life of pantoprazole in patients with renal impairment is comparable to the half-life of pantoprazole in healthy subjects. Pantoprazole is poorly dialysed. A slight increase in AUC and C_{max} occurs in elderly volunteers compared with younger people.

Poor metabolisers

Approximately 3 % of the European population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of pantoprazole is probably mainly catalysed by CYP3A4. After a single-dose administration of 40 mg pantoprazole, the mean area under the plasma concentration-time curve was approximately 6 times 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 pantoprazole.

Elderly

A slight increase in AUC and C_{max} in elderly volunteers compared with younger counterparts is also

not clinically relevant.

Paediatric population

Following administration of single oral doses of 20 or 40 mg pantoprazole to children aged 5 - 16 years AUC and C_{max} were in the range of corresponding values in adults.

Following administration of single intravenous doses of 0,8 mg/kg or 1,6 mg/kg pantoprazole to children aged 2 - 16 years there was no significant association between pantoprazole clearance and age or weight. AUC and volume of distribution were in accordance with data from adults.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard to humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

A two-year carcinogenicity study in rats found both neuroendocrine neoplasms and squamous cell papillomas in the fore stomach of rats.

The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic high-dose treatment.

In the two-year rodent study, an increased number of liver tumours was observed in rats and in female mice and was interpreted as being due to pantoprazole's high metabolic rate in the liver.

A slight increase of neoplastic changes of the thyroid was observed in the group of rats receiving the highest dose (200 mg/kg). The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in humans are low, no harmful effects on the thyroid glands are expected.

In a peri-postnatal rat reproduction study designed to assess bone development, signs of offspring toxicity (mortality, lower mean body weight, lower mean body weight gain and reduced bone growth) were observed at exposures (C_{max}) approximately 2x the human clinical exposure. By the end of the recovery phase, bone parameters were similar across groups, and body weights were also trending toward reversibility after a medicine-free recovery period. The increased mortality has only been reported in pre-weaning rat pups (up to 21 days of age), which is estimated to correspond to infants up to the age of 2 years old. The relevance of this finding to the paediatric population is unclear. A previous peri-postnatal study in rats at slightly lower doses found no adverse effects at 3 mg/kg compared with a low dose of 5 mg/kg in this study.

Investigations revealed no evidence of impaired fertility or teratogenic effects.

Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the foetus is increased shortly before birth.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Carmellose sodium

Colloidal anhydrous silica

Magnesium stearate

Mannitol

Sodium carbonate anhydrous

Sodium starch glycolate type A

Tablet coating:

Hypromellose

Methacrylic acid-ethyl acrylate copolymer

Propylene glycol

Titanium dioxide

Triethyl citrate

Yellow iron oxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Peploc 20 mg: 30 months

Peploc 40 mg: 36 months

6.4 Special precautions for storage

Store at or below 25 ºC. Protect from light and moisture.

Store blister in the outer carton until required for use.

6.5 Nature and contents of container

PEPLOC 20 mg and 40 mg are packed in aluminium-polyamide-

PVC/aluminium blister strips.

28 or 30 tablets are packed in an outer carton.

6.6 Special precautions for disposal

No special requirements.

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

8. REGISTRATION NUMBER(S)

PEPLOC 20 mg: RSA S4 A42/11.4.3/0056

PEPLOC 40 mg: RSA S4 A42/11.4.3/0057

9. DATE OF FIRST AUTHORISATION

Date of registration: 19 March 2010

10. DATE OF REVISION OF THE TEXT

22 March 2024

NAMIBIA:

PEPLOC 20 mg: NS2 10/11.4.3/0473

PEPLOC 40 mg: NS2 10/11.4.3/0474