CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-124

CORRESPONDENCE

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

Tel 908 598 7600
Fax 908 273 2869

NOVARTIS

May 4, 1999

Mellon Bank
Three Mellon Bank Center
27th Floor (FDA 360909)
Pittsburgh, PA 15259-0001

RE: **NDA #21-124 Terbinafine Hydrochloride Solution, 1%**
Rx – to – OTC Switch

USER FEE ID #3697

Please find enclosed a check in the amount of [redacted] the user fee for NDA #21-124. Approval is being sought for over-the-counter marketing of terbinafine hydrochloride solution, 1%, for the indications of tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm).

If you have any questions or require any additional information, please contact me at (908) 598-7823.

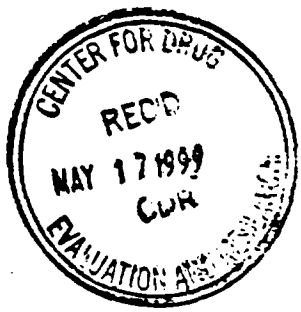
Very truly yours,

Cynthia Psaras

Cynthia Psaras, Ph.D.
Manager, Regulatory Affairs
Novartis Consumer Health, Inc.

Enclosure (Check #01042989)

cc: Mary Jean Kozma Fornaro, FDA, Division of Dermatologic and Dental Drug Products, HFD-540



NOVARTIS

May 14, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Rx-to-OTC Switch NDA

Dear Dr. Wilkin:

In accordance with 21 CFR §314.50, Novartis Pharmaceuticals Corporation herewith submits a New Drug Application for sale without prescription for terbinafine hydrochloride (HCl) solution, 1% for the treatment of interdigital-type tinea pedis, tinea cruris and tinea corporis. This application will incorporate by reference NDA 20-749 for Lamisil® Solution, 1%, approved October 17, 1997.

A pre-NDA meeting was held with the agency on December 21, 1998 to discuss the Rx-to-OTC switch of Lamisil® Solution, 1%. As agreed to in the meeting, this application includes:

- a re-analysis of the efficacy data submitted in the original application using a modified intent-to-treat (mITT) population which includes all randomized subjects
- an updated Integrated Summary of Efficacy (ISE) including the results of the mITT analysis
- an updated Integrated Summary of Safety (ISS) providing a breakout of the tinea cruris safety data from the original tinea corporis/cruris studies , post-marketing safety data, and a discussion of the potential for the development of fungal resistance to terbinafine
- synopses of the clinical and preclinical safety studies submitted in NDA 20-749
- data/information to support the use of the product in children 12 years and older

At this pre-NDA meeting, Novartis Consumer Health, Inc. stated that it would only market the spray form but have subsequently decided to seek OTC approval for both the dropper and spray products.

The proposed labeling for terbinafine HCl solution, 1%, marketed OTC differs from the Rx label currently in use in three ways. First, the indications are interdigital tinea pedis

(athlete's foot), tinea cruris (jock itch) and tinea corporis (ringworm); tinea versicolor will remain a prescriptive indication. Second, the OTC label states that the solution is not to be used in children under the age of 12 years. Third, labeling is also included for the dropper, which is not currently marketed by Novartis Pharmaceuticals Corporation in the United States.

Novartis Pharmaceuticals Corporation considers the information contained within this application to be confidential, and its contents are not to be disclosed without expressed written consent.

Please address any questions or comments regarding this application to:

Cynthia Psaras, PhD
Manager, Regulatory Affairs
Novartis Consumer Health, Inc.
560 Morris Avenue
Summit, New Jersey 07901-1312

Tel: 908-598-7823
FAX: 908-273-2869

Sincerely,

Patricia McGovern

Patricia McGovern
Associate Director, Regulatory Affairs
Novartis Pharmaceuticals Corporation

Attachments
Submitted in Duplicate
cc: Division of OTC Drug Products (in duplicate)

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

NEW CORRESP
NC

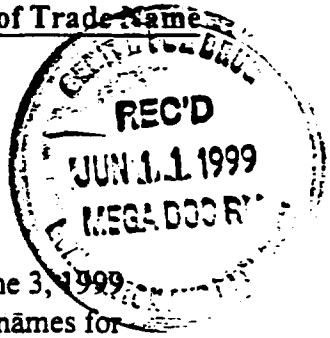
June 10, 1999

6/28/99

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride Solution, 1%

Rx-to-OTC Switch NDA:
Notification of Trade Name Selection



Dear Dr. Wilkin:

Reference is made to a conversation with Commander Frank Cross on June 3, 1999, requesting that Novartis Consumer Health, Inc. submit the selected trade names for terbinafine hydrochloride solution, 1%, to be marketed over-the-counter, for consideration by the FDA Nomenclature Committee.

The preferred trade name for the OTC spray version of terbinafine hydrochloride solution, 1%, is LAMISIL®AT™ SMART PUMP™. SMART PUMP refers to the fact that the non-aerosol pump functions even when inverted. The back-up trade name is LAMISIL®AT™ LIQUID PUMP SPRAY. The preferred trade name for the OTC dropper version of terbinafine hydrochloride solution, 1%, is LAMISIL®AT™ SOLUTION. The attachment lists the preferred and back-up trade names in a larger font to facilitate 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: Frank Cross by facsimile (301-827-2091)

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

NC

July 1, 1999

8/2/99

NEW CORRESP

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride Solution, 1%

Amendment to a Pending Application

SAS Datasets for Clinical Studies
Electronic Labeling

Dear Dr. Wilkin:

Reference is made to conversations with Commander Frank Cross on May 24, 1999 and June 3, 1999. In these conversations, Commander Cross requested that Novartis Consumer Health, Inc. (NCHI) submit (1) the Lamisil Solution, 1%, clinical study protocols on diskette, (2) the SAS datasets for these studies on diskette as well as loaded on a laptop computer and (3) the proposed over-the-counter (OTC) labeling in Word and PDF formats.

In this submission, NCHI is supplying the SAS datasets on diskette and the proposed OTC labeling in Word and PDF format. Duplicate SAS datasets and electronic labeling are being sent directly to Commander Frank Cross. The laptop computer loaded with SAS programming and SAS data will be forward to Commander Cross at a later date. On May 26, 1999, Commander Cross was notified by NCHI that the clinical study protocols were not available electronically.

The SAS datasets were originally submitted by Novartis Pharmaceuticals Corporation to NDA 20-749. The SAS datasets include studies SFF301, SFF303, SFF305, SFF309, SFF351 and SFF353. The tinea pedis studies are SFF351, SFF301, SFF309. The tinea cruris and tinea corporis study is SFF303. The remaining studies are tinea versicolor studies which were not submitted in NDA 21-124 for over-the-counter marketing. Raw data files and analysis data files are included for each of these studies. The files are in SAS transport format.

Please contact the undersigned at 908-598-7823 if additional information is required.

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Submitted in duplicate
Attachments sent to F. Cross (Mary Jean Kozma-Fornaro in his absence)
cc: Frank Cross/Mary Jean Kozma-Fornaro by facsimile, 301-827-2091

Manager
Regulatory Affairs

Summit, NJ 07901-1312

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

NOVARTIS

ORIGINAL

July 13, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Rx-to-OTC Switch NDA:
Request for Information

Dear Dr. Wilkin:

Reference is made to telephone conversations with Dr. James Vidra and Dr. Wilson DeCamp on June 28, 1999 and with Commander Frank Cross on July 6, 1999 requesting information on CMC issues, financial disclosure, and the pediatric rule. The following is the list of requested information.

1. Verify that the secondary packaging sites will not be filling bottles but just labeling them (Vidra and DeCamp).

2. State when the Basel facility will be ready for inspection (Vidra and DeCamp).

3. Re-submit information on container/closure system from NDA 20-749 (Novartis Pharmaceuticals Corporation) to NDA 21-124 (Rx-to-OTC switch) (Vidra and DeCamp).

4. List DMFs cited in NDA 20-749 plus any recent additions as well as letters of authorization. Drs. Vidra and DeCamp wanted to know if [redacted] new approved supplier of the bottles, has a DMF.

5. Submit the first annual report dated 3/3/99 for Lamisil Solution, 1% (NDA 20-749), to NDA 21-124 (Vidra and DeCamp).

6. Submit FDA form 3454 Certification: Financial Interests and Arrangements of Clinical Investigations for the original clinical studies submitted in NDA 20-749 (Cross).

7. Respond to pediatric rule stated in a letter sent to Novartis Pharmaceuticals Corporation on June 8, 1999 (Cross).

Our responses are arranged in the order listed above.

1. & 2. None of the four secondary packaging sites approved for NDA 20-749 or the four additional packaging sites submitted for approval in NDA 21-124 fill bottles with drug product. Lamisil Solution, 1%, is manufactured, packaged and released from Novartis Pharma AG, Lichtstrasse 35, 4002 Basel, Switzerland. The Basel manufacturing facility is ready for inspection at the agency's discretion.

3. The part of the CMC section covering the container/closure system from NDA 20-749 is attached for submission to NDA 21-124 . Additionally, any information on the container/closure submitted to NDA 20-749 is also being submitted to NDA 21-124.

4. The table below contains the Drug Master Files (DMF) submitted to NDA 20-749. The first three DMFs were referenced in NDA 20-749 at the time of submission. Novartis is the holder of all three DMFs, therefore, no letters of authorization are necessary. A fourth DMF was submitted during the review period for included in this submission.

5. The first annual report for Lamisil Solution, 1%, was submitted to NDA 20-749 on March 3, 1999. It is attached for submission to NDA 21-124.

6. FDA form 3454 Certification: Financial Interests and Arrangements of Clinical Investigations is included in this submission. It covers the original clinical studies submitted in NDA 20-749.

7. A letter from the FDA received by Novartis Pharmaceuticals Corporation on June 8, 1999 stated that we have 60 to 120 days from the date of the letter to respond to the

pediatric rule. Since we require additional time to appropriately respond, we are not addressing the pediatric issue in this submission. We will, however, provide our response within the time period designated in the June 8th letter.

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: Frank Cross by facsimile (301-827-2091)

DUPLICATE

Manager
Regulatory Affairs

560 Morris Avenue
Summit, NJ 07901-1312

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

NOVARTIS

NEW CORRESP
NC

August 2, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Request for
Pediatric Rule Waiver

Dear Dr. Wilkin:

Reference is made to NDA 21-124, Terbinafine Hydrochloride Solution, 1%, to 63 FR 66632 and to 21 CFR 314.55. The final rule states that the pediatric study requirement applies to all applications for new active ingredients, new indications, new dosage forms, new dosage regimens and new routes of administration. As stated in the NDA Summary of NDA 21-124, this Rx-to-OTC switch application does not meet any of these criteria. Terbinafine hydrochloride solution, 1%, is presently marketed by prescription only as Lamisil® Solution, 1%, for the topical treatment of tinea versicolor due to *Malassezia furfur*, and tinea pedis, tinea cruris or tinea corporis due to *Trichophyton rubrum, Trichophyton mentagrophytes,* or *Epidermophyton floccosum.* The frequency and duration of treatment of the prescriptive product is twice a day for one week for tinea versicolor and tinea pedis and once a day for one week for tinea cruris and corporis. The Rx-to-OTC switch application, NDA 21-124, seeks approval to market terbinafine hydrochloride solution, 1%, for the topical treatment of the same indications as the prescriptive product with the exception of tinea versicolor, which will remain a prescriptive indication. The proposed frequency and duration of treatment for the over-the-counter product does not differ from that of the prescriptive product. In view of the aforementioned facts, Novartis Consumer Health, Inc. requests a waiver for the pediatric study requirement for NDA 21-124.

Please contact the undersigned at 908-598-7823 if additional information is required.

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Submitted in quadruplicate
cc: Frank Cross by facsimile, 301-827-2091

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

DUPLICAT

NEW CORRESP

NC

NOVARTIS

August 27, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride Solution, 1%

Request for Information

Dear Dr. Wilkin:

Reference is made to a telephone conference between the FDA and the undersigned on August 18, 1999. The FDA participants were Frank Cross and Dr. James Vidra. Dr. Vidra asked for clarification of the following two CMC issues.

1. Confirm that a re-calculation of the Expected Introduction Concentration (EIC) of all terbinafine products (not just solution) would not result in an EIC beyond the 1 ppb limit for exclusion. Also include the manufacturing site for each terbinafine formulation.

The following are the responses of Novartis Consumer Health, Inc. (NCHI) on these issues.

1. Lamisil solution and tablets are manufactured in Basel, Switzerland while the cream is manufactured in Lincoln, NE. The calculation for all terbinafine products results in an EIC below the 1 ppb limit for exclusion. Therefore, NCHI requests a categorical exclusion for an Environmental Assessment.

2. The bottles made by the new supplier are physically and chemically identical to those made by the old supplier.

Please contact the undersigned at 908-598-7823 if additional information is required.

Sincerely,

for

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Submitted in quadruplicate
cc: Frank Cross by facsimile, 301-827-2091

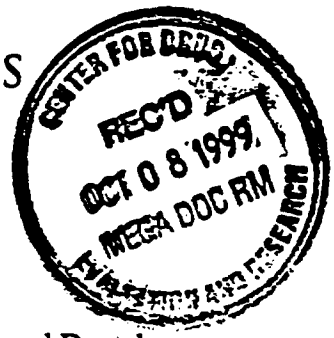
ORIGINAL

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



October 7, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT
BC

NDA 21-124
Terbinafine Hydrochloride Solution, 1%

Amendment to a Pending Application

Dear Dr. Wilkin:

In accordance with 21CFR§314.60(a), Novartis Consumer Health, Inc. herewith submits an amendment to a pending new drug application for terbinafine hydrochloride solution, 1%. This amendment provides for the withdrawal of a packaging site which is listed in the above cited pending new drug application.

Novartis Consumer Health, Inc. will not be using the facilities of the following site to label or package terbinafine hydrochloride solution, 1%, drug product:

[redacted]

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)
Ms. Regina Brown, New Jersey District Office; North Brunswick Resident Post—Certified Field Copy

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

October 12, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

ORIG AMENDMENT
BC

Amendment to a
Pending Application

Dear Dr. Wilkin:

In accordance with 21CFR§314.60(a), Novartis Consumer Health, Inc. herewith submits an amendment to a pending new drug application for terbinafine hydrochloride solution, 1%. While working on the withdrawal of [redacted] secondary packaging site, as discussed with Dr. James Vidra of your office, it was discovered that Novartis Pharmaceuticals Corp. does not currently have approval to label the primary package at the Lincoln, NE manufacturing site.

This amendment provides for the addition of the Novartis Consumer Health, Inc., Lincoln, NE site for the labeling of the primary package. Therefore, the manufacture and bottling of the drug product will be performed by Novartis Pharma, Basel, Switzerland. The unlabeled drug product will then be shipped to Novartis Consumer Health, Inc., Lincoln, NE for application of the primary package labeling and secondary packaging (boxes).

[redacted]

ORIGINAL

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)
Ms. Regina Brown, New Jersey District Office, North Brunswick Resident Post—Certified Field Copy

ORIGINAL

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

ORIG AMENDMENT
BM

October 21, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Request for Information

Dear Dr. Wilkin:

Reference is made to the Novartis Consumer Health, Inc. (NCHI) pending new drug application for over-the-counter sale of terbinafine hydrochloride (HCl) solution, 1% (NDA 21-124). On October 6, 1999, Mr. Kevin Darryl White, Project Manager in the Division of Dermatologic and Dental Drug Products, requested on behalf of the medical reviewer further information on adverse drug events reported during clinical trials, in the Novartis Worldwide Safety Database, and in the WHO database. The requested information is listed below.

1. Controlled studies on tinea pedis - bullous eruptions in 2 patients on Lamisil solution.
2. Controlled studies Series 300 - skin disorder in 8 patients on Lamisil solution.
3. Controlled study on seborrheic dermatitis - skin disorder in 1 patient on Lamisil solution.
4. Controlled study on candidiasis - 2 patients in the Lamisil solution treatment group discontinued because of adverse events, the nature of which were not specified. These were reported as severe and as definitely attributable to the drug.
5. Novartis worldwide safety database - 1 case each of exfoliative dermatitis, skin disorder, and vesiculobullous rash with Lamisil solution.
6. Novartis worldwide safety database - 3 cases of exfoliative dermatitis, 3 cases of erythema multiforme, 1 case of epidermal necrolysis, 3 cases of angioedema, 1 case of Stevens Johnson syndrome, 7 cases of vesiculobullous rash, and 6 cases of skin disorder with Lamisil cream.

7. WHO adverse event data for terbinafine - (some or all of these may be in the Novartis database) - 1 case of erythema multiforme, 2 cases of skin disorder, and 4 cases of vesiculobullous rash.

This submission contains our response to this request. Since we referenced the pre-NDA/Rx-to-OTC switch meeting held on December 21, 1998 in our response, this submission also includes a copy of that meeting's minutes. Additionally, please find FDA forms 3500A for the cited cases from the Novartis Worldwide Safety database and data from the WHO drug safety database for the cases in question from the WHO database.

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

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Submitted in duplicate
cc: Kevin Darryl White by facsimile, 301-827-2075

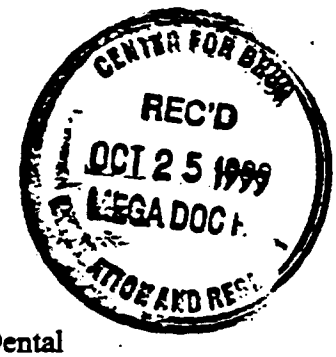
ORIGINAL

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



October 22, 1999

Kevin Darryl White
Project Manager
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride Solution, 1%

Request for Bottle Samples

Dear Kevin Darryl:

Enclosed are the bottle samples that you requested. Since the bottles are not assembled, I have placed the components of each bottle in a separate plastic bag.

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

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Note:
Bottle given
to KD White 10-25-99.
Smurphy

ORIGINAL

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

ORIG AMENDMENT

BC

October 27, 1999

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Request for Approval
for CMC Protocols

Dear Dr. Wilkin:

Reference is made to the Novartis Consumer Health, Inc. (NCHI) pending new drug application for sale without prescription of terbinafine hydrochloride (HCl) solution, 1% (NDA 21-124). We are currently planning a series of chemistry, manufacturing and controls (CMC) changes should the application be approved. At this time we are requesting that our proposals for these CMC changes be reviewed and approved by the chemistry reviewer prior to the start of the studies. Specifically, approval for all the changes to be submitted in a single supplement as well as for the bracketing stability protocol are requested. The proposed CMC changes are listed below.

1. Qualify the Novartis Consumer Health, Inc., Lincoln, Nebraska facility as the manufacturer of the drug product, terbinafine HCl solution, 1%

2. Qualify a new bottle supplier.

3. Qualify additional bottle sizes for over-the-counter marketing.

To qualify the Lincoln, NE facility as the manufacturer of terbinafine HCl solution, 1%, NCHI proposes to submit three (3) months of comparative accelerated stability data ——— and three (3) months of long-term stability data ———. from one (1) pilot scale batch. The container/closure system will be the same as that currently approved in the prescriptive NDA (20-749) as well as that submitted in the pending NDA

21-124. The comparison will be made to the three month stability data originally submitted in NDA 20-749.

To qualify a new bottle supplier of the 1oz. bottle, NCHI proposes to submit three (3) months of comparative accelerated stability data [redacted] and three (3) months of long-term stability data [redacted] from one (1) pilot scale batch. The bottle resins will be the same for the new supplier as that approved in NDA 20-749 and submitted in pending NDA 21-124. The pump assembly will also be the same as that approved in NDA 20-749 and submitted in pending NDA 21-124. The comparison will be made to the three month stability data originally submitted in NDA 20-749.

To qualify the additional bottle sizes, NCHI proposes to submit three (3) months of comparative accelerated stability data [redacted] and three (3) months of long-term stability data [redacted] from one (1) pilot scale batch. The comparison will be made to the three month stability data from the 1oz. bottle from the new supplier. The stability studies will bracket the range of bottle sizes with data collected from the smallest

The attached table summarizes the comparisons for the proposed CMC changes. The bracketing stability protocol is also included in this submission. Since all three studies are inter-related, can the results from all the studies be submitted, post-approval, in one CMC supplement?

Please contact the undersigned at 908-598-7823 if additional information is required.

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

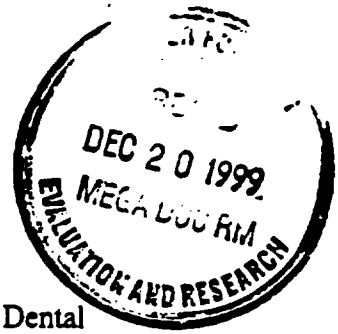
Submitted in quadruplicate
cc: Kevin Darryl White by facsimile, 301-827-2075

Manager
Regulatory Affairs

560 Morris Avenue
Summit, NJ 07901-1312

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

NOVARTIS



NDA ORIG AMENDMENT

December 17, 1999 BL

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Part 1 1/12/00

Request for Labels

Dear Dr. Wilkin:

Reference is made to the pending new drug application, NDA 21-124, Terbinafine Hydrochloride Solution, 1%, submitted May 14, 1999. On December 14, 1999, Elizabeth Yuan, Project Manager in the Division of Over-the-Counter Drug Products, requested the extended content labels for the solution spray and dropper bottles. Two non-functional extended content labels are included in this submission. The larger of the two labels wraps around the solution spray bottle serving as the principle display panel as well as the back panel. The smaller extended content label represents the "back panel" of the dropper bottle label; the principle display panel is a separate label which is not extended. The enclosed labels are non-functional since they do not include any adhesives. In the absence of approved labeling, these extended content labels are being provided for estimation of the label space for the Drug Facts format.

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)
Desk copy to Elizabeth Yuan, Division of Over-the Counter Drug Products

DUPLICATE

Manager
Regulatory Affairs

560 Morris Avenue
Summit, NJ 07901-1312

Tel 908-598-7823
Fax 908-277-2555

NOVARTIS

January 17, 2000

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

BC

Rx-to-OTC Switch NDA:
Request for Information

Dear Dr. Wilkin:

Reference is made to the telephone conversation with Dr. James Vidra and Dr. Wilson DeCamp on January 7, 2000 requesting information on the old and new bottle suppliers for terbinafine hydrochloride solution, 1%, dropper and spray bottles. On July 13, 1999, Novartis Consumer Health, Inc. (NCHI), at the request of Drs. Vidra and DeCamp, had submitted Novartis Pharmaceuticals Corporation's first annual report for Lamisil (terbinafine hydrochloride) Solution (NDA 20-749) to the Rx-to-OTC switch NDA 21-124. The annual report stated that with the permission of the chemistry reviewers from the Division of Dermatologic and Dental Drug Products, Novartis Pharmaceuticals Corporation was able to change suppliers of the bottles in the first annual report since the resins/raw materials by the old and new suppliers remain unchanged. Subsequently, on January 7, 2000, Drs. Vidra and DeCamp requested data from NCHI to support the Pharma statement that resins/raw materials of the old and new bottles remained unchanged. The analytical results of the Novartis Pharmaceuticals Corporation acceptance specifications are included in this submission.

ORIGINAL

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

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

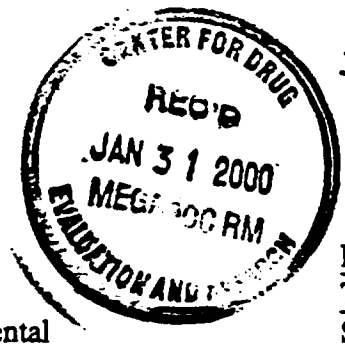
Attachment
Submitted in duplicate
cc: Kevin Darryl White by facsimile (301-827-2075)

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



January 28, 2000

NEW CC
NC

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Withdrawal of Amendment
CMC Protocols

Dear Dr. Wilkin:

Reference is made to a telephone conference between Novartis Consumer Health, Inc. (NCHI) and Dr. James Vidra and Dr. Wilson DeCamp from the Division of Dermatologic and Dental Drug Products on January 7, 2000. Drs. Vidra and DeCamp had requested the telephone conference after NCHI submitted stability protocols on October 27, 1999 for their approval prior to initiation of the studies. Drs. Vidra and DeCamp requested that NCHI withdraw this amendment since they gave us their direction on the stability protocols during the teleconference. NCHI withdraws the referenced amendment with this communication.

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

Sincerely,

Cynthia Psaras

Cynthia Psaras, PhD
Manager, Regulatory Affairs

Submitted in duplicate
cc: Kevin Darryl White by facsimile, 301-827-2075

ORIGINAL

Regulatory Affairs
Summit, NJ 07901-1312
Tel 908-598-7823
Fax 908-273-2869

NOVARTIS

NC

March 6, 2000

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Request for Information

Dear Dr. Wilkin:

Per Elizabeth Yuan's request, Novartis Consumer Health, Inc. is submitting information relating to the print specifications of the Drug Facts format on the labeling for terbinafine hydrochloride solution spray. The requested information is listed below.

Headings:
- Drug Facts: 14 pt Helvetica Bold/Italics
- Subheadings: 8 pt Helvetica Bold/Italic

Text: 6 pt Helvetica Regular
Hairline: 0.5pt
Barline: 2.5 pt

Attached is the actual Drug Facts section of the solution (dropper) label with each of the above components labeled for ease of 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)
Elizabeth Yuan by facsimile (301-827-2315)

[redacted]
Manager
Regulatory Affairs

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

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

NOVARTIS

March 17, 2000

Jonathan Wilkin, MD
Director
Division of Dermatologic and Dental
Drug Products/HFD-540
Office of Drug Evaluation V
Attn: Document Control Room
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NDA 21-124
Terbinafine Hydrochloride
Solution, 1%

Rx-to-OTC Switch NDA:
Labeling Commitments

Dear Dr. Wilkin:

Reference is made to the pending new drug application for terbinafine hydrochloride solution, 1% (NDA 21-124) for over-the-counter marketing. With this letter, Novartis Consumer Health, Inc. is accepting the labeling for Lamisil®AT™ Spray Pump and Solution Dropper as received electronically on March 9, 2000 with minor exceptions. These exceptions, as discussed with the agency on March 15 and 16, include the use of only one indication on the PDP of all cartons and immediate container labels rather than three indications, the use of Lamisil®AT™ Solution Dropper rather than Lamisil®AT™ Solution, the use of a carton for the solution dropper rather than a blister card and the use of the phrase "Call 1-800-xxx-xxxx 24 hours a day 7 days a week" indicating that we have live operators during that time.

Per our telephone conference on March 17, 2000, we will replace "CURES ATHLETE"S FOOT" with "CURES ATHLETE'S FOOT BETWEEN THE TOES*" on the PDP, and add the statement "*See back panel for Uses information" immediately below the picture of the spray bottle. The font size of the latter statement will be 8 which is equivalent to that of the statement "For Effective Relief of:..." also on the PDP. In addition, the statement "Effectiveness on the bottom or sides of foot is unknown." will follow "cures athlete's foot between the toes." in the Uses section in the Drug Facts box. Following this statement, a second bulleted statement will be "cures jock itch (tinea cruris) and ringworm (tinea corporis)." The third bulleted statement remains the same "relieves itching, burning, cracking, and scaling which accompany these conditions." All statements will be the same font size.

For the front panel on the immediate bottle container label, the asterisked statement will occur directly below the phrase "CURES ATHLETE'S FOOT BETWEEN THE TOES*." The font size will be 5 which is slightly larger than the statement of identity also on this panel.

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)