

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lamisil Once 1% cutaneous solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cutaneous solution contains 10 mg terbinafine (as hydrochloride).

Excipient(s) with known effect: ethanol 96% (863.75 mg/g).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous solution.

Clear to slightly opaque viscous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lamisil Once 1% cutaneous solution is indicated in the treatment of tinea pedis (athlete's foot) for adults (see section 4.4).

4.2 Posology and method of administration

Cutaneous use only.

Posology

Adults aged 18 years and over:

Duration and frequency of treatment

The film forming solution should be applied once on both feet, even if lesions are visible on one foot only. This ensures elimination of the fungi (dermatophytes) that might be found in areas of the feet where no lesions are visible.

Clinical symptoms usually start to improve within a few days.

If there are no signs of improvement within two weeks after completed treatment, patients should contact a pharmacist to verify that the product is correctly used or see a doctor to verify diagnosis. There is no data on repeated treatment with this product, therefore a second treatment cannot be recommended within a particular episode of tinea pedis.

Dosing in special populations

Pediatric population

Lamisil Once 1% cutaneous solution has not been studied in the paediatric population. Its use is therefore not recommended in patients below 18 years of age.

Elderly patients

There is no evidence to suggest that elderly patients require different dosages or experience side effects different to those in younger patients.

Method of administration

Patients should wash and dry both feet and hands before applying the medicinal product. They should treat one foot, then the other.

Starting between the toes, patients should apply a thin layer evenly between and all around the toes, as well as cover the sole and sides of the foot for up to 1.5 cm. The medicinal product should be applied in the same way to the other foot, even if the skin looks healthy. The medicinal product should be left to dry to a film for 1-2 minutes. Patients should then wash their hands. Lamisil Once 1% cutaneous solution should not be massaged into skin.

For the best results, the treated areas should not be washed for 24 hours after application. It is therefore recommended to apply Lamisil Once 1% cutaneous solution after a shower or bath and wait until the same time the following day before washing the feet gently again; after washing, the feet should be gently patted dry.

Patients should use the quantity they need to cover both feet as instructed above. Any unused medicinal product is to be discarded.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Lamisil Once 1% cutaneous solution should be used with caution in patients with lesions where alcohol could be irritating (after sun exposure or severe skin scaling). It should not be used on the face.

Lamisil Once 1% cutaneous solution is for external use only. It may be irritating to the eyes. In case of accidental contact with the eyes, rinse eyes thoroughly with running water.

Lamisil Once 1% cutaneous solution should be kept out of the sight and reach of children.

Lamisil Once 1% cutaneous solution is not recommended to treat hyperkeratotic chronic plantar tinea pedis (moccasin type).

In the event of allergic reaction, the film should be removed with an organic solvent such as denatured alcohol and the feet washed with warm soapy water.

Information concerning excipients

Lamisil Once 1% cutaneous solution contains ethanol; keep away from naked flames. This medicine contains 3316.8 mg alcohol (ethanol) in each daily dose which is equivalent to 863.75 mg/g of 96% ethanol. It may cause burning sensation on damaged skin.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions are known with Lamisil Once 1% cutaneous solution.

4.6 Pregnancy and lactation

Pregnancy

There is no clinical data for the use of terbinafine in pregnant women. Animal studies do not indicate any harmful effects with respect to pregnancy or the health of the foetus. Lamisil Once 1% cutaneous solution should not be used during pregnancy unless clearly necessary.

Breastfeeding

Terbinafine is excreted into breast-milk. After topical use, only a low systemic exposure is expected. Terbinafine should only be used in a nursing mother if the expected benefit justifies the risk to the infant. In addition, 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 (see section 5.3).

4.7 Effects on ability to drive and use machine

Lamisil Once 1% cutaneous solution has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Undesirable effects include mild and transient reactions at the site of application. In very rare instances, allergic reactions may occur.

Tabulated list of adverse reactions

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 (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Description of selected adverse reactions

Skin and subcutaneous tissue disorders:

Very rare (<1/10,000, including isolated reports): allergic reactions such as rash, pruritus, dermatitis bullous and urticaria.

Not known (cannot be estimated from available data): Skin exfoliation, skin discolouration, erythema.

General disorders and administration site conditions

Uncommon (>1/1,000, <1/100): application site reactions such as skin dryness, skin irritation or burning sensation.

Not known (cannot be estimated from available data): Application site pain.

Eye disorders:

Not known: eye irritation.

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 HPRRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

In case of accidental oral ingestion, the alcohol content (81.05% w/w) of Lamisil Once 1% cutaneous solution has to be considered.

Overdose is very unlikely to happen since the medicinal product is for single dose, cutaneous use, and the tube only contains the necessary quantity for one application. Accidental ingestion of one 4 g tube of product which contains 40 mg terbinafine is much lower than one 250 mg Lamisil tablet (adult oral unit dose). Should several tubes of Lamisil Once 1% cutaneous solution be inadvertently ingested however, adverse effects similar to those observed with an overdose of Lamisil tablets are to be expected. These include headache, nausea, epigastric pain and dizziness.

Treatment of overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antifungals for topical use
ATC code D01 A E15

Mechanism of action and pharmacodynamic effects

Terbinafine is an allylamine that 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. Terbinafine does not influence the metabolism of hormones or other drugs.

Terbinafine has a broad spectrum of antifungal activity in fungal infections of the skin caused by dermatophytes such as *Trichophyton* (e.g. *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*), *Microsporum canis* and *Epidermophyton floccosum*. At low concentrations terbinafine is fungicidal against dermatophytes.

Studies in patients have shown that a single dose application of Lamisil Once 1% cutaneous solution on both feet demonstrated efficacy in patients with tinea pedis (athlete's foot) presenting lesions between the toes, and extending to adjacent skin areas of the sides and soles of the feet.

Terbinafine has long lasting action, fewer than 12.5 % of athlete's foot sufferers treated with terbinafine 1 % solution show relapse or re-infection by 3 months after start of treatment.

5.2 Pharmacokinetic properties

Once applied to the skin, film forming solution forms a film on the skin. The film rapidly delivers terbinafine to the stratum corneum and terbinafine persists in the stratum corneum for up to 13 days.

Washing of the film decreased the terbinafine content in the stratum corneum and therefore washings should be avoided for the first 24h after application to permit as much stratum corneum penetration by terbinafine as possible.

The occlusive condition, likely to be encountered in therapeutic use, will result in 2.7-fold increased exposure of the stratum corneum to terbinafine following a single application of Lamisil Once 1% cutaneous solution. Although it has not been studied, penetration of terbinafine in the stratum corneum is likely to be higher in patients with tinea pedis than on the back of healthy volunteers. This is due to the occlusive effect found in the interdigital spaces, which is likely to be increased by wearing shoes, rather than any effect caused by an affected integrity of the stratum corneum.

Systemic bioavailability is very low in both healthy volunteers and patients. An application of Lamisil Once 1% cutaneous solution to the back, on an area 3 times the area of both feet, resulted in an estimated exposure to terbinafine of less than 0.5% of the exposure following oral administration of a 250 mg tablet.

Special Patient Populations

The pharmacokinetics of terbinafine in the stratum corneum is unlikely to be affected in sub populations. Any effects of sub populations on the systemic pharmacokinetics are also unlikely to be clinically significant, due to the very low levels of terbinafine that are found following topical application of terbinafine.

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 no associated 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.

Repeated dermal administration of Lamisil Once 1% cutaneous solution in rats and minipigs produces plasma terbinafine levels which are at least 50-100 times lower than the no-adverse-effect-levels established in terbinafine animal toxicity studies, so use of the medicinal product is not expected to produce any systemic adverse effect. Lamisil Once 1% cutaneous solution was well tolerated in a variety of tolerability studies and did not cause sensitisation.

The safety of acrylates/octylacrylamide copolymer, an excipient newly used in dermal topical medicinal products, has been established based on conventional studies of single and repeat dose toxicity, genotoxicity and local tolerability studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acrylates/octylacrylamide copolymer;
hydroxypropylcellulose;
medium chain triglycerides;
ethanol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original package in order to protect from light. Do not store above 30°C.

6.5 Nature and contents of container

4 g aluminium laminated tube (polyethylene-aluminium-polyethylene) with a polyethylene screwcap.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Karo Pharma AB
Box 16184
103 24 Stockholm
Sweden

8 MARKETING AUTHORISATION NUMBER(S)

PA22650/009/003

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 September 2006

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10 DATE OF REVISION OF THE TEXT

March 2024