TERBINAFINE HYDROCHLORIDE CREAM
1% W/W
TAJ PHARMA

1. NAME OF THE MEDICINAL PRODUCT

Terbinafine Hydrochloride Cream 1% w/w
Taj Pharma

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains:
Terbinafine hydrochloride equivalent to 8.89 mg of Terbinafine……10mg
Excipients…….q.s.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream

White or almost white cream, with a slight almond odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The treatment of tinea pedis (athlete's foot) and tinea cruris (dhobie itch/jock itch)

Fungal infections of the skin caused by dermatophytes such as species of Trichophyton (e.g. *T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum*), *Microsporum canis and Epidermophyton floc*cosum.

Infections of the skin caused by *Candida* (e.g. *Candida albicans*).

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

4.2 Posology and method of administration

Posology

Adults and adolescents (>12 years of age)

Duration and frequency of treatment:

Terbinafine can be applied once or twice daily.

The likely duration of each treatment is as follows:

Tinea pedis: 1 week.

Tinea cruris and Tinea corporis: 1 to 2 weeks.

Cutaneous candida: 2 weeks.

Pityriasis versicolor: 2 weeks.

Relief of symptoms is usually obtained within a few days.

Irregular use or an inadequate treatment period increases the risk of the symptoms returning. If no improvement is obtained after 2 weeks, the diagnosis should be re-evaluated.

Elderly

There has been nothing to indicate that elderly patients require a different dosage or have a side effects profile different from younger patients.

Paediatric population

Terbinafine 1 % Cream is not recommended for children below 12 years of age due to insufficient data on safety. The experience in children is limited.

Method of administration

For cutaneous use.

The skin should be clean and dry. The cream should be applied in a thin layer on and around the affected skin and rubbed in gently. In cases of reddened and weeping infection (under the breasts, between the fingers, buttocks or in the groin) the skin may be covered with a sterile compress after application of the cream, especially at night.

4.3 Contraindications

Hypersensitivity to the active substance, terbinafine, or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Terbinafine 1 % Cream cream is for external use only.

Terbinafine 1 % Cream cream may be irritating to the eyes. 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 reach of children.

In the event of allergic reaction, the cream should be removed and the treatment interrupted.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Candidiasis: It is not recommended to use acid pH soap. This provides favourable growth conditions for *Candida* spp.

Excipients

This medicine contains 10 mg benzyl alcohol in each gram of cream. Benzyl alcohol may cause allergic reactions and mild local irritation. This medicine also contains cetyl alcohol and cetostearyl alcohol which 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

There is no clinical experience with terbinafine in pregnant women. Foetal toxicity studies conducted in animals suggest no adverse effects (see section 5.3). Terbinafine 1 % Cream should not be used during pregnancy unless clearly necessary.

Breast-feeding

Terbinafine is excreted into breast-milk. After topical use, only a low systemic exposure is expected (see section 5.2). Terbinafine 1 % Cream 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 1 % Cream 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 including 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 the 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 be estimated from the 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

* 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.

4.9 Overdose

The low systemic absorption of topical terbinafine renders over dose extremely unlikely.

Symptoms

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 inadvertently ingested, adverse effects similar to those observed with an over dose of terbinafine tablets are to be expected. These include headache, nausea, epigastric pain and dizziness.

Treatment

If accidentally ingested, the recommended treatment of over dose 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 that has a broad spectrum of antimycotic activity. It has an antimycotic effect on fungal infections of the skin caused by dermatophytes such as *Trichophyton* (e.g. *T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum*), *Microsporum canis* and *Epdermophyton floccosum.* At low concentrations terbinafine has a fungicidal effect against dermatophytes and moulds. Its 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 P-450 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 low.

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, Benzyl alcohol, Sorbitan monostearate, Cetyl palmitate, Cetyl alcohol, Cetostearyl alcohol, Polysorbate 60, Isopropyl myristate, Purified water.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
4 years

Shelf life after opening 28 days

6.4 Special precautions for storage
Store in original container after first opening.

Do not freeze.

Keep the tube tightly closed.

6.5 Nature and contents of container
Collapsible aluminium tube with a polyethylene screw cap in pack sizes of 7.5 g, 15 g or 30 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Not applicable

7. MANUFACTURED IN INDIA BY:

TAJ PHARMACEUTICALS LTD.
Mumbai, India
Unit No. 214.Old Bake House,
Maharashtra chambers of Commerce Lane,
Fort, Mumbai - 400001
at:Gujarat, INDIA.
Customer Service and Product Inquiries:

1-800-TRY-FIRST (1-800-222-434 & 1-800-222-825)
Monday through Saturday 9:00 a.m. to 7:00 p.m. EST
E-mail: tajgroup@tajpharma.com