Professional Information for LIFANED 25, LIFANED 50 and LIFANED 100

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LIFANED 25 mg film-coated tablets

LIFANED 50 mg film-coated tablets

LIFANED 100 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

LIFANED 25: Each film-coated tablet contains sildenafil citrate equivalent to 25 mg sildenafil.

LIFANED 50: Each film-coated tablet contains sildenafil citrate equivalent to 50 mg sildenafil.

LIFANED 100: Each film-coated tablet contains sildenafil citrate equivalent to 100 mg sildenafil.

Excipients with known effect:

Contains sugar.

LIFANED 25: Each tablet contains 67,2 mg lactose monohydrate.

LIFANED 50: Each tablet contains 134,5 mg lactose monohydrate.

LIFANED 100: Each tablet contains 269 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

LIFANED 25: Blue coloured, diamond shaped, biconvex, film-coated tablets with "U" debossed on one side and "25" debossed on other side.

LIFANED 50: Blue coloured, diamond shaped, biconvex, film-coated tablets with "U" debossed on one side and "50" debossed on other side.

LIFANED 100: Blue coloured, diamond shaped, biconvex, film-coated tablets with "U" debossed on one side and "100" debossed on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LIFANED is indicated only for the treatment of erectile dysfunction.

THIS PRODUCT IS NOT AN APHRODISIAC.

4.2 Posology and method of administration

Posology

Use in adults:

The recommended dose is 50 mg, taken as needed approximately one hour before sexual activity. Based on efficacy and toleration, the dose may be increased to 100 mg or decreased to 25 mg. The maximum recommended dose is 100 mg. The maximum recommended dosing frequency is once per day.

The following factors are associated with increased plasma levels of LIFANED:

Age > 65 years (40 % increase in AUC), hepatic impairment (e.g. cirrhosis, 80 %), severe renal impairment (creatinine clearance < 30 mL/min, 100 %), and concomitant use of potent cytochrome P450 3A4 inhibitors (erythromycin 182 %, saquinavir 210 %, ketoconazole, itraconazole, 200 %, ritonavir 1 000 %).

Special populations

Use in patients with mild to moderately impaired renal function:

A starting dose of 25 mg should not be exceeded.

Use in patients with mild to moderately impaired hepatic function:

Since LIFANED clearance is reduced in patients with hepatic impairment (e.g. cirrhosis), a starting dose of 25 mg should not be exceeded.

Use in elderly patients:

Healthy elderly volunteers (65 years or over) had a reduced clearance of LIFANED. A starting dose of 25 mg should be considered in patients older than 65 years of age.

Use in patients using potent CYP 3A4 inhibitors:

Given the extent of the interaction with patients receiving concomitant therapy with cytochrome P450 3A4 inhibitors (e.g. ritonavir, erythromycin, saquinavir, ketoconazole, itraconazole), LIFANED should not be used concomitantly with these medicines (see section 4.3).
LIFANED was shown to potentiate the hypotensive effects of nitrates and its administration in patients who use nitric oxide donors or nitrates in any form is therefore contraindicated.

Use in children:

LIFANED is not indicated for use in children.

Method of administration

LIFANED tablets are for oral administration.

4.3 Contraindications

- Hypersensitivity to sildenafil citrate or to any of the excipients (see section 6.1).
- Consistent with its known effects on the nitric oxide/cGMP pathway (see section 5.1), LIFANED was shown to potentiate the hypotensive effects of acute and chronic nitrates, and its administration to patients who are concurrently using nitric oxide donors, organic nitrates or organic nitrites in any form either regularly or intermittently is therefore contraindicated.
- The co-administration of PDE5 inhibitors, including sildenafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension (see

section 4.5).

- Concomitant use of LIFANED with potent cytochrome P450 3A4 inhibitors e.g. ritonavir, erythromycin, saquinavir, ketoconazole and itraconazole is contraindicated.
- Medicines for the treatment of erectile dysfunction, including LIFANED, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure).
- LIFANED is contraindicated in patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure (see section 4.4).
- The use of LIFANED is contraindicated in patients with severe hepatic impairment and patients with severe impairment of renal function (creatinine clearance < 30 mL/min) not on haemodialysis or continuous ambulatory peritoneal dialysis.
- The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: hypotension (blood pressure < 90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases).

4.4 Special warnings and precautions for use

A thorough medical history and physical examination should be undertaken to diagnose erectile dysfunction, determine potential underlying causes, and identify appropriate treatment.

Cardiovascular risk factors

There is a potential for cardiac risk of sexual activity in patients with pre-existing cardiovascular disease. Therefore, treatment for erectile dysfunction, including LIFANED should not be generally used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status.

LIFANED has systemic vasodilatory properties that resulted in transient decreases in supine blood

pressure in healthy volunteers. Medical practitioners should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects, especially in combination with sexual activity. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g. aortic stenosis, hypertrophic obstructive cardiomyopathy), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure.

LIFANED potentiates the hypotensive effect of nitrates (see section 4.3).

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular dysrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of LIFANED. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of LIFANED without sexual activity. It is not possible to determine whether these events are related directly to these factors or to other factors.

Priapism

Medicines for the treatment of erectile dysfunction, including LIFANED, should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease), or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia).

Prolonged erections and priapism have been reported with sildenafil in post-marketing experience. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result.

Concomitant use with other PDE5 inhibitors or other treatments for erectile dysfunction

The safety and efficacy of combinations of sildenafil with other PDE5 inhibitors, or other pulmonary

arterial hypertension (PAH) treatments containing sildenafil, or other treatments for erectile dysfunction have not been studied. Therefore, the use of such combinations is not recommended.

Effects on vision

Cases of visual defects have been reported spontaneously in connection with the intake of sildenafil and other PDE5 inhibitors (see section 4.8).

A large-scale epidemiological study found evidence of an increased risk of retinal detachment with regular use of PDE5 inhibitors.

Cases of non-arteritic anterior ischaemic optic neuropathy, a rare condition, have been reported spontaneously and in an observational study in connection with the intake of sildenafil and other PDE5 inhibitors (see section 4.8). Patients should be advised that in the event of any sudden visual defect, they should stop taking LIFANED and consult a medical practitioner immediately (see section 4.3).

Concomitant use with ritonavir

Co-administration of LIFANED with ritonavir is contraindicated (see section 4.5).

Concomitant use with alpha-blockers

Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals (see section 4.5). This is most likely to occur within 4 hours post sildenafil dosing. In order to minimise the potential for developing postural hypotension, patients should be haemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25 mg should be considered (see section 4.2). In addition, medical practitioners should advise patients what to do in the event of postural hypotensive symptoms.

Effect on bleeding

Studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside *in vitro*. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore, LIFANED should be administered with caution to these patients.

Hearing loss

A sudden unilateral or bilateral decrease or loss of hearing (sensorineural deafness) with or without associated vestibular symptoms has been reported with the use of PDE5 inhibitors, including LIFANED. There is insufficient information regarding the reversibility of the hearing loss and the role of underlying risk factors for hearing loss in individual subjects.

Women

LIFANED is not indicated for use by women.

LIFANED contains lactose monohydrate

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take LIFANED.

4.5 Interaction with other medicines and other forms of interaction

Effects of other medicines on sildenafil

In vitro studies

The metabolism of sildenafil is principally mediated by the cytochrome P450 (CYP) isoforms 3A4 (major route) and 2C9 (minor route). Therefore, inhibitors of these isoenzymes may reduce sildenafil clearance and inducers of these isoenzymes may increase sildenafil clearance.

In vivo studies

Population pharmacokinetic analysis of clinical trial data indicated a reduction in sildenafil clearance

when co-administered with CYP3A4 inhibitors (such as ketoconazole, erythromycin, cimetidine). Although no increased incidence of adverse events was observed in these patients, when sildenafil is administered concomitantly with CYP3A4 inhibitors, a starting dose of 25 mg should be considered.

Co-administration of the human immunodeficiency virus (HIV) protease inhibitor ritonavir, which is a highly potent P450 inhibitor, at steady state (500 mg twice daily) with sildenafil (100 mg single dose) resulted in a 300 % (4-fold) increase in sildenafil C_{max} and a 1 000 % (11-fold) increase in sildenafil plasma AUC. At 24 hours, the plasma levels of sildenafil were still approximately 200 ng/mL, compared to approximately 5 ng/mL when sildenafil was administered alone. This is consistent with ritonavir's marked effects on a broad range of P450 substrates. Sildenafil has no effect on ritonavir pharmacokinetics. Based on these pharmacokinetic results co-administration of sildenafil with ritonavir is contraindicated (see section 4.3).

Co-administration of the HIV protease inhibitor saquinavir, a CYP3A4 inhibitor, at steady state (1 200 mg three times a day) with sildenafil (100 mg single dose) resulted in a 140 % increase in sildenafil C_{max} and a 210 % increase in sildenafil AUC. Sildenafil had no effect on saquinavir pharmacokinetics (see section 4.2). Stronger CYP3A4 inhibitors such as ketoconazole and itraconazole would be expected to have greater effects.

When a single 100 mg dose of sildenafil was administered with erythromycin, a moderate CYP3A4 inhibitor, at steady state (500 mg twice daily for 5 days), there was a 182 % increase in sildenafil systemic exposure (AUC).

In normal health male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC, C_{max}, t_{max}, elimination rate constant, or subsequent half-life of sildenafil or its principal circulating metabolite.

Cimetidine (800 mg), a cytochrome P450 inhibitor and non-specific CYP3A4 inhibitor, causes a 56 % increase in plasma sildenafil concentrations when co-administered with sildenafil (50 mg) to healthy volunteers.

Grapefruit juice is a weak inhibitor of CYP3A4 gut wall metabolism and may give rise to modest increases in plasma levels of sildenafil.

Single doses of antacid (magnesium hydroxide/aluminium hydroxide) did not affect the bioavailability of sildenafil.

Although specific interaction studies were not conducted for all medicines, population pharmacokinetic analysis showed no effect of concomitant treatment on sildenafil pharmacokinetics when grouped as CYP2C9 inhibitors (such as tolbutamide, warfarin, phenytoin), CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants), thiazide and related diuretics, loop and potassium sparing diuretics, angiotensin converting enzyme inhibitors, calcium channel blockers, beta-adrenoreceptor antagonists or inducers of CYP450 metabolism (such as rifampicin, barbiturates).

In a study in healthy male volunteers, co-administration of the endothelin antagonist, bosentan, (an inducer of CYP3A4 [moderate], CYP2C9 and possibly of CYP2C19) at steady state (125 mg twice a day) with sildenafil at steady state (80 mg three times a day) resulted in 62,6 % and 55,4 % decrease in sildenafil AUC and C_{max}, respectively. Therefore, concomitant administration of strong CYP3A4 inducers, such as rifampicin, is expected to cause greater decreases in plasma concentrations of sildenafil.

Nicorandil is a hybrid of potassium channel activator and nitrate. Due to the nitrate component, it has the potential to result in a serious interaction with sildenafil.

Effects of sildenafil on other medicines

In vitro studies

Sildenafil is a weak inhibitor of the cytochrome P450 isoforms 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 (IC50 > 150 µM). Given sildenafil peak plasma concentrations of approximately 1 µM after recommended doses, it is unlikely that LIFANED will alter the clearance of substrates of these isoenzymes. There are no data on the interaction of sildenafil and non-specific phosphodiesterase inhibitors such as theophylline or dipyridamole.

In vivo studies

Consistent with its known effects on the nitric oxide/cGMP pathway (see section 5.1), sildenafil was shown to potentiate the hypotensive effects of nitrates and its co-administration with nitric oxide donors or organic nitrates in any form is therefore contraindicated (see section 4.3).

Riociguat: Preclinical studies showed additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. In clinical studies, riociguat has been shown to augment the hypotensive effects of PDE5 inhibitors. There was no evidence of favourable clinical effect of the combination in the population studied. Concomitant use of riociguat with PDE5 inhibitors, including sildenafil, is contraindicated (see section 4.3).

Concomitant administration of sildenafil to patients taking alpha-blocker therapy may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing (see section 4.4). In three specific interaction studies, the alpha-blocker doxazosin (4 mg and 8 mg) and sildenafil (25 mg, 50 mg, or 100 mg) were administered simultaneously to patients with benign prostatic hyperplasia (BPH) stabilised on doxazosin therapy. In these study populations, mean additional reductions of supine blood pressure of 7/7 mmHg, 9/5 mmHg, and 8/4 mmHg, and mean additional reductions of standing blood pressure of 6/6 mmHg, 11/4 mmHg, and 4/5 mmHg, respectively, were observed. When sildenafil and doxazosin were administered simultaneously to patients stabilised on doxazosin therapy, there were

less frequent reports of patients who experienced symptomatic postural hypotension. These reports included dizziness and light-headedness, but not syncope.

No significant interactions were shown when sildenafil (50 mg) was co-administered with tolbutamide (250 mg) or warfarin (40 mg), both of which are metabolised by CYP2C9.

Sildenafil (50 mg) does not potentiate the increase in bleeding time caused by aspirin (150 mg).

Sildenafil (50 mg) does not potentiate the hypotensive effects of alcohol in healthy volunteers with mean maximum blood alcohol levels of 80 mg/dL.

Pooling of the following classes of antihypertensive medication; diuretics, beta-blockers, ACE inhibitors, angiotensin II antagonists, antihypertensive medicines (vasodilator and centrally-acting), adrenergic neurone blockers, calcium channel blockers and alpha-adrenoceptor blockers, showed no difference in the side effect profile in patients taking sildenafil compared to placebo treatment.

In a specific interaction study, where sildenafil (100 mg) was co-administered with amlodipine in hypertensive patients, there was an additional reduction on supine systolic blood pressure of 8 mmHg. The corresponding additional reduction in supine diastolic blood pressure was 7 mmHg. These additional blood pressure reductions were of a similar magnitude to those seen when sildenafil was administered alone to healthy volunteers.

Sildenafil (100 mg) did not affect the steady state pharmacokinetics of the HIV protease inhibitors, saquinavir and ritonavir, both of which are CYP3A4 substrates.

In healthy male volunteers, sildenafil at steady state (80 mg three times a day) resulted in a 49,8 % increase in bosentan AUC and a 42 % increase in bosentan C_{max} (125 mg twice a day).

4.6 Fertility, pregnancy and lactation

LIFANED is not indicated for use by women.

There are no adequate and well-controlled studies in pregnant or breastfeeding women.

No relevant adverse effects were found in reproduction studies in rats and rabbits following oral administration of sildenafil.

There was no effect on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers.

4.7 Effects on ability to drive and use machines

LIFANED may have a minor influence on the ability to drive and use machines. As dizziness and altered vision were reported in clinical trials with sildenafil, patients should be aware of how they react to LIFANED, before driving or operating machinery.

4.8 Undesirable effects

MedDRA system organ class	Frequency	Adverse reactions
Infections and infestations	Less frequent	Rhinitis
Immune system disorders	Less frequent	Hypersensitivity
Nervous system disorders	Frequent	Headache, dizziness
	Less frequent	Somnolence, hypoaesthesia, cerebrovascular accident, transient ischaemic attack, syncope
	Frequency unknown	Seizure, seizure recurrence
Eye disorders	Frequent	Visual colour distortions, visual disturbance, blurred vision
	Less frequent	Lacrimation disorders, eye pain, photophobia, photopsia, ocular

MedDRA system organ class	Frequency	Adverse reactions
		hyperaemia, visual brightness, conjunctivitis, retinal haemorrhage, arteriosclerotic retinopathy, retinal disorder, glaucoma, visual field defect, diplopia, visual acuity reduced, myopia, asthenopia, vitreous floaters, iris disorde mydriasis, halo vision, eye oedema, eye swelling, eye disorder, conjunctival hyperaemia, eye irritation, abnormal sensation in eye, eyelid oedema, scleral discolouration
	Frequency unknown	Non-arteritic anterior ischaemic optic neuropathy (NAION), retinal vascular occlusion
Ear and labyrinth disorders	Less frequent	Vertigo, tinnitus, deafness
Cardiac disorders	Less frequent	Tachycardia, palpitations, myocardial infarction, atrial fibrillation, unstable angi
	Frequency unknown	Sudden cardiac death, ventricular dysrhythmia
Vascular disorders	Frequent	Flushing, hot flush
	Less frequent	Hypertension, hypotension
Respiratory, thoracic and mediastinal disorders	Frequent	Nasal congestion
	Less frequent	Epistaxis, sinus congestion, throat tightness, nasal oedema, nasal dryness
Gastrointestinal disorders	Frequent	Nausea, dyspepsia
	Less frequent	Gastroesophageal reflux disease,

MedDRA system organ class	Frequency	Adverse reactions
		vomiting, abdominal pain upper, dry mouth, oral hypoaesthesia
Skin and subcutaneous tissue disorders	Less frequent	Rash
	Frequency unknown	Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)
Musculoskeletal and connective tissu disorders	Less frequent	Myalgia, pain in extremity
Renal and urinary disorders	Less frequent	Haematuria
Reproductive system and breast disorders	Less frequent	Penile haemorrhage, haematospermia, increased erection
	Frequency unknown	Priapism
General disorders and administration site conditions	Less frequent	Chest pain, fatigue, feeling hot, irritability
Investigations	Less frequent	Increased heart rate

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of LIFANED is important. It allows continued monitoring of the benefit/risk balance of LIFANED. Health care providers are requested 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's website.

4.9 Overdose

In single dose volunteer studies of doses up to 800 mg, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200 mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing, dizziness, dyspepsia, nasal congestion, altered vision) was increased. In cases of overdose, supportive

measures should be adopted as required. Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 7.1.5 Vasodilators – peripheral

Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction

ATC code: G04B E03

Mechanism of action

Sildenafil restores impaired erectile function by increasing blood flow to the penis, in response to sexual stimulation.

Sildenafil is a selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) which is responsible for degradation of cGMP in the corpus cavernosum. Sildenafil has no direct relaxant effect on isolated human corpus cavernosum but enhances the relaxant effect of NO on this tissue. When the NO/cGMP pathway is activated, during sexual stimulation, inhibition of PDE5 by sildenafil results in increased corpus cavernosum levels of cGMP, producing smooth muscle relaxation in the corpus cavernosum allowing the inflow of blood.

5.2 Pharmacokinetic properties

Absorption

Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 – 120 minutes (median 60 minutes) of oral dosing in the fasted state. The mean absolute oral bioavailability is approximately 40 % (range 25 – 63 %). The oral pharmacokinetics of sildenafil is proportional over the recommended dose range (25 – 100 mg). When sildenafil is taken with a high fat meal, the rate of absorption is reduced with a mean delay in T_{max} of 60 minutes and a mean reduction in C_{max} of 29 %.

Distribution

The mean steady state volume of distribution (Vss) for sildenafil is 105 L, indicating distribution into the tissues. Sildenafil and its major circulating N-desmethyl metabolite are both approximately 96 % bound to plasma proteins. Protein binding is independent of total drug concentrations. In healthy volunteers receiving sildenafil (100 mg single dose), less than 0,0002 % (average 188 ng) of the administered dose was present in ejaculate 90 minutes after dosing.

Biotransformation

Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes. The major circulating metabolite results from *N*-demethylation of sildenafil. This metabolite has a PDE selectivity profile similar to sildenafil and an *in vitro* potency for PDE5 approximately 50 % that of the parent compound. Plasma concentrations of this metabolite are approximately 40 % of those seen for sildenafil. The *N*-desmethyl metabolite is further metabolised, with a terminal half-life of approximately 4 hours.

Elimination

The total body clearance of sildenafil is 41 L/h with a resultant terminal phase half-life of 3 – 5 hours. After either oral or intravenous administration, sildenafil is excreted as metabolites predominantly in the faeces (approximately 80 % of administered oral dose) and to a lesser extent in the urine (approximately 13 % of administered oral dose).

Special populations

Elderly

Healthy elderly volunteers (65 years or over) had a reduced clearance of sildenafil, with free plasma concentrations approximately 40 % greater than those seen in healthy younger volunteers (18 – 45 years).

Renal insufficiency

In volunteers with mild (creatinine clearance (CLcr) = 50 – 80 mL/min) to moderate (CLcr = 30 – 49 mL/min) renal impairment, the pharmacokinetics of a single oral dose of sildenafil (50 mg) were not altered. In volunteers with severe (CLcr ≤ 30 mL/min) renal impairment, sildenafil clearance was reduced, resulting in mean increases in AUC (100 %) and C_{max} (88 %) compared to age-matched volunteers with no renal impairment.

Hepatic insufficiency

In volunteers with hepatic cirrhosis (Child-Pugh A and B) sildenafil clearance was reduced, resulting in increases in AUC (84 %) and C_{max} (47 %) compared to age-matched volunteers with no hepatic impairment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet:

Colloidal silica, anhydrous

Lactose monohydrate

Magnesium stearate (E572)

Maize starch

Povidone

Sodium starch glycolate

Film-coating:

Hypromellose (E464)

Macrogol 400

Opadry 06B50566 blue:

FD&C Blue indigo carmine (colourant) (E132)

Hypromellose (E464)

Macrogol 400

Sodium laurilsulfate

Titanium dioxide (E171)

Opadry OY-S-29019:

Hypromellose (E464)

Macrogol 6 000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30 °C.

Protect from moisture.

Keep the blister strips in the outer carton until required for use.

6.5 Nature and contents of container

Clear PVC/Aluminium blister strips placed in an outer carton.

Pack size: 2, 4, 8 or 12 tablets.

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

Unichem SA (Pty) Ltd

San Domenico

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8. REGISTRATION NUMBERS

LIFANED 25: 50/7.1.5/0061

LIFANED 50: 50/7.1.5/0062

LIFANED 100: 50/7.1.5/0063

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 February 2022

10. DATE OF REVISION OF THE TEXT

06 December 2024