LAMIRASE

Tablets

Composition
Each tablets contains Terbinafine (as hydrochloride) 250 mg.

Action
Terbinafine hydrochloride is a synthetic allylamine derivative. Terbinafine hydrochloride exerts its antifungal effect by inhibiting squalene epoxidase, a key enzyme in sterol biosynthesis in fungi. This action results in a deficiency in ergosterol and a corresponding accumulation of sterol within the fungal cell. Depending on the concentration of the drug and the fungal species tested *in vitro*, Terbinafine hydrochloride may be fungicidal; however, the clinical significance of these data is unknown. *In vitro*, mammalian squalene epoxidase is only inhibited at higher (4,000 fold) concentrations.

Terbinafine has been shown to be active against most strains of the following organisms both *in vitro* and in clinical infections of the nail. *Trichophyton rubrum, Trichophyton mentagrophytes*

Blood and tissue levels of Terbinafine following oral dosing with Terbinafine hydrochloride 250 mg QD exceed *in vitro* MICs against most strains of the following organisms that can infect the nail; however, the efficacy of Terbinafine in treating nail infections due to these organisms has not been studied in controlled clinical trials.
Epidermophyton floccosum, Microsporum gypseum, Microsporum nanum, Trichophyton verrucosum, Candida albicans, Scopulariopsis brevicaulis

Pharmacokinetics
Following oral administration Terbinafine is well absorbed (>70%) and the bioavailability of Terbinafine because of first-pass metabolism is approximately 40%. Peak plasma concentrations of 1 µ/ml appear within 2 h after a single 250 mg dose; the AUC (area under the curve) is approximately 4.56 mcg·h/ml. An increase in the AUC of Terbinafine of less than 20% is observed when Terbinafine hydrochloride is administered with food.

No effect of gender on the blood levels of Terbinafine was detected in clinical trials. In plasma, Terbinafine is >99% bound to plasma proteins and there are no specific binding sites. Prior to excretion, Terbinafine is extensively metabolized. No metabolites have been identified that have anti-fungal activity similar to Terbinafine. Approximately 70% of the administered dose is eliminated in the urine.

Indications
- Onychomycosis (fungal infection of the nail) caused by dermatophyte fungi.
- Tinea capitis
- Fungal infections of the skin for the treatment of tinea corporis, tinea cruris, tinea pedis and yeast infections of the skin caused by the genus candida (e.g. *Candida albicans*) where oral therapy is generally considered appropriate owing to the site, severity or extent of the infection

Contraindications
Contraindicated in individuals with hypersensitivity to Terbinafine.

Warnings
Rare cases of symptomatic hepatobiliary dysfunction including cholestatic hepatitis have been reported. Treatment with Terbinafine hydrochloride should be discontinued if hepatobiliary dysfunction develops. There have been isolated reports of serious skin reactions (*e.g.*, Stevens - Johnson syndrome and toxic epidermal necrolysis). If progressive skin rash occurs, treatment with Terbinafine hydrochloride should be discontinued.

Adverse Reactions

The most frequently reported adverse events observed are listed below. In general, the adverse events were mild, transient.

Adverse Event
Headache

Gastrointestinal Symptoms
Diarrhea, Dyspepsia, Abdominal Pain, Nausea and Flatulence

Dermatologic Symptoms
Rash, Pruritus, Urticaria, Liver Enzyme Abnormalities, Taste Disturbance, and Visual Disturbance

Rare adverse events, based on worldwide experience with Terbinafine hydrochloride use include: symptomatic idiosyncratic hepatobiliary dysfunction (including cholestatic hepatitis), serious skin reactions, severe neutropenia, and allergic reactions (including anaphylaxis). Rarely, Terbinafine hydrochloride may cause taste disturbance (including taste loss) which usually recovers within several weeks after discontinuation of the drug.

Precautions

General
Changes in the ocular lens and retina have been reported following the use of Terbinafine hydrochloride in controlled trials. The clinical significance of these changes is unknown. Hepatic function (hepatic enzyme) tests are recommended in patients administered Terbinafine hydrochloride for more than six weeks.
Pre-existing liver disease or renal impairment (creatinine clearance □50 ml/min), the use of Terbinafine hydrochloride has not been adequately studied, and therefore, is not recommended.

In patients with known or suspected immunodeficiency, physicians should consider monitoring complete blood counts in individuals using Terbinafine hydrochloride therapy for greater than six weeks.

Isolated cases of severe neutropenia have been reported. These were reversible upon discontinuation of Terbinafine hydrochloride with or without supportive therapy. If clinical signs and symptoms suggestive of secondary infection occur, a complete blood count should be obtained. If the neutrophil count is □1,000 cells/mm³, Terbinafine hydrochloride should be discontinued and supportive management started.

Pregnancy
Category B
There are no adequate and well-controlled studies in pregnant women, and because treatment of onychomycosis can be postponed until after pregnancy is completed, it is recommended that Terbinafine hydrochloride not be initiated during pregnancy.

Nursing Mothers
After oral administration, Terbinafine is present in breast milk of nursing mothers. The ratio of Terbinafine in milk to plasma is 7:1. Treatment with Terbinafine hydrochloride is not recommended in nursing mothers.

Pediatric Use
The safety and efficacy of Terbinafine hydrochloride have not been established in pediatric patients.

Drug Interactions

In vitro studies with human liver microsomes showed that Terbinafine does not inhibit the metabolism of tolbutamide, ethinylestradiol, ethoxycoumarin, and cyclosporine. *In vivo* drug-drug interaction studies conducted in normal volunteer subjects showed that Terbinafine does not affect the clearance of antipyrine, digoxin, and the antihistamine terfenadine. Terbinafine does not affect

the clearance of warfarin or warfarin effect on prothrombin time. Terbinafine decreases the clearance of intravenously administered caffeine by 19%. Terbinafine increases the clearance of cyclosporine by 15%.

Terbinafine clearance is increased 100% by rifampin, a CyP450 enzyme inducer, and decreased 33% by cimetidine, a CyP450 enzyme inhibitor. Terbinafine clearance is decreased 16% by terfenadine. Terbinafine clearance is unaffected by cyclosporine.

There is no information available from prospectively conducted drug interaction studies with the following classes of drugs: oral contraceptives, hormone replacement therapies, hypoglycemics, theophyllines, phenytoins, thiazide diuretics, beta-blockers, and calcium channel blockers.

Dosage and Administration

One 250 mg tablet of Lamirase should be taken once daily for 6 weeks by patients with fingernail onychomycosis. One 250 mg tablet of Lamirase should be taken once daily for 12 weeks by patients with toenail onychomycosis. 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.

Presentation

Lamirase tablets

Box of 14 tablets