Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Trade Name: TERBOFINE **(**Terbinafine Tablets USP 250 mg)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablets contains:

Terbinafine Hydrochloride USP250 mg

3 PHARMACEUTICAL FORM

Oral Tablets

Pink colour, caplet shaped, biconvex, film coated tablet one side plain & other side with break line.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Terbinafineis indicated in the treatment of:

- Oral Terbinafine is indicated in the treatment of ringworm (tinea corporis, tinea cruris and tinea pedis) where oral therapy is considered appropriate due to the site, severity or extent of the infection.
- Oral Terbinafine is indicated in the treatment of onychomycosis.

4.2 Route of administration, Posology and method of Administration:

Route of administration

Oral route administration

Mode of administration

The duration of treatment with terbinafineis dependent on the indication and the severity of the infection.

Posology

The usual recommended dosage in adults is 250 mg once daily.

Skin infections:

Likely durations of treatment are as follows:

Tinea pedis (interdigital, plantar/ moccasin type): 2 to 6 weeks.

Tinea corporis: 4 weeks

Tinea cruris: 2 to 4 weeks

Onychomycosis: The duration of treatment for the majority of patients is between 6 weeks and 3 months. Treatment periods of less than 3 months may be sufficient in younger patients or in patients with fingernail infection or toenail infection other than of the big toe.

Although a 3-month treatment period is usually sufficient in the treatment of toenail infections, a few patients may require treatment for 6 months or more. Poor nail outgrowth during the first weeks of therapy may help to identify the need for prolonged therapy.

Signs and symptoms of infection may persist after mycological cure and it may take several weeks for complete resolution to occur.

Children:

Due to limited data, use of terbinafinein children is not recommended.

Elderly:

There is n o evidence to suggest that elderly patients require different dosages or experience side-effects different to those of younger patients. The possibility of impairment of liver or kidney function should be considered in this age group.

Impaired renal function:

Patients with impaired renal function (creatinine clearance less than 50 mL/minute or serum creatinine of more than 300 mmol/L) should receive half the normal dose.

4.3 Contraindications:

- Hypersensitivity to terbinafine hydrochloride or any of the excipients.
- Severe renal impairment.
- Pregnancy and lactation, as safety has not been demonstrated.

4.4 Special warnings and precautions for use:

Liver function:

Terbinafine tablets are not recommended for patients with chronic or active hepatic disease. Before prescribing terbinafine tablets, liver function test should be performed. Hepatotoxicity

may occur in patients with and without pre-existing hepatic disease; therefore periodic monitoring (after 4-6 weeks of treatment) of liver function test is recommended. Terbinafine should be immediately discontinued in case of elevation of liver function test. Very rare cases of serious hepatic failure (some with a fatal outcome, or requiring hepatic transplant) have been reported in patients treated with terbinafine tablets. In the majority of hepatic failure cases the patients had serious underlying systemic conditions and a causal association with the intake of terbinafine tablets was uncertain.

Patients prescribed terbinafine tablets should be warned to report immediately any signs and symptoms of unexplained persistent nausea, decreased appetite, fatigue, vomiting, right upper abdominal pain, or jaundice, dark urine or pale faeces.

Patients with these symptoms should discontinue taking oral terbinafine and the patient's hepatic function should be immediately evaluated.

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

Terbinafine should be used with caution in patients with pre-existing psoriasis or lupus erythematosus.

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

Dermatological effects:

Serious skin reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis) have been very rarely reported in patients taking terbinafine tablets. If progressive skin rash occurs, terbinafine tablets treatment should be discontinued.

Haematological effects:

Very rare cases of blood disorders (neutropenia, agranulocytosis, thrombo-cytopenia, pancytopenia) have been reported in patients treated with terbinafine tablets. Aetiology of any blood disorders that occur in patients treated with terbinafine tablets should be evaluated and consideration should be given for a possible change in medication regimen, including discontinua-tion of treatment with terbinafine tablets.

Renal function: In patients with renal impairment the use of terbinafine tablets has not been adequately studied, and therefore, is not recommended.

Skin infections: The likely durations of treatment for Tinea pedis, Tinea corporis and Tinea cruris are 2 – 4 weeks. For Tinea pedis (interdigital, plantar/moccasin-type): recommended treatment periods may be up to 6 weeks. Complete disappearance of the symptoms of the infection may not occur until several weeks after mycological cure.

Onychomycosis (nail infection): In most patients the duration of successful treatment is 6-12 weeks.

Fingernail onychomycosis: In most cases 6 weeks' treatment is sufficient in fingernail onychomycosis.

Toenail onychomycosis: In most cases 12 weeks' treatment is sufficient in toenail onychomycosis although a few patients may require treatment up to 6 months. Complete resolution of the signs and symptoms of infection may not occur until several weeks after mycological cure and is only seen several months after stopping treatment, which is the time for growth of a healthy nail.

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

4.5 Interaction with other medicinal products and other forms of interaction

Medicines that induce metabolism (such as rifampicin) may result in accelerated plasma clearance of terbinafine, whereas plasma clearance may be reduced by medicines that inhibit cytochrome P450 (such as cimetidine). Adjustments in the dosage of terbinafine may be required where co-administration of such agents is necessary.

It has been reported that terbinafineinhibits the CYP2D6-mediated metabolism. Although this was an in vitro finding, it may become clinically relevant in patients who receive compounds that are predominantly metabolised by this enzyme, e.g. tricyclic antidepressants (TCA's), beta-blockers, selective serotonin reuptake inhibitors (SSRI's), and monoamine oxidase inhibitors (MAOI's) type B. Other in vitro studies as well as studies in healthy volunteers suggested that terbinafine has negligible potential to inhibit or induce the clearance of medicines that are metabolised via other cytochrome P450 enzymes (e.g. ciclosporin, tolbutamide, terfenadine, triazolam, oral contraceptives). However, some cases of menstrual disturbance (breakthrough

bleeding and irregular cycle) have been reported in patients who took terbinafine concomitantly with oral contraceptives.

4.6 Pregnancy and lactation

There is no clinical experience with terbinafine in pregnancy. Since terbinafine is excreted in breast milk, mothers should not receive treatment with terbinafinewhilst breast-feeding.

4.7 Effects on ability to drive and use machines

No studies on the effects of Terbinafine tablets treatment on the ability to drive and use machines have been performed. Patients who experience dizziness as an undesirable effect should avoid driving vehicles or using machines.

4.8 Undesirable effects

Side-effects:

Side effects are generally mild to moderate, and transient. The following adverse reactions have been observed in the clinical trials or during post-marketing experience.

Haematological system disorders:

Less frequent: Neutropenia, thrombocytopenia and agranulocytosis.

Nervous system disorders:

Less frequent: Psychiatric disturbances such as depression and anxiety, headache, paraesthesia, hypoaesthesia, dizziness, vertigo, malaise and fatigue.

Gastrointestinal system disorders:

Frequent: Dyspepsia, fullness, loss of appetite, nausea, mild abdominal pain, diarrhoea.

Taste loss and taste disturbance have been reported in approximately 0.6 % of patients treated with terbinafine. This usually resolves slowly on medicine discontinuation.

Hepatobiliary system disorders:

Frequent: Jaundice, cholestasis and hepatitis. If hepatic dysfunction develops, treatment with terbinafineshould be discontinued

(see also “Special Precautions”).

***Skin and subcutaneous disorders*:**

Less frequent: Stevens-Johnson syndrome, toxic epidermal necrolysis, rash, urticaria, photosensitivity and angioneurotic oedema, psoriasis. If progressive skin rash occurs, treatment with terbinafineshould be discontinued.

Other side-effects reported include:

Musculoskeletal disorders including arthralgia and myalgia. These may occur as part of a hypersensitivity reaction in association with allergic skin reactions.

Special Precautions:

Rarely, cases of cholestasis and hepatitis have been reported, these usually occur within two months of starting treatment.

Signs and symptoms suggestive of liver dysfunction include pruritus, unexplained persistent nausea, anorexia, tiredness, jaundice, vomiting, fatigue, abdominal pain, and dark urine or pale stools. If a patient presents with these signs or symptoms, hepatic origin should be confirmed and therapy with terbinafine should be discontinued. Pharmacokinetic studies in patients with pre-existing liver disease who received single doses have shown that the clearance of terbinafine may be reduced by approximately 50%. Since the therapeutic use of terbinafine in patients with chronic or active liver disease has not been studied in prospective clinical trials, its use in these circumstances is not recommended.

Due to reports of very rare cases of exacerbation of psoriasis, terbinafineshould be used with caution in patients with psoriasis.

4.9 Overdosage:

Few cases of overdose (up to 5g) have been reported, giving rise to headache, nausea, epigastric pain and dizziness. Recommended treatment for overdose consists of eliminating the active substance, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy if required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotheraupitic group: Antifungal

ATC CODE: D01BA02

Mechanism of Action:

Terbinafine is an allylamine, which has a broad spectrum of antifungal activity. At low concentrations terbinafine is fungicidal against dermatophytes, molds and certain dimorphic fungi. Its 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 cytochrome P450 system.

Pharmacodynamic effects

Terbinafine, an allylamine antifungal, has a broad spectrum of activity. Terbinafine is fungicidal against dermatophytes, moulds and certain fungi at low concentrations, whereas the activity against yeasts is either fungicidal or fungistatic, depending on the species.

Terbinafine exerts its fungicidal activity by specifically interfering with fungal sterol biosynthesis at an early stage. Fungal cell death is caused by a deficiency in ergosterol and an intracellular accumulation of squalene. Terbinafine inhibits squalene epoxidase in the fungal cell membrane. This enzyme squalene epoxidase is not related to the cytochrome P450 system. When administered orally, terbinafine concentrates in skin at levels associated with fungicidal activity.

5.2 Pharmacokinetic properties

A mean peak plasma concentration of 0.97 mg/mL is reached within 2 hours of administration of a single oral dose of 250 mg terbinafine. Terbinafine has an absorption half-life of 0.8 hours and a distribution half-life of 4.6 hours. It binds strongly to plasma proteins. Diffusion through the dermis occurs rapidly following which terbinafine concentrates in the lipophilic stratum corneum. Terbinafine is also secreted in sebum and therefore high concentrations are reached in hair follicles, hair and se bum-rich skins. Evidence indicates that terbinafine is distributed into the nail plate within the first few weeks of initiation of treatment. Biotransformation leads to the formation of metabolites with no antifungal activity and with predominantly renal excretion. The elimination half-life is 17 hours and there is no evidence of accumulation.

Although no age-dependent changes in pharmacokinetics have been observed with terbinafine, the elimination rate may be reduced in patients with impaired renal or hepatic function, thus resulting in higher blood concentrations of terbinafine.

Food does not affect the bioavailability of terbinafine.

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 rates, an increased incidence of liver tumours was observed in males at the highest dosage level of 69 mg/kg a day. 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, dogs or monkeys.

During high-dose studies in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level 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 mutagenic or clastogenic potential. 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

Dicalcium Phosphate

Starch

Microcrystalline Cellulose

Sodium Starch Glycolate

PVP K-30

Methyl Paraben Sodium

Propyl Paraben Sodium

Purified Water

Talcum Powder

Magnesium Stearate

Croscarmellose Sodium

Aerosil

Fine Coat

Isopropyl Alcohol

Methylene Dichloride

Erythrosine Lake

PEG 6000

Talcum Powder

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months from the date of manufacture

6.4 Special precautions for storage

Store at temperature below 30°C.

Keep out of reach of children.

Store the blisters in the outer carton until required for use.

6.5 Nature and contents of container

3 x 10 ALU-PVC Blister Pack with insert.

6.6 Special precautions for disposal and other handling:

No Special Requirements

7 MARKETING AUTHORISATION HOLDER

BDA HEALTHCARE PVT. LTD.,

Plot No.: B-1, B-2, B-3, Near Gov. ITI MIDC, Parseoni – 441105,

Taluka: Parseoni, District: Nagpur, M.S., India.

8. MARKETING AUTHORISATION NUMBER(S)

06428/08303/NMR/2020

9.MEDICAL PRESCRIPTION STATUS:

Prescription Only Medicinal Product (POM)

10.DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26.07.2021

11DATE OF REVISION OF THE TEXT:

02 July 2023