Lamisil Spray

1. Composition

Active substance Terbinafine hydrochloride.

Excipients

Ethanol, propylene glycol, macrogol cetostearyl ether, and purified water.

2. Pharmaceutical form and active substance quality per unit

Spray: 10 mg/g terbinafine hydrochloride (corresponds to 8.8 mg/g terbinafine).

4. Clinical Particulars

4.1Indications/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 epidermaphyton 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).

4.2 Dosage/Administration

Usual dosage

Cleanse and dry the affected skin areas thoroughly before applying Lamisil Spray.

Adults and adolescents aged 12 years and above:

Tinea pedis, Tinea Cruris, Tinea Corporis- apply Lamisil Spray once a day for one week.

Pityriasis versicolor (sun fungus) – apply twice a day for one week.

The affected area should be washed and dried thoroughly before each application of the medicine. Spray enough substance to make the treated area surrounding it wet.

If the treatment is applied to skin folds, the area can be covered with gauze dressing, especially at night. Change the gauze at each application.

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 month, the diagnosis should be verified.

Special dosage instructions

Elderly patients

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

Children less than 12 years of age

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

4.3 Contraindications

Hypersensitivity to the active substance terbinafine or to any of the excipients contained in the cream or spray (see *"Composition" section 1*).

4.4 Warnings and precautions

Lamisil Spray is for external use only.

Contact with the eyes should be avoided. In case of accidental contact with the eyes, eye irritation may occur. In case of accidental contact with the eyes, rinse the eyes and conjunctival sac thoroughly with running water.

Infants and young children should not come into contact with the treated skin areas.

Do not inhale Lamisil Spray.

In case of skin lesions, use Lamisil Spray with care because it contains alcohol and propylene glycol which can be irritating.

Excipients
This medicine contains 3.4165 g Ethanol in each bottle of 15 ml and 6.834 g Ethanol in each bottle of 30 ml which is equivalent to 25 mg/g of Lamisil Spray.
It may cause burning sensation on damaged skin.

This medicine contains 0.707 g Propylene Glycol in each bottle of 15ml and 1.414 g Propylene Glycol in each bottle of 30 ml which is equivalent to 50 mg/g of Lamisil Spray.

4.5 Interactions

No interaction studies have been performed with Lamisil Spray. There are no known drug interactions with Lamisil Spray.

4.6 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 Spray, less than 5% of the applied dose is absorbed. Lamisil Spray 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 Spray should not be used during lactation.

Infants and young children should not come into contact with the treated skin areas.

4.7 Effects on ability to drive and use machines

No corresponding study has been conducted.

4.8 Undesirable effects

The application can cause local reactions such as erythema, pruritus or desquamation. However, these benign symptoms must be distinguished from hypersensitivity reactions, which are reported in sporadic cases but require immediate discontinuation. These reactions can be accompanied by redness, papules, vesicles and pruritus, which can also occur beyond the contact zone (so-called dispersion reaction).

The following adverse effects are listed by system organ class and by frequency; they have been observed with the topical use of terbinafine. Frequencies are defined as follows:

Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000 <1/1000), very rare (<1/10,000).

Immune system disorders

Very rare: hypersensitivity reactions such as urticaria, allergic exanthema (including dispersion reactions), papules, vesicular changes.

Isolated cases: angio-oedema, anaphylactic shock.

Eye disorders

Rare: irritation.

Skin and subcutaneous tissue disorders

Common: desquamation, pruritus.

Uncommon: skin lesions, scabs, other 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: application site pain or irritation.

In rare cases, the underlying fungal infection may be aggravated.

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/
Additionally, please also report to GSK Israel (il.safety@gsk.com)

4.9 Overdose

The low systemic absorption of topical terbinafine renders overdose extremely unlikely.

In the event of accidental ingestion of Lamisil Spray, the 28.87% (v/v) alcohol content must be taken into account.

Treatment of overdose

In the event of accidental oral ingestion, additional symptomatic treatment may be administered if necessary. If ingestion is recent, activated charcoal can be administered.

5. Properties/Effects

ATC code

D01AE15

Mechanism of action

Terbinafine is an antifungal which has a broad spectrum of allylamine activity. It exerts a fungicidal action on dermatophytes.

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. 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

5.1 Pharmacodynamics Missing information.

5.2 Clinical efficacy

Lamisil Spray may be recommended for short-term treatment.

5.2 Pharmacokinetics

Absorption

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

Distribution

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

Metabolism

Systemically absorbed terbinafine is rapidly and completely metabolised in the liver to inactive metabolites by several CYP450 isoenzymes.

Elimination

Three quarters of terbinafine metabolites are eliminated in the urine and a quarter is eliminated in the faeces. After systemic administration, the elimination half-life is approximately 30 hours.

5.3 Preclinical data

Long-term toxicity

In long-term studies (up to 1 year) in rats and dogs on the oral administration of the active substance, terbinafine, no toxic effects have been observed at doses up to 100 mg/kg/day. At high oral doses, the liver and, to a lesser extent, the kidneys have been identified as potential target organs.

Mutagenicity

A standard battery of genotoxicity tests performed *in vitro* and *in vivo* revealed no mutagenic or clastogenic evidence of the 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.

Reproductive toxicity

No adverse event on fertility or other reproduction parameters were observed with the active substance terbinafine in studies in rats or rabbits. No malformations were observed; the peri- and post-natal development phases were also not affected.

Other data (local toxicity)

Repeated dermal use of Lamisil Once in rats and guinea pigs has resulted in 50– 100 times lower plasma terbinafine levels than those observed in routine animal toxicity studies. No systemic side effects are to be expected. Tolerance studies did not reveal any sensitisation due to Lamisil Once.

6. Other information

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

Special precautions for storage
Store below 30°C. Do not store in the refrigerator.
Keep out of the reach of children.

7. Authorisation number

117-13-29732-00

Packs Spray: 15 ml and 30 ml.

Not all the packs might be on the

market.

8. Manufacturer:

GSK Consumer Healthcare S.A., SWITZERLAND

ROUTE DE l'ETRAZ 1260 NYON, SWITZERLAND

9. Marketing authorisation holder

GSK CONSUMER HEALTHCARE, ISRAEL LTD

P.O.B 3256 Petach Tikva, Israel

10. Date of revision of the text

Revised in May 2021