

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Terbinafine hydrochloride 1% w/w topical cream
Lamisil cream 1%

2. Qualitative and quantitative composition

Terbinafine hydrochloride 1% w/w

Excipients with known effect

Each gram of cream contains 40mg cetyl alcohol, 40mg stearyl alcohol and 10mg benzyl alcohol.
See section 4.4.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

White cream in a tube.

4. Clinical particulars

4.1 Therapeutic indications

Fungal infections of the skin caused by *Trichophyton* (eg. *T. Rubrum*, *T. Mentagrophytes*, *T. Verrucosum*, *T. Violaceum*), *Microsporium canis* and *Epidermophyton floccosum*.
Yeast infections of the skin, principally those caused by the genus *Candida* (eg. *C. albicans*).
Pityriasis (tinea) versicolor due to *Pityrosporum orbiculare* (also known as *Malassezia furfur*).

4.2 Posology and method of administration

Lamisil can be applied once or twice daily.

Duration and frequency of treatment

The likely duration of each treatment is as follows:

Tinea corporis, cruris:	1 to 2 weeks
Tinea pedis:	1 week
Cutaneous candidiasis:	2 weeks
Pityriasis versicolor:	2 weeks

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Dosing in special populations:

Paediatric population

The experience with topical Lamisil in children is still limited and its use cannot therefore be recommended.

Elderly patients

There is no evidence to suggest that elderly patients require different dosages or experience side-

effects different to those of younger patients.

Method of administration

For cutaneous use.

Cleanse and dry the affected areas thoroughly before application of Lamisil. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (submammary, interdigital, intergluteal, inguinal) the application may be covered with a gauze strip, especially at night.

4.3 Contraindications

Hypersensitivity to terbinafine or any of the excipients contained in the cream, listed in section 6.1.

4.4 Special warnings and precautions for use

Lamisil Cream is for external use only. Contact with the eyes should be avoided. May be irritating to the eyes. In case of accidental contact with the eyes, rinse the eyes thoroughly with running water.

Lamisil Cream contains 36 mg benzyl alcohol in each daily dosage which is equivalent to 10 mg/g. Benzyl alcohol may cause allergic reactions.

Lamisil Cream contains cetyl alcohol and stearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

There are no known drug interactions with Lamisil Cream.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no clinical experience with Lamisil Cream in pregnant women, therefore, unless the potential benefits outweigh any potential risks, Lamisil Cream should not be administered during pregnancy.

Foetal toxicity studies in animals suggest no adverse effects (see section 5.3).

Breastfeeding

Terbinafine is excreted in breast milk. Therefore mothers should not receive Lamisil whilst breast-feeding. Infants must not be allowed to come into contact with any treated skin, including the breast.

Fertility

No effect of terbinafine on fertility have been seen in animal studies.

4.7 Effects on ability to drive and use machines

Lamisil Cream has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Local symptoms such as pruritus, skin exfoliation, application site pain, application site irritation, pigmentation disorder, skin burning sensation, erythema and scab may occur at the site of application.

These minor symptoms must be distinguished from hypersensitivity reactions such as widespread pruritis, rash, bullous eruptions and hives which are reported in sporadic cases but require discontinuation.

In case of accidental contact with the eyes terbinafine hydrochloride may be irritating to the eyes. In rare cases, the underlying fungal infection may be aggravated.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: *very common* ($\geq 1/10$); *common* ($\geq 1/100$ to $< 1/10$); *uncommon* ($\geq 1/1,000$ to $< 1/100$); *rare* ($\geq 1/10,000$ to $< 1/1,000$); *very rare* ($< 1/10,000$), or *not known* (can not to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Immune system disorders

Not known: Hypersensitivity

Eye disorders

Rare: Eye irritation

Skin and subcutaneous tissue disorders

Common: Skin exfoliation, pruritus

Uncommon: Skin lesion, scab, skin disorder, pigmentation disorder, erythema, skin burning sensation

Rare: Dry skin, dermatitis contact, eczema

Not known: Rash

General disorders and administration site conditions

Uncommon: Pain, application site pain, irritation

Rare: condition aggravated

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 e-PV desktop applications

(https://drive.google.com/file/d/16hwTz0587ZWtSWadbBAMwQPOD_KSExZP/view) or search for e-PV Mobile applications on the Google Play or Apple App Store.

4.9 Overdose

The low systemic absorption of topical terbinafine cream renders overdosage extremely unlikely. Accidental ingestion of the contents of one 30g tube of Lamisil Cream, which contains 300mg terbinafine hydrochloride, is comparable to one Lamisil 250mg tablet (adult oral unit dose).

Should a larger amount of Lamisil Cream be inadvertently ingested, adverse effects similar to those observed with an overdosage of Lamisil tablets are to be expected. These include headache, nausea, epigastric pain and dizziness.

If accidentally ingested, the recommended treatment of overdosage consists of eliminating the drug, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy, if needed.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacological Classification: 14.1.1 Topical Antibiotics

Terbinafine is an allylamine which has a broad spectrum of antifungal activity. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity versus yeasts is fungicidal or fungistatic depending of the species.

Terbinafine interferes specifically with fungal sterol biosynthesis at an early step. This leads to a deficiency in ergosterol and to an intracellular accumulation of squalene, resulting in fungal cell death. Terbinafine acts by inhibition of squalene epoxidase in the fungal cell membrane. The enzyme squalene epoxidase is not linked to the cytochrome P450 system.

5.2 Pharmacokinetic properties

Less than 5% of the dose is absorbed after topical application to humans; systemic exposure is therefore very slight.

5.3 Preclinical safety data

In long-term studies (up to 1 year) in rats and dogs no marked toxic effects were seen in either species up to oral doses of about 100 mg/kg a day. At high oral doses, the liver and possibly also the kidneys were identified as potential target organs.

In a two-year oral carcinogenicity study in mice, no neoplastic or other abnormal findings attributable to treatment were made up to doses of 130 (males) and 156 (females) mg/kg a day. In a two-year oral carcinogenicity study in rats at the highest dose level, 69 mg/kg a day, an increased incidence of liver tumours was observed in males. The changes, which may be associated with peroxisome proliferation, have been shown to be species-specific since they were not seen in the carcinogenicity study in mice or in other studies in mice, dogs or monkeys.

During the studies of high dose oral terbinafine in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level was 50 mg/kg). These irregularities were associated with the presence of a terbinafine metabolite in ocular tissue and disappeared after drug discontinuation. They were not associated with histological changes.

A standard battery of in vitro and in vivo genotoxicity tests revealed no evidence of a mutagenic or clastogenic potential for the drug.

No adverse effects on fertility or other reproduction parameters were observed in studies in rats or rabbits.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium hydroxide

benzyl alcohol

sorbitan monostearate

cetyl palmitate

cetyl alcohol

stearyl alcohol

polysorbate 60
isopropyl myristate
demineralised water

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Aluminium tube with membrane, with an interior coating of phenol-epoxy based lacquer, closed with a polypropylene cap, or laminated tube (low density polyethylene, aluminium, low density polyethylene) with a high density polyethylene shoulder, sealed with an aluminium/ethylene multilayer copolymer peel-off and closed with a polypropylene cap with built-in point to pierce the peel off, containing 15g or 30g Lamisil Cream.

Polypropylene dispenser tube with polypropylene screw-cap closure containing 15 or 30g Lamisil cream.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Applicant

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8. Manufacturer

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9. Registration Details

Zimbabwe registration number: 96/14.1.1/3077

Zimbabwe Category for Distribution: Pharmacist Initiated Medicines, (P.I.M.)

10. Date of revision of the text

January 2024