Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lamisil AT 1% Cutaneous Spray Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

10 mg terbinafine hydrochloride per 1 g spray solution.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Cutaneous spray, solution.
Clear, colourless to faintly yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Fungal infections of the skin caused by dermatophytes.
Pityriasis (tinea) versicolor.

4.2 Posology and method of administration

Adults:

Lamisil AT 1% Cutaneous Spray Solution is applied once or twice daily, depending on the indication. Cleanse and dry the affected areas thoroughly before applying Lamisil AT 1% Cutaneous Spray Solution. A sufficient amount of spray solution should be applied to wet the treatment area(s) thoroughly, and to cover the affected skin and surrounding area.

Duration and frequency of treatment:

Tinea corporis, cruris:	1 week once a day
Interdigital type tinea pedis:	1 week once a day
Pityriasis versicolor:	1 week twice a day

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

Use of Lamisil AT 1% Cutaneous Spray Solution in the elderly:
There is no evidence to suggest that elderly patients require different dosages or experience side effects different from those in younger patients.

Use of Lamisil AT 1% Cutaneous Spray Solution in children:
Experience with Lamisil AT 1% Cutaneous Spray Solution in children is limited and its use cannot, therefore, be recommended.

4.3 Contraindications

Known hypersensitivity to terbinafine or any of the excipients contained in the spray solution *(see 6.1 List of*

excipients).

4.4 Special warnings and precautions for use

Lamisil AT 1% Cutaneous Spray Solution should be used with caution in patients with lesions where alcohol could be irritating.

Lamisil AT 1% Cutaneous Spray Solution is for external use only. It may be irritating to the eyes. NCH B Terbinafine hydrochloride 1% Spray should not be used on the face.

In case of accidental contact with the eyes, rinse eyes thoroughly with running water.

In case of accidental inhalation, consult a physician if any symptoms develop or persist.

Lamisil AT 1% Cutaneous Spray Solution should be kept out of the reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions are known with Lamisil AT 1% Cutaneous Spray Solution.

4.6 Pregnancy and lactation

Animal studies did not reveal any teratogenic or embryofoetotoxic potential of terbinafine. No cases of malformations in humans have been reported with terbinafine to date. However, since clinical experience in pregnant women is very limited, Lamisil AT 1% Cutaneous Spray Solution should be used only if clearly indicated during pregnancy. Terbinafine is excreted in breast milk and therefore, mothers should not receive terbinafine whilst breast-feeding. In addition, infants must not be allowed to come into contact with any treated skin including the breast.

4.7 Effects on ability to drive and use machines

Cutaneous application of terbinafine does not affect the ability to drive and use machines.

4.8 Undesirable effects

Redness, itching or stinging may occur at the site of application; however, treatment rarely has to be discontinued for this reason. These harmless symptoms must be distinguished from allergic reactions such as pruritus, rash, bulbous eruptions and hives which are rare but require discontinuation.

4.9 Overdose

No case of overdose has been reported with Lamisil AT 1% Cutaneous Spray Solution. Should, however, Lamisil AT 1% Cutaneous Spray Solution be inadvertently ingested, adverse effects similar to those observed with an overdose of terbinafine tablets (e.g. headache, nausea, epigastric pain and dizziness) are to be expected. The alcohol content (23.5%) of the spray solution has to be taken into account.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungal for topical use
ATC code D01 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 drugs.

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 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 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
Propylene glycol
Macrogol cetostearyl ether

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

White, round HDPE bottle with a crimped mouth and spray pump.
Pack sizes: 15ml and 30ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For manipulation of the spray pump the bottle can be held in the upright or inverted position.

When using Lamisil AT 1% Cutaneous Spray Solution for the first time, the patient will need to depress the actuator a few times (usually up to 3 actuations) before the solution is dispensed.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 0030/056/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 October 2006