CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-124

ADMINISTRATIVE DOCUMENTS

SECTION 13: PATENT INFORMATION

Terbinafine HCl is covered by US Patent 4,680,291 (issued July 14, 1987 and expires on July 14, 2004) and US Patent 4,755,534 (issued July 5, 1988 and, in view of a 543 day extension, expires on December 30, 2006). Both patents cover terbinafine, pharmaceutical compositions containing the drug, and its use as an antimycotic agent. Terbinafine HCl solution spray is covered by US Patent 5,681,849 (issued October 28, 1997 and expires on October 28, 2014).

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA/BLA # 21-124 Supplement # _____ Circle one: SE1 SE2 SE3. SE4 SE5 (SE6)

HFD 540 Trade and generic names/dosage form: LAMISIL TERBINAFINE HYDROCHLORIDE SOLUTION, 1% Action: AP AE NA

Applicant NOVARTIS Therapeutic Class ANTI-FUNGAL

Indication(s) previously approved TINEA PEDIS, CORPORIS/CRURIS, VERSICOLOR

Pediatric information in labeling of approved indication(s) is adequate __ inadequate __

Proposed indication in this application INTERDIGITAL TINEA PEDIS, TINEA CORPORIS / CRURIS

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? __Yes (Continue with questions) ✓No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

__Neonates (Birth-1month) __Infants (1month-2yrs) __Children (2-12yrs) __Adolecents(12-16yrs)

__ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

X 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

__ 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

__ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

__ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

__ c. The applicant has committed to doing such studies as will be required.

- __ (1) Studies are ongoing.
- __ (2) Protocols were submitted and approved.
- __ (3) Protocols were submitted and are under review.
- __ (4) If no protocol has been submitted, attach memo describing status of discussions.

__ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

X 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

__ 5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? __Yes ✓No

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from MEDICAL OFFICER (e.g., medical review, medical officer, team leader)

/S/ 3/13/00 — 3/13/00

Signature of Preparer and Title — Date

Orig NDA/BLA # 21-124

HFD/Div File HFD-540

NDA/BLA Action Package

HFD-006/ KRoberts

(revised 10/20/97)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-6 (ROBERTSK)

LAMISIL® Solution 1% (terbinafine hydrochloride solution)
New Drug Application

SANDOZ CERTIFICATION
IN COMPLIANCE WITH THE
GENERIC DRUG ENFORCEMENT ACT OF 1992

SANDOZ PHARMACEUTICALS CORPORATION certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or 306(b) of the Federal Food, Drug and Cosmetic Act in connection with this application.

10/11/96
Date

Michael S. Perry, DVM, PhD
Vice President
Drug Registration and Regulatory Affairs

Meeting Date: December 21, 1998 Time: 1300 Location: S400
Meeting ID# 3457

NDA 20-749, Lamisil (terbinafine HCl) Solution, 1%

Sponsor: Novartis Consumer Health, Inc

Purpose of Meeting: Pre-NDA/Rx to OTC Switch

Meeting Chair: Jonathan K. Wilkin, M.D.

Meeting Recorder (CSO/Project Manager): Frank H. Cross, Jr., M.A., CDR

FDA Attendees, titles and offices:

Jonathan K. Wilkin, M.D., Division Director, DDDDP, HFD-540
Brenda Vaughan, M.D., Medical Officer, DDDDP, HFD-540
John Lipnicki, Team Leader, DOTCDP, HFD-560
Steve Aurecchia, M.D., Medical Officer, DOTCDP, HFD-560
Wilson DeCamp, Ph.D., Chemistry Team Leader, DNDCIII, HFD-830
Jim Vidra, Ph.D., Chemist, DNDCIII, HFD-830
Nahid Mokhtari, Ph.D., Interdisciplinary Scientist, DOTCDP, HFD-560
Barbara Hill, Ph.D., Pharmacologist/Toxicologist, DDDDP, HFD-540
R. Srinivasan, Ph.D., Biostatistics Team Leader, DOBIV, HFD-725
Steve Thomson, Biostatistician, DOBIV, HFD-725
Dennis Bashaw, Ph.D., Biopharmaceutics, DPEIII, HFD-880
Linda Gosey, Ph.D., Acting Microbiology Team Leader, ODEIV, DSPIDP, HFD-590
Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, DDDDP, HFD-540
Elizabeth Yuan, R.Ph., LTJG., Assistant Regulatory Management Officer, DOTCDP, HFD-560

Sponsor Attendees, titles and offices:

Novartis Consumer Health, Inc.

Frederic Huser, President, Novartis Consumer Health
Mark Gelbert, Ph.D., J.D., Vice President, Scientific Affairs
Russ Jones, Director, Regulatory Affairs
Christine Babiuk, Ph.D., Associate Director, Regulatory Affairs

Cynthia Psaras, Ph.D., Manager, Regulatory Affairs
Donald Reitberg, Pharm.D., Director, Medical Affairs and Clinical Operations
Eve del Rio, Ph.D., Associate Director, Clinical Operations
Morris Gold, Ph.D., Associate Director, Biostatistics/Data Management
Phyllis Schumann, Director, Global Development and Product Categories

Novartis Pharmaceuticals Corp.

Stephenie Barba, Executive Director, Drug Regulatory Affairs
Patricia McGovern, M.S., Associate Director, Regulatory Affairs
Sharon Olmstead, Assistant Director, Regulatory Affairs

Meeting Objectives:

Discussion of Rx to OTC Switch of Lamisil (terbinafine HCl) Solution, 1%.

Agency:

Project Management:

Please submit the Annual Report for NDA 20-749, Lamisil (terbinafine HCl) Solution, 1%. The Sponsor said that the Annual Report will be submitted in January 1999.

Chemistry, Manufacturing and Controls:

1. Containers: In NDA 20-749, two types of containers were approved, i.e., a 30 mL container with dropper and a 30 mL container with a spray device. Will both containers also be used with the OTC product? The Sponsor said that they will only be seeking approval for the Rx to OTC Switch of Lamisil Solution, 1%, spray delivery and not the dropper delivery.

2. Containers: Are these the identical containers from a physiochemical perspective to the 30 mL containers approved in NDA 20-749? The Sponsor said that the containers are identical for this new proposed NDA.

3. New Packaging Site: Per your December 2, 1998, briefing package, the solution will be analyzed, packed and released in the facilities of Novartis, Pharmaceuticals Ltd., Basel, prior to shipment to Novartis Pharmaceuticals, East Hanover, NJ, where it will be tested and released for commercial distribution." An alternate secondary packaging site to Lincoln, NE, will be identified in the U.S. This alternate secondary packaging site requires GMP inspection, therefore:

a. This site should either be identified at the time of the NDA submission with a statement that the site is prepared for FDA's GMP inspection, or

b. The proposed site change should be submitted as the first post approval supplement to the proposed NDA.

4. Stability data: The stability data received to date supports only an 18 month expiration and not the requested 24 months. NDA 20-749 was reviewed for additional stability data, however, no additional new data could be located. Please submit the 18 month stability data if the data exist.

5. CMC changes after NDA submission may affect the review of the NDA.

Pharmacology/Toxicology:

No issues identified.

Biopharmaceutics:

No issues identified.

Clinical Microbiology:

The Sponsor should address the following microbiology concern in the NDA submission:

In the proposed NDA submission please provide data showing the incidence of drug resistance development in the dermatophytic moulds and yeasts (i.e., *C. albicans*) when terbinafine is used chronically to treat T. pedis, T. cruris or T. corporis. The Sponsor is encouraged to consult the ICH, E1A document for further guidance on this subject.

Clinical (Division of Dermatologic and Dental Drug Products):

Clinical Topics:

1. Clinical Topic 1 of December 2, 1998, Meeting Briefing Package: With the exception of safety data (i.e., post-marketing safety update and adverse event reporting), no additional studies beyond those already submitted under NDA 20-749 in support of the proposed over-the-counter status of Lamisil Solution, 1%, in adult patients are needed.

   a. All adverse events for all causalities should be reported.

b. Safety data specifically for treatment of tinea cruris should be submitted in addition to the sponsor's proposed post-marketing safety update and adverse event data submitted under NDA 20-749.

c. The Sponsor's proposed post-marketing safety update should also include global post-marketing safety data.

d. The W.H.O. database should be queried in support of safety in addition to the safety update proposed by the sponsor.

2. Clinical Topic 2 of December 2, 1998, Meeting Briefing Package: Maintaining a prescription status for treatment of tinea versicolor is acceptable.

Regulatory Strategy Topics:

1. Regulatory Strategy Topic 1 of December 2, 1998, Meeting Briefing Package: Lamisil Solution, 1%, would not appear to qualify for expedited review by the Agency. The proposed Rx-to-OTC switch of Lamisil Solution, 1%, should be submitted as a new drug application.

2. Regulatory Strategy Topic 2 of December 2, 1998, Meeting Briefing Package: At this time, it does not appear that an Advisory Committee appearance would be required for consideration of the Rx to OTC switch of Lamisil Solution, 1%.

3. Regulatory Strategy Topic 3 of December 2, 1998, Meeting Briefing Package: The OTC indication for treatment of tinea pedis would be limited to a graphic representation of the interdigital clinical variant in patients 18 years or older.

a. An efficacy study in the treatment of moccasin type tinea pedis would be required for OTC marketing of Lamisil Solution, 1%, in the treatment of both clinical variants (interdigital and moccasin) of tinea pedis.

i. Clinical Studies SFF 301-E-100 and SFF351-E-100 submitted under NDA 20-749 support safety and efficacy in the treatment of interdigital tinea pedis only.

ii. Efficacy of Lamisil Solution, 1%, has not been demonstrated in the treatment of moccasin type tinea pedis.

b. A pediatric supplement is needed, because the proposed container label for Lamisil AT, Spray Liquid, would permit use in the pediatric age category 12 to 17 years of age. The pediatric supplement could be submitted separately or as a part of this NDA. Safety and efficacy for Lamisil Solution, 1%, have not been established in the pediatric population according to the approved label.

Clinical (Division of Over the Counter Drug Products):

Clinical Topics:

1. Clinical Topic 1 of December 2, 1998, Meeting Briefing Package: We would agree with the previous comment on this topic made by the Division of Dermatologic and Dental Drug Products.

2. Clinical Topic 2 of December 2, 1998, Meeting Briefing Package: We would agree with the previous comment on this topic made by the Division of Dermatologic and Dental Drug Products.

Regulatory Strategy Topics:

1. Regulatory Strategy Topic 1 of December 2, 1998, Meeting Briefing Package: We would agree with the previous comment on this topic made by the Division of Dermatologic and Dental Drug Products.

2. Regulatory Strategy Topic 2 of December 2, 1998, Meeting Briefing Package: We do not anticipate that a new label validation study will be required. Please note, however, that the label comprehension study for Lamisil Cream, 1%, is still under review. Similarly, we have not, at this juncture, identified any issue such that an Advisory Committee will be needed.

3. Regulatory Strategy Topic 3 of December 2, 1998, Meeting Briefing Package: With regard to labeling:

   a. The proposed OTC labeling extends usage of the product to age 12. The Sponsor was advised to submit data to support this usage extension. The Sponsor agreed. At this point in the development of this product, the Sponsor will label the product for use in the population ages 18 and over.

   b. The phrase "cures most" would be more appropriate than "cure," given the nature of the data on which the indications were approved and in light of NDA/OTC labeling precedent in this therapeutic area.

c. Given that studies in tinea pedis were limited to the interdigital form, and in the absence of a professional intermediary in the OTC consumer market, the OTC "athlete's foot" directions should direct consumers to use the product for the interdigital variant of tinea pedis.

d. We will defer further detailed comments on labeling to a future review.

Biostatistics:

The MITT population is defined as:

1. Randomized to treatment
2. All subjects that were dispensed study medication (active or vehicle)
3. Positive mycology (KOH and culture).

The Sponsor asked if the results from one large multi-centered trial vs. 2 confirmatory trials could be enough to extrapolate to future formulations of Lamisil (terbinafine HCl). The Agency suggested that the Sponsor submit its proposal for review. The Agency further suggested that the Sponsor consult the Guidance for Industry: Evidence of Clinical Effectiveness for further guidance on this subject.

Unresolved issues or issues requiring further discussion:

None.

Corrigendum:

Interdigital and plantar forms of tinea pedis have not been previously differentiated by indication in the OTC marketplace, and it may be more confusing than helpful to do so now. The Divisions suggest a Phase 4 Commitment from the Sponsor to conduct studies to demonstrate that the product is safe and effective for the entire OTC indication of athlete's foot by demonstrating efficacy and safety in plantar tinea pedis. Such data could then be used to change a more restrictive label (via illustrations only) to "standard" labels.

Signature, minutes preparer: _____
Concurrence Chair (or designated signatory): _____

cc:

Orig ND 20-749
HFD-540
HFD-540/DIV DIR/Wilkin
HFD-540/DERM TL/Walker
HFD-540/MO/Vaughan/12.21.98
HFD-540/PHARM TOX TL/Jacobs
HFD-540/PHARM TOX/Hill/12.21.98
HFD-540/PHARM TOX/Mainigi
HFD-540/CHEM TL/DeCamp/12.21.98
HFD-540/CHEM/Vidra/12.21.98
HFD-725/BIOSTAT TL/Srinivasan/12.21.98
HFD-880/BIOSTAT/Thomson/12.21.98
HFD-880/BIOPHARM TL/Bashaw/12.21.98
HFD-590/ACT MICRO TL/Gosey/12.21.98
HFD-540/SPM/Kozma-Fornaro
HFD-540/PM/Cross
HFD-560/DIV DIR/Bowen/12.22.98
HFD-560/DEP DIV DIR/Katz
HFD-560/MED TL/Lipnicki/12.21.98
HFD-560/MO/Aurecchia/12.21.98
HFD-560/IDS/Mokhtari-Rejali/12.21.98
HFD-560/SPM/Cook
HFD-560/PM/Walther
HFD-560/PM/Yuan/12.21.98
Drafted by: fhc/December 21, 1998

Initialed by:
final:

MEMORANDUM OF MEETING

MEMORANDUM OF TELECON

Meeting Date:	6-28-1999
Time:	9:30am
Location:	N225, 9201 Corporate Blvd., Rockville, MD 20850
Application:	NDA 21-124
Type of Meeting:	teleconference/information request
Meeting Chair/Recorder:	Elizabeth Yuan/Victoria Lutwak

FDA Attendees, titles, and Office/Division:
Kalyani Bhatt, Project manager, DDDDP, HFD-540
Wilson DeCamp, Ph.D., Chemistry Team Leader, ONDCIII, HFD-830
Victoria Lutwak, Project manager, DDDDP, HFD-540
James Vidra, Ph.D., Chemist, ONDCIII, HFD-830
Elizabeth Yuan, R.Ph., Project manager, DOTCDP, HFD-560

External Attendee:
Cynthia Psaras, Ph.D., Manager, Regulatory Affairs, Novartis Consumer Health, Inc., 560 Morris Avenue, Summit, NJ 07901

Background:
- Rx status of terbinafine hydrochloride (HCL) solution, 1% for the treatment of interdigital-type tinea pedis, tinea cruris, and tinea corporis was approved October 17, 1997 under NDA 20-749.
- Pre-NDA meeting for this efficacy supplement, type 6, was held on 12/21/1998.
- Application for the efficacy supplement, type 6, Rx-OTC Switch, was filed on 5/17/1999.

Meeting Objectives:
- To inform Novartis Consumer Health of information required for the chemistry review process for this drug product. They will be listed below:

1. Novartis needs to clarify the type of packaging that is performed at the various listed sites. (i.e. primary or secondary).

2. If actual filling occurs at any site, there needs to be a statement from Novartis stating that these sites are ready for inspection.

3. The information regarding the container closure system submitted under NDA 20-749 needs to be resubmitted under NDA 21-124 for review. Sponsor needs to reference the same and if applicable, any additional DMF information.

Minutes Prepared by: EY

Chair Concurrence:

Attachments/Handouts:

cc: NDA 21-124/Original
HFD-540/Div. Files
HFD-560/Div. Files
HFD-540/Meeting Miutes files
HFD-560/Meeting Minutes files
HFD-830/DeCamp/Vidra
HFD-540/Kozma-Fornaro/Lutwak/Bhatt
HFD-560/Yuan

Drafted by:ey 6/30/99
Initialed by:
Final:

MEETING MINUTES

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

January 7, 2000

MEMO OF RECORD: NDA 21-124 (Terbinafine HCl Solution, 1%, Rx-to-OTC Switch)

Author: Cynthia Psaras

Teleconference participants:

FDA
Kevin Darryl White, Project Manager, DDDDP
James Vidra, PhD, Chemist, DNDCIII
Wilson DeCamp, PhD, Chemistry Team Leader, DNDCIII

NCHI
Cynthia Psaras, PhD, Manager, Regulatory Affairs
Christine Babiuk, PhD, Associate Director, Regulatory Affairs
Randy Nelsen, Senior Associate, QA

Dr. Vidra stated that there were two purposes for the FDA to request this teleconference—the request for approval for CMC protocols dated October 27, 1999 and a deficiency in NDA 21-124 related to the October 27, 1999 submission.

The request for CMC protocols included (1) qualifying the Lincoln, NE facility as the manufacturing site of terbinafine HCl solution, 1%, (2) qualifying a new bottle supplier for terbinafine HCl solution and (3) qualifying additional bottle sizes for OTC marketing. Since it is not the policy of DDDDP to approve proposals prior to performing the stability studies, Drs. Vidra and DeCamp offered us direction in these areas. They also requested that this amendment be withdrawn since they are giving us their direction in this teleconference.

To qualify Lincoln, NE as the manufacturing site, six months of accelerated stability data and six months of long-term stability data are required at the time of submission of the prior approval supplement which can not occur until NDA 21-124 is approved. Three batches are required at the time of submission. Two of the three can be pilot scale batches and the third must be a full scale batch.

To qualify the additional bottle sizes, six months of accelerated stability data and six months of long-term stability data on the smallest and largest size bottles are required at the time of submission. This data can be included with the site qualification data submission. The same batch requirements as the site qualification apply. If the stability data from these two bottles sizes is within the range of the currently approved 1 oz. bottle, the expiration date will be 36 months similar to the currently approved Rx product.

At the time of submission of the supplemental NDA, NCHI must commit to place all bottle sizes on long-term stability. Three commercial batches are required for each size container.

To qualify a new bottle supplier, certificates of analysis from [redacted] are required. Additionally, six months of accelerated stability data and six months of long-term stability data on three batches are required at the time of submission. This data can be submitted in the same sNDA with the site qualification data and the alternate bottle size data.

Novartis Pharma submitted their first annual report for Lamisil Solution, 1%, to NDA 20-749 on March 3, 1999. The annual report was subsequently submitted to NDA 21-124 on July 13, 1999 at the request of Dr. Vidra. It was stated in the annual report that the [redacted] Drs. Vidra and DeCamp need to see data to support this statement before NDA 21-124 can be approved. Certificates of Analysis for both bottles have been requested ASAP. In the absence of the certificates of analysis, the Novartis acceptance specifications for the [redacted] bottle are required.

Cynthia Psaras, PhD
Manager
Regulatory Affairs

Novartis Consumer Health, Inc.
560 Morris Avenue
Summit, NJ 07901-1312

Tel 908-598-7823
Fax 908-273-2869

NOVARTIS

ORIGINAL BL
NAD 3/17/00
BDN

FAX

Date:	March 17, 2000
To:	Kevin Darryl White
Company:	FDA—DDDDP
From:	Cynthia Psaras
# of Pages (Including Cover)	3

Kevin Darryl,

Let me know if the attached is sufficient for your needs. If so, I will officially submit it to the NDA.

Cynthia

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Novartis Pharmaceuticals Corp.
59 Route 10
East Hanover, NJ 07936

2. TELEPHONE NUMBER *(Include Area Code)*

(908) 598-7823

3. PRODUCT NAME

Terbinafine Hydrochloride Solution, 1%

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

3697

6. LICENSE NUMBER / NDA NUMBER

21-124

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Cynthia Psaras	Manager Regulatory Affairs	May 14, 1999

LABELING REVIEW OF NDA

NDA 21-124

MAR 15 2000

Submission Date:	5/14/99	**Review Date:**	1/14/00 2/23/00 3/6/00

Applicant: Novartis Consumer Health, Inc.
560 Morris Avenue
Summit, New Jersey 07901-1312

Representative: Cynthia Psaras, Ph.D.
Manager, Regulatory Affairs
(908) 598-7823

Drug: Lamisil ® (Terbinafine Hydrochloride 1%) Solution

Pharmacologic Category: Antifungal

Reviewed:

1. Draft labeling of carton and immediate container for tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm) indications; 30 ml spray
2. Draft labeling of carton and immediate container for tinea cruris (jock itch) indication; 30 ml spray
3. Draft labeling of blister card and immediate container for tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm) indications; 30 ml dropper
4. Consumer educational brochure for the tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm); 30 ml spray product
5. Consumer educational brochure for the tinea cruris (jock itch); 30 ml spray product

Reviewer's Comments:

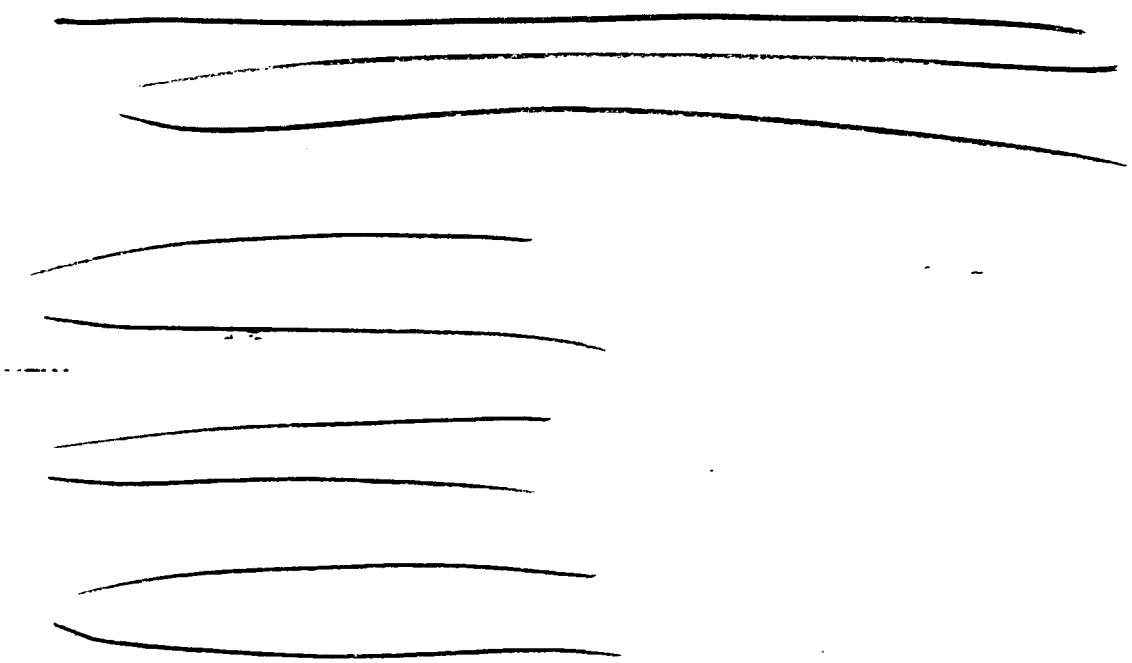
Background - This NDA is submitted in support of the switch of terbinafine hydrochloride solution, 1% to non-prescription status. Terbinafine hydrochloride solution, 1% was approved on October 17, 1997, for prescription (Rx) use for interdigital tinea pedis (athlete's foot), tinea cruris

(jock itch), tinea corporis (ringworm), and tinea versicolor under NDA 20-749. The applicant is seeking over-the-counter (OTC) marketing approval of terbinafine hydrochloride solution, 1% for interdigital tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm) in a spray pump and dropper applicator form; and, for tinea cruris (jock itch) in a spray pump form. Thus, the only remaining Rx indication for this product is tinea versicolor. The dropper applicator product is not currently marketed in the United States. **Note:** The sponsor is not requesting a plantar (moccasin type) tinea pedis indication as was approved for the OTC Lamisil cream product (NDA 20-980).

Labeling review – The proposed labeling for terbinafine hydrochloride solution, 1% for OTC use is different from the Rx label as follows:

a. The proposed OTC indications are interdigital tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm). Tinea versicolor is not indicated on the OTC label.
b. The proposed OTC label states that the solution is not to be used in children under the age of 12 years, rather than 18 years in the Rx label.
c. The proposed OTC labeling for terbinafine hydrochloride solution, 1% with a dropper applicator was not approved under NDA 20-749.

A Consumer Educational Brochure was not submitted for the athlete's foot, jock itch, and ringworm 30 ml dropper product and the sponsor states that there is no educational brochure associated with this product. The sponsor intends to market both the 30 ml spray product and the 30 ml dropper product upon approval.



11 page(s) of revised draft labeling has been redacted from this portion of the review.

Recommendations:

1. Attached is the mock-up labeling based on the OTC labeling format and content requirements published in the Federal Register on March 17, 1999 (64 FR 13254). This review provides labeling content only and does not address appropriate font, type size, or barline/hairline thickness as specified in section 201.66.
2. Inform the sponsor that the word "New" and the statements "Now Available Without a Prescription" and "Full Prescription Strength" on the principal Display Panel are allowed for no more than 6 months after initial introduction to the market place.
3. Inform the sponsor that a consumer educational brochure needs to be included with the athlete's foot, jock itch, and ringworm 30ml dropper product. Recommend to the sponsor that a draft educational brochure be submitted for review.
4. After labeling day, mock-up labeling and comments should be sent by fax to the Sponsor for their concurrence prior to the issuance of the action letter based on the PDUFA due date

/S/

IDS: Donald Dobbs

CC:
NDA 21-124 archival
HFD-540/division files
HFD-540/Wilkin
HFD-540/Huene
HFD-540/White
HFD-540/Kozma-Fornaro
HFD-560/Ganley
HFD-560/Katz
HFD-560/Lipnick
HFD-560/Shetty
HFD-560/Dobbs
HFD-560/Cook
HFD-560/Yuan
HFD-560/Miguele

/S/ 3/17/00
/S/ 11:57:00

NDA 21-124 Labeling Review

Please contact the undersigned with any questions or comments at 908-598-7823.

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Attachment
Submitted in duplicate
cc: Kevin Darryl White by facsimile (301-827-2075)