SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Terbinafine Hydrochloride 10 mg/g cream
Cuplex Athletes Foot 1% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

10 mg terbinafine hydrochloride (equivalent to 8.89 mg terbinafine) in 1 g cream.

Excipients with known effect: 40 mg cetyl alcohol, 40 mg cetostearyl alcohol and 10 mg benzyl alcohol in 1 g cream.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream

White or almost white cream, with slight almond odour.

4.

4.1 Therapeutic indications

The treatment of tinea pedis (athlete's foot) and tinea cruris (dhobie itch/jock itch) caused by *Trichophyton* (e.g. *T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum)* and *Epidermophyton floccosum*.

4.2 Posology and method of administration

Posology

Adults and adolescents over 16 years of age
Terbinafine cream is applied once daily.

Duration of treatment is one week for tinea pedis and tinea cruris.
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 two weeks, the diagnosis should be verified by a physician.

Paediatric population
The experience with topical terbinafine in children is still limited and its use in children and adolescents under 16 years cannot therefore be recommended.

Elderly
There is no evidence to suggest that older patients require different dosages or experience side-effects different to those of younger patients.

Method of administration
For cutaneous use.
Cleanse and dry the affected areas thoroughly before application of Terbinafine cream. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (interdigital, intergluteal, inguinal), the application may be covered with a gauze strip, especially at night.

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 for external use only.

Should be used with caution in patients with lesions where alcohol could be irritating. Should not be used on the face.
Contact with the eyes should be avoided. It may be irritating to the eyes. In case of accidental contact with the eyes, rinse eyes thoroughly with running water and contact an ophthalmologist if necessary.

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

This medicinal product contains cetyl alcohol and cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).
This medicinal product contains 10 mg benzyl alcohol in each gram of cream. Benzyl alcohol may cause allergic reactions and mild local irritation.

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

Breast-feeding
Terbinafine is excreted in breast milk. 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.

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

4.7 Effects on ability to drive and use machines

Terbinafine 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 and scab may occur at the site of application. These minor symptoms must be distinguished from hypersensitivity reactions such as widespread pruritus, rash, bullous eruptions and hives, which are reported in sporadic cases and require discontinuation.
In case of accidental contact with the eyes, terbinafine hydrochloride 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), or *not known* (can not to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

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

Not known: Rash

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 www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Terbinafine cream is for external use only. 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).

Symptoms
Should a larger amount of terbinafine cream be inadvertently ingested, adverse effects similar to those observed with an overdosage of terbinafine tablets are to be expected. These include headache, nausea, epigastric pain and dizziness.

Treatment
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: Antifungals for dermatological use; Other antifungals for topical use. ATC code: D01AE15

Terbinafine is an allylamine, which has a broad-spectrum of anti-fungal activity. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts, e.g. *Candida* species is fungicidal 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 the 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 and other drugs.
Terbinafine provides long-lasting protection. More than 90% of patients with interdigital tinea pedis (athlete’s foot) treated with Terbinafine 1% cream for one week show no mycological

evidence of relapse or re-infection by three months after start of treatment. No such data on tinea cruris are available.

Terbinafine is used for the treatment of fungal infections of the skin and nails, which is caused by *Trichophyton* (e.g. *T. rubrum, T. mentagrophytes*) and *Epidermophyton floccosum*. The following table outlines the range of minimum inhibitory concentrations (MIC) against the dermatophytes.

Organism	**MIC range (µg/ml)**
Trichophyton rubrum	0.001-0.15
Trichophyton mentagrophytes	0.0001-0.05
Epidermophyton floccosum	0.001-0.05

5.2 Pharmacokinetic properties

Absorption
Less than 5% of the dose is absorbed after topical application; systemic exposure is therefore 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 mg/kg (males) and 156 mg/kg (females) 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. There were no associated 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,

Benzyl alcohol,

Sorbitan stearate,

Cetyl palmitate,

Cetyl alcohol,

Cetostearyl alcohol,

Polysorbate 60,

Isopropyl myristate,

Water purified.

6.2 Incompatibilities

None known.

6.3 Shelf life

4 years

Shelf life after opening: 1 month

6.4 Special precautions for storage

No special precautions for storage.

Store in original container.

6.5 Nature and contents of container

Aluminium tube closed by polyethylene cap. The tubes are containing 7.5 g and 15 g cream.

6.6 Special precautions for disposal

No special instructions.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Gedeon Richter Plc.
H-1103 Budapest
Gyömrői út 19-21
Hungary

8 MARKETING AUTHORISATION NUMBER(S)

PL 04854/0044

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