NOVARTIS

LAMPRENE® (clofazimine)

50 and 100 mg capsules

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1. NAME OF THE MEDICINE

LAMPRENE® 50 mg Soft Gelatin Capsules

LAMPRENE® 100 mg Soft Gelatin Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

LAMPRENE 50 mg Soft Gelatin Capsules: Each capsule contains 50 mg clofazimine present as a microcrystalline suspension in an oil-wax base.

LAMPRENE 100 mg Soft Gelatin Capsules: Each capsule contains 100 mg micronised clofazimine suspended in an oil-wax base.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

LAMPRENE 50 mg soft gelatin capsule: Spherical, brown, opaque soft gelatin capsules with no imprint on the capsules. Diameter approximately 7,2 mm.

LAMPRENE 100 mg soft gelatin capsule: Brown, opaque, oblong, soft gelatin capsules. One side carries the imprint “GEIGY”, the other side carries imprint “GM” in white. Diameter approximately 6,5 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Leprosy:

LAMPRENE 50/100 mg soft gelatin capsules, used only in combination with rifampicin and dapsone, is indicated as treatment for multibacillary (MB) forms of leprosy, including erythema nodosum leprosum (ENL).

Multidrug therapy (MDT) is necessary in order to prevent the emergence of resistant strains of *Mycobacterium leprae*.

Multidrug-resistant Tuberculosis (MDR-TB):

LAMPRENE 50/100 mg soft gelatin capsules is indicated for the treatment of pulmonary multidrug-resistant tuberculosis, MDR-TB in adults and children 10 years and older, including rifampicin resistant tuberculosis (RR-TB).

4.2 Posology and method of administration

Multibacillary leprosy:

LAMPRENE is administered as part of a multidrug therapy, in combination with dapsone and rifampicin for the treatment of multibacillary leprosy. Multidrug therapy (MDT) is necessary in order to prevent the emergence of resistant strains of *Mycobacterium leprae*.
For the treatment of leprosy, the WHO recommends the following regimens:

Table 1- MDT dosage

	Dapsone	**Rifampicin**	**LAMPRENE (clofazimine)**
Adults and adolescents (15 years and above)	Days 1-28 100 mg once daily as self-medication	Day 1 only of each cycle* 600 mg under supervision	Day 1 only of each cycle* 300 mg under supervision and Days 2-28 50 mg once daily as self-medication
Children (10 to 14 years)	Days 1-28 50 mg once daily as self-medication	Day 1 only of each cycle* 450 mg under supervision	Day 1 only of each cycle* 150 mg under supervision and Days 2-28 50 mg on alternate days (i.e. day 3, 5, 7, …) as self-medication

This triple combination should be administered for 12 months (i.e.*12 consecutive 28-day treatment cycles). An additional 12 months of this triple combination may be necessary for

MB patients showing evidence of relapse.

Children below 10 years: The dose should be adjusted according to body weight: 1 to 2 mg/kg clofazimine + 10 to 20 mg/kg rifampicin + 1 to 2 mg/kg dapsone. As an example, LAMPRENE (clofazimine) 100 mg soft gelatin capsule once a month under supervision + 50 mg twice a week as self-medication + rifampicin 300 mg once a month under supervision + dapsone 25 mg once a day as self-medication.

Treatment of children below 10 years of age is possible only if dapsone tablets of 25 mg are commercially available.

Patients with erythema nodosum leprosum (ENL)

Adults and children: If the patient develops erythema nodosum leprosum, treatment with dapsone and rifampicin should be continued as before, and the dosage of LAMPRENE 50/100 mg soft gelatin capsules should be raised to 200 to 300 mg per day, given under medical supervision. These high daily doses must not be given for longer than 3 months (see section 4.4 Special warnings and precautions for use). The dose of LAMPRENE 50/100 mg soft gelatin capsules should be gradually reduced, first to 100 mg twice daily for 12 weeks and then to 100 mg once daily for a further 12 to 24 weeks.

Multidrug-resistant tuberculosis (MDR-TB)

Dosage:

For the treatment of pulmonary MDR-TB:

Adults and adolescents:

- For adults weighing at least 30 kg, the recommended dosage is 100 mg/day.
- For adults weighing less than 30 kg, the recommended dosage is 50 mg/day.

Children (10 years of age and over):

- For children weighing at least 30 kg, the recommended dosage is 2-5 mg/kg/day, not exceeding 100 mg/day.
- For children weighing less than 30 kg, the recommended dosage is 2-5 mg/kg/day, not exceeding 50 mg/day. If a dose lower than 50 mg/day is required, the 50 mg dose can be given every other day.

Dosing in special populations

Safety and efficacy have not been established in HIV infected patients on antiretroviral therapy.

Renal impairment

There are no data available in patients with renal impairment.

Caution is advised when administered to patients with renal impairment.

Hepatic impairment

There are no data available in patients with hepatic impairment. LAMPRENE 50/100 mg soft gelatin capsules should not be administered to patients with hepatic impairment (see section 4.4 Special warnings and precautions for use and section 5 Pharmacological properties).

No dosing recommendations can be made in the following groups of patients as efficacy and safety have not been established:

- Patients co-infected with HIV and treated for HIV infection
- Patients with hepatic impairment
- Women who are pregnant
- Patients co-infected with hepatitis B and/ or C

Method of administration

LAMPRENE 50/100 mg soft gelatin capsules should be taken with a meal or with a glass of milk to ensure maximum absorption.

4.3 Contraindications

- Known hypersensitivity to clofazimine or to any of the excipients of LAMPRENE 50/100 mg soft gelatin capsules.
- Patients with acquired or congenital QT interval prolongation including Torsades de Pointes (see Warning and Special Precautions).
- Concomitant use with medicines known to prolong QTc interval up to the time intervals known to induce serious dysrhythmias.

4.4 Special warnings and precautions for use

- Efficacy and safety have not been investigated in children, pregnancy, patients with impaired liver function, and not established in patients co-infected with HIV and treated for HIV infection, hepatitis B and/ or C.
- QTc interval prolongation may occur with LAMPRENE 50/100 mg soft gelatin capsules administration, which is likely to be augmented by co-administration of other medicines known to cause QTc prolongation (see section 4.3 Contraindications).

Patient adherence

LAMPRENE 50/100 mg soft gelatin capsules should never be used as monotherapy for the treatment of leprosy or MDR-TB. LAMPRENE 50/100 mg soft gelatin capsules must be used in combination with other medicines (see section 4.2 Posology and method of administration).

Patients should be informed of the importance of adherence with the prescribed treatment regimen in order to prevent medicine resistance. Irregularity in administration of medication and poor adherence can lead to delayed and failed treatment, rendering the patient a source of contamination.

Patients should be trained to recognise the signs and symptoms of reactions and relapses following completion of treatment and should be made aware of the importance of immediately reporting the earliest manifestations of these signs to the relevant healthcare professional.

Lepra reactions

It is recommended to not interrupt MDT during lepra reactions. See section 4.2 Posology and method of administration, for LAMPRENE 50/100 mg soft gelatin capsules dosing in patients who develop ENL (erythema nodosum leprosum) reactions. Some data indicate a trend towards reduction in the frequency and severity of ENL in leprosy patients treated with MDT. This trend may be attributed to the anti-inflammatory properties of LAMPRENE 50/100 mg soft gelatin capsules. Nevertheless, temporary, unexplained increases in the reporting of reversal reactions have also been observed in leprosy patients, usually during the first year of treatment with MDT.

Lepra reactions usually respond satisfactorily to standard anti-inflammatory therapy.

Accumulation of clofazimine

The deposition of large amounts of clofazimine in the intestinal mucosa causes irritation, leading to gastrointestinal disturbances (e.g. abdominal pain (sometimes intermittent), nausea, vomiting and diarrhoea), sometimes with more severe clinical manifestations such as gastrointestinal haemorrhage and intestinal obstruction. Clofazimine has heterogeneous distribution throughout the body and a slow elimination rate, accumulating mainly in fatty tissue, the reticuloendothelial system (macrophages, histiocytes and spleen), and the skin. Adverse reactions to clofazimine are mainly linked to its uptake by tissue and organs. Because of this, the use of high doses for long periods should be avoided. After prolonged administration in high doses, clofazimine may accumulate in various organs, body fluids and tissues as crystals. Among the viscera, the jejunum has the highest drug deposition, closely followed by the spleen. If crystals are deposited in the mesenteric lymph nodes and/or histiocytes at the lamina propria of the jejunal mucosa, this may lead to intestinal obstruction. Fatalities have been reported following gastrointestinal side effects. If gastrointestinal symptoms develop during treatment, the dosage should be reduced or the interval between doses prolonged.

Symptoms may slowly regress on withdrawal of LAMPRENE 50/100 mg soft gelatin capsules.

In the event of persistent diarrhoea or vomiting, the patient should be hospitalised.

Skin discolouration

Medical practitioners should be aware that skin discolouration due to LAMPRENE 50/100 mg soft gelatin capsules may result in depression (cases of depression with suicide have been reported).

Patients should be warned that LAMPRENE 50/100 mg soft gelatin capsules may cause discolouration of the conjunctiva, lacrimal fluid, sweat, sputum, urine, faeces, nasal secretions, semen and breast milk, and reddish to brownish-black discolouration of the skin. Patients should be told that discolouration of the skin may take several months or years to disappear after the end of therapy with LAMPRENE 50/100 mg soft gelatin capsules.

Torsades de Pointes and QT prolongation

Cases of Torsades de Pointes with QT prolongation have been reported in patients receiving LAMPRENE 50/100 mg soft gelatin capsules mostly at doses higher than usually recommended or in combination with other QT-prolonging medicines (such as bedaquiline, fluoroquinolones, delamanid, rilpivirine, lopinavir, atazanavir, nelfinavir, saquinavir). Concomitant administration with other medicines known to prolong QTc interval up to the time intervals known to induce serious dysrhythmias is contraindicated (see section 4.3 Contraindications and section 4.5 Interaction with other medicines and other forms of interaction). LAMPRENE 50/100 mg soft gelatin capsules should be discontinued if the QTc prolongation exceeds 500 milliseconds (ms) and/or the Qtc prolongation exceeds 60 milliseconds (ms) from baseline or if the patient develops dysrhythmias. Patients receiving LAMPRENE 50/100 mg soft gelatin capsules at recommended doses and/or doses higher than usually recommended and/or in combination with QT-prolonging medicines, should have regular clinical

monitoring at baseline and regular ECGs performed to monitor for QT prolongation and cardiac dysrhythmias.

Paradoxical reactions:

Some patients may experience paradoxical reactions during treatment with anti-tuberculosis drugs, manifesting as the worsening of TB symptoms or the appearance of new symptoms. Monitor for these reactions and manage appropriately.

Interactions

As clofazimine is predicted to be a moderate to strong inhibitor of CYP3A (CYP3A4 and CYP3A5) substrates, caution should be exercised while co-administering LAMPRENE 50/100 mg soft gelatin capsules with other medicines which are CYP3A substrates (see section 4.5 Interaction with other medicines and other forms of interaction).

4.5 Interaction with other medicines and other forms of interaction

Dapsone

LAMPRENE appears to have no important effects on the pharmacokinetics of dapsone, although a transient increase in the urinary excretion of dapsone occurred in a few patients. Limited data suggesting that dapsone inhibits the anti-inflammatory activity of LAMPRENE 50/100 mg soft gelatin capsules have not been confirmed. If leprosy-associated inflammatory reactions develop in patients being treated with dapsone and LAMPRENE 50/100 mg soft gelatin capsules, it is still advisable to continue treatment with both medicines.

Rifampicin

LAMPRENE reduces rifampicin absorption in leprosy patients, increasing the time it takes

for the peak serum concentration to be reached and prolonging the elimination half-life. Total exposure (AUC) of rifampicin was not affected, so this interaction is unlikely to be clinically significant.

Isoniazid

In volunteers receiving clofazimine (150 mg daily) and standard doses of isoniazid (300 mg daily), elevated concentrations of LAMPRENE 50/100 mg soft gelatin capsules were detected in plasma and urine, compared to clofazimine alone.

Interaction with QT prolonging medicines

Cases of Torsades de Pointes with QT prolongation have been reported in patients receiving LAMPRENE 50/100 mg soft gelatin capsules in combination with QT prolonging medicines. Caution is recommended when clofazimine is administered with other medicines (e.g: bedaquiline, fluoroquinolones, delamanid, azithromycin, rilpivirine, lopinavir, atazanavir, nelfinavir, saquinavir) with known QT interval prolonging potential (see section 4.3 Contraindications, section 4.4 Special warnings and precautions for use).

Effects of LAMPRENE 50/100 mg soft gelatin capsules on CYP3A (CYP3A4 and CYP3A5) substrates:

As LAMPRENE 50/100 mg soft gelatin capsules is predicted to be a moderate to strong inhibitor of CYP3A (CYP3A4 and CYP3A5) substrates, caution should be exercised while co-administering LAMPRENE 50/100 mg soft gelatin capsules with other medicines which are CYP3A substrates.

No clinical interaction studies have been performed with other CYP3A

substrates. Clofazimine inhibits the CYP3A enzyme *in vitro*. Based on Physiologically Based Pharmacokinetic Modelling (PBPK) modeling results, clofazimine is predicted to be a moderate to strong CYP3A inhibitor.

Hence, caution should be exercised with the concomitant administration of LAMPRENE 50/100 mg soft gelatin capsules and CYP3A substrates (e.g.: anti-mycobacterial medicines (bedaquiline, delamanid, clarithromycin), selected unboosted anti-retrovirals (amprenavir, delaviridine, efavirenz, etravirine, indinavir, nelfinavir, raltegravir, rilpivirine, simeprevir, maraviroc), anti-hyperlipidaemic medicines and anti-hypertension medicines (simvastatin, lovastatin, losartan, verapamil, diltiazem, nitrendipine, amlodipine, nislodipine, nifedipine, eplerenone, felodipine, lercanidipine), anti-diabetics (pioglitazone, repaglinide, saxagliptin)).

Effects of other medicines on LAMPRENE 50/100 mg soft gelatin capsules:

In a healthy volunteer study of a combination regimen including clofazimine, cycloserine, ethionamide, para-aminosalicyclic acid, and pyridoxine, the C_{max} and T_{max} values of clofazimine were similar to those reported in other studies where clofazimine was administered alone, suggesting no major effects of these medicines on the pharmacokinetics of clofazimine. In patients with pulmonary TB, where clofazimine was dosed alone and in combination with bedaquiline, pyrazinamide and pretomanid, the C_{max} and AUC values of clofazimine were similar between the groups suggesting no major effects of these medicines on the pharmacokinetics of clofazimine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety of clofazimine in pregnancy has not been established and experience with

LAMPRENE 50/100 mg soft gelatin capsules in pregnancy is limited. Clofazimine crosses the placenta and harm to the foetus cannot be excluded. Skin discolouration has been observed in newborn babies exposed to clofazimine in utero. Use of LAMPRENE 50/100 mg soft gelatin capsules in pregnancy can be considered in patients with limited treatment options. Appropriate counselling of pregnant woman and her partner should be done.

Animal studies revealed no evidence of teratogenicity but adverse effects in the foetus were observed at high doses. In the mouse, there were signs of foetotoxicity (e.g. retardation of foetal skull ossification at high doses).

Breastfeeding:

Safety of clofazimine in lactation has not been established.

Clofazimine passes into the breast milk, and skin discolouration may occur in the infant. Women using LAMPRENE 50/100 mg soft gelatin capsules should not breastfeed their infants.

Fertility

There was evidence of impaired fertility in one study in female rats receiving clofazimine 50 mg/kg/day.

The effect of clofazimine on fertility in humans is unknown.

4.7 Effects on ability to drive and use machines

Dizziness, reduced visual acuity, nausea, fatigue and headache have been reported on LAMPRENE 50/100 mg soft gelatin capsules therapy. Patients experiencing such adverse reactions should not drive a vehicle or operate machines.

4.8 Undesirable effects

Summary of the safety profile

The safety profile of LAMPRENE 50/100 mg soft gelatin capsules is similar when used in leprosy and DR-TB.

Tabulated summary of side effects

Side effects are listed in Table 2. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first.

Table 2: Summary of side effects

Blood and lymphatic system disorders	
Less frequent:	Lymphadenopathy, splenic infarction, anaemia
Cardiac disorders	
Less frequent:	QT prolongation, cardiac dysrhythmias including Torsade de Pointes
Psychiatric disorders	
Less frequent:	Depression
Nervous system disorders	
Less frequent:	Headache, dizziness
Eye disorders	
Frequent:	Conjunctival discolouration, corneal pigmentation, tear discolouration, visual acuity reduced, dry eye, eye irritation

Less frequent:	Maculopathy, corneal deposits
Respiratory, thoracic and mediastinal disorders	
Frequent:	Sputum discoloured
Gastrointestinal disorders	
Frequent:	Nausea, vomiting, abdominal pain, diarrhoea, faeces discoloured
Less Frequent:	Gastroenteritis eosinophilic, decreased appetite, intestinal obstruction, gastrointestinal haemorrhage, abdominal discomfort, abdominal pain upper, constipation
Hepatobiliary disorders	
Less Frequent:	Hepatitis, blood bilirubin increased, jaundice, aspartate aminotransferase increased
Skin and subcutaneous tissue disorders	
Frequent:	Sweat discolouration, skin discolouration, hair colour changes, ichthyosis, dry skin, rash, pruritus
Less Frequent:	Photosensitivity reaction, dermatitis acneiform, dermatitis exfoliative
Renal and urinary disorders	
Frequent:	Chromaturia
General disorders and administration site conditions	
Less Frequent:	Fatigue, pyrexia
Investigations	
Frequent:	Weight decreased
Less Frequent:	Blood sugar increased

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Please refer to the Torsades de Pointes and QT prolongation subsection in the Special warnings and precautions for use section.

No specific data are available on the treatment of overdose with LAMPRENE 50/100 mg soft gelatin capsules. In cases of acute overdosage, symptomatic and supportive treatment may be given as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group, ATC: Drugs for the treatment of lepra, *J04BA01*.

Clofazimine is thought to exert its anti-mycobacterial effect through multiple mechanisms. The primary mechanism of action for the antimicrobial activity of clofazimine can be postulated through its membrane-directed activity, including the bacterial respiratory chain and ion transporters. Intracellular redox cycling, involving oxidation of reduced clofazimine, leads to the generation of antimycobacterial reactive oxygen species (ROS), superoxide-hydrogen peroxide (H_2O_2).

Secondly, interaction of clofazimine with membrane phospholipids results in the generation of antimycobacterial lysophospholipids, which promote membrane dysfunction, resulting in interference with K^+ uptake. Both mechanisms result in interference with cellular energy metabolism by disrupting ATP production.

The third proposed mechanism of action is binding preferentially to mycobacterial deoxyribonucleic acid (DNA) with particular affinity to guanine bases and inhibiting mycobacterial replication and growth.

Clofazimine also displays an anti-inflammatory effect, which may contribute to the effect of clofazimine in controlling erythema nodosum leprosum (ENL) reactions.

Anti-inflammatory activity of clofazimine is primarily through inhibition of T lymphocyte activation and proliferation. Clofazimine may indirectly interfere with the proliferation of T cells by promoting the release of ROS and E-series prostaglandins (PGs), especially PGE2 from neutrophils and monocytes.

Clofazimine may also exert anti-mycobacterial activity by its effect on tissue macrophages. Clofazimine has a tendency to concentrate selectively in cells of the reticuloendothelial system.
Clofazimine has shown apoptosis inducing properties in activated macrophages. Clofazimine has been shown to inhibit MtSerB2, a phosphatase produced by M. tuberculosis that is believed to help the pathogen to evade the host's immune response.

Leprosy:

Clofazimine exerts a mycobacteriostatic and weakly mycobactericidal effect on Mycobacterium leprae.

Clofazimine appears to bind preferentially to mycobacterial DNA and inhibit mycobacterial replication and growth.

The minimum inhibitory concentration of clofazimine for M. leprae in mouse tissue has been estimated at between 0.1 and 1 microgram per gram; uneven tissue distribution precludes a more accurate estimate. The onset of antimicrobial activity of clofazamine is slow, and can only be demonstrated after about 50 days of therapy.

No cross-resistance occurs with dapsone and rifampicin, probably because clofazimine has a different mode of action. M. leprae resistant to clofazimine have been reported in isolated cases.

Multidrug-Resistant Tuberculosis (MDR-TB)

The MIC of clofazimine against drug susceptible as well as single drug-resistant, multidrug-resistant and extensively drug resistant TB strains ranges from < 0.0625 µg/mL to > 1 µg/mL. The majority [84.7 % (95 % CI: 69.5 %, 93.1 %)] of the tested strains have a reported MIC value of ≤ 0.5 µg/mL for clofazimine.

Clofazimine does not show cross-resistance with isoniazid or rifampin. In vitro resistance to clofazimine in mycobacterium tuberculosis has been mapped to mutations in the transcriptional regulator Rv0678 which results in the upregulation of MmpS5-MmpL5, an efflux pump. These mutants show cross-resistance to bedaquiline. Two additional mutations

(Rv1979c and Rv2535c) have also been associated with clofazimine resistance in vitro; however, the mechanism and clinical relevance of these mutations is yet to be determined.

5.2 Pharmacokinetic Properties

Absorption

Clofazimine is absorbed slowly. Bioavailability of the micronised suspension in an oil-wax base is up to 70 % after a 100 mg dose and decreases with higher doses.
The time to reach peak plasma concentration (median time) of clofazimine decreases from 12 to 8 hours under fed conditions relative to the fasted state. Administration of the medicine with food increases its bioavailability in terms of AUC (area under the concentration-time curve) by about 60 %, and tends to accelerate the absorption rate.

After administration of a single oral dose of 200 mg clofazimine with a morning meal, mean (± SD) peak plasma concentrations of 0.41 (± 0.14) micrograms per mL
(861 (± 289) pmol/g) were measured in healthy volunteers. When clofazimine is taken on an empty stomach, the peak plasma concentration was approximately 20 % lower.

After repeated administration of clofazimine to leprosy patients in daily doses of 50 mg and 100 mg, mean trough concentrations of 0.27 and 0.43 micrograms / mL (580 pmol/g and 910 pmol/g), respectively, were measured after 42 consecutive days when concentrations were still increasing. The time to achieve steady state concentration has not been studied. From modelling studies, steady state concentrations were not reached after 20 weeks of treatment. The accumulation ratios after 50 and 100 mg daily doses of clofazimine on day 42 were 9.88 and 11.61, respectively.

Distribution

Clofazimine is strongly lipophilic and accumulates chiefly in fatty tissue and in the macrophages of the reticuloendothelial system. After long-term treatment, clofazimine was detectable as crystals particularly in the following organs, tissues and body fluids: subcutaneous fat, mesenteric lymph nodes, bile, gall bladder, adrenals, spleen, small intestine, liver, muscle tissue, bones and skin. Clofazimine does not appear to cross the intact blood-brain barrier.

Clofazimine crosses the placenta and passes into breast milk in sufficient quantities to cause discolouration of the milk.
Clofazimine bound to the alpha- and beta-lipoproteins in serum, particularly the beta-lipoproteins, and the binding was saturable at approximately 10 microgram/mL (21141 pmol/g) concentrations. Binding to gamma-globulin and albumin was negligible.

Biotransformation/ Metabolism

Information on the metabolism of clofazimine is limited. Three metabolites, two of which are glucuronides, have been identified in urine.

Elimination

Clofazimine is eliminated very slowly from the plasma. The mean elimination half-life of unchanged substance following a single dose of 200 mg in healthy volunteers was 10.6 (± 4.0) days. After repeated administration of 50 mg and 100 mg daily to leprosy patients, the elimination half-life was about 25 days.

Unchanged clofazimine is excreted via the bile mainly in the faeces. Within 3 days on

average, 35 % of the dose is recovered in faeces. No more than 0.4 % of the dose is found in the urine as unchanged clofazimine after 24 hours. Urinary metabolites account for about 0.6 % of the daily dose. However, clofazimine could still be detected in faeces several months after discontinuation of treatment.

Special populations

No data is available on the effects of renal or hepatic dysfunction, or of age, on the pharmacokinetics of clofazimine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Capsule content:

Butylated hydroxytoluene;

Citric acid (anhydrous);

Propylene glycol;

Rapeseed oil (refined);

Lecithin (E322);

Beeswax (yellow);

Soybean oil (hydrogenated);

Soya-bean oils (partially hydrogenated)

Capsule shell:

Ethyl parahydroxybenzoate sodium;

Propyl parahydroxybenzoate sodium;

Ethyl vanillin;

Gelatin;

Glycerol 85 %;

Black iron oxide (E172);

Red iron oxide (E172);

P-methoxyacetophenone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

6.4 Special precautions for storage

Store at or below 25 °C and protect from moisture.

Keep out of the reach of children.

6.5 Nature and contents of container

LAMPRENE 50/100 mg soft gelatin capsules are either packaged in white to off-white high density polyethylene (HDPE) bottles with a HDPE screw cap with a yellow tamper proof ring, further packaged in paper board carton or can be packaged in low density polyethylene (LDPE) bags inserted in high density polyethylene (HDPE) bottle with a HDPE screw cap.

Kindly note that not all strengths may be marketed.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novartis South Africa (Pty) Ltd

Magwa Crescent West

Jukskei View

Waterfall City

Johannesburg

2090

Tel. (011) 347 6600

8. REGISTRATION NUMBERS

LAMPRENE 50 mg soft gelatin capsules: 53/20.2.4/0472

LAMPRENE 100 mg soft gelatin capsules: B/20.2.4/108

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 April 2018

10. DATE OF REVISION OF THE TEXT

22 August 2025

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