Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lamisil 1% cutaneous solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: 10 mg terbinafine hydrochloride per 1 g solution (1% w/w).
Excipient(s) with known effect: propylene glycol (E1520) (50 mg/g)

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cutaneous solution

Clear, colourless to faintly yellow liquid

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lamisil solution is indicated in the treatment of fungal infections of the skin caused by dermatophytes and pityriasis (tinea) versicolor in adults (see section 4.4)

4.2 Posology and method of administration

Cutaneous use.

Posology

Adults.
Lamisil solution is applied once or twice daily, depending on the indication.

Duration and frequency of treatment.

Interdigital type tinea pedis:	Once a day for 1 week
Tinea corporis, cruris:	Once a day for 1 week
Pityriasis versicolor:	Twice a day for 1 week

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence.

Method of administration
The affected area should be cleaned and dried thoroughly before the application of Lamisil Solution. A sufficient amount of solution should be applied to wet the treatment area(s) thoroughly, and to cover the affected skin and surrounding area.

Dosing in special populations:
Pediatric population
Lamisil solution is not recommended for use in children due to insufficient data on safety and efficacy.

Elderly patients
There is no evidence to suggest that elderly patients require different dosages or experience side effects different from

those in younger patients.

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 solution should be used with caution in patients with lesions where alcohol could be irritating.
It should not be used on the face.

Lamisil 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 solution should be kept out of the reach of children.

Information concerning excipients

Lamisil solution contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions are known with Lamisil solution.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no clinical experience with terbinafine in pregnant women. Foetal toxicity studies in animals suggest no adverse effects (see section 5.3).
Lamisil solution should not be used during pregnancy unless clearly necessary.

Breast-feeding
Terbinafine is excreted in breast milk . Lamisil solution should not be used during breast-feeding.

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 machines

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

4.8 Undesirable effects

Summary of the safety profile

Local symptoms such as pruritus, skin exfoliation, application site pain, application site irritation, pigmentation disorder, skin burning sensation, erythema, scab, etc. may occur at the site of application. These harmless symptoms must be distinguished from hypersensitivity reactions incl. rash, which are reported in sporadic cases and require discontinuation of therapy. In case of accidental contact with the eyes terbinafine may be irritating to the eyes. In rare cases the underlying fungal infection may be aggravated.

Tabulated list of adverse reactions
Adverse reactions 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* (can not to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Class (SOC) Frequency	Adverse Reaction
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
Unknown	Rash*
General disorders and administration site conditions	
Uncommon	Pain, application site pain, application site irritation
Rare	Condition aggravated

*: Based on post-marketing experience

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

4.9 Overdose

The low systemic absorption of topical terbinafine solution renders overdosage extremely unlikely.

Accidental ingestion of the contents of one 30 ml bottle of Lamisil solution, which contains 300 mg terbinafine hydrochloride, is comparable to ingestion of one Lamisil 250 mg tablet (adult oral unit dose).

Should a larger amount of Lamisil solution 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.

In case of accidental oral ingestion, the alcohol content (28.87% v/v) of Lamisil solution has to be considered.

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

Terbinafine is an allylamine which 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 and moulds. The activity against yeasts is fungicidal (e.g. *Pityrosporum orbiculare* or *Malassezia furfur)* or fungistatic, depending on 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. Terbinafine does not influence the metabolism of hormones or other substances.

5.2 Pharmacokinetic properties

Less than 5% of the dose is absorbed after topical application to humans; systemic exposure is thus 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 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

Purified water
Ethanol 96%
Propylene glycol (E1520)
Macrogol cetostearyl ether

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.
12 weeks after first opening.

6.4 Special precautions for storage

Do not store above 30^{o}C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Lamisil solution is available in 30 ml, white oval high-density polyethylene (HDPE) squeeze bottles, with a low density polyethylene dropper insert and HDPE screw closure.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Novartis Pharmaceuticals UK Limited
Frimley Business Park
Frimley Camberley
Surrey
GU16 7SR
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 13/45/4

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Date of last renewal: 9th May 2007

10 DATE OF REVISION OF THE TEXT

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