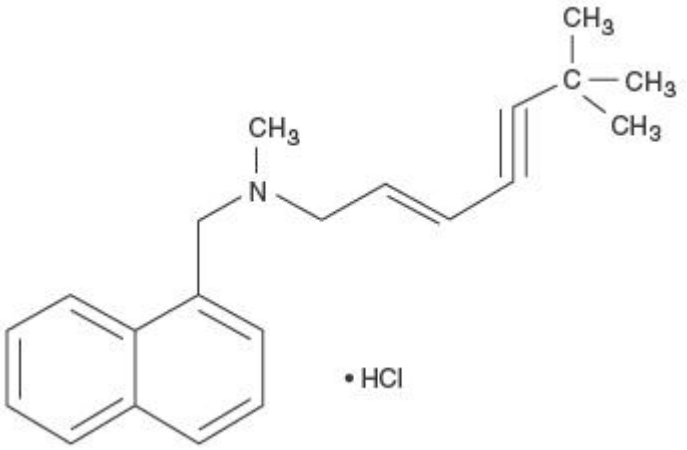
PRODUCT INFORMATION

1. Name of the product

LAMISIL ONCE

2. Active ingredient

Terbinafine hydrochloride 10mg/g



Chemical structure:

3. **Pharmaceutical form**

Topical solution.

4. **Therapeutic indications**

Treatment for athlete's foot.

5. Description

Lamisil once also contains, as excipients, Ethyl alcohol 96% (v/v), acrylates/octylacrylamide copolymer (e.g. Dermacryl 79), medium chain triglycerides, hydroxypropylcellulose(e.g. Klucel MF) ,.

6. Pharmacology

6.1. Pharmacodynamics

Pharmacotherapeutic group: Antifungal for topical use (ATC code D01A E15).

Terbinafine is an allylamine with antifungal activity mainly against dermatophytes.

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. Terbinafine does not influence the metabolism of hormones or other drugs.

A phase III, randomized, double-blind, placebo-controlled clinical trial has been conducted to investigate the efficacy and safety of Lamisil Once in patients aged 12 years and over with tinea pedis. In this study, 273 patients which were treated with a single application of Lamisil Once (190 patients) or vehicle (83 patients) according to the directions for use were analysed for the efficacy. The primary efficacy variable was the number of patients 'effectively treated' (negative microscopy, negative culture, total clinical signs and symptoms score ≤2 using a scoring scale of 0-3 for each individual sign/symptom, with no individual sign/symptom for pustules, incrustation, vesiculation and an individual score ≤1 for erythema, desquamation, pruritus,) 6 weeks after treatment. Secondary efficacy parameters included negative culture, negative microscopy, negative mycology (both negative microscopy and negative culture), clinical cure (total signs/symptoms score = 0), complete cure (negative mycology and clinical cure) and reinfection/relapse rate 12 weeks after treatment in patients effectively treated at week 6. Lamisil Once was significantly superior to placebo in effective treatment at week 6, with 63.2% of patients effectively treated compared to 16.9% in the placebo group. Lamisil Once was also significantly superior to placebo for all secondary measures of efficacy. Twelve weeks after the single application the reinfection/relapse rate was low (12.5% of effectively treated patients in the terbinafine group had a positive culture at Week 12).

A total of five patients experienced adverse events thought to be treatment related. One patient in each of the placebo and Lamisil Once groups experienced a mild burning sensation, one patient in the placebo group experienced a moderate peripheral oedema, and one patient each in the Lamisil Once group experienced a mild pain and a moderate aggravation of pruritus.

6.2. Pharmacokinetics

Upon application of Lamisil Once to the skin of the back, terbinafine in the film stays on the skin for up to 72 hours, or 96 hours under occlusion, condition which mimics the natural occlusion occurring in the interdigital spaces. The film quickly delivers terbinafine to the stratum corneum: in a study using 5% terbinafine, at 60 minutes after application to the skin of the back, 16-18% of the applied dose was present in the stratum corneum. Delivery progressively continues and terbinafine persists in the stratum corneum for up to 13 days at levels which are in excess of the in vitro Minimum Inhibitory Concentration for terbinafine against dermatophytes.

Systemic bioavailability is very low. An application of terbinafine 10 mg/g film forming solution on the back, on an area of 3 times the area of both feet, resulted in exposure to terbinafine of less than 0.5% of the exposure following oral administration of a 250 mg tablet. In patients with tinea pedis, application of Lamisil Once resulted in plasma terbinafine levels below the level of detection in 13/14 patients, and a level of 1.12 ng/mL at 120 hours after application of the film in the remaining patient.

7. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 5.

8. Precautions

Lamisil Once is not recommended to treat hyperkeratotic chronic plantar tinea pedis (moccasin type). The efficacy of Lamisil Once has not been tested in patients with hyperkeratotic chronic plantar tinea pedis (moccasin type) and patients with this condition generally require oral therapy or long-term topical therapy.

Lamisil ONCE Film Forming Solution is for external use only. It should not be used on the face; it may be irritating to the eyes. In case of accidental contact with the eyes, rinse eyes thoroughly with running water. Do not swallow.

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.

Lamisil ONCE Film Forming Solution should be used with caution in patients with lesions where alcohol could be irritating, such as lesions which are markedly inflamed or fissured.

8.1. Use in pregnancy

Category B1: Drugs that have been taken by only a limited number of pregnant women and women of childbearing age without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Since clinical experience in pregnant women is very limited, Lamisil ONCE should not be used during pregnancy unless the potential benefit to the mother has been weighed against the potential risk to the fetus.

8.2. Effects on fertility

Foetal toxicity and fertility studies in animals suggest no adverse effects.

8.3. Use in lactation

Terbinafine is excreted in breast milk. The amounts absorbed through the skin after dermal application are small, but the effects on the infant are unknown. Therefore Lamisil should not be used during lactation.

8.4. Use in the elderly

There is no evidence to suggest that elderly patients require different doses of terbinafine, or experience adverse effects different from those in younger patients after use of Lamisil dermal formulations.

8.5. Paediatric use

Experience with Lamisil ONCE in children under the age of 15 is limited. Therefore use in children under the age of 15 years is not recommended.

8.6. Effects on Ability to Drive or Use Machines

Lamisil Once Film Forming Solution has no or negligible influence on the ability to drive and use machines.

9. Interactions with other drugs

No drug interactions are known with Lamisil ONCE Film Forming Solution.

10. Adverse effects

Undesirable effects include transient reactions at the site of application. Note that some of the application site reactions (e.g. pruritus) are also symptoms of tinea pedis.

In very rare instances, allergic reactions may occur.

Adverse reactions (Table 1) are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 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.

Skin and subcutaneous tissue disorders:

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

General disorders and administration site conditions:

Uncommon, may affect up to 1 in 100 people (>1/1,000, <1/100): application site reactions (skin dryness, skin irritation or burning sensation, pruritus), peripheral oedema, pain.

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. 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/*

11. Dosage and administration

Adults and children aged 15 years and over:

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

Patients should wash and dry both feet and hands before applying the 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 product should be applied in the same way to the other foot, even if the skin looks healthy. The product should be left to dry to a film for 1-2 minutes. Patients should then wash their hands. Lamisil Once should not be massaged into skin.

For the best results, the treated area should not be washed for 24 hours after application. It is therefore recommended to apply Lamisil Once after a shower or bath and wait until the same time the following day before washing the feet again.

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

Relief of clinical symptoms usually occurs within a few days. If there are no signs of improvement after one week, patients should see a doctor.

There are no data on repeated treatment with Lamisil Once. Therefore a second treatment cannot be recommended within a particular episode of athlete's foot.

12. Overdosage

12.1. Signs and symptoms

Overdose is very unlikely to happen since the 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 be 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. The alcohol content of Lamisil Once (81.05%w/w) has to be considered in case of accidental oral ingestion.

12.2. Treatment

In case of overdose, contact the Poisons Information Centre.

13. Presentation and storage conditions

Lamisil **Once** is a clear to slightly opaque viscous solution. It is supplied as a single dose preparation in an individual 4 g tube.

Store below 30°C. Store in original container to protect from light.

Highly flammable. Keep away from naked flames.

The product contains alcohol. Do not light a cigarette or expose

yourself to fire until the gel is completely dried

The expiry date of the product is indicated on the packaging materials.

14. Manufacturer

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

15. License Holder and Importer

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

16. Marketing Authorization Number

137-26-31486

17. Date of revision of the text

Revised in May 2025.