SCHEDULING STATUS

S4

1 NAME OF THE MEDICINAL PRODUCT

ISONIAZID 300 UNIMED (300 mg tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300mg isoniazid.

Sugar free

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

White to off-white, circular, biconvex, uncoated tablets, plain on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ISONIAZID 300 UNIMED is indicated alone for the prophylaxis and treatment of tuberculosis and in conjunction with other antituberculosis medicines.

4.2 Posology and method of administration

Posology

Adult and Adolescent Dose:

Prophylaxis: 5 mg/kg body mass (maximum 300mg) once daily.

It may be used in combination with rifampicin for prophylaxis against multidrug-resistant tuberculosis.

Treatment: In combination with other antituberculosis medicines: 5-15 mg per kg of body weight (up to 900 mg) once daily or in divided doses (maximum 900 mg per day), based on the type of tuberculosis and sensitivity pattern. Higher doses are used for CNS tuberculosis and multidrug-resistant tuberculosis.

Paediatric Dose:

Prophylaxis: 10 mg per kg of body weight, up to 300 mg, once daily.

Treatment: In combination with other antituberculosis medicines:10 to 20 mg per kg of body weight, up to 300 mg, once daily. Higher doses are used for CNS tuberculosis and multidrug-resistant tuberculosis.

Special Populations

Slow or fast acetylators

The rate of acetylation is determined genetically.

The mean half-life in fast acetylators is approximately 70 minutes, whereas 2 to 5 hours is characteristic of slow acetylators.

Patients who are slow acetylators may be more prone to adverse effects and may require lower than usual doses. Tuberculosis therapy must be continued for 6 months to 2 years, depending on the treatment given.

Paediatrics

The rate of medicine metabolism is influenced by the youth / age of the patient: a particular dose of isoniazid in mg/kg when given to a young child (under 5 years) may not reach the same blood levels as when given to an older child or adult.

Higher mg/kg dosages are therefore required in younger children to achieve levels that are considered effective to produce bactericidal activity.

Elderly patients (65 years of age and older)

No dosage reduction is necessary in the elderly, but caution should be exercised due to the possible decrease in renal and hepatic function.

Hepatic impairment

ISONIAZID 300 UNIMED should be used with caution in patients with mild to moderate hepatic impairment as the half-life of isoniazid may be prolonged in the presence of hepatic insufficiency. (see section 4.4).

Renal impairment

Patients who are slow acetylators with severe renal failure (glomerular filtration rate of less than 10 mL/minute) (creatinine clearance < 30 mL/min) might require a dose reduction of about 100 mg to maintain trough plasma levels at less than 1 mcg/mL.

No dosage reduction of isoniazid is necessary when given to patients with mild renal failure.

Method of administration

For oral administration

ISONIAZID 300 UNIMED tablets should be taken preferably on an empty stomach, at least 30 minutes before a meal or 2 hours after a meal.

It may be taken with meals if gastrointestinal irritation occurs, but oral absorption may be reduced.

Aluminium-containing antacids may delay and decrease absorption and serum concentrations of isoniazid. ISONIAZID 300 UNIMED should therefore be taken/administered at least 1 hour before taking antacids.

4.3 Contraindications

When used in combination with other anti-tuberculosis medicines, the contraindications of these medicines should be consulted and adhered to, in addition to that of isoniazid.

ISONIAZID 300 UNIMED is contraindicated in:

- hypersensitivity to isoniazid, ethiomide, pyrazinamide, niacin, or other chemically related compounds or to any of the excipients (see section 6.1).
- alcoholism
- hepatic function impairment and medicine-induced liver disease
- severe renal failure
- patients with uncontrolled seizures
- The use of ISONIAZID 300 UNIMED in pregnancy should take into account the woman and/or her developing foetus where these need to be used (see section 4.6).
- Isoniazid in combination with other antituberculosis medicines can lead to optic neuritis.

4.4 Special warnings and precautions for use

Severe and sometimes fatal hepatitis associated with isoniazid as in ISONIAZID 300 UNIMED therapy has been reported and may occur or may develop even after many months of treatment. The risk of developing hepatitis is age related. Approximate case rates by age are: less than 1 per 1,000 for persons under 20 years of age, 3 per 1,000 for persons in the 20 to 34 year age group, 12 per 1,000 for persons in the 35 to 49 year age group, 23 per 1,000 for persons in the 50 to 64 year age group and 8 per 1,000 for persons over 65 years of age. The risk of hepatitis is increased with daily consumption of alcohol. Precise data to provide a fatality rate for ISONIAZID 300 UNIMED-related hepatitis is not available. Patients given isoniazid as in ISONIAZID 300 UNIMED should be carefully monitored and interviewed at monthly intervals. For persons 35 and older, in addition to monthly symptom reviews, hepatic enzymes (specifically, AST and ALT [formerly SGOT and SGPT, respectively]) should be measured prior to starting ISONIAZID 300 UNIMED therapy and periodically throughout treatment. Isoniazid as in ISONIAZID 300 UNIMED-associated hepatitis usually occurs during the first three months of treatment. Usually, enzyme levels return to normal despite continuance of medicine, but in some cases progressive liver dysfunction occurs. Other factors associated with an increased risk of hepatitis include daily use of alcohol, chronic liver disease and injection drug use. The risk may also be increased during the post-partum period. More careful monitoring should be considered in these groups, possibly including more frequent laboratory monitoring. If abnormalities of serum ALT exceed three times the upper limit of normal, or there is an increase in bilirubin, ISONIAZID 300 UNIMED should be discontinued. Liver function tests are not a substitute for a clinical evaluation at monthly intervals or for the prompt assessment of signs or symptoms of adverse reactions occurring between regularly scheduled evaluations. Patients should be instructed to

immediately report signs or symptoms consistent with liver damage or other adverse effects. These include any of the following: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, persistent paraesthesias of the hands and feet, persistent fatigue, weakness or fever of greater than 3 days duration and/or abdominal tenderness, especially right upper quadrant discomfort. If these symptoms appear or if signs suggestive of hepatic damage are detected, ISONIAZID 300 UNIMED should be discontinued promptly, since continued use of the medicine in these cases has been reported to cause a more severe form of liver damage. Patients with tuberculosis who have hepatitis attributed to ISONIAZID 300 UNIMED should be given appropriate treatment with alternative medicines. If ISONIAZID 300 UNIMED must be re-instituted, it should be re-instituted only after symptoms and laboratory abnormalities have cleared. The medicine should be restarted in very small and gradually increasing doses and should be withdrawn immediately if there is any indication of recurrent liver involvement. Preventive treatment should be deferred in persons with acute hepatic diseases.

ISONIAZID 300 UNIMED should not be given to patients who have experienced severe adverse reactions, including isoniazid-induced liver disease.

Care should be taken in giving ISONIAZID 300 UNIMED to patients suffering from: convulsive disorders, diabetes mellitus, chronic alcoholism, or impaired liver or kidney function or to patients taking other potentially hepatoxic medicines.

If symptoms of hepatitis such as malaise, fatigue, anorexia, and nausea develop, ISONIAZID 300 UNIMED treatment should be discontinued immediately. (see boxed warning above)

Advanced age, female gender, slow acetylators, malnutrition, HIV infection, pre-existing liver disease, and extrapulmonary tuberculosis were identified as risk factors for isoniazid-induced hepatotoxicity.

ISONIAZID 300 UNIMED should be used with caution in patients with mild to moderate hepatic or renal impairment or patients taking other potentially hepatotoxic medicines. If symptoms of hepatitis deteriorate in these patients, ISONIAZID 300 UNIMED should be discontinued immediately.

Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

Cases of severe cutaneous reactions including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), some with fatal outcome, have been reported (see section 4.8). Patients should be advised of these signs and symptoms (e.g. progressive skin rash often with blisters or mucosal lesions), and cautioned to consult their doctor immediately, if they experience this. Treatment should be permanently discontinued if an alternative cause for these signs and symptoms cannot be established.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Fatal cases of severe, systemic hypersensitivity reactions, including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome have been observed during antituberculosis therapy (see section 4.8).

It is important to note that early manifestations of hypersensitivity, such as fever, lymphadenopathy or biological abnormalities (including eosinophilia, liver abnormalities) may be present even though rash is not evident. If such signs or symptoms are present, the patient should be advised to consult their doctor immediately.

Treatment should be discontinued if an alternative cause for the signs and symptoms cannot be established.

ISONIAZID 300 UNIMED should be used with caution in patients with a history of psychosis.

Pyridoxine

Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic, pregnant, or infected with HIV, should be given pyridoxine. The administration of 10 to 15 mg pyridoxine daily, with a maximum of 30 mg/day during treatment with ISONIAZID 300 UNIMED is recommended.

Isoniazid in combination with other anti-tuberculosis medicines causes optic neuritis which can lead to optic atrophy and blindness (see section 4.8). Periodic eye examinations during treatment are recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Antiturberculous medicines

Paraminosalicyclic acid

When ISONIAZID 300 UNIMED is given to patients who inactivate it slowly or to patients receiving paraminosalicyclic acid concurrently, plasma concentrations may be enhanced, and adverse effects are more likely to appear.

Rifampicin

There may be an increased risk of liver damage in patients receiving rifampicin and ISONIAZID 300 UNIMED but liver enzymes are raised only transiently.

Cycloserine & Disulfiram

Increased central nervous system adverse effects have occurred when isoniazid as in

ISONIAZID 300 UNIMED is given concomitantly with potentially neurotoxic medicines such as cycloserine or disulfiram.

Anti-epileptics and Benzodiazepines

ISONIAZID 300 UNIMED can inhibit the hepatic metabolism of a number of medicines, in some cases leading to increased toxicity. These include the antiepileptics carbamazepine, primidone, phenytoin, and ethosuximide and the benzodiazepines diazepam and triazolam, chlorzoxazone, and disulfiram.

Hepatotoxic medicines

Hepatotoxic reactions have been reported with concurrent use of paracetamol and isoniazid. Chronic alcoholism, may increase the potential for isoniazid-induced hepatotoxicity (see section 4.4)

Paracetamol

A report of severe paracetamol toxicity was reported in a patient receiving isoniazid. It is believed that the toxicity may have resulted from a previously unrecognized interaction between isoniazid and paracetamol and a molecular basis for this interaction has been proposed. However, current evidence suggests that isoniazid does induce P-450IIE1, a mixed-function oxidase enzyme that appears to generate the toxic metabolites, in the liver. Furthermore, it has been proposed that isoniazid resulted in induction of P-450IIE1 in the patient's liver which, in turn, resulted in a greater proportion of the ingested paracetamol being converted to the toxic metabolites. Studies have demonstrated that pre-treatment with isoniazid potentiates paracetamol hepatotoxicity in rats.

Carbamazepine

ISONIAZID 300 UNIMED has been reported to cause substantial elevations of plasma concentrations of carbamazepine and symptoms of carbamazepine toxicity at isoniazid doses of 200 mg daily or more. The concurrent use is not recommended unless the effects can be closely monitored and suitable downward dosage adjustments made (a reduction between one-half or one-third was reported effective).

Diazepam

Concomitant benzodiazepine (diazepam) and isoniazid as in ISONIAZID 300 UNIMED therapy has been reported to result in an increased risk of benzodiazepine toxicity (sedation, respiratory depression).

Levodopa

ISONIAZID 300 UNIMED may reduce the therapeutic effects of levodopa.

Itraconazole & ketoconazole

Concomitant administration of ISONIAZID 300 UNIMED with itraconazole and ketoconazole may result in significant decreases in plasma concentrations and therapeutic failure. Concurrent use should be well monitored and dosage increases made if necessary.

Zalcitabine

Because the clearance of isoniazid was found doubled when zalcitabine was given in HIV-positive patients, concurrent use of ISONIAZID 300 UNIMED and zalcitabine should be

monitored to ensure ISONIAZID 300 UNIMED effectiveness.

Stavudine

There may be an increased risk of distal sensory neuropathy when ISONIAZID 300 UNIMED is used in patients taking stavudine (d4T).

Theophylline

Concomitant administration of ISONIAZID 300 UNIMED and theophylline may cause elevated plasma concentrations of theophylline and in some instances, a slight decrease in the elimination of isoniazid. Since the therapeutic range of theophylline is narrow, theophylline serum levels should be monitored closely and appropriate dosage adjustments of theophylline should be made.

Warfarin

Isoniazid can inhibit hepatic metabolism, leading to increased toxicity of coumarin anticoagulants, such as warfarin.

Prednisolone

Prednisolone may increase hepatic metabolism and/or excretion of ISONIAZID 300 UNIMED.

Antacids

Aluminium-containing antacids may delay and decrease absorption and serum concentrations of isoniazid. It is therefore recommended that ISONIAZID 300 UNIMED be administered at least 1 hour before taking antacids (see section 4.2).

Interactions with food

Isoniazid, as in ISONIAZID 300 UNIMED, is an inhibitor of monoamine oxidase (MAO) and diamine oxidase (DAO), can therefore reduce tyramine and histamine metabolism, causing symptoms such as headache, sweating, palpitations, flushing, conjunctiva! irritation, tachycardia, tachypnoea and hypotension.

Patients should be advised against ingesting foods rich in tyramine and/or histamine during treatment with isoniazid, such as cured meat, some cheeses (e.g. matured cheeses), wine, beer and some fish (e.g. tuna, mackerel, salmon).

4.6 Fertility, pregnancy and lactation

Use of MYZID in pregnancy should take into account the safety of other anti-tuberculosis medicines in pregnancy, and the risk to the pregnant woman and/or her embryo/developing foetus where these medicines are to be used in combination with isoniazid.

Women of childbearing potential

Women of child-bearing potential should be advised to avoid becoming pregnant while on treatment with ISONIAZID 300 UNIMED.

Pregnancy

Isoniazid crosses the placenta. The safe use of isoniazid in pregnancy has not been established, and harm to the embryo/developing foetus cannot be excluded (see section 4.3).

Pyridoxine supplementation is recommended.

Breastfeeding

Women on treatment with ISONIAZID 300 UNIMED should not breastfeed their infants.

The safety of infants receiving breast milk of mothers on treatment with ISONIAZID 300 UNIMED has not been established.

Fertility

No data on the effect of isoniazid on fertility is available.

4.7 Effects on ability to drive and use machines

ISONIAZID 300 UNIMED may influence the ability to drive and use machines. Since adverse reactions such as dizziness, vertigo, optic neuritis, and convulsions have been reported in patients receiving isoniazid. Patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that ISONIAZID 300 UNIMED 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 reactions are those affecting the nervous system and the liver.

b. Tabulated summary of the adverse effects

Assessment of undesirable effects is based on the following frequency groupings:

Undesirable effects are listed by MedDRA System Organ Classes and frequency:

Frequent

Less frequent

Frequency not known: cannot be estimated from the available data

MedDRA System Organ Classification (SOC) according to the sequence:	**Adverse Reaction**	**Frequency per patient**
Blood and lymphatic system disorders	Blood dyscrasias	Less frequent
	agranulocytosis, aplastic anaemia, sideroblastic anaemia, haemolytic anaemia, thrombocytopenia; and eosinophilia	Frequency not known
Immune system disorders	Hypersensitivity reactions (fever, skin rashes, joint pain)	Less frequent
Metabolism and nutrition disorders (see section c below)	hypoglycaemia, nicotinic acid deficiency, pyridoxine deficiency pellagra, hyperglycemia, metabolic acidosis.	Frequency not known
Psychiatric disorders (see section c below)	elevated mood, psychotic disorder.	Frequency not known
Nervous System disorders (see section c below)	peripheral neuritis	Frequent
	neurotoxicity	Less frequent

	peripheral neuropathy, optic neuritis, seizure. Hyperreflexia	Frequency not known
Eye disorders	Optic neuritis, which can lead to optic atrophy and blindness*	Frequency not known
Ear and labyrinth disorders (see section c below)	deafness, tinnitus, vertigo	Frequency not known
Vascular disorders	vasculitis	Frequency not known
Respiratory, thoracic and mediastinal disorders	interstitial lung disease	Frequency not known
Gastrointestinal disorders	constipation, dry mouth, nausea, pancreatitis, gastrointestinal irritation, vomiting and other gastrointestinal effects, including epigastric distress (nicotinic acid deficiency (pellagra)	Frequency not known
Hepatobiliary disorders (see section c below)	hepatitis prodromal symptoms (loss of appetite, nausea or vomiting, unusual tiredness or weakness)	Frequent
	hepatitis	Less frequent
	acute hepatic failure, liver injury, jaundice	Frequency not known

Skin and subcutaneous tissue disorders	toxic epidermal necrolysis, eosinophilia systemic symptoms	Less frequent
	erythema multiforme, Stevens-Johnson syndrome	Frequency not known
Musculoskeletal and connective tissue disorders	systemic lupus erythematosus, lupus-like syndrome, rheumatoid syndrome	Frequency not known
Renal and urinary disorders	dysuria, urinary retention	Frequency not known
Reproductive System and breast disorders	gynaecomastia	Frequency not known
General disorders and administration site conditions	pyrexia	Frequency not known
Investigations	increased hepatic enzymes	Frequency not known
Miscellaneous (see section c below)	headache, insomnia, excessive dreaming, irritability, nervousness	Frequency not known

c. Description of selected adverse reactions

Nervous System Reactions

Peripheral neuropathy is the most common adverse effect. It is dose-related, occurs most often in the malnourished and in those predisposed to neuritis (e.g., alcoholics and diabetics) and is usually preceded by paraesthesias of the feet and hands. The incidence is higher in "slow inactivators".

Other neurotoxic effects, which are uncommon with conventional doses, are convulsions, toxic encephalopathy, optic neuritis and atrophy, memory impairment and toxic psychosis.

Hepato-biliary Reactions

Elevated serum transaminase (SGOT; SGPT), bilirubinaemia, bilirubinuria, jaundice and occasionally severe and sometimes fatal hepatitis. The common prodromal symptoms of hepatitis are anorexia, nausea, vomiting, fatigue, malaise and weakness. Mild hepatic dysfunction, evidenced by mild and transient elevation of serum transaminase levels occurs in 10 to 20 percent of patients taking ISONIAZID 300 UNIMED. This abnormality usually appears in the first 1 to 3 months of treatment but can occur at any time during therapy. In most instances, enzyme levels return to normal and generally, there is no necessity to discontinue medication during the period of mild serum transaminase elevation. In occasional instances, progressive liver damage occurs, with accompanying symptoms. If the SGOT value exceeds three to five times the upper limit of normal, discontinuation of the ISONIAZID 300 UNIMED should be strongly considered. The frequency of progressive liver damage increases with age, especially over the age of 35; it may be serious and sometimes fatal with the development of necrosis. It is rare in persons under 20, but occurs in up to 2,3 percent of

those over 50 years of age. (see boxed warning, section 4.4)

Miscellaneous

Cessation of treatment may result in certain withdrawal symptoms, including headache, insomnia, excessive dreaming, irritability and nervousness.

Psychiatric disorders

Although ISONIAZID 300 UNIMED usually has a mood elevating effect, mental disturbances, ranging from minor personality changes to major mental derangement have been reported; these are usually reversed on withdrawal of the medicine.

Ear and Labyrinth disorders

Vertigo may be troublesome with doses of 10mg per kg body weight. This has been reported in patients with end-stage renal failure.

Eye disorders

Isoniazid causes optic neuritis which in combination with other anti-tuberculosis medicines, can lead to optic atrophy and blindness.

Hepato-biliary disorders

The risk of these undesirable effects increases with age, especially over the age of 35; it may be serious and sometimes fatal with the development of necrosis.

Metabolism and nutrition disorders

Nicotinic acid deficiency may be related to an isoniazid-induced pyridoxine deficiency which affects the conversion of tryptophan to nicotinic acid.

Nervous system disorders

Hyperreflexia may be troublesome with doses of 10 mg per kg body weight.

d. Paediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

As vertigo is a dose-related adverse effect, it may be expected more frequently amongst the paediatric population.

e. Other special populations

The occurrence of deafness, tinnitus and vertigo has been reported in patients who have end-stage renal impairment.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

Patients may be asymptomatic for 30 minutes to 2 hours after an acute overdose. Early adverse events associated with isoniazid as in ISONIAZID 300 UNIMED overdose are nausea, vomiting, dizziness, slurred speech, lethargy, disorientation, visual hallucinations (including bright colours and strange designs) and hyper-reflexia. With more severe overdosage, respiratory distress and central nervous system toxicity such as seizures and coma may be expected. Seizures usually occur within 1 to 3 hours after ingestion and are often repetitive and refractory to usual anticonvulsants. Metabolic acidosis occurs within a few hours. Hyperglycaemia, glycosuria and ketonuria have been reported.

Treatment

Treatment for overdosage is symptomatic and supportive therapy. Including the control of convulsions by diazepam given intravenously, together with large doses of pyridoxine. Metabolic acidosis is corrected with sodium bicarbonate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Medicine Class: A 20.2.3 Tuberculostatics

Pharmacotherapeutic group: - drugs for treatment of tuberculosis; ATC code: J04AC01

Mechanism of action

Isoniazid is a synthetic, bactericidal antitubercular medicine, which is active against many mycobacteria, primarily those that are actively dividing. Its exact mechanism of action is not

known, but it may relate to inhibition of mycolic acid synthesis and disruption of the cell wall in susceptible organisms.

Resistance

Resistance to isoniazid occurs because of mutations in the *katG, inhA, kasA and ahpC* genes. Resistance in *M. tuberculosis* develops rapidly when isoniazid monotherapy is administered.

5.2 Pharmacokinetic properties

Absorption

Readily absorbed from gastrointestinal tract after oral administration, but may however undergo significant first pass metabolism. Absorption and bio-availability are reduced when administered with food.

Distribution

The plasma half-life for isoniazid ranges from about 1 to 4 hours. Readily diffuses into all tissues and fluids including the cerebrospinal fluid, pleural and ascitic fluids, skin, sputum, saliva, lungs, muscle, and caseous tissue. Isoniazid is retained in the skin and in infected tissue; it crosses the placenta and is secreted in the breast milk.

Biotransformation

The primary metabolic route is acetylation.

Others include hydrolysis and glycine conjugation, hydrazone formation, and n-methylation;

acetylation is polymorphic and two groups of acetylators have been identified, rapid and slow acetylators. The rate of hydrolysis is more rapid in the rapid acetylators than in the slow ones. The metabolites formed include acetyl isoniazid, isonicotinic acid, isonicotinuric acid, isonicotinoyl-hydrazones of pyruvic and glutaric acids, and n-methyl isoniazid.

Elimination

Approximately 75 to 95 % is excreted by the kidneys within 24 hours, mainly as metabolites. Small amounts are excreted in the faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Intragranular ingredients: Microcrystalline cellulose 101, maize starch, crospovidone XL, purified water.

Extragranular ingredients: Polyplasdone XL, colloidal silicon dioxide, microcrystalline cellulose 102, magnesium stearate (vegetable grade).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

Multiple blisters may be packed in a vanished, printed cardboard carton (PVC/PVdC aluminium foil blister packs of 10 or 28 tablets each). Keep the blisters in the carton until required for use.

Opaque, white, HDPE bottles with caps containing 500 or 1000 tablets. These tablets are packed within a triple laminate pouch (Polyester/Aluminum/Polyethylene). Each pouch contains 500 or 1000 tablets and is heat sealed.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Unimed Healthcare (Pty) Ltd

Corner Birch Road & Bluegum Avenue,

Anchorville,

Lenasia,

1827

8 REGISTRATION NUMBER

57/20.2.3/0903

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 September 2024

10 DATE OF REVISION OF THE TEXT