TERBINAFINE HYDROCHLORIDE 1% CREAM

PL 21300/0001-11

UKPAR

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TERBINAFINE HYDROCHLORIDE 1% CREAM

PL 21300/0001-11

UKPAR

LAY SUMMARY

The MHRA granted MPX International Limited Marketing Authorisations (licences) for the medicinal products Terbinafine Hydrochloride 1% Cream (PL 21300/0001, 3, 4, 9, and 10) which are prescription only medicines (POM) and (PL 21300/0002, 5, 6, 7, 8, and 11) are available on general sale list (GSL). These products are used for the local treatment of fungal infections of the skin.

Terbinafine is an anti-fungal preparation. It kills fungi, which cause skin infections.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Terbinafine Hydrochloride 1% Cream outweigh the risks, hence Marketing Authorisations have been granted.
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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Terbinafine Hydrochloride 1% Cream on 29th March 2007. Terbinafine Hydrochloride 1% Cream (PL 21300/0001, 3, 4, 9, and 10) are prescription only medicines (POM) and (PL 21300/0002, 5, 6, 7, 8, and 11) are available on general sale list (GSL).

The proposed products are submitted under article 10.3 last paragraph, as ‘hybrid’ applications. These products are cross referring to Lamisil Cream 1%, PL 00101/0305, granted 3 October 1990, and marketed by Novartis Pharmaceuticals UK Ltd.

Terbinafine Hydrochloride 1% Cream (PL 21300/0001, 3, 4, 9, and 10) are used to treat fungal infections of the skin caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum.

Yeast infections of the skin, principally those caused by the genus Candida (e.g. C. albicans).

Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

Terbinafine Hydrochloride 1% Cream (PL 21300/0002, 5, 6, 7, 8, and 11) are used for the treatment of tinea pedis (Athlete’s foot) and tine cruris (jock itch) caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes) and Epidermophyton floccosum.

Terbinafine is an antimycotic with a broad-spectrum of anti-fungal activity belonging to the allylamine group. This product interferes with fungal sterol biosynthesis by the inhibition of squalene epoxidase in the fungal cell membrane, which leads to an intracellular accumulation of squalene, resulting in fungal cell death.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Nomenclature
INN: Terbinafine hydrochloride

Chemical name: (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalene methylamine hydrochloride

CAS number: 78628-80-5

Structure

\[
\text{Molecular formula: } C_{21}H_{25}N\cdot\text{HCl}
\]

Molecular Weight: 327.9

General properties
An almost white to pale creamy coloured crystalline powder. Soluble in absolute ethanol, in ethanol 96%, methanol and chloroform; slightly soluble in water, acetone, isopropyl alcohol; insoluble in toluene and ethyl acetate. There are no chiral C atoms in the structure.

Melting range: 198-207°C

The active substance used in the manufacture of the final product is in compliance with GMP and letter of access to the Drug Master File has been provided.

An appropriate specification has been provided for the active substance terbinafine hydrochloride.

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

Batch analysis data have been provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Active terbinafine hydrochloride is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.
Based upon the results obtained, a preliminary retest period of 3 years has been proposed. This is acceptable. Storage conditions for the drug substance are given as: ‘Store at 15-30°C, in commercial packaging, protected from light.’

**DRUG PRODUCT**

**Other ingredients**
Other ingredients consist of pharmaceutical excipients, namely Sodium Hydroxide, Benzyl Alcohol, Sorbitan Stearate, Cetyl Palmitate, Cetyl Alcohol, Cetostearyl Alcohol, Polysorbate 60, Isopropyl Myristate, and Water purified.

All excipients comply with satisfactory European Pharmacopoeial monograph. None of the excipients used contain material of animal or human origin.

**Pharmaceutical development**
The objective of the pharmaceutical development programme was to produce products containing 1% Terbinafine Hydrochloride cream that are tolerable and which could be considered as generic products to the originator products Lamisil Cream.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

**Manufacture**
A description and flow-chart of the manufacturing method have been provided and are satisfactory.

In-process controls are satisfactory based on process validation data and controls on the finished product. Satisfactory controls for temperature, appearance and pH of the manufacturing process and filling of the assembly process are described.

**Finished product specification**
The finished product specification is satisfactory. 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 product is packed in to an aluminium tube, inside double lacquered with epoxy resin and closed by polyethylene caps. Specifications and certificates of analysis for all packaging materials have been provided. These are satisfactory.

The applicant has confirmed that all packaging that comes into direct contact with the drug product complies with European Directive 90/128/EEC with respect to their contact with food.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 4 years with storage condition ‘Store in the original container’ has been set, and this is satisfactory.
SPC, PIL, Labels
The SPCs, PILs, and Labels are pharmaceutically acceptable.

The PIL is in compliance with current guidelines. The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

Conclusion
It is recommended that Marketing Authorisations are granted for these applications.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for applications of this type.
CLINICAL ASSESSMENT

1 INTRODUCTION
These are national abridged, standard applications, for Terbinafine 1% Cream containing 1% Terbinafine hydrochloride, submitted on the basis of generic medicinal product of Lamisil Cream, PL 00101/0305, granted on 3rd Oct, 1990 to Novartis Pharmaceuticals Ltd. The applicant has provided a hybrid application with literature references and a therapeutic equivalence study in tinea pedis in lieu of a bioequivalence study.

1.1 GCP aspects
The applicant claims that all studies have followed GCP guidance and are compliant with the guideline.

1.2 Therapeutic Class
Terbinafine is an antifungal drug for topical use; ATC code is D01A E15.

1.3 Background
Terbinafine is a well established antifungal agent used both orally and as a topical application for cutaneous mycoses, depending upon the severity and specific nature of the mycoses. The current applications are for treatment of skin infections caused by trichophyton verrucosum, Microsporum canis, Candida albicans and pityrosporum orbiculare (tinea), applied locally for 1-2 weeks.

1.4 Regulatory Status
The MPX international application for Terbinafine Cream have not been authorised in any other EU member state or elsewhere. There have been no refusals.

1.5 Indications, Dose and Dose Regimen
The applicant submits the following:

Indications:

The Prescription only medicines are used for fungal infections of the skin caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum.
Yeast infections of the skin, principally those caused by the genus Candida (eg. C. albicans).
Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

Posology
Terbinafine cream can be applied once or twice daily. Cleanse and dry the affected areas thoroughly before application of Terbinafine cream. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (submammary, interdigital, intergluteal, inguinal) the application may be covered with a gauze strip, especially at night.

The likely durations of treatment are as follows:
Tinea corporis, cruris: 1 to 2 weeks  
Tinea pedis: 1 week  
Cutaneous candidiasis: 2 weeks  
Pityriasis versicolor: 2 weeks

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Children  
The experience with topical terbinafine in children is still limited and its use cannot therefore be 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.

Method of administration  
Via the topical route.

Posology  
The General sale list are used for treatment of tinea pedis (Athlete’s foot) and tinea cruris (jock itch) caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes) and Epidermophyton floccosum.

The likely durations of treatment are as follows:  
Tinea cruris: 1 to 2 weeks  
Tinea pedis: 1 week

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Children  
The experience with topical Terbisil in children aged 16 and under is still limited and its use cannot therefore be 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.

Method of administration  
Via the topical route.
1.6 Consideration for Paediatric use
There is no experience with terbinafine in children and hence its use is not recommended.

2 CLINICAL PHARMACOLOGY
2.1 Pharmacokinetics
This is a locally acting locally applied preparation with minimal systemic absorption (<5%). Hence systemic pharmacokinetics is not relevant.

2.2 Pharmacodynamics
The pharmacodynamic effects of Terbinafine have been well established both as a topical agent and for systemic administration in the indications sought. The applicant has provided sufficient published literature to support the claims. These are considered acceptable.

2.3 Bioavailability & Bioequivalence
Bioavailability and bioequivalence are not deemed appropriate nor are considered feasible for locally applied, locally acting preparations (see the relevant guideline CPMP/EWP/239/96).

3 CLINICAL EFFICACY
3.1 Introduction
The applicant has provided a review of clinical efficacy for terbinafine (Lamisil) in the indications sought and a therapeutic equivalence study in tinea pedis that is detailed and discussed below.

Therapeutic Equivalence study:
This was a randomised, prospective, comparative, double-blind, active controlled, parallel group, multi-centre study.

Patients with a clinical diagnosis of interdigital tinea pedis were included. There were 3 clinic visits with centralised evaluation of all cultures.

The sample sizes were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Terbinafine</th>
<th>Lamisil (Novartis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised</td>
<td>733</td>
<td>366</td>
</tr>
<tr>
<td>Efficacy Population</td>
<td>718</td>
<td>362</td>
</tr>
<tr>
<td>Clinical PP population</td>
<td>538</td>
<td>270</td>
</tr>
<tr>
<td>Mycology Full Population</td>
<td>447</td>
<td>214</td>
</tr>
<tr>
<td>Complete per-protocol</td>
<td>296</td>
<td>144</td>
</tr>
</tbody>
</table>

The complete Per protocol population formed the population for primary efficacy criterion.

Study Flow Chart:

![Study Flow Chart](image)
End points:

Primary Efficacy Variable
- Mycological cure at Visit -3

Secondary efficacy variables:
- Mycological cure at Visit-2
- Clinical Cure (visit -2 & 3)
- Complete Cure (Visit 2 and 3)
- Score of Clinical signs & symptoms

The applicant employed the following scale:
- 0: None  Complete absence of any signs
- 2: mild  Obvious but minimal involvement
- 3: moderate  Something that is easily noted
- 4: Severe  Quite marked.
- Sum of scores of Clinical signs and Symptoms

The sum of scores was calculated from scores of signs- fissuring, erythema, maceration, vesiculation, exudation, desquamation and from the symptoms; pruritus, burning/stinging.
- Investigator’s Rating
  The investigator’s rating based on 75%, 50% or less improvement. These however appear to have been arbitrary assessment.
- Patient’s assessment of efficacy.

Statistical methods:
The confidence interval approach to assess therapeutic equivalence of efficacy was used. Equivalence was concluded if the centre-weighted two-sided 95% CI for the difference between the two treatments lay entirely within the equivalence range (10% ±).

Results:

Efficacy evaluation: Mycological cure was achieved in patients in the mycological PP population; cure rates of 77.8 % and 78.3% respectively. Calculated CI was -9.9%; 8.9% which was entirely within the equivalence range (-10%; +10%), therapeutic equivalence was concluded.

Analysis of the full mycological population appear to confirm the above results; Cure rates of 70.6% and 71.2 % for trebisil (Generic terbinafine) and lamisil respectively, a difference of 0.7% (CI -9.1 to +7.7%).

Secondary efficacy parameters:
- Mycological cure at visit 2 showed wider confidence intervals with the cure rates being lower than at visit -3 and difference between cure rates (for terbinafine and lamisil) being higher.

- Clinical cure rates at visit 2 and 3; Clinical cure (no residual sign /symptoms) were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Trebisil</th>
<th>Lamisil</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-2</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>V-3</td>
<td>33.7%</td>
<td>28.7%</td>
</tr>
</tbody>
</table>

- Cure rates in clinical population were similar in the clinical full population.
The following table summarises the efficacy data:

<table>
<thead>
<tr>
<th>Endpoint and analysis population</th>
<th>Terbinafine</th>
<th>Lamisil</th>
<th>Difference and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycological cure Visit 3 – PP</td>
<td>77.8</td>
<td>78.3</td>
<td>-0.5 (-9.9, 8.9)</td>
</tr>
<tr>
<td>Mycological cure Visit 3 – FAS</td>
<td>70.6</td>
<td>71.2</td>
<td>-0.7 (-9.1, 7.7)</td>
</tr>
<tr>
<td>Mycological cure Visit 2 - PP</td>
<td>75.7</td>
<td>68.4</td>
<td>7.3 (-2.9, 17.5)</td>
</tr>
<tr>
<td>Mycological cure Visit 2 – FAS</td>
<td>64.5</td>
<td>69.5</td>
<td>-5.0 (-13.8, 3.7)</td>
</tr>
<tr>
<td>Clinical cure Visit 3 – PP</td>
<td>33.7</td>
<td>28.7</td>
<td>5.0 (-2.8, 12.8)</td>
</tr>
<tr>
<td>Clinical cure Visit 3 – FAS</td>
<td>27.3</td>
<td>25.8</td>
<td>1.5 (-5.0, 8.0)</td>
</tr>
<tr>
<td>Clinical cure Visit 2 - PP</td>
<td>10.0</td>
<td>10.1</td>
<td>-0.1 (-5.2, 5.0)</td>
</tr>
<tr>
<td>Clinical cure Visit 2 – FAS</td>
<td>9.1</td>
<td>8.1</td>
<td>1.0 (-3.1, 5.1)</td>
</tr>
<tr>
<td>Complete cure Visit 3 – PP</td>
<td>29.9</td>
<td>23.7</td>
<td>6.2 (-3.9, 16.3)</td>
</tr>
<tr>
<td>Complete cure Visit 3 – FAS</td>
<td>26.6</td>
<td>21.5</td>
<td>5.2 (-2.8, 13.1)</td>
</tr>
<tr>
<td>Complete cure Visit 2 - PP</td>
<td>11.1</td>
<td>5.9</td>
<td>5.2 (-1.2, 11.5)</td>
</tr>
<tr>
<td>Complete cure Visit 2 – FAS</td>
<td>8.9</td>
<td>5.2</td>
<td>3.7 (-1.0, 8.5)</td>
</tr>
</tbody>
</table>

The rates were higher in the terbisetil group but not statistically significant. The other secondary efficacy parameters were not statistically significant between treatment groups as per clinical study report.

4 CLINICAL SAFETY
4.1 Introduction

The expert claims that safety of terbinafine has been well established (as Lamisil) that has been in clinical use since 1990. This is applicable to the topical formulation and simultaneously, the orally administered form is also available. Whilst submitting a therapeutic equivalence study, the applicant claims this to be a substitute for the bioequivalence study and claims essential similarity to the topical Lamisil cream. Safety aspects arising out of the “therapeutic equivalence study” are discussed by the expert and summarised here.

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Terbinafine</th>
<th>Lamisil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 9</td>
<td>N= 11</td>
</tr>
<tr>
<td>Burning at application site</td>
<td>5 6 %</td>
<td>8 9.6%</td>
</tr>
<tr>
<td>Erythema</td>
<td>1 1.2%</td>
<td>0 0</td>
</tr>
<tr>
<td>Pain</td>
<td>1 1.2%</td>
<td>0 0</td>
</tr>
<tr>
<td>Pruritus (site)</td>
<td>2 2.4%</td>
<td>1 1.2%</td>
</tr>
<tr>
<td>Warmth</td>
<td>0 0</td>
<td>2 2.4%</td>
</tr>
<tr>
<td>Total</td>
<td>9 10.85</td>
<td>11 13.2%</td>
</tr>
</tbody>
</table>

As no differences were demonstrated in this reasonably sized study, the expert concludes that there are no safety concerns related to this generic formulation and claims this is supported by the published literature relating to Lamisil.
4.2 Assessor’s overall conclusions on clinical safety
There are no new safety concerns arising out of the “therapeutic equivalence study” submitted by the applicant. The assessor concurs with the expert that based on the published data relating to Lamisil, no major safety issues exist.

5 CLINICAL EXPERT REPORT
The clinical expert report has been written by a pharmaceutical physician. It is an adequate summary of the clinical data provided in the dossier.

6 PRODUCT LITERATURE

6.1 SPC: Summary of Product Characteristics
The SPC is consistent with the reference product.

6.2 PIL; Patient Information Leaflet
The Patient information leaflet is consistent with the reference product.

6.3 Labels
The packagings are consistent with the reference product.

7 DISCUSSIONS

7.1 Pharmacodynamics & Pharmacokinetics
The kinetics of terbinafine has been well established previously and the expert discusses these issues sufficiently in the expert report. There are no major dynamic interactions of terbinafine when used as cutaneous cream and hence this issue is not of major concern.

7.2 Bioequivalence
The applicant has not submitted any bioequivalence data for this cutaneous cream. This is considered appropriate as the systemic absorption of such a cutaneous formulation is considered minimal and bioequivalence is not expected. Therapeutic equivalence with the established product is has been provided.

7.3 Efficacy & Safety
The applicant has not provided new safety or efficacy data. This is acceptable for an application of this type.

7.4 Risk – benefit
The risk benefit for terbinafine cream is favourable and therefore acceptable.

8 CLINICAL AND PRE-CLINICAL ASSESSORS’ CONCLUSIONS
There are no pre-clinical issues with the use of Terbinafine as this product has been in clinical use for a number of years both as local application and as an oral formulation (terbinafine tablets).

From a clinical standpoint, the applicant has provided a therapeutic equivalence study comparing the generic product with the brand leader, lamisil. This is satisfactory.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Terbinafine Hydrochloride 1% Cream 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 application of this type.

EFFICACY
The efficacy of Terbinafine Hydrochloride 1% Cream has been well documented in the past. No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable. Extensive clinical experience with Terbinafine Hydrochloride 1% Cream is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
### STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 2\textsuperscript{nd} June 2004</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 2\textsuperscript{nd} July 2004</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the applications the MHRA requested information relating to the quality dossiers on 1\textsuperscript{st} March 2005, 2\textsuperscript{nd} February 2006, 19\textsuperscript{th} July 2006, and 24\textsuperscript{th} October 2006</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 20\textsuperscript{th} January 2006, 14\textsuperscript{th} July 2006, 12\textsuperscript{th} October 2006, and 7\textsuperscript{th} January 2007,</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 29\textsuperscript{th} March 2007</td>
</tr>
</tbody>
</table>
### STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>12/06/2007</td>
<td>Type IB</td>
<td>To add own label supplier</td>
<td>Approved 19/10/2007</td>
</tr>
<tr>
<td>22/06/2007</td>
<td>Type II</td>
<td>To update SPC and consequentially the PIL and Labelling only for the GSL</td>
<td>Approved 12/07/2007</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Terbinafine Hydrochloride 1 % cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
10 mg terbinafine hydrochloride (equivalent to 8.89 mg terbinafine) in 1 g cream.

Excipient: 80 mg cetyl alcohol and cetostearyl alcohol in 1 g cream.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Cream
White or almost white cream, with slight almond odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Fungal infections of the skin caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum.
Yeast infections of the skin, principally those caused by the genus Candida (e.g. C. albicans).
Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

4.2 Posology and method of administration
Terbinafine cream can be applied once or twice daily. Cleanse and dry the affected areas thoroughly before application of Terbinafine cream. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (submammary, interdigital, intergluteal, inguinal) the application may be covered with a gauze strip, especially at night.

The likely durations of treatment are as follows:

- Tinea corporis, cruris: 1 to 2 weeks
- Tinea pedis: 1 week
- Cutaneous candidiasis: 2 weeks
- Pityriasis versicolor: 2 weeks

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Children
The experience with topical terbinafine in children is still limited and its use cannot therefore be 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.

Method of administration

Via the topical route.

4.3 Contraindications

Known hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and precautions for use

Terbinafine cream is for external use only. Contact with the eyes should be avoided. If it gets into the eyes accidentally, the eyes should be washed with plenty of water and the patient should turn to an ophthalmologist if necessary.

The cream contains cetyl alcohol and cetostearyl alcohol which may cause local reactions (i.e. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

There are no known drug interactions with Terbinafine cream.

4.6 Pregnancy and lactation

Foetal toxicity and fertility studies in animals suggest no adverse effects.

There is no clinical experience with Terbinafine cream in pregnant women, therefore, unless the potential benefits outweigh any potential risks, Terbinafine cream should not be administered during pregnancy.

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

4.7 Effects on ability to drive and use machines

There are no data available that terbinafine would affect driving ability or any other activity requiring concentration.

4.8 Undesirable effects

In the Therapeutic equivalence study with Terbisil 1% cream and Lamisil 1% cream (EQUATE) a total of 733 patients were exposed to either Terbisil (n=366) or Lamisil (n=367) during the 1 week of the treatment period, where 10.1% of the patients (74 patients) experienced at least one adverse event. A total number of adverse events related to the study medications were 20 events during the study.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Common</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary System</td>
<td>&gt;1/100, &gt;1/10</td>
<td>MedDRA V. 8.0</td>
<td></td>
</tr>
<tr>
<td>Organ Class</td>
<td>Application site irritation</td>
<td></td>
<td>15.6 %</td>
</tr>
<tr>
<td>Application site pruritus</td>
<td></td>
<td></td>
<td>3.6 %</td>
</tr>
<tr>
<td>Application site warmth</td>
<td></td>
<td></td>
<td>2.4 %</td>
</tr>
</tbody>
</table>
Table: Adverse reactions

<table>
<thead>
<tr>
<th>Event</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site pain</td>
<td>1.2 %</td>
</tr>
<tr>
<td>Application site erythema</td>
<td>1.2 %</td>
</tr>
<tr>
<td>Pain*</td>
<td></td>
</tr>
<tr>
<td>Application site hypersensitivity*</td>
<td></td>
</tr>
</tbody>
</table>

* These adverse reactions did not occur during the study “Equate”.

Erythema, pruritus, warmth, pain or irritation (stinging, burning sensation) occasionally occur at the site of application. Treatment generally does not have to be discontinued for this reason. These symptoms must be distinguished from application site hypersensitivity reactions, which are rare but require discontinuation of therapy.

4.9 Overdose
Terbinafine cream is for external use only. If accidental ingestion of the cream occurs, appropriate method of gastric lavage can be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Antifungals for topical use
ATC code: D01A E15

Terbinafine is an antimonycotic with a broad-spectrum of anti-fungal activity belonging to the allylamine group. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts, e.g. Candida species is fungicidal or fungistatic depending on the species.

Terbinafine interferes with fungal sterol biosynthesis by the inhibition of squalene epoxidase in the fungal cell membrane, which leads to an intracellular accumulation of squalene, resulting in fungal cell death.

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.

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC range (µg/ml)</th>
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</thead>
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</tr>
<tr>
<td>Trichophyton mentagrophytes</td>
<td>0.0001 – 0.05</td>
</tr>
<tr>
<td>Trichophyton verrucosum</td>
<td>0.001 – 0.006</td>
</tr>
<tr>
<td>Trichophyton violaceum</td>
<td>0.001 – 0.1</td>
</tr>
<tr>
<td>Microsporum canis</td>
<td>0.0001 – 0.1</td>
</tr>
<tr>
<td>Epidermophyton floccosum</td>
<td>0.001 – 0.05</td>
</tr>
</tbody>
</table>
5.2 Pharmacokinetic properties
Less than 5% of the dose is absorbed after topical application; systemic exposure is therefore very slight.

5.3 Preclinical safety data
Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium hydroxide,
Benzyl alcohol,
Sorbitan stearate,
Cetyl palmitate,
Cetyl alcohol,
Cetostearyl alcohol,
Polysorbate 60,
Isopropyl myristate,
Water purified.

6.2 Incompatibilities
None known.

6.3 Shelf life
4 years
Shelf life after opening: 1 month

6.4 Special precautions for storage
No special precautions for storage.
Store in original container.

6.5 Nature and contents of container
Aluminium tube closed by polyethylene cap. The tubes are containing 7.5 g, 15 g or 30 g cream.

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
MPX International Ltd.
127 Shirland Road, London W9 2EP, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 21300/0001
PL 21300/0003
PL 21300/0004
PL 21300/0009
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
29/03/2007

10 DATE OF REVISION OF THE TEXT
29/03/2007
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Terbinafine Hydrochloride 1% cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
10 mg terbinafine hydrochloride (equivalent to 8.89 mg terbinafine) in 1 g cream.

Excipient: 80 mg cetyl alcohol and cetostearyl alcohol in 1 g cream.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Cream

White or almost white cream, with slight almond odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
The treatment of tinea pedis (Athlete’s foot) and tinea cruris (jock itch) caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes) and Epidermophyton floccosum.

4.2 Posology and method of administration
Terbinafine cream can be applied once or twice daily. Cleanse and dry the affected areas thoroughly before application of Terbinafine cream. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly.

The likely durations of treatment are as follows:
Tinea cruris: 1 to 2 weeks
Tinea pedis: 1 week

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Children
The experience with topical Terbisil in children aged 16 and under is still limited and its use cannot therefore be 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.

Method of administration
Via the topical route.
4.3 **Contraindications**
Known hypersensitivity to the active substance or any of the excipients.

4.4 **Special warnings and precautions for use**
Terbinafine cream is for external use only. Contact with the eyes should be avoided. If it gets into the eyes accidentally, the eyes should be washed with plenty of water and the patient should turn to an ophthalmologist if necessary.

The cream contains cetyl alcohol and cetostearyl alcohol which may cause local reactions (i.e. contact dermatitis).

4.5 **Interaction with other medicinal products and other forms of interaction**
There are no known drug interactions with Terbinafine cream.

4.6 **Pregnancy and lactation**
Foetal toxicity and fertility studies in animals suggest no adverse effects.

There is no clinical experience with Terbinafine cream in pregnant women, therefore, unless the potential benefits outweigh any potential risks, Terbinafine cream should not be administered during pregnancy.

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

4.7 **Effects on ability to drive and use machines**
There are no data available that terbinafine would affect driving ability or any other activity requiring concentration.

4.8 **Undesirable effects**
In the Therapeutic equivalence study with Terbisil 1% cream and Lamisil 1% cream (EQUATE) a total of 733 patients were exposed to either Terbisil (n=366) or Lamisil (n=367) during the 1 week of the treatment period, where 10.1% of the patients (74 patients) experienced at least one adverse event. A total number of adverse events related to the study medications were 20 events during the study.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Common</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary System</td>
<td>&gt;1/100, &gt;1/10</td>
<td></td>
</tr>
<tr>
<td>Organ Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MedDRA V. 8.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Application site irritation</td>
<td>15.6 %</td>
</tr>
<tr>
<td></td>
<td>Application site pruritus</td>
<td>3.6 %</td>
</tr>
<tr>
<td></td>
<td>Application site warmth</td>
<td>2.4 %</td>
</tr>
<tr>
<td></td>
<td>Application site pain</td>
<td>1.2 %</td>
</tr>
<tr>
<td></td>
<td>Application site erythema</td>
<td>1.2 %</td>
</tr>
<tr>
<td></td>
<td>Pain*</td>
<td></td>
</tr>
<tr>
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</tbody>
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* These adverse reactions did not occur during the study “Equate”.

24
Erythema, pruritus, warmth, pain or irritation (stinging, burning sensation) occasionally occur at the site of application. Treatment generally does not have to be discontinued for this reason. These symptoms must be distinguished from application site hypersensitivity reactions, which are rare but require discontinuation of therapy.

4.9 Overdose
Terbinafine cream is for external use only. If accidental ingestion of the cream occurs, appropriate method of gastric lavage can be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Antifungals for topical use
ATC code: D01A E15

Terbinafine is an antimycotic with a broad-spectrum of anti-fungal activity belonging to the allylamine group. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts, e.g. Candida species is fungicidal or fungistatic depending on the species.

Terbinafine interferes with fungal sterol biosynthesis by the inhibition of squalene epoxidase in the fungal cell membrane, which leads to an intracellular accumulation of squalene, resulting in fungal cell death.

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) and Epidermophyton floccosum. The following table outlines the range of minimum inhibitory concentrations (MIC) against the dermatophytes.

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5.2 Pharmacokinetic properties
Less than 5% of the dose is absorbed after topical application; systemic exposure is therefore very slight.

5.3 Preclinical safety data
Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium hydroxide,
Benzyl alcohol,
Sorbitan stearate,
Cetyl palmitate,
Cetyl alcohol,
Cetostearyl alcohol,
Polysorbate 60,
Isopropyl myristate,
Water purified.

6.2 Incompatibilities
None known.

6.3 Shelf life
4 years
Shelf life after opening: 1 month

6.4 Special precautions for storage
No special precautions for storage.
Store in original container.

6.5 Nature and contents of container
Aluminium tube closed by polyethylene cap. The tubes are containing 7.5 g and 15 g cream.

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
MPX International Ltd, 127 Shirland Road, London W9 2EP, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 21300/0002
PL 21300/0005
PL 21300/0006
PL 21300/0007
PL 21300/0008
PL 21300/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
29/03/2007

10 DATE OF REVISION OF THE TEXT
29/03/2007
UKPAR Terbinafine Hydrochloride 1% Cream

PL 21300/0001, 3, 4, 9, AND 10

PATIENT INFORMATION LEAFLET

TERBINAFINE HYDROCHLORIDE 1% Cream

Terbinafine hydrochloride

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:
1. What Terbinafine Hydrochloride 1% cream (hereafter Terbinafine) is and what it is used for
2. Before you use Terbinafine
3. How to use Terbinafine
4. Possible side effects
5. How to store Terbinafine
6. Further information

1. WHAT TERBINAFINE IS AND WHAT IT IS USED FOR

Terbinafine is an anti-fungal preparation. It kills fungi, which cause skin infections.

Terbinafine is used for the local treatment of fungal infections of the skin.

For external use only.

2. BEFORE YOU USE TERBINAFINE

DO NOT USE Terbinafine
- If you are allergic (hypersensitive) to terbinafine hydrochloride or any of the other ingredients of Terbinafine.

TAKE SPECIAL CARE with Terbinafine
- For external use only.

- Avoid contact of the cream with your eyes. If it gets into the eyes accidentally, the eyes should be washed with plenty of water and the patient should consult an ophthalmologist if necessary.
- After application you should always wash your hands.

Taking or using other medicines
Please tell your doctor or pharmacist if you are taking/using or have recently taken/used any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Pregnancy
Ask your doctor or pharmacist for advice before using Terbinafine. If you do become pregnant whilst using Terbinafine, tell your doctor.

Breast-feeding
Ask your doctor or pharmacist for advice before using Terbinafine.

Driving and using machines
Terbinafine cream will not affect your ability to drive or operate machinery when used as directed and only externally.

Important information about some of the ingredients of Terbinafine
Cetyl alcohol and cetostearyl alcohol, which are among the other ingredients of the cream, may cause local skin reactions (e.g. contact dermatitis).
3. HOW TO USE TERBINAFINE

Your doctor will decide the right amount of Terbinafine for you to use and will tell you how long to use your medicine. Follow your doctor's instructions exactly.

Unless otherwise instructed by your doctor, apply the cream once or twice daily. The cream is generally used for 1 to 2 weeks, but this will depend upon the type and area of infection. Make sure that you have cleaned and dried the affected skin and surrounding areas thoroughly before applying Terbinafine cream in a thin layer. The cream should be rubbed in gently and the affected areas may be covered with a gauze dressing, especially at night.

If there are no signs of improvement after two weeks of therapy, consult your doctor.

If you USE MORE Terbinafine than you should
If you or someone else including a child, accidentally swallow the cream, contact your doctor immediately.

If you FORGET TO USE Terbinafine
If you forget to use your cream, apply the cream as soon as possible, until your treatment is completed as usual.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Terbinafine can have side effects, although not everybody gets them.

Redness, itching or stinging occasionally occur at the site of application. If these side effects occur, contact your doctor. Hypersensitivity reactions may develop with any medicine. Therefore, if you experience any of the following symptoms, such as swelling of the treated area, pain and redness, you should stop treatment and contact your doctor.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE TERBINAFINE

Do not use after the expiry date stated on the pack. The expiry date refers to the last day of that month.

No special precautions for storage.

Store in original container.

Do not use Terbinafine if you notice visible signs of deterioration.

Keep out of the reach and sight of children.

If your doctor decides to stop your treatment, return any leftover medicine to the pharmacist. Only keep it if your doctor tells you to.

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.

6. FURTHER INFORMATION

What Terbinafine contains

The active substance is terbinafine hydrochloride
The other ingredients are sodium hydroxide, benzyl alcohol, sorbitan stearate, ceteryl palmitate, cetaryl alcohol, cetostearyl alcohol, polysorbate 60, isopropyl myristate, water purified.

What Terbinafine looks like and contents of the pack

White or almost white cream, with slight almond odour.

Packs contain 1 tube of cream (7.5 g, 15 g or 30 g)

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Application held by:
MPX International Ltd. 127 Shirland Road, London W9 2EP, United Kingdom

Manufactured by:
Gedeon Richter Ltd. 1103 Budapest, Győrői út 19-21, Hungary

Leaflet revised in November 2006.
UKPAR Terbinafine Hydrochloride 1% Cream

PL 21300/0001-11

TERBINAFINE HYDROCHLORIDE 1% Cream

Terbinafine hydrochloride

Read all of this leaflet carefully before you start using this medicine.

This medicine is available without prescription. Nevertheless you still need to use Terbinafine cream carefully to get the best results from it.

- Keep this leaflet. You may want to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve within two weeks of starting treatment.

In this leaflet:
1. What Terbinafine 1% cream (hereafter Terbinafine) is and what it is used for
2. Before you use Terbinafine
3. How to use Terbinafine
4. Possible side effects
5. How to store Terbinafine
6. Further information

1. WHAT TERBINAFINE IS AND WHAT IT IS USED FOR

Terbinafine cream is an antifungal preparation. It kills fungi, which cause skin infections.

Terbinafine cream is used for the local treatment of fungal infections such as Athlete's foot and jock itch.

You can treat mild, transient complaints before seeking medical attention or supervision.

To achieve optimal effect you should use this medicine carefully and expertly.

For external use only.

Fungal infections can develop in the following areas of the body:
- Fungal infection of the foot (Athlete’s foot) appears on the feet, mainly between the toes. It can spread to the soles, edges or the instep of the feet. It may affect one or both feet.
- The most common symptoms can be inflammation, cracking or scaling of the skin, unpleasant itching. In more severe cases, small weeping blisters, peeling skin and painful, deep cracks can appear.
- Terbinafine is NOT for nail infections

2. BEFORE YOU USE TERBINAFINE

- if you are allergic (hypersensitive) to terbinafine hydrochloride or any of the other ingredients of Terbinafine
- you are not sure about the nature of your skin problem, you should consult your doctor before starting to use Terbinafine cream
- you are younger than 16 years of age

TAKE SPECIAL CARE with Terbinafine
- For external use only.
- Avoid contact of the cream with your eyes. If it gets into the eyes accidentally, the eyes should be washed with plenty of water and the patient should consult an ophthalmologist if necessary.
- After application you should always wash your hands.

Taking or using other medicines
Please tell your doctor or pharmacist if you are taking/using or have recently taken/used any other medicines, including medicines obtained without a prescription.

Pregnancy and breastfeeding
Pregnancy
Ask your doctor or pharmacist for advice before using Terbinafine. If you do become pregnant whilst using Terbinafine, tell your doctor.

Breastfeeding
Ask your doctor or pharmacist for advice before using Terbinafine.

Driving and using machines
Terbinafine does not affect your ability to drive or operate machinery when used as directed and only externally.

Important information about some of the ingredients of Terbinafine
Cetyl alcohol and cetostearyl alcohol, which are among the other ingredients of the cream, can cause local skin reactions (e.g. contact dermatitis).

3. HOW TO USE TERBINAFINE

You can open the sealed tube by using the spike at the top of the cap. Always clean and dry your hands before using the cream.
Usage of the cream:
The cream should be applied once or twice daily on the previously
drenched and dried area. The cream should be applied to the
affected skin and surrounding area in a thin layer and rubbed in
lightly.

Duration of treatment according to types of infections:

**Fungal infection of the foot:**
1 week/orcer or twice daily

Treatment should be continued for one week, even if the affected
area starts healing earlier. This way you can avoid the return of
infection and treatment will be successful.
The effect of use of the cream will stop the infection quickly due
to the killing of the pathogenic fungus. However, complete healing
may take longer depending on the extent of inflammation. The effect
of Terbinafine cream persists after treatment, even when you have
finished using the preparation.

If there are no signs of improvement after two weeks of therapy,
consult your doctor.

To avoid re-infection it is important to take the following hygienic
measures:
The affected area should be kept clean; after use of the cream you
should always wash your hands; you should use your own towel;
you should frequently change underwear; you should wear cotton
socks and it is advised to disinfect footwear.
Avoid scratching the affected area, although it may be itchy
because it can cause further damage to the skin and slow down the
healing process or spread the infection.

If you USE MORE Terbinafine than you should
If you or someone else including a child, accidentally swallow the
cream, contact your doctor immediately.

If you FORGET TO USE Terbinafine
If you forget to use your cream, apply the cream as soon as possible,
and then continue the rest of your treatment as usual.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Terbinafine can have side effects, although not
everybody gets them.
Redness, itching or sting occasionally occur at the site of application.
If these side effects occur, contact your doctor.

Hypersensitivity reactions may develop with any medicine.
Therefore, if you experience any of the following symptoms, such
as swelling of the treated area, pain and redness, you should stop
treatment and contact your doctor.

If any of the side effects gets serious, or if you notice any side
effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE TERBINAFINE

Do not use after the expiry date stated on the pack. The expiry date
refers to the last day of that month.

No special precautions for storage.

Store in original container.

Do not use Terbinafine if you notice visible signs of deterioration.

Keep out of the reach and sight of children.

Only keep it if your doctor tells you to.

If your doctor decides to stop your treatment, return any left over
medicine to the pharmacist.

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.

6. FURTHER INFORMATION

What Terbinafine contains

The active substance is terbinafine hydrochloride
The other ingredients are sodium hydroxide, benzyl alcohol,
sorbitan stearate, cetyl palmitate, cetyl alcohol, cetearyl alcohol,
polysorbate 60, isopropyl myristate, water purified.

What Terbinafine looks like and contents of the pack

White or almost white cream, with slight almond odour.

Packs contain 1 tube of cream (7.5 g and 15 g)

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Application held by:
MPX International Ltd. 127 Shipton Road,
London W9 2EP, United Kingdom

Manufactured by:
Gedeon Richter Ltd. 1103 Budapest, Gyömrői út 19-21, Hungary

Leaflet revised in June 2007
LABELLING

TERINAfine Hydrochloride 1% Cream

For External Use Only.

TERINAfine Hydrochloride 1% Cream

Officinalus Laboratories Ltd.
1237 Pilkington Road
London W9 2EF
United Kingdom

7.5 g

TERINAfine Hydrochloride

1% Cream

Each gram contains 10 mg Terbinafine hydrochloride.

In addition, the following substances are included in the preparation:

- Propylene glycol, sorbitol, disodium edetate, dihydrogen phosphate,
sodium hydroxide, and water for suspensions.

For cutaneous use only. 

For external use only. 

Keep out of the reach of children. 

This product contains Paraben, which may cause sensitisation. 

In the event of skin irritation or sensitisation, discontinue use and consult your healthcare provider.

Batch No:

Terbinafine Hydrochloride 1% Cream

For External Use Only.
TERBINAFINE HYDROCHLORIDE 1% Cream

Each tube contains 50g of Terbinafine Hydrochloride.

For external use only. Keep out of the reach and sight of children.

PL 21300/0001
UKPAR Terbinafine Hydrochloride 1% Cream

TERBINAFINE HYDROCHLORIDE 1% Cream

For Externally Use Only

TINICINE HYDROCHLORIDE
1% Cream

MPP International Ltd.
127 Stratford Road
Londom W7 2PF
United Kingdom

TERBINAFINE HYDROCHLORIDE
1% Cream

1 g cream contains 10 mg Terbinafine hydrochloride.

Exipients: sodium hydroxide, benzyl alcohol,
sorbitol stearate, cetyl palmitate, cetyl alcohol,
macroxyly alcohol, polysorbate 60, naproxyni
syrup and purified water.

For external use.

Please read the enclosed leaflet before use.
Keep out of the reach and sight of children.
No special precautions for storage.
Store in original container.
Use as directed by medical practitioner.
PL 213000/0001
TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only

7.5 g

TERBINAFINE HYDROCHLORIDE
1% Cream

APL LIFE SCIENCES LTD
137-141 Highbridge Road
London NW 2PZ
United Kingdom

TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only
The cream should be applied once or twice daily.
For indicated use:
It is not recommended for children under 10 years.
It is not recommended for pregnant or breastfeeding mothers.
For use in skin infections such as Athlete's Foot.

TERBINAFINE HYDROCHLORIDE 1% Cream

PL 21300/0002

GSL
TERBINAFINE HYDROCHLORIDE 1% Cream

1 g cream contains 10 mg Terbinafine hydrochloride.

Excipients: sodium hydroxide, benzyl alcohol, sodium laurate, cetyl palmitate, cetyl alcohol, cetostearyl alcohol, polyethylene glycol 60, isopropyl myristate, purified water.

For cutaneous use.

Please read the enclosed leaflet before use.

Keep out of the reach and sight of children.

No special precautions for storage.

Store in original container.

Use as directed by medical practitioner.

PL 21300/0003
TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only

Each tube contains 30g Terbinafine hydrochloride.

For cutaneous use. Please read the enclosed leaflet before use.

Keep out of the reach of children.

For special precautions, see the leaflet.

For use on skin only.

For more information, see the leaflet.

Ingredients: water, propylene glycol, hydroxypropyl methylcellulose, polyethylene glycol, methylparaben, ethylparaben.

PL 21300/0004

TERBINAFINE HYDROCHLORIDE 1% CREAM
TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only.

15 g

TERBINAFINE HYDROCHLORIDE
1% Cream

Excipients: sodium hydroxide, benzyl alcohol, sodium stearate, cetyl palmitate, cetyl alcohol, cetearyl alcohol, polyethylene 60, isopropyl myristate, purified water.

For the treatment of...

PL 21300/0004

TERBINAFINE HYDROCHLORIDE 1% CREAM

Please read the enclosed leaflet before use.

Keep out of the reach and sight of children.

No special precautions for storage.

Store in original container.

Use as directed by medical practitioner.

PL 21300/0004

Terbinafine Hydrochloride 1% Cream
UKPAR Terbinafine Hydrochloride 1% Cream

**TERBINAFINE HYDROCHLORIDE 1% Cream**

For External Use Only

30 g

**TERBINAFINE HYDROCHLORIDE**

1% Cream

MPH International Ltd.
157 Shenpin Road
London NWF 2BF
United Kingdom

**Rush No/Fig/Date**

Batch No: T0001

1 g cream contains 10 mg Terbinafine hydrochloride.

Excipients: sodium hydroxide, benzy alcohol, sorbitan sesquioleate, propylene glycol, octyl alcohol, polysorbate 60, isopropyl myristate, purified water.

For external use.

Please read the enclosed leaflet before use.

Keep out of the reach of children.

No special precautions for storage. Store in unopened container.

Use as directed by medical practitioner.

PL 21300/0004
UKPAR Terbinafine Hydrochloride 1% Cream

TERBINAFINE HYDROCHLORIDE 1% Cream

7.5 g

For External Use Only

TERBINAFINE HYDROCHLORIDE 1% Cream

May be obtained from the regulatory authority.

9999 9999 9999 9999 9999 9999 9999 9999 9999

TERBINAFINE HYDROCHLORIDE 1% Cream

1 g cream contains 10 mg Terbinafine hydrochloride.

Applying daily of the affected area. Do not cover with adhesive bandages, cloth, or bandages. Do not use on the face, eyes, or mouth. Aqueous skin irritant; avoid contact with eyes, mouth, and mucous membranes.

The cream should be applied once or twice daily.

Not subject to medical prescription.

PL 21300/0005

TERBINAFINE
HYDROCHLORIDE
1% CREAM
UKPAR Terbinafine Hydrochloride 1% Cream

TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only

15 g

TERBINAFINE HYDROCHLORIDE

1% Cream

1.94 g cream contains 40 mg terbinafine hydrochloride.

Excipients: mineral oil, white petrolatum, methyl parahydroxybenzoate, propyl parahydroxybenzoate, deodorant

It is supplied in a protective tube with a dosage measure applicator

The cream should be applied twice or more daily.

For cutaneous use only.

Not for use in children under 16 years.

Not to be used on the face.

No special precautions for storage.

Not subject to medicinal prescription.

UKPAR 21300/0001-11
UKPAR Terbinafine Hydrochloride 1% Cream

For External Use Only

TERBINAFINE HYDROCHLORIDE 1% Cream

1 g contains 10 mg Terbinafine hydrochloride.

Ingredients: Terbinafine hydrochloride, purified water, propylene glycol, polyethylene glycol, purified water.

Packaging: Tube of 100 g.

For dermatological use.

Please read the enclosed leaflet before use.

Keep out of the reach and sight of children.

For specific precautions for storage, see package leaflet.

For treatment over 30 days, consult a doctor.

PL 21300/0009
UKPAR Terbinafine Hydrochloride 1% Cream

PL 21300/0001-11

TERBINAFINE HYDROCHLORIDE 1% Cream

For External Use Only

TERBINAFINE HYDROCHLORIDE 1% Cream

75 g

TERBINAFINE HYDROCHLORIDE 1% Cream

1 g cream contains 125 mg Terbinafine hydrochloride.

For the treatment of scalp ringworm infections, dermatophytosis of the fingers, nails or body resulting from infections caused by certain species of dermatophytes.

Not for use in children under 18 years.

Pregnancy Category B. Do not use in pregnancy unless clearly necessary. There is no evidence of harm to the foetus but this does not exclude the possibility of such harm. As with all drugs, use during pregnancy should only be prescribed on medical grounds.

Lactation: No information is available. Use with caution.

The cream should be applied once or twice daily. For scalp ringworm infections, the area should be washed with a mild shampoo before application.

The cream should be applied to the skin and scalp at night, leaving it on overnight to work most effectively. Do not remove before the next application. Avoid getting the cream on the eyes, ears or nose. Avoid contact with broken skin.

It is usual to apply the Stock Solution to the skin and scalp at night, leaving it on overnight to work most effectively. Do not remove before the next application. Avoid contact with broken skin.

Do not use near the eyes or nose, or on the broken or damaged skin.

Care should be taken to avoid contact with broken skin.

If a rash occurs, discontinue use and seek medical advice.

R 2130/0011