ANNOTATED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LIDONIT film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 600 mg linezolid.

LIDONIT -contains sugar (lactose monohydrate 200 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablets.

White to off white coloured, oval shaped, bevelled edges, biconvex, tablets having score line on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LIDONIT is indicated for the treatment of patients with the following infections caused by susceptible strains of the designated micro-organisms. LIDONIT is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy must be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected (see 4.4).

Vancomycin-resistant: *Enterococcus faecium* infections, which includes cases with concurrent bacteraemia.

Nosocomial pneumonia: caused by *Streptococcus pneumoniae* (including multi-drug resistant *S. pneumoniae* (MDRSP) strains) or *Staphylococcus aureus* (methicillin-susceptible and -resistant strains).

Community-acquired pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains) or *Streptococcus pneumoniae* (including multi-drug resistant *S. pneumoniae* (MDRSP) strains), including cases with concurrent bacteraemia.

Prescribers should carefully consider alternatives before initiating treatment with LIDONIT in the outpatient setting due to the concern regarding the inappropriate use of antibiotics leading to an increase in resistant organisms.
Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and their susceptibility to linezolid. Therapy may be introduced empirically while waiting for the test results. Once these tests are available, antimicrobial therapy should be adjusted accordingly.

4.2 Posology and method of administration

LIDONIT tablets may be used as initial therapy. Patients who commence treatment on intravenous linezolid may be switched to LIDONIT when clinically indicated. In such circumstances, no dose adjustment is required as LIDONIT has an oral bioavailability of approximately 100 %. LIDONIT film coated tablets can be taken with or without food.

The recommended dose for LIDONIT is indicated in the table below:

Adult and adolescent (12 years and older) patients:

Infections (including those associated with concurrent bacteraemia)	**Dosage and route of administration**	**Duration of treatment**
Community-acquired pneumonia, including concurrent bacteraemia	600 mg orally every 12 hours	10 – 14 consecutive days
Nosocomial pneumonia including concurrent bacteraemia		
Enterococcal infections, including vancomycin-resistant infections, and those with concurrent bacteraemia	600 mg orally every 12 hours	14 – 28 consecutive days

Special populations

Elderly patients:

No dose adjustment is necessary.

Patients with renal insufficiency:

No dose adjustment is necessary.

Patients with severe renal insufficiency (CL_{CR} < 30 mL/min):

No dose adjustment is required.

LIDONIT should be used with special caution in patients with severe renal insufficiency due to the unknown clinical significance of higher exposure (up to 10-fold) to the two primary metabolites of LIDONIT. In these patients LIDONIT should only be considered when the theoretical risk is outweighed by the anticipated benefit.

Approximately 30 % of a LIDONIT dose is removed during 3 hours of haemodialysis, therefore LIDONIT should be given after dialysis in patients receiving such treatment.

Haemodialysis removes the primary metabolites of LIDONIT to some extent, although the concentrations of these metabolites are still considerably higher following dialysis than those observed in patients with normal renal function or mild to moderate renal insufficiency.

LIDONIT should be used with special caution in patients with severe renal insufficiency who are undergoing dialysis. In these patients LIDONIT should only be considered when the theoretical risk is outweighed by the anticipated benefit.

No clinical data is available for LIDONIT administration to patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or alternative treatments for renal failure (other than haemodialysis).

Patients with hepatic insufficiency:

Although no dose adjustment is required, due to limited clinical data, it is recommended that LIDONIT should be used with special precaution in patients with hepatic impairment and should only be considered when the theoretical risk is outweighed by the anticipated

benefit.

Method of administration

LIDONIT film coated tablets are for oral use.

LIDONIT may be taken with or without food.

Missed dose:

Doctors should advise patients who forget to take LIDONIT to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to linezolid or to any of the ingredients of LIDONIT
- LIDONIT should not be used in patients treated with monoamine inhibitor oxidases A or B (e.g. phenelzine, isocarboxazid, moclobemide, selegiline) or within two weeks after discontinuation of taking such medicines
- LIDONIT should not be administered to patients with the following underlying clinical conditions or on the following types of concomitant medicines:
    - patients with uncontrolled hypertension, pheochromocytoma, carcinoid syndrome, hyperthyroidism, bipolar depression, schizoaffective disorder, acute confusional states
    - patients taking any of the following: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT_1 receptor agonists (triptans), serotonin-norepinephrine reuptake inhibitors (SNRIs), dopaminergic medicines (e.g.

dopamine, dobutamine), direct and indirect acting sympathomimetic medicines including the adrenergic bronchodilators, pseudoephedrine and phenylpropanolamine, vasopressor medicines (e.g. epinephrine (adrenaline), norepinephrine (noradrenaline)), meperidine, pethidine or buspirone (see sections 4.4 and 4.5)

- pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Serotonin syndrome

Spontaneous reports of serotonin syndrome associated with the co-administration of LIDONIT and serotonergic medicines, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been reported. Co-administration of LIDONIT and serotonergic medicines is therefore contraindicated (see section 4.3).

Myelosuppression

Reversible Myelosuppression (including anaemia, granulocytopenia, leucopenia, pancytopenia and thrombocytopenia) has been reported in patients receiving linezolid, as in LIDONIT .

Cases of sideroblastic anaemia have been reported post-marketing. Where time of onset was known, most patients had received linezolid therapy for more than 28 days. Most patients fully or partially recovered following discontinuation of linezolid with or without treatment for their anaemia.

Thrombocytopenia may occur more commonly in patients with severe renal insufficiency, whether or not on dialysis. Elderly patients treated with LIDONIT may be at greater risk of experiencing blood dyscrasias than younger patients.

Monitoring of complete blood counts should therefore be considered for patients who have pre-existing myelosuppression, who are at increased risk for bleeding, patients who receive concomitant medicines that may decrease haemoglobin levels or platelet count or function, have severe renal insufficiency or are receiving LIDONIT treatment for more than 2 weeks.

Therapy with LIDONIT should be stopped if significant myelosuppression occurs. In this case, intensive monitoring of blood counts and appropriate management strategies should be implemented.

Antibiotic-associated diarrhoea and colitis

Antibiotic-associated diarrhoea and antibiotic-associated colitis, including pseudomembranous colitis and *Clostridium difficile*-associated diarrhoea (CDAD) have been reported in association with the use of LIDONIT , and may range in severity from mild diarrhoea to fatal colitis.

In antibiotic-associated colitis, treatment with LIDONIT should be discontinued. Appropriate therapy should be instituted. Therefore, it is important to consider this diagnosis in patients who develop severe diarrhoea during or after the use of LIDONIT .

Medicines inhibiting gut motility/peristalsis are contraindicated in this situation.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. CDAD has been

reported to occur over two months after the administration of antibacterial medicines such as LIDONIT , therefore careful medical history is necessary.

Lactic acidosis

Lactic acidosis has been reported with the use of LIDONIT . Patients who develop signs and symptoms of metabolic acidosis, including recurrent nausea or vomiting, abdominal pain, a low bicarbonate level, or hyperventilation while receiving LIDONIT
should receive immediate medical attention.

Mitochondrial dysfunction

Linezolid inhibits mitochondrial protein synthesis when given for prolonged courses. There is a decrease in cellular energy production in tissues that are highly dependent on oxidative phosphorylation such as the optic nerve, liver, skeletal muscles and kidneys. Adverse events, such as lactic acidosis, anaemia and neuropathy (optic and peripheral), may occur as a result of this inhibition; these events are more common when LIDONIT is used for longer than 28 days.

Peripheral and optic neuropathy

Peripheral neuropathy, as well as optic neuropathy and optic neuritis sometimes progressing to loss of vision, have been reported in patients treated with LIDONIT .
Patients should be advised to report symptoms of visual impairment, such as changes in visual acuity, changes in colour vision, blurred vision or visual field defect. Prompt evaluation is recommended with referral to an ophthalmologist.

There may be an increased risk of neuropathies when LIDONIT is used in patients currently taking or who have recently taken antimycobacterial medicines for the treatment of tuberculosis (see section 4.5).

Visual function should be monitored in all patients taking LIDONIT for extended periods (3 months and more) as well as in those patients reporting new visual symptoms, regardless of the length of therapy. If peripheral or optic neuropathy occurs, the continued use of LIDONIT in these patients should be weighed against the potential risks.

Convulsions

Convulsions have been reported in patients treated with LIDONIT . Patients should be advised to inform their medical practitioner if they have a history of seizures.

Use with tyramine-rich foods

Patients should be advised against consuming tyramine rich foods (see section 4.5).

Superinfection

The effects of linezolid therapy on normal flora have not been established.

The use of LIDONIT may result in an overgrowth of non-susceptible organisms.

Should superinfection occur during therapy, appropriate measures should be taken.

Bacteriological examination of appropriate specimens should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to linezolid. While awaiting these test results, therapy may be instituted empirically. Once these results become available, antimicrobial therapy should be adjusted accordingly.

Other

LIDONIT is not indicated for the treatment of Gram-negative infections. Patients with mixed Gram-negative and Gram-positive infections are at a higher risk of mortality when linezolid, as in LIDONIT , is given as monotherapy. LIDONIT must therefore be used concomitantly with appropriate antibacterial cover for Gram-negative organisms in such patients.

In patients treated with linezolid excess mortality was seen in comparison to vancomycin/dicloxacillin/oxacillin. The most important factor influencing the mortality rate was the Gram-positive infection status at baseline. The greatest imbalance occurred during treatment and within 7 days following discontinuation of study medicine. More patients in the linezolid arm acquired gram negative pathogens during the study and died from infections caused by gram negative pathogens and polymicrobial infections. This clinical study was an open-label randomised study comparing linezolid to vancomycin, oxacillin or dicloxacillin in the treatment of seriously ill patients with intravascular catheter-related bloodstream infections.

LIDONIT should be used with special caution in patients at high risk for life threatening systemic infections, such as those with infections related to central venous catheters in intensive care units.

LIDONIT is not approved for the treatment of patients with catheter-related bloodstream infections.

The safety and efficacy of LIDONIT has not been established when administered for periods longer than 28 days.

Experience in the use of linezolid in the treatment of patients with diabetic foot lesions, decubitus or ischaemic lesions, severe burns or gangrene is limited.

Special populations

Caution is advised when LIDONIT is used in patients with severe renal and/or hepatic insufficiency.

Lactose

LIDONIT contains lactose. Patients with the rare hereditary conditions of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take LIDONIT .

4.5 Interaction with other medicines and other forms of interaction

Linezolid, as in LIDONIT , does not induce or inhibit the activities of clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4) and is not detectably metabolised by the cytochrome P450 (CYP) enzyme system. Therefore, no CYP450-induced medicine interactions are expected. Medicines such as phenytoin and warfarin, which are CYP2C9 substrates, may be given with LIDONIT without changes in dosage regimen.
Adding warfarin to steady-state linezolid therapy resulted in a 10 % reduction in the mean maximum INR on co-administration with a 5 % reduction in AUC INR. The data is insufficient on patients who received warfarin and linezolid and thus the clinical significance cannot be established.

No interactions have been observed in pharmacokinetic studies with either aztreonam or gentamicin.

Linezolid, as in LIDONIT is a reversible, non-selective monoamine oxidase inhibitor (MAOI). It produces a reversible enhancement of pressor responses which is started by pseudoephedrine and phenylpropanolamine hydrochloride (as proven by clinical studies). Thus, the potential interaction with adrenergic or sympathomimetic medicines should be considered and doses of medicines, such as dopamine or epinephrine (adrenaline), should
be titrated to attain the desired response.

Linezolid when co-administered with pseudoephedrine or phenylpropanolamine hydrochloride enhanced the increases in blood pressure in normotensive healthy volunteers.
Systolic blood pressure increased in the range of 30-40 mmHg. It is recommended that doses of medicine with vasopressive action, including dopaminergic agents, should be carefully titrated to achieve the desired response when co-administered with linezolid.

No significant pressor response was observed in subjects receiving both LIDONIT and less than 100 mg tyramine. This suggests that it is only necessary to avoid ingesting large amounts of food and beverages with a high tyramine content (e.g. un-distilled alcoholic beverages, mature cheese, yeast extracts and fermented soya bean products such as soy sauce).

Although LIDONIT has the potential for interaction with serotonergic agents, no serotonin effects (e.g. confusion, delirium, restlessness, tremors, blushing, diaphoresis and hyperpyrexia) were observed in subjects receiving linezolid and dextromethorphan.

Spontaneous reports of serotonin syndrome associated with the co-administration of LIDONIT, and serotonergic medicines, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs) have been reported. Where administration of LIDONIT and concomitant serotonergic agents is clinically appropriate, patients should be closely observed for signs and symptoms of serotonin syndrome such as cognitive dysfunction, hyperpyrexia, hyperreflexia and incoordination. If signs or symptoms occur, doctors should consider discontinuation of either one or both agents. If the concomitant serotonergic agent is withdrawn, discontinuation symptoms can be observed.

Rifampicin: Concomitant administration with LIDONIT may cause a decrease of about 21 % and 32 % in linezolid C_{max} and AUC, respectively. The mechanism of this interaction and the clinical significance is not known.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of LIDONIT in pregnancy is contraindicated as safety has not been established (see section 4.3).

Breastfeeding

The use of LIDONIT in lactation is contraindicated as safety has not been established (see section 4.3).

Animal data revealed that linezolid as well as its metabolites can possibly pass into breast milk – It is recommended that breastfeeding should be discontinued prior to and throughout administration.

Fertility

Study results in male rats revealed fertility and reproductive performance decreased at exposure levels approximately equal to those expected in humans. Prostrate, testes and epididymis weight changes were evident in dogs treated for 1 month.

However, it is not known whether these findings have an impact on human fertility.

4.7 Effects on ability to drive and use machines

Patients should be warned about the potential for dizziness or symptoms of visual impairment whilst receiving LIDONIT and should be advised not to drive or operate machinery if any of these symptoms occur.

4.8 Undesirable effects

Summary of the safety profile

Headache, diarrhoea, nausea and candidiasis (particularly oral and vaginal candidiasis) were the most commonly reported adverse effects, with those leading to discontinuation of treatment including headache, diarrhoea, nausea and vomiting.

Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Infections and Infestations	Frequent	Candidiasis (moniliasis), oral candidiasis, fungal infections
	Less frequent	Antibiotic-associated colitis including pseudo-membranous colitis

Blood and lymphatic system disorders	Frequent Less frequent Frequency unknown	Anaemia Reversible anaemia, eosinophilia leukopenia, neutropenia, pancytopenia, thrombocytopenia Myelosuppression, sideroblastic anaemia
Immune system disorders	Frequency unknown	Anaphylaxis
Metabolism and nutrition disorders	Less frequent	Increased serum creatine phosphokinase, hyperglycaemia, lactic acidosis, hyponatraemia
Psychiatric disorders	Frequent	Insomnia
Nervous system disorders	Frequent Less frequent Frequency unknown	Headache, taste perversion (metallic taste), dizziness Convulsions, hypoesthesia, peripheral neuropathy, paraesthesia Serotonin syndrome
Eye disorders	Less frequent Frequency unknown	Blurred vision, peripheral and optic neuropathy, changes in visual field defect Loss of vision, changes in visual acuity, changes in colour vision, optic neuritis
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Less frequent	Dysrhythmia (tachycardia)
Vascular disorders	Frequent Less frequent	Hypertension Hypotension, transient ischaemic attacks, phlebitis, thrombophlebitis

Gastrointestinal disorders	Frequent Less frequent	Abdominal pain, cramps or distension, diarrhoea, nausea, vomiting, constipation, dyspepsia Dry mouth, gastritis, glossitis, increased thirst, pancreatitis, loose stools, stomatitis, tongue discolouration or disorder, superficial tooth discolouration
Hepatobiliary disorders	Frequent Less frequent	Abnormal liver function test; increased AST, ALT or alkaline phosphatase Increased total bilirubin
Skin and subcutaneous tissue disorders	Frequent Less frequent Frequency unknown	Pruritus, rash Dermatitis, diaphoresis, urticaria, angioedema, bullous disorders such as those described as Stevens-Johnson syndrome Toxic epidermal necrolysis, alopecia
Renal and urinary disorders	Less frequent	Renal failure, polyuria
Reproductive system and breast disorders	Frequent Less frequent	Vaginal moniliasis Vulvovaginal disorder, vaginitis
General disorders and administrative site conditions	Frequent Less frequent	Fever, localised pain Chills, fatigue, increased thirst

Investigations	Frequent	*Chemistry*: Increased total bilirubin, AST, ALT, LDH, alkaline phosphatase, blood urea, creatine kinase, lipase, amylase or non-fasting glucose, decreased total protein, albumin, sodium, calcium, increased or decreased potassium or bicarbonate *Haematology*: Increased neutrophils or eosinophils, decreased haemoglobin, haematocrit or red blood cell count, increased or decreased platelet or white blood cell counts
	Less frequent	*Chemistry*: Increased creatinine, sodium, calcium; decreased non fasting glucose, increased or decreased chloride *Haematology*: Increased reticulocyte count; decreased neutrophils

Description of selected adverse reactions

Localised abdominal pain, transient ischaemic attacks and hypertension are, in less frequent cases, considered to be serious.

Linezolid, administered for up to 28 days, revealed that less than 0,1% of the patients reported anaemia.

2,5 % (33/1326) as compared with 12,3 % (53/430) of patients with life-threatening infections and underlying co-morbidities developed anaemia, with 9 % (3/33) and 15 % (8/53) developing serious medicine-related anaemia that required a blood transfusion were reported in patients treated with linezolid for ≤ 28 and >28 days respectively.

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 following the link: https://www.sahpra.org.za/Publications/Index/8.

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:

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8)

Management of overdose:

In the event of overdosage with LIDONIT , supportive care is advised together with maintenance of glomerular filtration.

Approximately 30 % of a LIDONIT dose is removed during 3 hours of haemodialysis, however, no data are available for the removal of LIDONIT by peritoneal dialysis or haemoperfusion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antibacterials

ATC code: J01XX08

Pharmacological classification: Pharmacological classification: A 20.1.1 Broad and medium spectrum antibiotic.

Mechanism of action

Linezolid, of the oxazolidinone class of antimicrobials, is a synthetic antibacterial medicine.

Linezolid prevents the formation of a functional 70S-initiation complex which is an essential component of the translation process. It selectively inhibits bacterial protein synthesis by binding to the P site of the 50S ribosomal subunit and preventing formation of the larger ribosomal-fMet-tRNA complex that initiates protein synthesis.

Resistant organisms:	
Inherently resistant organisms:	
Haemophilus influenza *Enterobacteriaceae*	*Neisseria* species *Pseudomonas* species

Resistance

There is no cross-resistance between linezolid and other classes of medicines, such as aminoglycosides, beta-lactams, folic acid antagonists, glycopeptides, lincosamides, quinolones, rifamycins, streptogramins, tetracyclines and chloramphenicol.
Resistance to linezolid develops slowly and by multiple step mutation in 23S ribosomal RNA occurring at frequencies of less than 1×10^{-9} to 1×10^{-11} as proven by *in vitro* studies.

5.2 Pharmacokinetic properties

Linezolid is biologically active and is metabolised to form inactive metabolites.

Absorption:

Maximum plasma concentrations are reached within 2 hours of dosing and absolute bioavailability is approximately 100 %. It is not affected by food. The $t_{½}$ is 4-6 hours

Distribution:

Plasma protein binding is approximately 31 %. The volume of distribution at steady-state averages at about 40 to 50 litres and approximates to total body water.

Linezolid concentrations have been determined in various fluids following multiple dosing. The ratio of linezolid in saliva and sweat relative to plasma was 1,2:1,0 and 0,55:1,0 respectively. The ratio for epithelial lining fluid and alveolar cells of the lung was 4,5:1,0 and 0,15:1,0, when measured at steady-state C_{max} respectively. In patients with ventricular-peritoneal shunts and essentially non-inflamed meninges, the ratio of linezolid in cerebrospinal fluid to plasma at C_{max} was 0,7:1,0 after linezolid dosing.

Biotransformation:

Linezolid is metabolised by a non-enzymatic process. Two inactive open-ring carboxylic acid derivatives mainly result from metabolic oxidation of the morpholine ring. The hydroxyethyl glycine metabolite (B) is the predominant human metabolite and the amino ethoxy acetic acid metabolite (A) is less abundant. Linezolid does not inhibit the activities of clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4) and is not detectably metabolised by

cytochrome P450 (CYP) isoenzymes *in vitro*. Linezolid does not induce human CYP2C9 nor significantly induce major cytochrome P450 isoenzymes in rats.

Elimination:

Linezolid is primarily excreted in the urine as metabolite B (40 %), parent compound (30 – 35 %) and metabolite A (10 %), under steady-state conditions. The elimination half-life of the parent compound averages at about 5 – 7 hours. Non-renal clearance accounts for approximately 65 % of the total clearance of linezolid.

Pharmacokinetics in special patient groups

Elderly:

In elderly patients aged 65 and over, the pharmacokinetics of linezolid are not significantly altered.

Renal insufficiency:

In patients with either mild, moderate or severe renal insufficiency, no dose adjustment is necessary since linezolid clearance is independent of creatinine clearance. In patients with severe renal insufficiency (CL_{CR} < 30 mL/min), there is evidence that the primary metabolites of linezolid accumulate, however the clinical significance of this has not yet been established. Linezolid should be given after dialysis, since approximately 30 % of a dose is removed during 3 hours of haemodialysis (beginning 3 hours after administration).

Hepatic insufficiency:

In patients with mild to moderate hepatic insufficiency, the pharmacokinetics of linezolid are not altered. Therefore, dose adjustment in these patients is not required. In patients with severe hepatic insufficiency, the pharmacokinetics of linezolid have not been evaluated. However, since linezolid is metabolised by a non-enzymatic process, hepatic function impairment is not expected to significantly alter its metabolism.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

Colloidal silicon dioxide

Hypromellose

Lactose monohydrate

Magnesium stearate

Polacrilin potassium

Coating:

Wincoat white consisting of:

Hydroxypropyl methyl cellulose

Polyethylene glycol 6000

Polyethylene glycol 400

Titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 °C. Protected from moisture.

Keep blisters in the carton until required for use.

6.5 Nature and contents of container

Blister containing 25-micron aluminium foil as lidding material and clear PVC/PVDC 40 GSM foil as base material containing 10 tablets per blister, inside an outer carton containing a leaflet.

Blister containing 25-micron aluminium foil as lidding material and clear PVC foil as base material containing 10 tablets per blister, inside an outer carton containing a leaflet.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

Manufacturer:

LUPIN LTD.

EPIP, SIDCO Industrial Complex,

Kartholi, Bari Brahmana,

Jammu (J&K)

181133

India

8. REGISTRATION NUMBER

A54/20.1.1/0591

9. DATE OF FIRST AUTHORISATION

21 July 2020

10. DATE OF REVISION OF THE TEXT

05 January 2023