Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fungasil 10mg/g cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of cream contains 10 mg of terbinafine hydrochloride.

Excipients with known effect: 40 mg Cetyl alcohol and 40 mg Cetostearyl alcohol per gram cream.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.

White or almost white cream

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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.

Yeast infections of the skin, principally those caused by the genus Candida (e.g. Candida albicans).

Pityriasis (tinea) versicolor, caused by Pityrosporum orbiculare (Malassezia furfur).

4.2 Posology and method of administration

Adults and adolescents (>12 years of age):
Duration and frequency of the treatment:

Tinea pedis: once daily for one week.

Tinea cruris and tinea corporis: once daily for one week

Cutaneous candidiasis: once daily for 1 to 2 weeks

Pityriasis versicolor: once or twice daily for 2 weeks

Fungasil 10 mg/g cream can be applied once or twice daily. The skin should be dry and clean. The cream should be applied to the affected skin and surrounding area in a thin layer and then rubbed in gently. If the event of intertriginous infection (submammary, interdigital, intergluteal or inguinal) the skin may be covered with a sterile gauze following application of the cream, especially at night.

Relief of symptoms usually occurs within a few days.
Irregular use or premature discontinuation increase the risk of recurrence of the symptoms. If no improvement is seen after two weeks, the diagnosis should be reconsidered.

Elderly:
There are no indications that elderly patients require different dosages or experience side-effects different to those of younger patients.

Children:
Fungasil 10 mg/g cream is not recommended for use in children below 12 years of age due to insufficient data on safety. The experience in children is limited.

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

Terbinafine cream is intended for external use only. It may be irritating to the eyes; therefore contact with the eyes should be avoided. In case of accidental contact with the eyes, rinse eyes thoroughly with running water.

Terbinafine cream should be kept out of the sight and reach of children.

Fungasil 10 mg/g cream contains Cetyl alcohol and Cetostearyl alcohol. May cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions are known with the topical forms of terbinafine.

4.6 Fertility, pregnancy and lactation

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

Breast-feeding
Terbinafine cream 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. Terbinafine is excreted in breast milk. After topical administration only low systemic exposure is anticipated (see section 5.2). Fungasil

Fertility
No effect of terbinafine on fertility has been seen in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Terbinafine cream has no influence on the ability to drive and use machines.

4.8 Undesirable effects

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.

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); not known (cannot to be estimated from available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Immune system disorders
Rare: Allergic reactions such as pruritus, rash, dermatitis bullous and urticaria.
Not known: Hypersensitivity (based on post-marketing experience)

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
Not known: Rash (based on post-marketing experience)

General disorders and administration site conditions
Uncommon: Pain, application site pain, application site irritation
Rare: Condition aggravated

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: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

The low systemic absorption of topical terbinafine renders overdosage extremely unlikely. Accidental ingestion of one 30 g tube of terbinafine cream, which contains 300 mg terbinafine hydrochloride, is comparable to ingestion of one terbinafine 250 mg tablet (adult oral unit dose).

Should a larger amount of terbinafine cream be ingested accidentally, adverse effects similar to those observed with an overdose of tablets containing terbinafine (e.g. headache, nausea, epigastric pain and dizziness) are to be expected.

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: D01AE15

Terbinafine, an allylamine, is an antimycotic with a broad spectrum of activity. At low concentrations terbinafine is fungicidal against moulds forming fungi (dermatophytes and others) and some dimorph fungi. Its activity against yeasts is fungicidal or fungistatic, depending on the species.

Terbinafine specifically inhibits fungal sterol synthesis at an early stage. This leads to a deficiency in ergosterol and intracellular accumulation of squalene, which leads to fungal cell death.

Terbinafine acts by inhibition of the enzyme squalene epoxidase in the fungal cell membrane. This enzyme does not have any relationship with the cytochrome P450-system. As far as known, terbinafine does not influence the metabolism of other medicinal products or hormones.

5.2 Pharmacokinetic properties

Less than 5% of the dose is absorbed following topical application in humans; as a result, systemic exposure is very marginal.

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

Sodium hydroxide (E524)
Benzyl alcohol
Sorbitan stearate (E491)
Cetyl palmitate
Cetyl alcohol
Cetostearyl alcohol
Polysorbate 60 (E435)
Isopropyl myristate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years
Shelf life after opening: 3 months

6.4 Special precautions for storage

Store in the original package in order to protect from light.
Do not freeze.
Keep the tube tightly closed.

6.5 Nature and contents of container

Aluminium tube with a polyethylene screw cap in pack sizes of 7.5g, 15g or 30 g.

Not all pack sizes may be marketed.

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road
Clonmel
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 126/166/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th January 2007

Date of last renewal: 14 October 2010

10 DATE OF REVISION OF THE TEXT

April 2015