CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-124

CHEMISTRY REVIEW(S)

DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS FEB 20 2000
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-124 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 01/27/00

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
NDA 21-124/000	05/14/99	05/19/99	05/25/99
NC	06/10/99	06/11/99	06/22/99
Telecon	06/28/99	NA	NA
BC	07/13/99	07/14/99	07/22/99
NC	08/27/99	09/01/99	09/13/99
BC	10/07/99	10/08/99	10/25/99
BC	10/12/99	10/13/99	10/25/99
BC (Withdrawn)	10/27/99	10/28/99	11/17/99
Telecon	01/07/00	NA	NA
BC	01/17/00	01/18/00	02/01/00
BC	01/26/00	01/27/00	02/02/00

NAME & ADDRESS OF APPLICANT: Novartis Consumer Health, Inc.
560 Morris Avenue
Summit, New Jersey 07901-1312
Cynthia Psaras, Ph.D.
Manager, 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 (athlete's foot), tinea cruris (jock itch), and tenia corporis (ringworm).

DOSAGE FORM:	Solution/Spray
STRENGTHS:	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 20-749/000, Approved 10/17/97.
NDA 20-749/Y-001, Annual Report, 3/3/99.

REMARKS/COMMENTS:

New Drug Application 21-124/000 provides for the Over-the-Counter sale of LAMISIL (terbinafine HCl) Solution, 1%, therefore this is a Rx-to-OTC Switch NDA. The prescription counterpart NDA to this OTC NDA is NDA 20-749, approved October 17, 1997.

The majority of CMC data were referred to in NDA 20-749/000. There were three Phase 4 commitments stemming from the approval of NDA 20-749 which were adequately addressed in their July 13, 1999 BC as well as in the Y-001 Annual Report, dated March 3, 1999.

The applicant, Novartis Consumer Health, Inc., stated the drug substance, the drug product composition, specifications, manufacturing process and controls, container closure systems and drug product stability essentially remained the same as in the previously approved NDA 20-749. New drug product stability data on six individual lots now indicate 36 months of acceptable aging data thus increasing the permitted expiry date from three to four years. As before, there are two previously approved containers, a one ounce dropper and a one ounce spray pump. Neither containers provide metered dosages.

The reported differences between the current NDA 21-124/000 and the original prescription NDA 20-749/000 were: new trademarks, new OTC labeling, new secondary packaging sites, updated stability data and environmental assessment questions. These differences were emphasized in this review.

Minor chemistry amendment, dated 10/27/99, requested three CMC changes, e.g. 1) FDA approval of a new drug product manufacturing facility; 2) FDA approval for additional bottle sizes; and 3) FDA approval for a new bottle supplier. During the 1/7/00 teleconference, FDA suggested the 10/27/99 amendment be withdrawn and resubmitted as two prior approval supplements (for the new manufacturing facility and new bottle sizes). Approval of the new bottle supplier and comparative bottle data was subsequently submitted in the applicant's Minor amendment dated 1/26/00 which provided acceptable comparative data. FDA recommendations 1) and 2) were agreed to by the applicant. The request for a new drug product manufacturing facility involves the transfer of the current LAMISIL Solution drug product manufacturing from the Novartis Pharma AG, Basle, Switzerland, location to the Novartis Consumer Health, Inc., manufacturing facility located in Lincoln, Nebraska. As stated above, FDA recommended this manufacturing facility transfer be submitted as a PAS following this NDA's approval.

CONCLUSIONS & RECOMMENDATIONS:
This Rx-to-OTC Switch NDA 21-124 is Recommended for Approval.

It should be reiterated to the applicant that the FDA review for the transfer of the drug product manufacturing facility from Basle, Switzerland to Lincoln, Nebraska and for qualifying additional bottle sizes can occur as Post Approval Supplements following approval of this NDA.

/S/ 1/25/00
James D. Vidra, Ph.D.
Review Chemist

Attachments (2)

cc: Orig. NDA #21-124
HFD-540/Division File
HFD-540/DivDir/Wilkin
HFD-540/ProjMan/Cross
HFD-540/Pharm/Mainigi
HFD-540/MedOfF/Huene
HFD-540/PharmTox/Mainigi
HFD-540/ChemSup/DeCamp /S/ 1/20/00

/S/ 2/24/00

7 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21124/000
Priority: 6S
Org Code: 540
Stamp: 17-MAY-1999 Regulatory Due: 17-MAR-2000
Action Goal:
District Goal: 17-JAN-2000
Applicant: NOVARTIS PHARMS
59 RT 10
EAST HANOVER, NJ 079361080
Brand Name: LAMISIL AT SMART PUMP/SOLUTION (TERBINAF
Established Name:
Generic Name: TERBINAFINE HCL 1% SOLUTION
Dosage Form: SOL (SOLUTION)
Strength: 1%

FDA Contacts:
F. CROSS JR (HFD-540) 301-827-2023 , Project Manager
J. VIDRA (HFD-540) 301-827-2065 , Review Chemist
W. DECAMP II (HFD-540) 301-827-2041 , Team Leader

Overall Recommendation:

ACCEPTABLE on 24-JAN-2000 by M. EGAS (HFD-322) 301-594-0095
WITHHOLD on 20-OCT-1999 by S. ADAMS (HFD-320) 301-594-0095

Establishment: [redacted]
DMF No:
AADA No:

Profile: LIQ OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 20-OCT-1999
Decision: WITHHOLD
Reason: FACILITY (FIRM) WITHDRAWN
Responsibilities: [redacted]

Establishment: 9611204
NOVARTIS PHARMA INC (SANDOZ)
CH-4002
BASEL, , SZ
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 05-JAN-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
Responsibilities: [redacted]

Profile: LIQ OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-JAN-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: 9612715
NOVARTIS PHARMA INC (SANDOZ)
DMF No:
AADA No:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

RINGASKIDDY/CORK, RINGASKIDD

Profile: **CSN** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **05-JAN-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21124/000
Priority: 6S
Org Code: 540
Stamp: 17-MAY-1999 Regulatory Due: 17-MAR-2000
Action Goal:
District Goal: 17-JAN-2000
Applicant: NOVARTIS PHARMS
59 RT 10
EAST HANOVER, NJ 079361080
Brand Name: LAMISIL AT SMART PUMP/SOLUTION (TERBINAF
Established Name:
Generic Name: TERBINAFINE HCL 1% SOLUTION
Dosage Form: SOL (SOLUTION)
Strength: 1%

FDA Contacts:
F. CROSS JR (HFD-540) 301-827-2023 , Project Manager
J. VIDRA (HFD-540) 301-827-2065 , Review Chemist
W. DECAMP II (HFD-540) 301-827-2041 , Team Leader

Overall Recommendation:

ACCEPTABLE on 24-JAN-2000 by M. EGAS (HFD-322) 301-594-0095
WITHHOLD on 20-OCT-1999 by S. ADAMS (HFD-320) 301-594-0095

Establishment: [redacted]
DMF No:
AADA No:

Profile: LIQ OAI Status: NONE
Responsibilities: [redacted]
Last Milestone: OC RECOMMENDATION
Milestone Date: 20-OCT-1999
Decision: WITHHOLD
Reason: FACILITY (FIRM) WITHDRAWN

Establishment: 9611204
NOVARTIS PHARMA INC (SANDOZ)
CH-4002
BASEL, , SZ
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Responsibilities: [redacted]
Last Milestone: OC RECOMMENDATION
Milestone Date: 05-JAN-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
Profile: LIQ OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-JAN-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: 9612715
NOVARTIS PHARMA INC (SANDOZ)
DMF No:
AADA No:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

RINGASKIDDY/CORK, RINGASKIDD'

Profile: **CSN** OAI Status: **NONE** Responsibilities: [redacted]
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **05-JAN-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**