# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

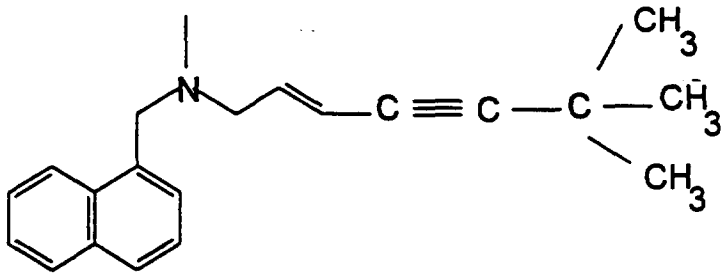
**21-124**

# PHARMACOLOGY REVIEW

NOV 17 1999

**REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA**

KEY WORDS:
**Reviewer Name:** Kumar D. Mainigi
**Division Name:** Dermatologic and Dental Drug Products, HFD-540
Review Completion Date: 11-17-1999
Electronic file number:
**NDA 21, 124** 000/05-17-1999/initial application
Information to Sponsor: No (X)
Sponsor: Novartis Pharmaceuticals Corporation
59 Route 10, East Hanover, NJ
Manufacturer: Novarits Pharma Ltd. Basel, Switzerland
Drug: **Terbinafine Hydrochloride Solution 1%**
Code name: SF 86-327
Generic Name: Terbinafine hydrochloride
Trade name: **Lamisil**
Chemical name: (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalenemethanmine hydrochloride
Structure:




HCl

**Related submissions:**

**INDs**

[redacted]

**NDAs**
20-192; Lamisil Cream 1% (approved, 12-30-1992)
20-539; Lamisil Tablets (approved,05-10-1996)
20-749; Lamisil Solution 1% ( approved,10-17-1997)
20-846; Lamisil DermGel 1% (approved , 04-29-1998)

**Drug class:** Antifungal

**Indication:** Treatment of interdigital tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm).

**Clinical formulation (and components):**

| Names of ingredients | Function | Formula (g) |
|---|---|---|
| Terbinafine hydrochloride | Active compound | |
| Cetomacrogol . | | |
| Propylene glycol | | |
| Ethanol (96%) | | |
| Purified water | | |
| | | 1.000 |
| Nitrogen | | |

* Equivalent to polyoxyl 20 cetostearyl ether

**Background:** Over the years, a number of applications have been submitted to support different antifungal formulations of the active ingredient, terbinafine hydrochloride. To evaluate the safety of this compound, the sponsor has extensively tested it in a wide spectrum of animal and *in vitro* studies. These studies were conducted with the tablet, cream, solution and gel formulations. The 1% solution formulation approved by the FDA in1997 is also sold as prescription drug in 37 other countries and as an OTC product in three countries. No adverse effects of any clinical significance have been reported for the topical solution. The OTC formulation will be identical to the approved 1% solution formulation currently marketed under prescription.

**Label:** The OTC reviewer shall draft the label of the OTC product. However, this label will be different from the Rx label in three ways. Of the currently approved four indications (athlete's foot; jock itch; ringworm; plantar tinea pedis), only plantar tinea pedis will be maintained under the prescription status. The label will state that the solution is not to be used in children under 12 years of age. Third, the labeling for dropper not currently marketed by the sponsor in the United States will be included.

**Regulatory Conclusions:** The animal safety profile for terbinafine hydrochloride has been well established, therefore, there are no non-clinical safety issues involved in Rx-to-OTC switch of this drug. The dosing regimen and the route of administation are identical to the Rx product. **I have no objection to Rx-to-OTC switch for Terbinafine Hydrochloride Solution 1%.**

/S/ 11/17/99

Kumar D. Mainigi, Ph.D., M.P.H., D.A.B.T.
Toxicologist

CC: NDA 21, 124
HFD-540
CSO/White
Chem/Vidra
Pharm/Mainigi
MO/Huene
MO/DOTCDP/Shetty
DOTCDP Label/Dobbs

/S/ 3/17/00

Concurrence:
Jacobs.A TL/HFD-540 /S/ 11/17/99 for DFS
Wilkin.J. Dir/HFD-540 /S/ 11/21/99 DFS