Lamisil Cream 1%

Pharmaceutical form and active substance content per unit
Cream: 10 mg/g Terbinafine hydrochloride (corresponds to 8.8 mg/g terbinafine).

Indications/Possible uses
Fungal infections of the skin caused by dermatophytes such as trichophyton (e.g.T. rubrum T. mentagrophytes T. verrucosum T. violaceum) Microsporum canis and Epidemophyton floccosum.
Yeast infections of the skin principally those caused by the genus Candida (e.g. candida albicans).
Pityriasis (tinea versicolor due to pityrosporum orbiculare (also known as malassezia furfur).
For the treatment of plantar-type tinea pedis (Moccasin type).

Composition
Active substance: Terbinafine hydrochloride.
Excipients: Isopropyl myristate, Polysorbate 60, Cetyl alcohol, Stearyl alcohol, Cetyl palmitate, Sorbitan Stearate, Benzyl alcohol, Sodium Hydroxide, Purified Water

Posology/Use
Usual posology
Cleanse and dry the affected skin areas thoroughly before application of Lamisil.

Adults and children over 12 years of age
Apply Lamisil Cream 1-2 times per day, based on indication. Apply the cream to the affected skin and surrounding area in a thin layer and rub-in lightly. In case of intertriginous infection (inframammary, interdigital, internatal, inguinal) the application site may be covered with a gauze strip, especially at night.

Usual treatment regimens
Tinea pedis (interdigital), Tinea corporis/cruris: **Once** per day for 1 week.
Tinea pedis plantaris (moccasin-type): Twice per day for 2 weeks.
Skin candidiasis: 1-2 times per day for 1 week.
Tinea versicolor: 1-2 times per day for 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 one week, the diagnosis should be verified.
The effectiveness of Lamisil Cream has not been studied in patients with Tinea pedis and concomitant severe Onychomycosis.

Special dosage recommendations
Elderly patients
There is no evidence to suggest that elderly patients require different dosages or experience adverse reactions different from those of younger patients.

Paediatric population
The safety and efficacy of Lamisil Cream in children less than 12 years of age have not been established. Due to limited clinical data, application of Lamisil Cream in children less than 12 years of age is not recommended.

Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section "composition".

Warnings and precautions
Lamisil is for external use only. Contact with the eyes should be avoided.
In case of accidental contact with the eyes, rinse the eyes and conjunctival sac thoroughly with running water.
Lamisil Cream contains cetyl alcohol and stearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

Important information about the excipients in Lamisil Cream:
This medicine contains:
150mg benzyl alcohol in each 15g tube and 300mg benzyl alcohol in each 30g tube which is equivalent to 10 mg/g.
Benzyl alcohol may cause allergic reactions. and mild local irritation.
Stearyl alcohol May cause local skin reactions (e.g. contact dermatitis).
Cetyl alcohol May cause local skin reactions (e.g. contact dermatitis).

Interactions
There are no known drug interactions with the cream.

Pregnancy/Lactation
Pregnancy
No controlled studies are available in pregnant women. Reproduction studies in animals did not demonstrate any risk for the foetus.
In case of local application of Lamisil, less than 5% of the applied quantity is absorbed. Lamisil should not be used during pregnancy unless absolutely necessary.

Lactation
Terbinafine is excreted in small quantities in breast milk. It is not known if this small amount present in the breast milk may have a deleterious effect on the infant. Lamisil should not be used while breastfeeding. Young children should not come in contact with the treated skin areas.

Effects on ability to drive and use machinery
No corresponding study has been conducted.

Adverse events
The application may cause local reactions such as pruritus, desquamation, pain or irritations, pigmentation disorder, burning sensations, erythema or scab. However, these benign symptoms must be distinguished from hypersensitivity reactions including skin eruptions, which are reported in sporadic cases but require immediate discontinuation. In case of accidental contact with the eyes, eye irritation may occur. In rare cases, the underlying fungal infection may be aggravated.

Adverse events are listed below by system organ class and frequency. Frequencies are defined as follows:
Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing severity.

Immune system disorders

The following hypersensitivity reactions have been observed:
Very rare: urticarial.
Isolated cases: angio-oedema, anaphylactic shock.

Eye disorders
Rare: irritation.

Skin and subcutaneous tissue disorders
Common: desquamation, pruritus.
Uncommon: skin lesions, scabs, skin changes, pigmentation disorders, erythema, burning sensation.

Rare: dry skin, contact dermatitis, eczema.
Very rare: skin eruption or papula.

General disorders and administration site conditions
Uncommon: pain, application site pain or irritation.
Rare: primary disease aggravation.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

Overdose
The low systemic absorption of topical terbinafine renders overdose extremely unlikely.
Accidental ingestion of 2 tubes of Lamisil Cream containing 300 mg terbinafine hydrochloride is comparable to the ingestion of a 250 mg Lamisil tablet (corresponding to a standard adult oral dose). If a larger quantity of topical Lamisil is inadvertently ingested, adverse reactions similar to those observed with an overdose of Lamisil tablets are to be expected, such as headaches, nausea, epigastric pain and dizziness.

Treatment of overdose
If accidentally ingested, the recommended treatment of overdose consists of eliminating the medicinal product by the administration of activated charcoal, and giving symptomatic supportive therapy, if needed.

Properties/Effects
ATC Code: D01AE15
Terbinafine is an allylamine which has a broad spectrum of antifungal activity. It has a fungal activity on dermatophytes, moulds and some dimorphic fungi. The activity on yeasts is fungicidal or fungistatic depending of the species.
Terbinafine interferes specifically with ergosterol biosynthesis in the fungal cell membrane at an early step. Inhibition of squalene epoxidase enzyme leads to ergosterol deficiency and accumulation of intracellular squalene, resulting in fungal cell lysis, particularly because of the change in membrane function. Terbinafine inhibits squalene epoxidase in the fungal cell membrane. The enzyme squalene epoxidase is not linked to the cytochrome P450 system.
Therefore, terbinafine has no effect on the metabolism of hormones or other medicinal products.

Minimum inhibitory concentration in vitro

Fungal species	µg/ml
Susceptible:	
Trichophyton rubrum	0.003–0.006
T. mentagrophytes	0.003–0.01
T. tonsurans	0.003
T. verrucosum	0.003
T. schönleinii	0.006
Microsporum canis	0.006–0.01
M. versicolor	0.003
M. gypseum	0.006
Epidermophyton floccosum	0.003–0.006
Partly susceptible:	
Aspergillus fumigatus	0.1–1.56
Sporothrix schenckii	0.1–0.4
Candida albicans:	
yeast	25–100
mycelium	0.23–0.7
C. parapsilosis	0.8–3.1
Pityrosporum ovale	0.2–0.8
P. orbiculare	0.8

Lamisil may be recommended for short-term treatment (1-2 weeks based on indication). In most patients with interdigital mycosis, no relapse occurred for 2 months after a Lamisil treatment for one week.

In two double-blind studies controlled by vehicle (8 weeks observation period) conducted in a total of n = 193 patients, the effectiveness of Lamisil Cream has also been demonstrated for plantar mycosis (called tinea pedis moccasin type). During these studies, following twice a day application for two weeks, no pathogen was detectable anymore in the smear in approx. 70% of patients. Patients with concomitant severe onychomycosis were not included in that study. For other topical administration forms, effectiveness for that indication has not been studied.

Pharmacokinetics

After local application, terbinafine penetrates the skin and accumulates in the stratum corneum. At the end of a 7-day topical application, terbinafine can be measured at a fungicidal concentration in the stratum corneum for an additional 7 days.

In humans, less than 5% of the applied topical dose is absorbed. Systemic exposure during topical treatment is therefore very low.

Preclinical data

Reproductive toxicity

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

Mutagenicity

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

Carcinogenicity
In a two-year carcinogenicity study with oral administration in mice, no neoplastic or other abnormal findings were observed at dosages up to 130 mg/kg (males) and 156 mg/kg (females) per day. In a two-year carcinogenicity study with oral administration in rats at the highest dose level of 69 mg/kg per day, an increased incidence of liver tumours was observed in males. These 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.

Specific comments
Stability
The expiry date of the product is indicated on the packaging materials.
Notes regarding storage
Store below 30°C.
Keep out of the reach of children.

Authorisation number
115-55-27562-05

How supplied
Lamisil Cream: Lamisil Cream is a white cream packaged in a varnished laminated tube with or without a membrane (aluminum) and closed with polypropylene screw cap. Pack sizes 15 g and 30 g. Not all pack sizes may be marketed.

Manufacturer:
Karo Healthcare AB, Sweden
Box 16184, 10324 Stockholm, Sweden

Authorisation holder
Chemipal Ltd., 44 Giborei Israel st., Netanya 4250432

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