

**TERBINAFINE 250 MG TABLETS  
(TERBINAFINE HYDROCHLORIDE)**

**PL 08137/0129**

**UKPAR**

**TABLE OF CONTENTS**

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 12
Summary of Product Characteristics	Page 13
Product Information Leaflet	Page 17
Labelling	Page 19

**TERBINAFINE 250 MG TABLETS  
(TERBINAFINE HYDROCHLORIDE)**

**PL 08137/0129**

**LAY SUMMARY**

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Neolab Limited a Marketing Authorisation (licence) for the medicinal product Terbinafine 250 mg Tablets (PL 08137/0129) on 30<sup>th</sup> October 2007. This is a prescription-only medicine (POM) used for the treatment of a variety of fungal infections of the skin and nails.

Terbinafine 250 mg Tablets contain the active ingredient terbinafine hydrochloride, which belongs to a group of medicines called antifungals. Terbinafine hydrochloride attacks and kills the fungus that is causing your infection.

The test product was considered to be a generic product of the reference product Lamisil 250 mg Tablets (Novartis Pharmaceuticals UK Ltd) based on the bioequivalence study submitted, and no new safety issues arose as a result of this study.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Terbinafine 250 mg Tablets outweigh the risk, hence a Marketing Authorisation has been granted.

**TERBINAFINE 250 MG TABLETS  
(TERBINAFINE HYDROCHLORIDE)**

**PL 08137/0129**

**SCIENTIFIC DISCUSSION**

**TABLE OF CONTENTS**

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 8
Clinical assessment	Page 9
Overall conclusion and risk benefit assessment	Page 11

## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the UK granted Neolab Limited a Marketing Authorisation for the medicinal product Terbinafine 250 mg Tablets (PL 08137/0129) on 30<sup>th</sup> October 2007. The product is a prescription-only medicine (POM) indicated for the treatment of a variety of fungal infections of the skin and nails, including ringworm where oral therapy is considered appropriate.

The application was submitted as a national, abridged, complex application, according to Article 10.1 (a) (iii) first paragraph (now article 10(1)) of Directive 2001/83/EC. The application refers to the innovator product, Lamisil 250 mg Tablets (PL 00101/0304; Novartis Pharmaceuticals UK Ltd) that was granted a UK licence on 03/10/1990.

The product contains the active ingredient terbinafine hydrochloride, a broad spectrum antifungal agent which acts by inhibiting fungal sterol synthesis and is indicated for the treatment of a variety of fungal infections of the skin and nails, including ringworm where oral therapy is considered appropriate

The application depends upon the bioequivalence study presented by the applicant comparing the test product with the reference product Lamisil 250 mg Tablets (PL 00101/0304; Novartis Pharmaceuticals UK Ltd).

## PHARMACEUTICAL ASSESSMENT

### ACTIVE SUBSTANCE

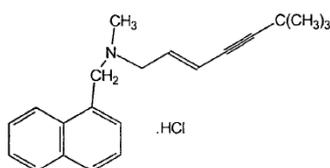
#### Terbinafine hydrochloride

Nomenclature:

INN: Terbinafine hydrochloride

Chemical name: (2E)-N,6,6-Trimethyl-N-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine hydrochloride.

Structure:



Molecular formula: C<sub>21</sub>H<sub>26</sub>ClN

Molecular weight: 327.9

CAS No: 78628-80-5

Physical form: A white or almost white powder

Solubility: Very slightly or slightly soluble in water, freely soluble in anhydrous ethanol and in methanol, slightly soluble in acetone.

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate active substance specification has been provided based on the European Pharmacopoeia specification.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active terbinafine hydrochloride is stored in appropriate packaging. It is packed in 2 clear low density polythene (LDPE) bags enclosed in a black polythene bag (all individually sealed using plastic fasteners and cellophane tape) and placed in fibre drums. Specifications and certificates of analysis have been provided. The polyethylene bags in direct contact with the drug substance satisfy Directive 2002/72/EC (as amended), and are suitable for contact with foodstuffs.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated for active substance stored in similar immediate packaging to the commercial packaging. This data demonstrates the stability of the drug substance and supports a retest period of 2 years at a storage condition of 25 °C/60 % RH, when stored in the proposed packaging.

**DRUG PRODUCT****Other ingredients**

Other ingredients consist of pharmaceutical excipients, namely microcrystalline cellulose, sodium starch glycollate, hypromellose, colloidal anhydrous silica, magnesium stearate, and purified water. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeial monographs. Satisfactory certificates of analysis have been provided for all excipients.

There are no materials of human or animal origin contained in or used in the manufacturing process for the proposed product.

There were no novel excipients used and no overages.

**Pharmaceutical development**

Details of the pharmaceutical development of the drug product have been supplied and are satisfactory.

**Manufacture**

A description and flow-chart of the manufacturing method has been provided.

In-process controls have been provided and are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on validation batches. The results are satisfactory.

**Finished product specification**

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

**Container Closure System**

The tablets are packed in blisters. This primary packaging is composed of a PVC (polyvinylchloride)/Aluminium foil. The blister strips are packaged with the PIL into cardboard outer cartons. The product is packaged in sizes of 14 and 28 tablets.

Specifications and Certificates of Analysis for all packaging components used have been provided. These are satisfactory.

All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

**Stability**

Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 2 years has been set, which is satisfactory. The storage instruction is “Store in the original package”.

**Bioequivalence Study**

A bioequivalence study was submitted comparing the test product, Terbinafine 250 mg Tablets, to the innovator product, Lamisil 250 mg Tablets (PL 00101/0304; Novartis Pharmaceuticals UK Ltd).

**Product Information**

The updated, approved SPC, leaflet, and labelling are satisfactory.

**Conclusion**

The test product is pharmaceutically equivalent to the reference product which has been licensed in the UK for over 10 years. On this basis, and considering the bioequivalence data provided, the applicant’s claim that Terbinafine 250 mg Tablets is a generic medicinal product of Lamisil 250 mg Tablets appears justified. A more detailed evaluation of the bioequivalence study is found in the clinical assessment.

The quality grounds for this application are considered adequate. It is recommended that a Marketing Authorisation is granted.

## **PRECLINICAL ASSESSMENT**

The application was submitted as a national, abridged, complex application, according to Article 10.1 (a) (iii) first paragraph (now article 10(1)) of Directive 2001/83/EC.

No new preclinical data have been supplied with this application and none are required for an application of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.

## CLINICAL ASSESSMENT

### INDICATIONS

Terbinafine 250 mg Tablets are indicated for the treatment of a variety of fungal infections of the skin and nails, including ringworm where oral therapy is considered appropriate.

### CLINICAL PHARMACOLOGY

#### Pharmacokinetics - General

Terbinafine is well absorbed orally with a  $C_{max}$  of approximately 1 mg/L at 2 hours after a single 250 mg oral tablet. Bioavailability is 70% and food delays absorption by about an hour, but does not affect bioavailability. Kinetics are linear between 125-750 mg doses and steady state plasma is reached after 10-14 days in healthy volunteers with 125 or 250 mg daily doses.

Terbinafine is lipophilic with a large volume of distribution of about 1,000-2,000 L. It is >95% plasma protein bound and tissue concentrations are higher in skin and nails, than in plasma.

It is extensively metabolised in the liver, partly first pass, and oxidised by CYP enzymes. At least 7 CYP enzymes, particularly CYP2C9, CYP1A2, CYP3A4, and CYP2C8, are involved and it is a competitive inhibitor of CYP2D6. There are nearly 15 known inactive metabolites. Although it inhibits CYP2D6, its metabolism by multiple enzyme pathways means few interactions, other than anti-mycotics and important interactions with tricyclic antidepressants.

#### Pharmacokinetics - Bioequivalence Study

This bioequivalence study compared the test product, Terbinafine 250 mg Tablets (PL 08137/0129, Neolab Limited), to the reference product Lamisil 250 mg Tablets (PL 00101/0304; Novartis Pharmaceuticals UK Ltd).

This was an open label, single dose, randomised, two period cross over trial in 32 healthy male volunteers. Of the 32 subjects, two were standby and one was withdrawn after the first period because of raised liver enzymes. Thus, 31 subjects successfully completed the study. The data from 30 subjects were used for the analysis. Subjects were fasting until 2 hours after dosing. Blood samples were taken for 96 hours post dose.

The report is stated to conform to GCP. The assay was HPLC with a detection limit of 10 ng/ml.

### Results

**Table 1 – Terbinafine mean pharmacokinetic data**

Variable	Terbinafine Test	Lamisil (reference)	T/R ratio 90% CI
$C_{max}$ (ng/ml)	1274	1213	1.05 (97-114%)
$T_{max}$ (h)	2.3	2.2	
$AUC_{0-\infty}$ (ng.h/ml)	7931	7927	1.00 (94-106%)

**Pharmacodynamics**

Terbinafine blocks ergosterol biosynthesis in the fungal cell wall, inhibiting enzyme squalene epoxidase, leading to toxic accumulation of squalene. Terbinafine has a low affinity to mammalian cells compared to fungal cells, although ergosterol synthesis is similar to cholesterol synthesis. The mean MIC and the mean minimal fungicidal concentration (MFC) for terbinafine in 39 dermatophyte isolates is 0.004 µg/ml, a value lower than other antifungal agents. In contrast to ketoconazole, terbinafine has little effect on mammalian steroid hormone synthesis.

**Clinical Pharmacology - Clinical Assessor's Comments**

The applicant appears to have shown bioequivalence for terbinafine within accepted limits.

**EFFICACY**

No new data are submitted and none are required for this type of application.

Efficacy is reviewed in the clinical expert report. The reference product is established and the application depends upon the ability to show bioequivalence with the reference product.

**SAFETY**

No new data are submitted and none are required for this type of application.

Safety is reviewed in the clinical expert report. The reference product is established and the main basis of the application depends upon the bioequivalence study. The present product has not been marketed and no post marketing surveillance data are available.

**EXPERT REPORT**

A satisfactory clinical expert report has been submitted with appropriate CV.

**PRODUCT INFORMATION:****Summary of Product Characteristics**

The approved SPC is satisfactory.

**Patient Information Leaflet**

The PIL is in line with the approved SPC and is satisfactory.

**Labelling**

Colour mock-ups of the labelling have been provided. The labelling is satisfactory.

**DISCUSSION AND CONCLUSION**

All issues have been adequately addressed by the applicant. The bioequivalence of the test and reference products was shown within general acceptance limits. The approved SPC and PIL of the test product are in line with the SPC and PIL of the reference product.

Sufficient clinical information has been submitted to support this application. When used as indicated, Terbinafine 250mg Tablets has a favourable benefit-to-risk ratio. Therefore, a Marketing Authorisation may be granted on medical grounds.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The important quality characteristics of Terbinafine 250mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for an application of this type.

### **EFFICACY**

Bioequivalence has been demonstrated between the applicant's Terbinafine 250mg Tablets and the reference product Lamisil 250 mg Tablets (Novartis Pharmaceuticals UK Ltd).

No new or unexpected safety concerns arise from this application.

### **PRODUCT LITERATURE**

The approved SPC, PIL and labelling are satisfactory and consistent with that for Lamisil 250 mg Tablets.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Extensive clinical experience with terbinafine hydrochloride is considered to have demonstrated the therapeutic value of the active substance. The risk benefit is, therefore, considered to be positive.

**TERBINAFINE 250 MG TABLETS  
(TERBINAFINE HYDROCHLORIDE)**

**PL 08137/0129**

**STEPS TAKEN FOR ASSESMENT**

- 1 The MHRA received the marketing authorisation application on 16<sup>th</sup> January 2004
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 13<sup>th</sup> February 2004
- 3 Following assessment of the application the MHRA requested further information relating to the clinical dossier on 25<sup>th</sup> June 2004, and further information relating to the quality dossier on 1<sup>st</sup> July 2004
- 4 The applicant responded to the MHRA's requests, providing further information for the clinical sections on 30<sup>th</sup> June 2004 and the quality sections in September 2004
- 5 Following assessment of the response the MHRA requested further information relating to the quality dossier on 21<sup>st</sup> September 2004
- 6 The applicant responded to the MHRA's request, providing further information for the quality sections on 31<sup>st</sup> August 2005 and 30<sup>th</sup> November 2005
- 7 Following assessment of the response the MHRA requested further information relating to the quality dossier on 18<sup>th</sup> July 2006
- 8 The applicant responded to the MHRA's request, providing further information for the quality sections on 18<sup>th</sup> June 2007
- 9 Following assessment of the response the MHRA requested further information relating to the quality dossier on 1<sup>st</sup> August 2007
- 10 The applicant responded to the MHRA's request, providing further information for the quality sections on 28<sup>th</sup> August 2007
- 11 The application was determined on 30<sup>th</sup> October 2007

## SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SPC) for Terbinafine 250 mg Tablets is as follows:

### 1 NAME OF THE MEDICINAL PRODUCT

Terbinafine 250 mg Tablets.

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 281.25 mg terbinafine hydrochloride, equivalent to 250 mg terbinafine.

For excipients, see 6.1.

### 3 PHARMACEUTICAL FORM

Tablet.

Terbinafine 250 mg Tablets are white, circular, biconvex tablets with a deep score plus "TBF" and "NEO" on one side and plain on the other side.

### 4 CLINICAL PARTICULARS

#### 4.1 THERAPEUTIC INDICATIONS

Fungal infections of the skin and nails caused by *Trichophyton* (e.g. *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*), *Microsporum canis* and *Epidermophyton floccosum*.

1. Terbinafine Tablets are 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.

2. Terbinafine Tablets are indicated in the treatment of onychomycosis.

Consideration should be given to official guidance on the appropriate use of antifungal agents.

#### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults: 250 mg once daily.

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

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 most patients is between 6 weeks and 3 months. Treatment periods of less than 3 months can be anticipated in patients with fingernail infection, toenail infection other than of the big toe, or patients of younger age. In the treatment of toenail infections, 3 months is usually sufficient although a few patients may require treatment of 6 months or longer. Poor nail outgrowth during the first weeks of treatment may enable identification of those patients in whom longer therapy is required. Complete resolution of the signs and symptoms of infection may not occur until several weeks after mycological cure.

#### Children

A review of safety experience with terbinafine in children, which includes 314 patients involved in a UK post marketing surveillance study, has shown that the adverse event profile in children is similar to that seen in adults. No evidence of any new, unusual or more severe reactions to those seen in the adult population have been noted. However, as data are still limited its use is not recommended.

#### Use in the elderly

There is no 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 (see Precautions).

Method of administration: Via the oral route.

#### **4.3 CONTRAINDICATIONS**

Hypersensitivity to terbinafine or to any of the other constituents of Terbinafine Tablets.

#### **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

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 pruritus, 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 (see 4.8 Undesirable effects). Single dose pharmacokinetic studies in patients with pre-existing liver disease have shown that the clearance of terbinafine may be reduced by about 50%. The 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. Patients with impaired renal function (creatinine clearance less than 50ml/minute or serum creatinine of more than 300µmol/l) should receive half the normal dose.

#### **4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION**

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 agents is necessary, the dosage of terbinafine may need to be adjusted accordingly.

In vitro studies have shown, that terbinafine inhibits the CYP2D6-mediated metabolism. This in vitro finding may be of clinical relevance for patients receiving compounds predominantly metabolised by this enzyme, such as tricyclic antidepressants (TCA's), B-blockers, selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors (MAOIs) Type B.

Other studies undertaken in vitro and in healthy volunteers suggest that terbinafine shows negligible potential to inhibit or induce the clearance of drugs that are metabolised via other cytochrome P450 enzymes (e.g. cyclosporin, tolbutamine, terfenadine, triazolam, oral contraceptives). However, some cases of menstrual disturbance (breakthrough bleeding and irregular cycle) have been reported in patients taking terbinafine concomitantly with oral contraceptives.

#### **4.6 PREGNANCY AND LACTATION**

Foetal toxicity and fertility studies in animals suggest no adverse effects. There is no clinical experience with terbinafine in pregnant women, therefore, unless the potential benefits outweigh any potential risks, terbinafine should not be administered during pregnancy. Terbinafine is excreted in breast milk and therefore mothers should not receive terbinafine treatment whilst breast-feeding.

#### **4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**

None.

#### **4.8 UNDESIRABLE EFFECTS**

Side effects are generally mild to moderate, and transient. The most common are gastrointestinal symptoms (dyspepsia, fullness, loss of appetite, nausea, mild abdominal pain, diarrhoea), allergic skin reactions (rash, urticaria) and headache. Paraesthesia, hypoaesthesia, dizziness, malaise and fatigue have also been reported rarely. Extremely rare cases of vertigo have been reported. Musculo-skeletal disorders including arthralgia and myalgia have been

reported. These may occur as part of a hypersensitivity reaction in association with allergic skin reactions.

Rare cases of serious skin reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, photosensitivity and angioneurotic edema) have been reported. If progressive skin rash occurs, terbinafine treatment should be discontinued.

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

Rare cases of serious hepatic dysfunction, including jaundice, cholestasis and hepatitis have been reported. If hepatic dysfunction develops, treatment with terbinafine should be discontinued (see 4.4 Special warnings and special precautions for use).

Haematological disorders such as neutropenia, thrombocytopenia and agranulocytosis have been reported very rarely.

Exacerbation of psoriasis has been reported very rarely (see 4.4 Special warnings and special precautions for use). Psychiatric disturbances such as depression and anxiety have been reported very rarely.

#### **4.9 OVERDOSE**

A few cases of overdose (up to 5g) have been reported, giving rise to headache, nausea, epigastric pain and dizziness. 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**

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. Terbinafine does not influence the metabolism of hormones or other drugs.

When given orally, the drug concentrates in skin at levels associated with fungicidal activity.

#### **5.2 PHARMACOKINETIC PROPERTIES**

A single oral dose of 250 mg 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.

#### **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 rats, 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**

Microcrystalline cellulose

Sodium starch glycollate

Hypromellose

Colloidal anhydrous silica

Magnesium stearate.

### **6.2 INCOMPATIBILITIES**

Not applicable.

### **6.3 SHELF LIFE**

24 months.

### **6.4 SPECIAL PRECAUTIONS FOR STORAGE**

Store in the original package.

### **6.5 NATURE AND CONTENTS OF CONTAINER**

Blister strips comprising PVC/Aluminium foil enclosed in an outer carton. Pack sizes of 14 or 28 tablets (not all packs may be marketed).

### **6.6 SPECIAL PRECAUTIONS FOR DISPOSAL**

Not applicable.

## **7 MARKETING AUTHORISATION HOLDER**

Neolab Limited

57 High Street

Odiham

Hants

RG29 1LF

UK

## **8 MARKETING AUTHORISATION NUMBER(S)**

PL 08137/0129

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

30/10/2007

## **10 DATE OF REVISION OF THE TEXT**

30/10/2007

## PATIENT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET  
**Terbinafine 250 mg Tablets**  
 Terbinafine hydrochloride



### What you should know about Terbinafine Tablets

Please read this leaflet carefully before you start to take your medicine. This leaflet provides a summary of the information available on your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

### What's in your medicine

Each tablet contains 250 mg of the active ingredient, terbinafine (as terbinafine hydrochloride). Other ingredients include: microcrystalline cellulose, sodium starch glycolate, hypromellose, colloidal anhydrous silica and magnesium stearate.

Terbinafine Tablets are white, round tablets with a deep score plus 'TBF' and 'NEO' on one side and plain on the other side.

The tablets are available in packs containing 14 and 28 tablets.

### What is Terbinafine?

The active ingredient in your tablets, terbinafine, belongs to a family of medicines called antifungals. It is used in the treatment of a variety of fungal infections of the skin and nails. It attacks and kills the fungus that is causing your infection. The Marketing Authorisation Holder and manufacturer responsible for batch release is Neolab Ltd, 57 High Street, Odiham, Hants, RG29 1LF.

### Before taking your medicine

Before you start taking this medicine, tell your doctor if:

- You suspect that you are allergic to terbinafine or any of the other ingredients of the tablets (listed above)
- You have any liver problems or have had any disease which may have affected your liver
- You have any kidney problems
- You suffer from psoriasis
- You are pregnant, or planning to become pregnant. If you become pregnant whilst taking Terbinafine Tablets, tell your doctor.
- You are breastfeeding
- You are taking any other medicines, either bought or prescribed. Some medicines can interfere with these tablets, so check with your doctor or pharmacist before taking any other medicines. In particular, tell your doctor if you are taking any of the following:
  - rifampicin
  - cimetidine
  - oral contraceptives. Irregular periods and breakthrough bleeding may occur in some patients
  - antidepressants
  - beta-blockers

Terbinafine Tablets are not recommended for children.

### Taking your medicine

Take your Terbinafine Tablets as prescribed by your doctor and as stated on the carton label. Swallow your tablets whole with a glass of water.

The usual dose is 250 mg a day.

Treatment for skin infections usually lasts for between 2 and 6 weeks. For nail infections treatment usually lasts between 6 weeks and 3 months, although some patients with toenail infections may need to be treated for 6 months or longer.

**If you forget to take your medicine:**

If you miss a dose, do not worry. Take another as soon as you remember or wait until it is time to take your next dose. Then go on as before.

**If you take too many tablets:**

If you accidentally take too much of your medicine, tell your doctor or go to the nearest casualty department **AS SOON AS POSSIBLE**. If you go to the hospital/doctor, remember to take this leaflet and any remaining tablets with you so the doctor knows what you have taken.

Please read the back of this leaflet.

**After taking your medicine**

Most people have no problems when taking these tablets. Like all medicines, however, Terbinafine Tablets can cause unwanted side effects in some people. Side effects are often mild to moderate and may wear off after a while.

The most common side effects are

- Headache
- Reduced appetite or slight nausea (sick feeling)
- Indigestion
- Mild abdominal pain or fullness
- Diarrhoea
- Itching, rash or swelling.

Rare side effects include

- Feeling unwell, tired or dizzy
- Numbness or tingling

There have been reports of muscle and joint pains. These may happen as part of a hypersensitivity (allergic) reaction along with allergic skin reactions (rash, swelling).

Taste loss and taste disturbance have been reported by a small number of patients. This usually resolves when the medicine is discontinued.

Rare side effects may include yellowing of your skin or eyes (jaundice; this may indicate liver problems) and severe skin rash (swelling, blistering or wheals). If you notice any of these symptoms, stop taking your tablets and tell your doctor immediately.

Very rarely people may experience a decrease in the number of some blood cells, depression and anxiety or a worsening of psoriasis symptoms.

Vertigo has been reported extremely rarely.

**Storing your medicine**

Do not keep this medicine after the expiry date shown on the carton. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Store the tablets in the original package.

Keep all medicines out of the reach and sight of children. Your medicine can harm them.

These tablets have been prescribed for you. Only a doctor can prescribe these tablets for you.

Never give them to anyone else even if their symptoms are the same as yours. It may harm them.

This leaflet was prepared August 2007.

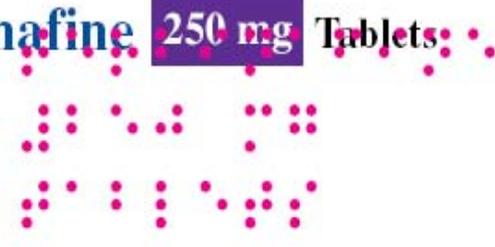
This leaflet applies to Terbinafine 250 mg Tablets only.

**LABELLING**

**Pack size 14**

	<p><b>Terbinafine</b>  <b>250 mg</b> Tablets</p> <p>Each tablet contains 281.25 mg terbinafine hydrochloride, equivalent to 250 mg terbinafine. For oral administration. Use as directed by a physician. Please read the enclosed leaflet. Store in the original package.</p> <p><b>KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN</b></p>	
	<p>14 tablets</p> <p><b>Terbinafine 250 mg</b> Tablets</p>	<p>Item Code</p>
<p><b>Terbinafine 250 mg</b> Tablets          14 tablets</p>	<p><b>Terbinafine 250 mg</b> Tablets</p> <p>14 tablets</p> 	
	<p><b>Terbinafine 250 mg</b> Tablets</p> <p>PL 08137/0129          PL Holder: Neolab Ltd, 57 High Street, Odiham, Hants, RG29 1LF</p>	<p>POM</p> <p>14 tablets</p> <p>XXXXX</p>

Pack size 14 with braille

	<p><b>Terbinafine</b>  <b>250 mg</b> Tablets</p> <p>Each tablet contains 281.25 mg terbinafine hydrochloride, equivalent to 250 mg terbinafine. For oral administration. Use as directed by a physician. Please read the enclosed leaflet. Store in the original package.</p> <p><b>KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN</b></p>	<p>for all responses label</p>
	<p>14 tablets</p> <p><b>Terbinafine 250 mg</b> Tablets</p>	<p>Bar Code</p>
<p>Terbinafine  <b>250 mg</b> Tablets          14 tablets</p>	<p><b>Terbinafine 250 mg</b> Tablets</p>  <p>14 tablets</p> 	
	<p><b>Terbinafine 250 mg</b> Tablets</p> <p>PL 08137/0129          PL Holder: Neolab Ltd, 57 High Street, Odiham, Hants, RG29 1LF</p>	<p>POM</p> <p>14 tablets</p> <p>XXXXX</p>

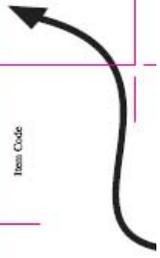
Pack size 28

<p><b>Terbinafine</b>  <b>250 mg Tablets</b></p> <p>Each tablet contains 281.25 mg terbinafine hydrochloride, equivalent to 250 mg terbinafine. For oral administration. Use as directed by a physician. Please read the enclosed leaflet. Store in the original package.</p> <p><b>KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN</b></p>	<p>Bar Code</p> <p style="writing-mode: vertical-rl; transform: rotate(180deg);">for dispensing label</p>	
<p>28 tablets</p> <p><b>Terbinafine 250 mg Tablets</b></p>		<p>Item Code</p>
<p style="writing-mode: vertical-rl; transform: rotate(180deg);">28 tablets</p> <p style="writing-mode: vertical-rl; transform: rotate(180deg);"><b>Terbinafine 250 mg Tablets</b></p>	<p><b>Terbinafine 250 mg Tablets</b></p> <p>28 tablets</p>  <p>neolab</p>	
<p><b>Terbinafine 250 mg Tablets</b></p> <p>PL 08137/0129          PL Holder: Neolab Ltd, 57 High Street, Odiham, Hants, RG29 1LF</p>	<p>POM</p>	<p>XXXXX</p>

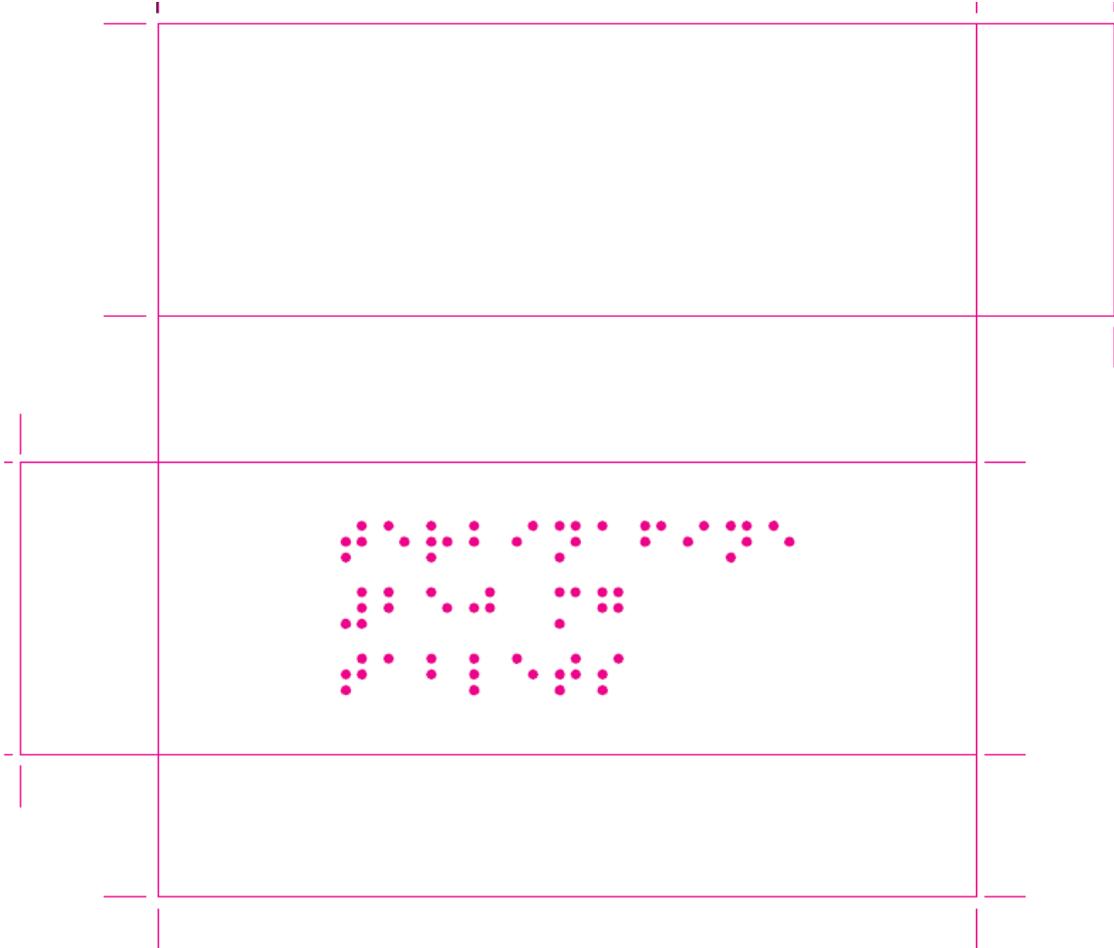


Pack size 28 with braille

	<p><b>Terbinafine</b>  <b>250 mg Tablets</b></p> <p>Each tablet contains 281.25 mg terbinafine hydrochloride, equivalent to 250 mg terbinafine. For oral administration. Use as directed by a physician. Please read the enclosed leaflet. Store in the original package.</p> <p><b>KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN</b></p>	<p>for dispensing label</p>
	<p>28 tablets</p> <p><b>Terbinafine 250 mg Tablets</b></p>	<p>Item Code</p>
<p>Terbinafine 250 mg Tablets                  28 tablets</p>	<p><b>Terbinafine 250 mg Tablets</b></p> <p>28 tablets</p> 	
	<p><b>Terbinafine 250 mg Tablets</b></p> <p>PL 08137/0129                  PL Holder: Neolab Ltd, 57 High Street, Odiham, Hants, RG29 1LF</p> <p><b>28 tablets</b></p>	<p>POM</p> <p>XXXXX</p>



### Braille



250 mg

t e r b i n a f i n e

Number sign → 2 5 0 m g

t a b l e t s

Blister

