Summary of Product Characteristics

TERBINAFORCE-250

(Terbinafine Tablets USP 250 mg)

1. NAME OF MEDICINAL PRODUCT

TERBINAFORCE-250 (Terbinafine Tablets USP 250 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TERBINAFORCE-250: Each uncoated tablet contains Terbinafine Hydrochloride USP equivalent to Terbinafine 250 mg.

Excipients of known effect;

Each tablet contains Lactose.....108.5m mg

: For a full list of excipients, please refer Section 6.1.

3. PHARMACEUTICAL FORMS

TERBINAFORCE-250: A white to off-white, circular, bevel edged, flat, scored on one side, uncoated tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Terbinafine is an allylamine antifungal indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes, ringworm infections (including tinea pedis, cruris, and corporis) where oral therapy appropriate (due to site, severity or extent).

4.2 Dosage and Administration

An oral dose of 250 mg is given once daily for 2-4 weeks for tinea cruris; treatment may be continued for up to 6 weeks for tinea pedis infections; a 4 week course is used in tinea corporis infection.

Dermatophyte infections of the nails are treated with the equivalent of Terbinafine 250 mg orally once daily for 6 to 12 weeks although longer treatment may be necessary in toe-nail infections.

In Children of over 1 year of age, body-weight 10–20 kg, 62.5 mg once daily; body-weight 20–40 kg, 125 mg once daily; body-weight over 40 kg, 250 mg once daily

Mode of Administration: For oral use

4.3 Contraindications

TERBINAFORCE-250 is contraindicated in individuals with a history of allergic reaction to oral Terbinafine because of the risk of anaphylaxis or any excipients of this medication.

4.4 Special Warning and Precautions for use

TERBINAFORCE**-250** contains Lactose. Patients with rare hereditary problems of galactose intolerance, or glucose-galactose malabsorption should not take this medicine.

Terbinafine is not recommended for patients with chronic or active liver disease. Before prescribing Terbinafine, any pre-existing liver disease should be assessed. Hepatotoxicity

may occur in patients with and without pre-existing liver disease.

Taste disturbance, including taste loss, has been reported with the use of Terbinafine. Taste disturbance can be severe, may be prolonged, or may be permanent. Discontinue Terbinafine if taste disturbance occurs.

Smell disturbance, including loss of smell, has been reported with the use of Terbinafine. Smell disturbance may be prolonged, or may be permanent. Discontinue Terbinafine if smell disturbance occurs.

Depressive symptoms have been reported with Terbinafine use. Prescribers should be alert to the development of depressive symptoms.

Severe neutropenia has been reported. If the neutrophil count is $\leq$ 1,000 cells/mm^3, Terbinafine should be discontinued.

Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported with oral use of Terbinafine. If progressive skin rash occurs, treatment with Terbinafine should be discontinued.

Precipitation and exacerbation of cutaneous and systemic lupus erythematosus have also been reported.

4.5 Interaction with other medicinal products and other forms of interaction

Plasma concentrations of Terbinafine may be increased by drugs that inhibit its metabolism by cytochrome P450, such as cimetidine, and decreased by drugs that induce cytochrome P450 enzymes, such as rifampicin Menstrual disturbances including breakthrough bleeding have been reported in patients taking oral contraceptives and Terbinafine.

Terbinafine has been shown *in vitro* to inhibit metabolism mediated by the cytochrome P450 isoenzyme CYP2D6. Hence it may affect the plasma concentrations of drugs predominantly metabolised by this enzyme such as tricyclic antidepressants, beta blockers.

4.6 Pregnancy and Lactation

Use in Pregnancy *Pregnancy Category B.* Should be used during pregnancy only if clearly needed. Use in Lactation

Terbinafine is excreted in breast milk and therefore mothers should not receive Terbinafine whilst breast- feeding.

4.7 Effect on ability to drive and use machines

Patients who experience dizziness as an undesirable effect should avoid driving vehicles or using machines.

4.8 Undesirable Effects

Abdominal discomfort, anorexia, nausea, diarrhoea; headache; rash and urticaria occasionally with arthralgia or myalgia are some of the undesirable effects; less commonly taste disturbance; rarely liver toxicity (including jaundice, cholestasis and hepatitis) have been reported, in such cases discontinue treatment, Angioedema, dizziness, malaise, paraesthesia, hypoaesthesia,

photosensitivity, serious skin reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis), discontinue treatment if progressive skin rashes occurs; Very rarely reported side effects are: psychiatric disturbances, blood disorders (including leucopenia and thrombocytopenia), lupus erythematosus-like effect, and exacerbation of psoriasis.

Reporting of suspected adverse reactions:

Healthcare professionals are requested to report any suspected adverse reactions to the National Regulatory Agents

4.9 Overdose

Doses up to 5 grams have been reported without inducing serious adverse reactions. The symptoms of overdose included nausea, vomiting, abdominal pain, dizziness, rash, frequent urination, and headache. The recommended treatment of overdosage consists in eliminating the drug, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy if needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic

Properties Pharmacotherapeutic group: Antifungals for systemic use. ATC Code: D01BA02

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 versus 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.

5.2 Pharmacokinetic Properties

Terbinafine Hydrochloride is well absorbed from the gastrointestinal tract. The bioavailability is about 40% because of first-pass hepatic metabolism. Peak plasma concentrations of 1 µg/mL appear within 2 hours after a single 250 mg dose. Terbinafine is extensively bound to plasma proteins. Terbinafine is distributed into the stratum corneum of the skin, the nail plate, and hair where it reaches concentrations considerably higher than those found in plasma. It appears in breast milk. Terbinafine is metabolised in the liver to inactive metabolites which are excreted mainly in the urine. A plasma elimination half-life varying from 17 to 36 hours has been reported and a terminal elimination half-life of up to 400 hours in patients given prolonged therapy, probably representing elimination from skin and adipose tissue. Fungicidal concentrations in nails are maintained for several weeks after therapy is stopped. The elimination rate may be altered in patients

with liver or kidney disease.

5.3 Pre-Clinical Safety Data

No relevant additional information is available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Lactose (DC Grade), Povidone k-30, LHPC (Low-substituted Hydroxypropyl Cellulose)-11, Colloidal Anhydrous Silica, Magnesium Stearate and Crospovidone.

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 months from the date of manufacture.

6.4 Special

Precautions for Storage Store below 30°C. Protect from light & moisture. Keep all medicines out of the reach of children.

6.5 Nature and Contents of Container

TERBINAFORCE-250: 10 Tablets packed in a PVC Blister. Three such Blisters are packed in a carton along with a package insert.

6.6 Special Precautions for Disposal

No special requirements.

7. Marketing Authorization Holder

MANKIND PHARMA LTD.
208, Okhla Industrial Estate, Phase-3, New Delhi-110 020 (INDIA)

8. MARKETING AUTHORISATION NUMBER

CTD2350

9. DATE OF FIRST AUTHORISATION IN KENYA

10. DATE OF REVISION OF THE TEXT