Terbinafine

TAFINE ®

Composition
Tablet:
Each tablet contains:
Terbinafine Hydrochloride USP equivalent to Terbinafine 250 mg

Cream:
Terbinafine Hydrochloride USP 1% w/w
Benzyl Alcohol USP (as preservative) 1% w/w

MOLECULAR INTRODUCTION

Terbinafine is an allylamine which has a broad spectrum of antifungal activity. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts 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 inhibition of squalene epoxidase in the fungal cell membrane. The enzyme squalene epoxidase is not linked to the cytochromeP450 system. Terbinafine does not influence the metabolism of hormones of other drugs. When given orally, the drug concentrates in skin, hair and nails at levels associated with fungicidal activity. Relapse with **TAFINE** are very low (8.75%) as compared to azoles which are used in the current therapy.

MECHANISM OF ACTION

Terbinafine is hypothesized to act by inhibiting squalene monooxygenase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. This inhibition also results in an accumulation of squalene, which is a substrate catalyzed to 2,3-oxydo squalene by squalene monooxygenase. The resultant high concentration of squalene and decreased amount of ergosterol are both thought to contribute to terbinafine's antifungal activity.

INDICATIONS

Tablets: Fungal infections of the skin, hair and nails caused by dermatophytes such as trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. tonsurans, T. violaceum), Microsporum canis and Epiderphyton floccosum.
Oral **TAFINE** is indicated in the treatment of ringworm (tinea corporis, tinea cruris, tinea pedis and tinea capitis) and yeast infections of the skin caused by the genus Candida (e.g. Candida

albicans) where oral therapy is considered appropriate owing to the site, severity or extent of the infection, Onychomycosis (fungal infection of the nail) caused by dermatophyte fungi.
Note: In contrast to topical TAFINE, oral TAFINE is not effective in pityriasis versicolor.

Cream: Fungal infection of the skin caused by dermatophytes such as Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epiderphyton floccosum. Yeast infections of the skin, principally those caused by the genus Candida (e.g. Candida albicans) Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

PHARMACOKINETICS

Tablets: A single oral dose of 250 mg terbinafine result in peak plasma concentrations of 0.97mcg/ml within 2 hours of administration. The absorption half-life is 0.8 hours and the distribution half-life is 4-6 hours. The bioavailability of terbinafine is moderately affected by food, but not sufficiently to require dosing adjustments. Terbinafine binds strongly to plasma proteins (99%). It rapidly diffuses through the dermis and concentrates in the lipophilic stratum corneum. Terbinafine is also secreted in the sebum, thus achieving high concentrations in hair follicles, hair sebum-rich skin. There is also evidence that terbinafine is distributed into the nail plate in the first few weeks after commencing therapy. Biotransformation results in metabolites with no antifungal activity which are excreted predominantly in the urine. The terminal elimination half-life is 17 hours. There is no evidence of accumulation, no age dependent changes in steady-state plasma concentrations of **TAFINE** have been observed, but the elimination rate may be reduced in patients with renal or hepatic impairment, resulting in higher blood levels of terbinafine.
Cream: Less than 5% of the dose is absorbed after topical application to humans; systemic exposure is thus very slight.

DOSAGE AND ADMINISTRATION

The duration of treatment varies according to the indication and severity of the infection.

TABLETS
Children: No Data are available in children under two years of age (usually<12kg.)
Children weighing <20kg / 62.5 mg once daily
Children weighing 20-40kg / 125 mg once daily
Children weighing >40kg / 250 mg once daily
Adults: 250 mg once daily

Skin Infections
Likely duration of treatment:
Tinea pedis (interdigital, plantar/moccasin type): 2 to 6 weeks
Tinea corporis, cruris: 2 to 4 weeks
Cutaneous candidiasis: 2 to 4 weeks

Complete resolution of the signs and symptoms of infection may not occur until several weeks after mycological cure.

Hair and scalp infections
Likely duration of treatment:
Tinea capitis: 4 weeks (Tinea capitis occurs primarily in children.)

Onychomycosis
For most patients the duration for successful treatment is between 6 weeks to 3 months.
Less than 3 months can be anticipated for the treatment of fingernail infections of moderate infections of toenails. In the remaining cases, 3 months of therapy is usually sufficient, although some patients, particularly those with nail infection of the big toes, may require treatment of 6 months or longer. Poor nails outgrowth, as observed during the first weeks of therapy may enable identification of those patients in whom treatment longer than 3 months is indicated.
In fungal nail infection the optimal clinical effect is seen some months after mycological cure and cessation of treatment. This is related to the period required for outgrowth of healthy nail tissue.

CREAM
TAFINE can be applied once or twice daily. Cleanse and dry affected areas thoroughly before treating with ***TAFINE.*** Apply the cream to the affected skin and surrounding area in a thin layer and rub lightly. In the case of intertriginous infection (submammary, interdigital, intergluteal, inguinal) the application may be covered gauze, especially at night.

Likely duration of treatment:
Tinea corporis, cruris: 1 to 2 weeks
Tinea pedis: 2 to 4 weeks: when applied twice daily. 1 week's treatment is usually sufficient.
Cutaneous candidiasis: 1 to 2 weeks
Pityriasis versicolor: 2 weeks (Relief of clinical symptoms usually occurs within a few days)
Irregular use or premature discontinuation of treatment carries risk or recurrence. If there are no signs of improvement after two weeks the diagnosis should be verified.

Use of TAFINE in the elderly: there is no evidence to suggest that elderly patients require dosages different from those in younger patients. When using tablets in this age group, the possibility of impairment of liver or kidney function should be considered (see Precaution)

Use of TAFINE in children: In children above 2 years of age. Oral ***TAFINE*** has been found to be well tolerated. Experience with topical ***TAFINE*** in children is limited.

CONTRA-INDICATIONS
Hypersensitivity to terbinafine.
Contraindicated in lactation

PRECAUTIONS

Tablets: Patients with pre-existing, stable chronic liver dysfunction or impaired renal function (creatinine clearance less than 50 ml/min or serum creatinine of more than 300 umol/L) should receive half the normal dose.
Cream: ***TAFINE*** cream is for external use only. Contact with eyes should be avoided.

SIDE EFFECTS

Tablets: Anorexia, nausea, abdominal pain, taste disturbances, diarrhoea, rash, urticaria. Potentially Fatal: Liver failure, Stevens-Johnson syndrome, neutropaenia.
Cream: Redness, itching or stinging occasionally occur at the site of application; however, treatment rarely has to be discontinued for this reason. These harmless reactions must be distinguished from allergic reactions which are rare but require discontinuation.

STORAGE

Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it in cool & dark place. DO NOT FREEZE.

PRESENTATION

Tablets: 10 Tablets X 10 Blisters
Cream: 15 gm Tube

For further information, please contact:
Market Planning Department
Deurali-Janta Pharmaceuticals Pvt. Ltd.
GPO Box 4239, 355 Hattisar Road, Kamalpokhari, Kathmandu, Nepal.
Tel: 4435167/68/69 E-mail: mplanning@deuralijanta.com Website: www.deuralijanta.com