CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-749

CHEMISTRY REVIEW(S)

16
OCT 17 1997
FAX

DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-749 CHEM.REVIEW #: 1 REVIEW DATE: 7/21/97

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
NDA 20-749, Original,	10/17/96	10/18/96	10/23/96
NDA 20-749/BC,	8/29/97	9/2/97	9/11/97
NDA 20-749/BC,	9/5/97	9/9/97	9/11/97
NDA 20-749/BC,	9/16/97	9/17/97	9/18/97
NDA 20-749/BC,	9/23/97	9/26/97	10/2/97
NDA 20-749/FAX,	10/6/97	10/6/97	-

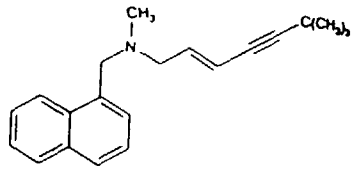
NAME & ADDRESS OF APPLICANT: Novartis Pharmaceuticals Corporation
Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080
Stephenie Barba
Director
Drug Registration and Regulatory Affairs

DRUG PRODUCT NAME

Proprietary:	Lamisil
Nonproprietary/USAN:	terbinafine HCl
Code Names/#'s:	4030410
Chemical Type/	3S
Therapeutic Class:	Antifungal (topical)

ANDA Suitability Petition/DESI/Patent Status: Not Applicable!

PHARMACOLOGICAL CATEGORY/INDICATION: Topical treatment of tinea pedis, tinea cruris, tenia corporis and pityriasis versicolor.
DOSAGE FORM: Solution/Spray
STRENGTHS:f 1%
ROUTE OF ADMINISTRATION: Topical
DISPENSED: X Rx ____ OTC
CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:
(E)-N-(6,6-Dimethyl-2-hepten-4-yn-yl)-N-methyl-1-naphthalenemethanamine hydrochloride
Empirical Formula: $C_{21}H_{26}NCl$
Molecular Formula:



Molecular Weight: 327.90
CAS No.: 78628-80-5

SUPPORTING DOCUMENTS:

NDA 20-192/SCS-004	NDA 20-192	DMF
NDA 20-192/SCS-005	NDA 20-539	DMF
NDA 20-539	DMF	DMF

In addition to the above, APPENDIX #1 provides additional documents.

CONSULTS:

(1) Nomenclature & Labeling Committee - Trademark Reviewed on 3/4/97 (See APPENDIX #2).
(2) Environmental Assessment and FONSI dated 7/10/97 (See APPENDIX #3).
(3) Establishment Evaluation Request (EER), (See APPENDIX #4).

REMARKS/COMMENTS:

NDA 20-749 has a 3-S classification for a new drug dosage form, LAMISIL Topical Solution, 1%, and LAMISIL Topical Spray, 1%. Both solutions are identical in their formulations, both contain 1% terbinafine hydrochloride and both differ only by the design of their 30 ml containers. The topical LAMISIL Solution is simply packaged in both 30 ml squeeze and spray bottles. The indication for this product is a topical antifungal, specifically for the treatment of tinea pedis, tinea cruris, and tinea corporis caused by *Trichophyton rubrum, Epidermophyton floccosum,* or *Trichophyton mentagrophytes,* and in the treatment of pityriasis versicolor due to *Pityrosporum* species. Both drug substance, terbinafine hydrochloride, and drug product are manufactured by Sandoz Pharmaceutical Corporation, currently owned by Novartis Pharmaceutical Corporation, of Basel, Switzerland.

The synthesis of terbinafine hydrochloride is a new synthesis which was previously reviewed and approved by FDA in NDA Supplement 20-192/S-009 on 12/6/96.

This drug product has the following Informational Requests associated with it:

- In the drug product's Methods of Manufacturing & Packaging, Manufacturing Controls Section, there was no indication or statement of a Reprocessing Operations.
- In the Regulatory Specifications and Methods for Drug Product (RSMDP), Sampling Procedures Section, there was a lack of specific sampling plans. No sampling plans were noted for the production batches or for the selection of sub-samples for analytical procedures;
- In the RMSDP, the pH Method Section lacked a standardization procedure and composition of standardization buffers;
- An Informational Request Letter has issued for DMF
- Container/component extractables data on both containers was requested as a Phase IV Study.

CONCLUSIONS & RECOMMENDATIONS:
This original NDA 20-749 is recommended for APPROVAL. A listing of informational requests associated with this NDA is provided in the Remarks Section of this cover letter.

10/10/97

James D. Vidra, Ph.D.
Review Chemist

cc: Orig. NDA #20-749
HFD-540/Division File
HFD-540/ProjMan/Cross
HFD-540/Pharm/Mainigi
HFD-540/MedOfF/Huene
HFD-540/ChemSup/DeCamp 10/16/97
HFD-830/ChemDir/Chen 10/17/97
filename: N20749