TERBINAFINE TABLETS 250 mg

Pack Insert:
Enclosed

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

TERBICIP 250 mg Tablets

Terbinafine Tablets 250 mg

COMPOSITION
Each uncoated tablet contains:
Terbinafine Hydrochloride equivalent to
Terbinafine ..... 250 mg

Description
White, circular, biconvex tablets with 'TF' debossed on one side and score line on the other side.

Dosage Form
Tablets

Pharmacology

Pharmacodynamics
Terbinafine is an allyl-amine which has a broad spectrum of antifungal activity. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity versus yeasts is fungicidal or fungistatic depending on the species.
Terbinafine interferes selectively with fungal sterol biosynthesis at an early stage through inhibition of the enzyme squalene epoxidase. This leads to a deficiency in ergosterol and to an intracellular accumulation of squalene in the fungal cell membrane. Both the deficiency in ergosterol and the accumulation of squalene are responsible for fungal cell death.
When given orally, the active substance concentrates in skin, hair and nails at levels associated with fungicidal activity. Measurable concentrations of the active substance are still evident 15 – 20 days after cessation of treatment.
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, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum. The following table outlines the range of minimum inhibitory concentrations (MIC) against the dermatophytes.

Organism	MIC rang (µg/ml)
Trichophyton rubrun	0.001 – 0.15
Trichophyton mentagrophytes	0.0001 – 0.05
Trichophyton verrucosum	0.001 – 0.006
Trichophyton violaceum	0.001 – 0.1
Microsporum canis	0.0001 – 0.1
Edidermorphyton fluccosum	0.001 – 0.05

Terbinafine exhibits poor efficacy against many yeasts of the Candida species.
Terbicip 250 mg tablets in contrast to locally administered terbinafine treatment, has no effect in the treatment of Pityriasis (Tinea) versicolor.

Pharmacokinetics
A single oral dose of 250mg terbinafine results in mean peak plasma concentrations of 0.97µg/ml within 2 hours after administration. The absorption half-life is 0.8 hours and the distribution half-life is 4.6 hours. Terbinafine binds strongly to plasma proteins. It rapidly diffuses through the dermis and concentrates in the lipophilic stratum corneum. Terbinafine is also secreted in sebum, thus achieving high concentrations in hair follicles, hair and sebum rich skins. There is also evidence that terbinafine is distributed into the nail plate within the first few weeks of commencing therapy.
Biotransformation results in metabolites with no antifungal activity, which are excreted predominantly in the urine. The elimination half-life is 17 hours. There is no evidence of accumulation.
No age-dependent changes in pharmacokinetics have been observed but the elimination rate may be reduced in patients with renal or hepatic impairment, resulting in higher blood levels of terbinafine.
The bioavailability of terbinafine is unaffected by food.

Indications
TERBICIP is indicated in the following conditions:
- Fungal infections of the skin, including 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.
- Tinea capitis
- Onychomycosis (fungal infection of the nails) caused by dermatophyte fungi.

Dosage and Administration
Children
No data are available in children under 2 years of age (usually < 12 kg)
Children weighing 20-40 kg: Half tablet of **TERBINAFINE 250 mg** once a day.
Children weighing >40 kg: one tablet of **TERBINAFINE 250 mg** once a day.

Adults
One tablet of **TERBINAFINE 250 mg** once a day.
The duration of treatment varies according to the indication and the severity of the infection.

Skin Infections
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
Recommended duration of treatment.

Tinea capitis: 4 weeks
Tinea capitis occurs primarily in children.

Onychomycosis
For most patients the duration of successful treatment is 6-12 weeks.

Fingernail onychomycosis
6 weeks of therapy is sufficient for toenail infections in most cases.

Toenail onychomycosis
12 weeks of therapy is sufficient for toenail infections in most cases.

Some patients with poor nail outgrowth may require longer treatment. The optimal clinical effect is seen some months after mycological cure and cessation of treatment. This is related to the period required for the outgrowth of healthy nails.

Mode of Administration
Oral

Contraindications
Terbinafine Tablets are contraindicated in individuals with hypersensitivity to terbinafine or to any other ingredients of the formulation.

Warnings and Precautions
Rarely, cases of cholestasis and hepatitis have been reported, these usually occur within two months of starting treatment. If a patient presents with signs or symptoms suggestive of liver dysfunction such as pruritis, unexplained persistent nausea, anorexia or tiredness, or jaundice, vomiting, fatigue, abdominal pain or dark urine, or pale stools, hepatic origin should be verified and terbinafine therapy should be discontinued.

Patients on terbinafine who develop a high fever or sore throat should be examined concerning possible hematological reactions.

Single dose pharmacokinetic studies in patients with pre-existing liver disease have shown that the clearance of terbinafine can be reduced by 50%.

Therapeutic use of terbinafine in patients with chronic or active liver disease has not been studied in prospective clinical trials, and therefore cannot be recommended.
Terbinafine should be used with caution in patients with psoriasis, as very rare cases of exacerbation of psoriasis have been reported.

Terbinafine is a potent inhibitor of the isoenzyme CYP2D6, which should be considered if terbinafine is combined with medicinal products metabolized by this isoenzyme that are titrated individually. Dose adjustments may be necessary.

Interaction with other Medicaments
The plasma clearance of terbinafine may be accelerated by drugs which induce metabolism (such as rifampicin) and may be inhibited by drugs which inhibit cytochrome P450 (such as cimetidine). Where co-administration of such drugs is required, it may be necessary to adjust the dose of terbinafine accordingly.

In vitro studies have shown that terbinafine inhibits the CYP2D6-mediated metabolism. For this reason, it is important to monitor patients who are treated simultaneously with drugs that are mainly metabolized by this enzyme, such as tricyclic antidepressants, β-blockers, selective serotonin re-uptake inhibitors and monoamine oxidase inhibitors type B if the co-medication has a narrow therapeutic index.

Other in vitro and clinical studies suggest that terbinafine shows negligible potential to inhibit or induce the clearance of drugs that are metabolised via other cytochrome P450 enzymes (e.g. ciclosporin, tolbutamine, terfenadine, triazolam, oral contraceptives). There have been some cases reported of menstrual disturbances such as breakthrough bleeding and irregular cycle in patients taking Terbinafine concomitantly with oral contraceptives.

Rare cases of changes in INR and/or prothrombin time have been reported in patients receiving terbinafine concomitantly with warfarin.

Pregnancy
Pregnancy Category B
Foetal toxicity and fertility studies in animals suggest no adverse effects. Since clinical experience in pregnant women is very limited, **TERBINAFINE** should not be used during pregnancy unless the potential benefits outweigh any potential risks.

Lactating Women
Terbinafine is excreted in breast milk; therefore, mothers receiving oral treatment with **TERBINAFINE** should not breastfeed.

Paediatric Use
Oral terbinafine has been found to be well tolerated in children above 2 years of age.

Geriatric Use
There is no evidence to suggest that elderly patients require different dosages or experience different side effects than younger patients. When prescribing tablets for patients in this age group, the possibility of pre-existing impairment of liver or kidney functions should be considered.

Undesirable Effect:
In general, **TERBINAFINE Tablets** are well tolerated. Side effects are usually mild to moderate and transient.
Common Side Effects (>1%): Gastrointestinal symptoms (feeling of fullness, loss of appetite, dyspepsia, nausea, mild abdominal pain, diarrhoea), non-serious forms of skin reaction (rash, urticaria), musculoskeletal reactions (arthralgia, myalgia).

Uncommon Side Effects (0.1-1%): Taste disturbances, including taste loss, which usually recover within several weeks after discontinuation of the drug. Isolated cases of prolonged taste disturbances have been reported. A decrease of food intake leading to significant weight loss was observed in very few severe cases.

Rare Side Effects (0.001-0.1%): Hepatobiliary dysfunction (primarily cholestatic in nature) has been reported in association with Terbinafine 250 mg tablets treatment, including very rare cases of liver failure.

Very Rare Side Effects (<0.01%): Serious skin reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis) and anaphylactoid reactions (including angio-oedema) have been reported.
If progressive skin rash occurs, **TERBINAFINE** treatment should be discontinued.
Haematological disorders such as neutropenia, agranulocytosis, or thrombocytopenia have been reported.

Overdosage
A few cases of overdosage of up to 5 g (20 times the daily therapeutic dose) have been reported, giving rise to headache, nausea, epigastric pain, and dizziness. The recommended treatment for overdosage consists of eliminating the drug, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy, if needed.

Shelf life
36 months

Storage
Store below 30°C.Protect from light.

Presentation
Carton containing 2 blisters of 14 tablets each

Product Registration Holder in Malaysia
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Cipla

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SAP Code: XXXXXXXX (Ver. 02)
Leaflet size: 160 x 200 mm
Colours:
Black

Reference : 21079089
Ph_code / 2D code :
Country : Malaysia
Date: 22/05/2023

Path: D:\OneDrive - Cipla Limited\Shashi\International\Vinod\Malaysia Reg\Terbicip Tablets 2023\Terbicip 250mg Tablets Leaflet Malaysia.ai