

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 77-511

Name: Terbinafine Hydrochloride Cream, 1%

Sponsor: Taro Pharmaceuticals

Approval Date: July 2, 2007

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-511

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-511

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 77-511

Taro Pharmaceuticals U.S.A., Inc.
Attention: Sirinivasa Rao
Director Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 30, 2004, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Terbinafine Hydrochloride Cream, 1%.

Reference is also made to the tentative approval letter issued by this office on March 22, 2006, and to your amendments dated October 4, 2006; and March 30, 2007.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective the date of this letter. The Division of Bioequivalence has determined your Terbinafine Hydrochloride Cream, 1%, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Lamisil® Cream of Novartis Pharmaceutical Corporation. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

We remind you of your commitment specified in your amendment dated June 25, 2007. To alert the Office of Generic Drugs staff that you are submitting information to address the post-approval commitment, please state "Post- Approval Commitment Response" at the top of your cover letter.

Sincerely yours,

(See appended electronic signature page)

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Gary Buehler

7/2/2007 09:09:53 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-511

TENTATIVE APPROVAL LETTER

ANDA 77-511

MAR 22 2006

Taro Pharmaceuticals U.S.A. Inc.
Attention: Kalpana Rao
5 Skyline Drive
Hawthorne, NY 10532

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated December 30, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Terbinafine Hydrochloride Cream, 1%.

Reference is also made to your amendments dated August 23, 2005, and March 21, 2006.

We have completed the review of this abbreviated application, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your application at this time because of the patent/exclusivity issue noted below. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Lamisil® Cream of Novartis Consumer Health Inc. is currently subject to a period of patent protection. As noted in the Agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book", U.S. Patent No. 4755534 (the '534 patent) is scheduled to expire on December 30, 2006. Your application contains a Paragraph III Certification to the '534 patent under Section 505(j)(2)(A)(vii)(III) of the Act. This certification states that Taro Pharmaceuticals U.S.A. Inc. (Taro) will not market this Terbinafine Hydrochloride Cream prior to the

your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the '534 patent has expired, i.e., December 30, 2006.

In order to reactivate your application prior to final approval, please submit a "MINOR AMENDMENT - FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your application will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval, and it should also identify changes, if any, in the conditions under which the product was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made. This amendment should be designated clearly in your cover letter as a "MINOR AMENDMENT - FINAL APPROVAL REQUESTED".

In addition to the amendment requested above, the Agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

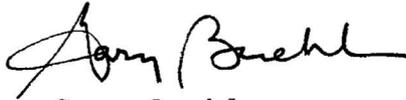
Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made. Such changes should be submitted as an amendment to the ANDA and categorized as representing either "major" or "minor" changes. The amendment will be reviewed according to OGD policy in effect at the time of receipt. Your submission of multiple amendments prior to final approval may also lead to a delay in the issuance of the final approval letter.

Please note that this drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final

approval letter prior to December 30, 2006, you should amend your application accordingly.

For further information on the status of this application or upon submitting an amendment to the application, please contact Benjamin Danso, Pharm.D, Project Manager, at 301-827-5848.

Sincerely yours,



Gary Buehler

Director

3/22/06

Office of Generic Drugs

Center for Drug Evaluation and Research

cc: ANDA 77-511
Division File
Field Copy
HFD-610/R. West
HFD-205
HFD-610/Orange Book Staff

W. Wickham
3/22/06

Endorsements:

HFD-629/K.Woodland/*K Woodland 1/23/06*
HFD-623/R.Bykadi/*S. Bykadi 1-24-2006*
HFD-617/B.Danso/*BD 1-24-06*
HFD-613/R.Wu/*via Email 1-23-06*
HFD-613/J.Grace/*via Email 1-24-06*

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E/T by

TENTATIVE APPROVAL

ps 1/31/06

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-511

LABELING

(b) (4)



**ATTACHED LEGEND TO ALL
DIGITAL MECHANICALS**

(b) (4)

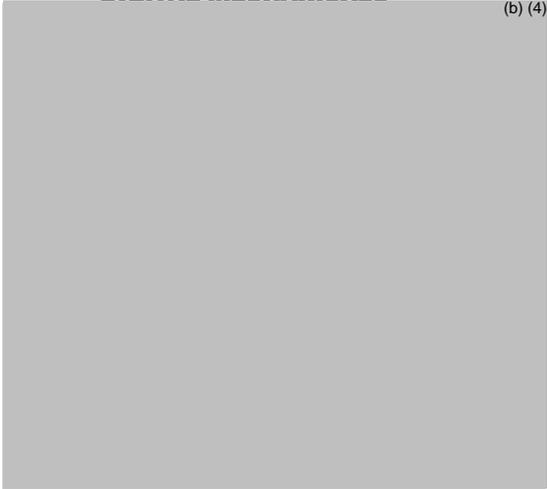


(b) (4)



**ATTACHED LEGEND TO ALL
DIGITAL MECHANICALS**

(b) (4)



Compare to the active ingredient in Lamisil AT®*

Cures Most Athlete's Foot

Terbinafine Hydrochloride Cream 1% Antifungal Cream



- Relieves Itching & Burning
- Full Prescription Strength



LPK-0000-0
0505-0
M000

T 27

Cures Most Athlete's Foot

Full Prescription Strength

Terbinafine Hydrochloride Cream 1% Antifungal Cream

NET WT 1/2 oz (15 g)

Terbinafine Hydrochloride Cream 1% Antifungal Cream



Drug Facts (continued)
Inactive ingredients: benzyl alcohol, ethyl alcohol, polyethylene glycol, sorbitan monostearate, stearyl alcohol, isopropyl myristate, polysorbate 80, purified water, sodium hydroxide, sorbitan monostearate, stearyl alcohol.



TERBINAFINE Hydrochloride Cream 1%
Lamisil AT®
Lamellar Pharmaceuticals
Lamellar, NY
10522
U.S.A.
Made in Canada.

Drug Facts

Active ingredient
Terbinafine hydrochloride 1%

Purpose
Antifungal

Uses
• Cures most athlete's foot (tinea pedis)
• Cures most foot itch (tinea cruris) and ringworm (tinea corporis)
• Relieves itching, burning, cracking and scaling which accompany these conditions

Warnings For external use only
• Do not use on nails or scalp • In or near the mouth or the eyes • For vaginal yeast infections
When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.
Stop use and ask a doctor if too much irritation occurs or gets worse.
Keep out of reach of children. If swallowed, get medical help or contact a poison control center right away.

Directions
• Adults and children 12 years and older
• Wash the tip of the cap to break the seal and open the tube
• Apply the cream to the affected skin with soap and water and dry completely before applying
• For athlete's foot wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.
• Between the toes only; apply twice a day (morning and night) for 1 week or as directed by a doctor.
• On the bottom or sides of the feet; apply twice a day (morning and night) for 2 weeks or as directed by a doctor.
• For foot itch and ringworm apply once a day (morning or night) for 1 week or as directed by a doctor.
• Wash hands after each use
• Children under 12 years: ask a doctor

Other information
• Do not use if seal on tube is broken or is not visible
• Store at controlled room temperature 20°-25°C (68°-77°F)
• See carton or tube crimp for lot number and expiration date

Other information
• Children under 12 years: ask a doctor
• Wash hands after each use
• Children under 12 years: ask a doctor

ATTACHED LEGEND TO ALL DIGITAL MECHANICALS

(b) (4)



(b) (4)

7/8" DIAMETER
MASTER TEMPLATE

(b) (4)

Cures Most Athlete's Foot Full Prescription Strength

Terbinafine Hydrochloride

Cream 1% Antifungal Cream NET WT 1/2 oz (15 g)

Active ingredient	Purpose	Directions
Terbinafine hydrochloride 1%	Antifungal	<ul style="list-style-type: none"> adults and children 12 years and older use the tip of the cap to break the seal and open the tube wash the affected skin with soap and water and dry completely before applying for athlete's foot wear well-fitting, ventilated shoes. Change shoes and socks at least once daily. between the toes only: apply twice a day (morning and night) for 1 week or as directed by a doctor. on the ball of or sides of the foot: apply twice a day (morning and night) for 2 weeks or as directed by a doctor. for jock itch and ringworm: apply once a day (morning or night) for 1 week or as directed by a doctor. wash hands after each use children under 12 years: ask a doctor

Warnings
For external use only.
Do not use
• on nails or scalp • in or near the mouth or the eyes
• for vaginal yeast infections.

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.

Stop use and ask a doctor if too much irritation occurs or gets worse.

Keep out of reach of children. If swallowed, get medical help or contact a poison control center right away.

Store at controlled room temperature 20°-25°C (68°-77°F). See crimp of tube for lot number and expiration date.

Dist. by: Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532 Made in Canada.
LPI-0000-0 0595-0 000

(b) (4)

ATTACHED LEGEND TO ALL
DIGITAL MECHANICALS

(b) (4)

Cures Most Athlete's Foot

Compare to the active ingredient in Lamisil AT®*

Terbinafine Hydrochloride Cream 1% Antifungal Cream



- Relieves Itching & Burning
- Full Prescription Strength

LP-000-0
0305-0
M000

T30

Cures Most Athlete's Foot

Full Prescription Strength

Terbinafine Hydrochloride Cream 1% Antifungal Cream

NET WT 0.85 oz (24 g)

Terbinafine Hydrochloride Cream 1% Antifungal Cream



Drug Facts (continued)

Other Antifungals:

- do not use if seal on tube is broken or is not viable
- store at controlled room temperature 20°-25°C (68°-77°F)
- see carton or tube cap for lot number and expiration date

Inactive Ingredients: benzyl alcohol, cetyl palmitate, isopropyl myristate, polyethylene glycol, purified water, sodium hydroxide, xanthan monohydrate, stearyl alcohol.

NO COPY NO COLOR



Drug Facts

Active ingredient: Terbinafine hydrochloride 1% Antifungal

Uses:

- cures most athlete's foot (tinea pedis)
- cures most itch (tinea corporis) and ringworm (tinea capitis)
- relieves itching, burning, cracking and scaling which accompany these conditions

Warnings:

- For external use only
- Do not use • on rash or scab • if or near the mouth or the eyes • for vaginal yeast infections
- If the medicine does not get into the eye, if eye contact occurs, rinse thoroughly with water
- Keep use and seal intact. If top mouth infection occurs or gets worse.
- Keep use and seal intact. If eye contact occurs, rinse thoroughly with water.

Directions:

- adults and children 12 years and older
- use the tip of the cap to break the seal and open the tube
- 1 week between the toes
- between the toes apply twice a day (morning and night) for 1 week or as directed by a doctor.
- on the bottom or sides of the feet apply twice a day (morning and night) for 1 week or as directed by a doctor.
- for itch that has spread to the body apply once a day (morning and night) for 1 week or as directed by a doctor.
- wash hands after each use
- children under 12 years: ask a doctor

How to use:

- wash the affected area with soap and water and dry completely before applying
- use the tip of the cap to break the seal and open the tube
- between the toes apply twice a day (morning and night) for 1 week or as directed by a doctor.
- on the bottom or sides of the feet apply twice a day (morning and night) for 1 week or as directed by a doctor.
- for itch that has spread to the body apply once a day (morning and night) for 1 week or as directed by a doctor.
- wash hands after each use
- children under 12 years: ask a doctor

How to use:

- wash the affected area with soap and water and dry completely before applying
- use the tip of the cap to break the seal and open the tube
- between the toes apply twice a day (morning and night) for 1 week or as directed by a doctor.
- on the bottom or sides of the feet apply twice a day (morning and night) for 1 week or as directed by a doctor.
- for itch that has spread to the body apply once a day (morning and night) for 1 week or as directed by a doctor.
- wash hands after each use
- children under 12 years: ask a doctor

Cures Most Athlete's Foot Antifungal Cream

Terbinafine Hydrochloride Cream 1%

ATTACHED LEGEND TO ALL DIGITAL MECHANICALS

(b) (4)



(b) (4)

7/8" DIAMETER
MASTER TEMPLATE

(b) (4)

Full Prescription Strength

Cures Most Athlete's Foot

Terbinafine Hydrochloride

Cream 1% Antifungal Cream

NET WT 0.85 oz (24 g)

Active Ingredient	Purpose	Directions
Terbinafine Hydrochloride 1% Uses • cures most athlete's foot (tinea pedis) • cures most jock itch (tinea cruris) and ringworm (tinea corporis) • relieves itching, burning, cracking and scaling which accompany these conditions Warnings For external use only. Do not use • on nails or scalp • in or near the mouth or the eyes • for vaginal yeast infections. Always using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Stop use and ask a doctor if too much irritation occurs or gets worse. Keep out of reach of children. If swallowed, get medical help or contact a poison control center right away. Store at controlled room temperature 20°-25°C (68°-77°F) See crimp of tube for lot number and expiration date	Antifungal • adults and children 12 years and older • use the tip of the cap to break the seal and open the tube • wash the affected skin with soap and water and dry completely before applying • for athlete's foot wear well-fitting, ventilated shoes. Change shoes and socks at least once daily. • between the toes only: apply twice a day (morning and night) for 1 week or as directed by a doctor. • on the bottoms or sides of the feet: apply twice a day (morning and night) for 2 weeks or as directed by a doctor. • for jock itch and ringworm: apply once a day (morning or night) for 1 week or as directed by a doctor. • wash hands after each use • children under 12 years: ask a doctor	  

Div. by: Taro Pharmaceuticals U.S.A., Inc.
 Hawthorne, NY 10532 Made in Canada.
 LPR-0000-0 0505-0 000

(b) (4)

(b) (4)

**ATTACHED LEGEND TO ALL
DIGITAL MECHANICALS**

(b) (4)

Cures Most Athlete's Foot

Compare to the active ingredient in Lamisil AT®*

Terbinafine Hydrochloride Cream 1% Antifungal Cream



- Relieves Itching & Burning
- Full Prescription Strength

LPK-0000-0
0606-0
M000

T 30

Cures Most Athlete's Foot

Full Prescription Strength

Terbinafine Hydrochloride Cream 1% Antifungal Cream

NET WT 1 oz (30 g)

Terbinafine Hydrochloride Cream 1% Antifungal Cream



Drug Facts (continued)

Other Information

- Do not use if seal on tube is broken or is not visible
- Store at controlled room temperature 20°-25°C (68°-77°F)
- See carton or tube strip for lot number and expiration date
- Contains 100 mg terbinafine hydrochloride (1% w/w) per 10 g (0.35 oz) of cream

NO COPY
NO COLOR

Decanted by: **Terbinafine HCL, N.A., Inc.**
 1470 is a registered trademark of **Terbinafine HCL, N.A., Inc.**
 Made in Canada.

Warnings

- Do not use if seal on tube is broken or is not visible
- Do not use if you are allergic to terbinafine hydrochloride or any of the other ingredients
- Do not use if you are allergic to any of the ingredients listed on the label
- Do not use if you are allergic to any of the ingredients listed on the label
- Do not use if you are allergic to any of the ingredients listed on the label



Directions

- Adults and children 12 years and older:
 - Wash the affected area with soap and water and dry completely before applying.
 - Use the tip of the cap to break the seal and open the tube.
 - Apply the cream to the affected area once a day (morning and night) for 1 week or as directed by a doctor.
 - Wash hands after each use.
- Children under 12 years: ask a doctor.

Uses

- Cures most athlete's foot (tinea pedis)
- Cures most foot itch (tinea cruris) and ringworm (tinea corporis)

Warnings

- Relieves itching, burning, cracking and scaling which accompany these conditions
- Do not use if you are allergic to terbinafine hydrochloride or any of the other ingredients
- Do not use if you are allergic to any of the ingredients listed on the label
- Do not use if you are allergic to any of the ingredients listed on the label
- Do not use if you are allergic to any of the ingredients listed on the label

Other Information

- Do not use if seal on tube is broken or is not visible
- Store at controlled room temperature 20°-25°C (68°-77°F)
- See carton or tube strip for lot number and expiration date
- Contains 100 mg terbinafine hydrochloride (1% w/w) per 10 g (0.35 oz) of cream

Drug Facts

Active ingredient: Terbinafine hydrochloride 1%
Purpose: Antifungal Cream 1%
 Cures Most Athlete's Foot

ATTACHED LEGEND TO ALL DIGITAL MECHANICALS

(b) (4)



(b) (4)

(b) (4)

Full Prescription Strength

Cures Most Athlete's Foot

Terbinafine Hydrochloride

Cream 1% Antifungal Cream

NET WT 1 oz (30 g)

Active ingredient	Purpose	Directions
Terbinafine Hydrochloride 1% Indications • cures most athlete's foot (tinea pedis) • cures most jock itch (tinea cruris) and ringworm (tinea corporis) • relieves itching, burning, cracking and scaling which accompany these conditions Warnings For external use only. Do not use: • on nails or scalp • in or near the mouth or the eyes • for vaginal yeast infections. While using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Stop use and ask a doctor if too much irritation occurs or gets worse. Keep out of reach of children. If swallowed, get medical help or contact a poison control center right away. Store at controlled room temperature 20°-25°C (68°-77°F) See crimp of tube for lot number and expiration date	Antifungal	• adults and children 12 years and older • use the tip of the cap to break the seal and open the tube • wash the affected skin with soap and water and dry completely before applying • for athlete's foot wear well-fitting, ventilated shoes. Change shoes and socks at least once daily. • between the toes only: apply twice a day (morning and night) for 4 weeks or as directed by a doctor. • on the bottom or sides of the feet: apply twice a day (morning and night) for 2 weeks or as directed by a doctor. • for jock itch and ringworm: apply once a day (morning or night) for 4 weeks or as directed by a doctor. • wash hands after each use • children under 12 years: ask a doctor



1 week between the toes



2 weeks on the bottom or sides of the feet



Dist. by: Taro Pharmaceuticals U.S.A., Inc.
 Hawthorne, NY 10532 Made in Canada.
 LPK-0000-0 0505-0 000

(b) (4)

(b) (4)

ATTACHED LEGEND TO ALL DIGITAL MECHANICALS

(b) (4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-511

LABELING REVIEWS

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 77-511

Date of Submission: December 30, 2004 (e-submission)

Applicant's Name: Taro Pharmaceuticals USA, Inc.

Established Name: Terbinafine Hydrochloride Cream, 1% (OTC)

Labeling Deficiencies:

1. GENERAL COMMENTS:

- a. Revise "Terbinafine Hydrochloride 1% Cream" to read "Terbinafine Hydrochloride Cream 1%".
- b. In order for us to verify your compliance with the labeling format requirements of 21 CFR 201.66, please submit a format legend for each size of your container and carton labels.

2. CONTAINER (b) (4) 12 g, 15 g, 24 g, and 30 g tubes)

Refer to GENERAL COMMENTS

3. CARTON (one tube)

- a. Refer to GENERAL COMMENTS
- b. 12 g and 15 g Cartons: In the electronic submission, text is cut-off. Please realign the horizontal barlines (refer to attachment).

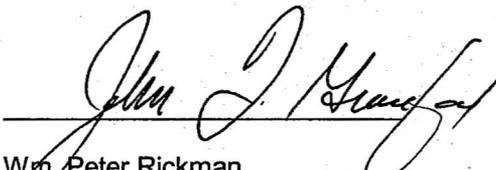
4. CONSUMER EDUCATIONAL BROCHURE

- a. Refer to GENERAL COMMENT 1.a.
- b. Picture #1: add the caption "1 week between the toes"

Please revise your labels and labeling, as instructed above, and submit final printed labels and labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes- <http://www.fda.gov/cder/cdernew/listserv.html> or <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>

To facilitate review of your next submission, please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.



Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachment: electronic submissions of the 12 g and 15 g Cartons

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N/A
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 28 (checked 5/11/05)		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)			
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	

Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. NONE	X		

NOTE TO THE CHEMIST:

FOR THE RECORD:

****First Generic****

- Labeling review based on the approved labeling for the OTC reference listed drug (Lamisil AT® Cream NDA 20-980.) The original application and labeling was approved March 9, 1999. There have been no labeling supplements approved since this date. However, a letter was issued by the New Drug division on October 26, 2000 requesting the following: *In the FEDERAL REGISTER of August 29, 2000 (65 FR 52302), the Food and Drug Administration (FDA) published an amendment of the final monograph for over-the-counter (OTC) topical antifungal drug products to make a minor change in the indications for these drug products. The change inserted the word "most" between the introductory phrase and the name of the condition(s) for which the OTC topical antifungal drug product is to be used.*
- Packaging
The RLD packages product in 12 g, 24 g and 30 g tubes.
ANDA: (b) (4)
12 g, 15 g, 24 g, and 30 g (b) (4) tubes
Inner seal (b) (4) permanent seal
 - Lot number and expiration date will be stamped on the container labels at the time of print. [vol. B1.1, section 1.4.2. pg. 1]
 - Taro's 1-800 number will be provided prior to print for commercial use. [Vol. b1.1, section 1.4.2., pg. 1]
- Manufacturing facility [Vol. B1.4. section 3.2.P.3.1, pg. 1]
Taro Pharmaceuticals Inc.
130 East Drive,
Brampton, Ontario
Canada, L6T 1C1
- Inactive ingredients
There does not appear to be a discrepancy in inactives between the product labeling and the Component and Composition statements. [Vol. B1.2, section 2.3, pg. 16]
Purified water, Polysorbate, Cetyl alcohol, Steryl alcohol, Cetyl palmitate, Isopropyl myristate, Sorbitan Monosterate, Sodium hydroxide, Benzyl alcohol
- Storage
Not a USP item
RLD – Store at Controlled Room Temperature (20°-25°C (68°-77°F)
ANDA – Store at Controlled Room Temperature (20°-25°C (68°-77°F)

6. Patent and Exclusivity for NDA 20-980

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Patent Use Code	How Filed	Labeling Impact
020980	001	4680291	JUL 14, 2004	U-73	Expired	None
020980	001	4755534	DEC 30, 2006	U-73	P III (V1.1, section 1.3.3, pg. 2)	None

Exclusivity Data

There is no unexpired exclusivity for this product.

7. Bioequivalence Issues – Pending review as of May 10, 2005

Date of Review:	May 11, 2005	Date of Submission:	December 30, 2004 (Original Submission)
Primary Reviewer:	Ruby Wu <i>RWu</i>	Date:	5/11/05
Team Leader:	John Grace <i>John Grace</i>	Date:	5-11-05

cc: ANDA: 77-511
DUP/DIVISION FILE
HFD-613/RWu/JGrace (no cc)
V:\FIRMSNZ\TARO\LTRS&REV\77511.na1.L.doc
Review

(b) (4)



(b) (4)



div.

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 77-511
Date of Submission: May 25, 2005 (Amendment: e-submission)
Applicant's Name: Taro Pharmaceuticals USA, Inc.
Established Name: Terbinafine Hydrochloride Cream, 1% (OTC)

APPROVAL SUMMARY

1. Do you have Final Printed Labels and Labeling? Yes.

2. CONTAINER ^{(b) (4)} 12 g, 15 g, 24 g, and 30 g tubes)
Satisfactory in final print as of the May 25, 2005 e-submission.
^(b)
⁽⁴⁾
12 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb12gT0000-0S.pdf
15 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb15gT0000-0S.pdf
24 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb24gT_0000-0S.pdf
30 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb30gT_0000-0S.pdf

3. CARTON (one tube)
Satisfactory in final print as of the May 25, 2005 e-submission.
^(b)
⁽⁴⁾
12 g: \\CdseSubogd1\N77511\N_000\2005-05-25\Terb12gC0000-0S.pdf
15 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb15gC0000-0S.pdf
24 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb24gC_0000-0S.pdf
30 g: \\CDSESUBOGD1\N77511\N_000\2005-05-25\Terb30gC_0000-0S.pdf

4. CONSUMER EDUCATIONAL BROCHURE
Satisfactory in final print as of the May 25, 2005 e-submission.
\\CDSESUBOGD1\N77511\N_000\2005-05-25\TerbInsert_0000-0S.pdf

Revisions needed post-approval: No.

BASIS OF APPROVAL

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Lamisil ® Cream (Same as OB...not modifier "AT")
NDA Number: 20-980
NDA Drug Name: Terbinafine Hydrochloride Cream, 1%
NDA Firm: Novartis
Date of Approval of NDA Insert and supplement: The original application and labeling was approved March 9, 1999.
There have been no labeling supplements approved since this date.
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container & Carton Labels: Side-by-side comparison with innovator labels in jacket.

Patent and Exclusivity for NDA 20-980

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Patent Use Code	How Filed	Labeling Impact
020980	001	4680291	JUL 14, 2004	U-73	Expired	None
020980	001	4755534	DEC 30, 2006	U-73	P.III (V1.1, section 1.3.3, pg. 2)	None

Exclusivity Data

There is no unexpired exclusivity for this product.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N/A
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 28 (checked 7/13/05)		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N/A
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	

Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. NONE	X		

NOTE TO THE CHEMIST:

FOR THE RECORD:

****First Generic****

- Labeling review based on the approved labeling for the OTC reference listed drug (Lamisil AT® Cream NDA 20-980.) The original application and labeling was approved March 9, 1999. There have been no labeling supplements approved since this date. However, a letter was issued by the New Drug division on October 26, 2000 requesting the following:
In the FEDERAL REGISTER of August 29, 2000 (65 FR 52302), the Food and Drug Administration (FDA) published an amendment of the final monograph for over-the-counter (OTC) topical antifungal drug products to make a minor change in the indications for these drug products. The change inserted the word "most" between the introductory phrase and the name of the condition(s) for which the OTC topical antifungal drug product is to be used.
- Packaging
The RLD packages product in 12 g, 24 g and 30 g tubes.
ANDA: (b) (4)
12 g, 15 g, 24 g, and 30 g (b) (4) tubes
Inner seal (b) (4) permanent seal
 - Lot number and expiration date will be stamped on the container labels at the time of print. [vol. B1.1, section 1.4.2. pg. 1]
 - Taro's 1-800 number will be provided prior to print for commercial use. [Vol. b1.1, section 1.4.2., pg. 1]
- Manufacturing facility [Vol. B1.4. section 3.2.P.3.1, pg. 1]
Taro Pharmaceuticals Inc.
130 East Drive,
Brampton, Ontario
Canada, L6T 1C1
- Inactive ingredients
There does not appear to be a discrepancy in inactives between the product labeling and the Component and Composition statements. [Vol. B1.2, section 2.3, pg. 16]
Purified water, Polysorbate, Cetyl alcohol, Steryl alcohol, Cetyl palmitate, Isopropyl myristate, Sorbitan Monosterate, Sodium hydroxide, Benzyl alcohol
- Storage
Not a USP item
RLD – Store at Controlled Room Temperature (20°-25°C (68°-77°F))
ANDA – Store at Controlled Room Temperature (20°-25°C (68°-77°F))

6. Patent and Exclusivity for NDA 20-980

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Patent Use Code	How Filed	Labeling Impact
020980	001	4680291	JUL 14, 2004	U-73	Expired	None
020980	001	4755534	DEC 30, 2006	U-73	P III (V1.1, section 1.3.3, pg. 2)	None

Exclusivity Data

There is no unexpired exclusivity for this product.

7. Bioequivalence Issues – Pending review as of July 13, 2005

Date of Review:	July 13, 2005	Date of Submission:	May 25, 2005 (Amendment)
Primary Reviewer:	Ruby Wu	Date:	
Team Leader:	John Grace	Date:	

cc: ANDA: 77-511
DUP/DIVISION FILE
HFD-613/RWu/JGrace (no cc)
V:\FIRMSNZ\TAROLTRS&REV\77511.OTC.ap.L.doc
Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-511

CHEMISTRY REVIEWS

#1
ANDA 77-511

Terbinafine Hydrochloride Cream, 1%

Taro Pharmaceuticals U.S.A., Inc.

**Kathy P. Woodland
Division of Chemistry I
Team 5**



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Chemistry Review Data Sheet

1. ANDA 77-511
2. REVIEW #:1
3. REVIEW DATE: May 8, 2005
Revised June 10, 2005
4. REVIEWER: Kathy P. Woodland

5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Original Submission

December 30, 2004

Acceptable for Filing

January 3, 2005

Amendment (add alternate source of drug
substance)

March 9, 2005

Amendment (labeling)

May 26, 2005

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals U.S.A.

Address: 5 Skyline Drive
Hawthorne, N.Y. 10532



Chemistry Review Data Sheet

Representative: Kalpana Rao

Telephone: 914-345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None

b) Non-Proprietary Name (USAN): Terbinafine Hydrochloride Cream, 1%

9. LEGAL BASIS FOR SUBMISSION:

a. The basis of Taro's proposed ANDA for Terbinafine Hydrochloride Cream, 1% is the approved listed drug, Lamisil, NDA 20980, held by Novartis Consumer Health Inc.

b. There is no unexpired exclusivity for Lamisil Cream, 1%. There is one patent #4755534, which will expire on Dec. 30, 2006.

10. PHARMACOL. CATEGORY: Treatment of Athlete's foot.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 10 mg/g (1%)

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: ___ Rx ___ x ___ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

___ SPOTS product – Form Completed

___ x ___ Not a SPOTS product

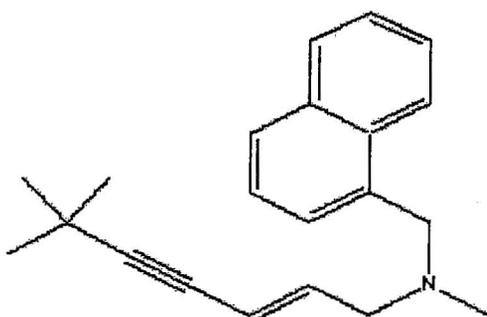
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemistry Review Data Sheet

TRANS-N-(6,6-DIMETHYL-2-HEPTEN-4-YNYL)-N-METHYL-; Lamisil (free base);
 Lamosil; 1-Naphthalenemethanamine, N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-, (E)-,
 monohydrochloride;

Molecular Formula: $C_{21}H_{26}ClN$

Molecular Weight: 327.90



HCL

17. RELATED/SUPPORTING DOCUMENTS: None

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCE D	CODE1	STATUS2	DATE REVIEW COMPLETED	COMMENTS
(b) (4)				3	Adequate	5/10/04 B.Lim	
				1	Inadequate	6/7/005 K. Woodland	
				4			
				4			
				4			
				4			
				4			
				4			
				4			



CHEMISTRY REVIEW



Chemistry Review Data Sheet

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Pending		
Methods Validation	Not Required		
Labeling	Pending		
Bioequivalence	Pending		
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 77-511

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This product is a FIRST GENERIC. Not approvable. Minor Chemistry, Labeling is deficient and Bioequivalence is pending.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Substance:

Terbinafine Hydrochloride drug substance is a white to off-white crystalline powder. The drug substance is soluble in methylene chloride and methanol; sparingly soluble in acetone, ethanol, 2-propanol; slightly soluble in water; practically insoluble in toluene.

Drug Product:

The product is

(b) (4)

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g). The IT is (b) (4)%, the QT is (b) (4)%.

B. Description of How the Drug Product is Intended to be Used

The drug product Terbinafine Hydrochloride Cream, 1% is an OTC product used for the treatment of Athlete's Foot (tinea pedis), jock itch (tinea cruris), and body ringworm (tinea corporis) (antifungal).

The treatment is one week for Athlete's Foot between the toes, jock itch, and body ringworm, and two weeks for Athlete's Foot on the bottoms or sides of the foot.

The market sizes are (b) (4) 12 gram, 15 gram, 24 gram, and 30 gram (b) (4) tubes.

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g) The IT is (b) (4)%, the QT is (b) (4)%.



Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

Not Approvable

III. Administrative

A. Reviewer's Signature

Kathy P. Woodland

B. Endorsement Block

HFD-627/K. Woodland/ *K Woodland 6/24/05*
HFD-627/A. Mueller, PhD/ *A Mueller 6-24-05*
HFD-617/B. Danso, Pharm D., PM/
V:\FIRMSNZ\TAROLTRS&REV\77511.CR1.DOC

C. CC Block

15 pages have been withheld as b4 (CCI/TS) immediately following this page

cc: ANDA 77-511
ANDA DUP 75-511
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/K. Woodland/ *K Woodland 6/29/05*
HFD-627/A. Mueller, PhD/ *A Mueller 6-29-05*
HFD-617/B. Danso, Pharm D., PM/6-28-05

V:\FIRMSNZ\TARO\LTRS&REV\77511.CR1.DOC

TYPE OF LETTER: NOT APPROVABLE - MINOR

#2

**ANDA 77-511
FIRST GENERIC**

Terbinafine Hydrochloride Cream, 1%

Taro Pharmaceuticals U.S.A., Inc.

**Kathy P. Woodland
Division of Chemistry I
Team 5**

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III. Administrative.....	8
A. Reviewer's Signature	8
B. Endorsement Block	8
C. CC Block.....	8
Chemistry Assessment	9



#2

Chemistry Review Data Sheet

- 1. ANDA 77-511
- 2. REVIEW #:2
- 3. REVIEW DATE: September 20, 2005
Revised January 30, 2006
- 4. REVIEWER: Kathy P. Woodland
- 5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

Original Submission	December 30, 2004
Acceptable for Filing	January 3, 2005
Amendment (add alternate source of drug substance)	March 9, 2005
Amendment (labeling)	May 25, 2005

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Amendment	August 23, 2005
-----------	-----------------

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals U.S.A., Inc.
Address: 5 Skyline Drive
Hawthorne, N.Y. 10532
Representative: Kalpana Rao
Telephone: 914-345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:



Chemistry Review Data Sheet

- a) Proprietary Name: None
b) Non-Proprietary Name (USAN): Terbinafine Hydrochloride Cream, 1%

9. LEGAL BASIS FOR SUBMISSION:

a. The basis of Taro's proposed ANDA for Terbinafine Hydrochloride Cream, 1% is the approved listed drug, Lamisil, NDA 20980, held by Novartis Consumer Health Inc.

b. There is no unexpired exclusivity for Lamisil Cream, 1%. There is one patent #4755534, which will expire on Dec. 30, 2006.

10. PHARMACOL. CATEGORY: Treatment of Athlete's foot.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 10 mg/g (1%)

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: ___ Rx ___ x ___ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

___ SPOTS product – Form Completed

___ x ___ Not a SPOTS product

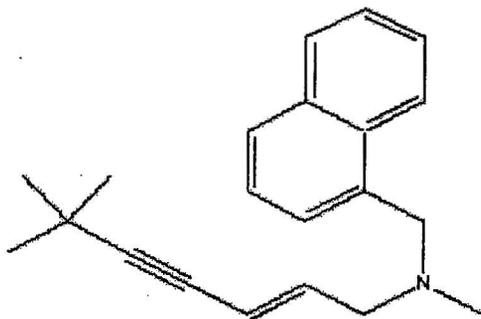
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

TRANS-N-(6,6-DIMETHYL-2-HEPTEN-4-YNYL)-N-METHYL-; Lamisil (free base); Lamosil; 1-Naphthalenemethanamine, N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-, (E)-, monohydrochloride;

Chemistry Review Data Sheet

Molecular Formula: C₂₁H₂₆ClN

Molecular Weight: 327.90



HCL

17. RELATED/SUPPORTING DOCUMENTS: None

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCE D	CODE1	STATUS2	DATE REVIEW COMPLETED	COMMENTS
(b) (4)				1	Adequate	9/23/05 K. Woodland	
				1	Adequate	1/26/06 K. Woodland	
				4			
				4			
				4			
				4			
				4			
				4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review



CHEMISTRY REVIEW



Chemistry Review Data Sheet

- 4 – Sufficient information in application
- 5 – Authority to reference not granted
- 6 – DMF not available
- 7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
BES	Pending		
Methods Validation	Not Required		
Labeling	Acceptable	7/13/05	Ruby Wu
Bioequivalence	Acceptable	1/6/06	C. Kim
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:

The Chemistry Review for ANDA 77-511

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This product is a FIRST GENERIC. Approvable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Substance:

Terbinafine Hydrochloride drug substance is a white to off-white crystalline powder. The drug substance is soluble in methylene chloride and methanol; sparingly soluble in acetone, ethanol, 2-propanol; slightly soluble in water; practically insoluble in toluene.

Drug Product:

The product is

(b) (4)

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g). The IT is (b) (4)%, the QT is (b) (4)%.

B. Description of How the Drug Product is Intended to be Used

The drug product Terbinafine Hydrochloride Cream, 1% is an OTC product used for the treatment of Athlete's Foot (tinea pedis), jock itch (tinea cruris), and body ringworm (tinea corporis) (antifungal).

The treatment is one week for Athlete's Foot between the toes, jock itch, and body ringworm, and two weeks for Athlete's Foot on the bottoms or sides of the foot.

The market sizes are (b) (4), 12 gram, 15 gram, 24 gram, and 30 gram (b) (4) tubes.

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g) The IT is (b) (4)%, the QT is (b) (4)%.



Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

Approvable

III. Administrative

A. Reviewer's Signature

Kathy P. Woodland

B. Endorsement Block

HFD-620/K. Woodland/ *K Woodland 1/30/06*
HFD-620/G. Bykadi, PhD/ *G. Bykadi 1-31-2006*
HFD-617/B. Danso, Pharm D., PM/
V:\FIRMSNZ\TARO\LTRS&REV\77511.CR2.DOC

C. CC Block

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CHEMISTRY REVIEW



Chemistry Assessment Section

cc: ANDA 77-511
ANDA DUP 75-511
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/K. Woodland/ *K. Woodland 1/30/06*
HFD-627/G. Bykadi, PhD/ *A. Bykadi 1-31-2006*
HFD-617/B. Danso, Pharm D., PM/1-19-06

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TYPE OF LETTER: CMC APPROVABLE

**ANDA 77-511
(FIRST GENERIC)**

Terbinafine Hydrochloride Cream, 1%

Taro Pharmaceuticals U.S.A., Inc.

**Kathy P. Woodland
Division of Chemistry I
Team 5**



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Chemistry Review Data Sheet

1. ANDA 77-511
2. REVIEW #: 3
3. REVIEW DATE: April 30, 2007
Revised June 26, 2007
4. REVIEWER: Kathy P. Woodland
5. PREVIOUS DOCUMENTS:

Previous DocumentsDocument Date

Original Submission	December 30, 2004
Acceptable for Filing	January 3, 2005
Amendment (add alternate source of drug substance)	March 9, 2005
Amendment (labeling)	May 25, 2005
Amendment	August 23, 2005

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) ReviewedDocument Date

Amendment	October 4, 2006
Amendment (Gratuitous amendment)	March 21, 2006
Amendment (Final approval requested)	March 30, 2007
Amendment	June 25, 2007

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals U.S.A., Inc.
Address: 3 Skyline Drive
Hawthorne, N.Y. 10532



CHEMISTRY REVIEW



Chemistry Review Data Sheet

Representative: Kalpana Rao

Telephone: 914-345-9001

Fax 914-593-0078

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None

b) Non-Proprietary Name (USAN): Terbinafine Hydrochloride Cream, 1%

9. LEGAL BASIS FOR SUBMISSION:

a. The basis of Taro's proposed ANDA for Terbinafine Hydrochloride Cream, 1% is the approved listed drug, Lamisil, NDA 20980, held by Novartis Consumer Health Inc.

b. There is no unexpired exclusivity for Lamisil Cream, 1%. There is one patent #4755534*PED, which will expire on June 30, 2007.

10. PHARMACOL. CATEGORY: Treatment of Athlete's foot.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 10 mg/g (1%)

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: ___Rx ___x___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

___ SPOTS product – Form Completed

___x___ Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



CHEMISTRY REVIEW

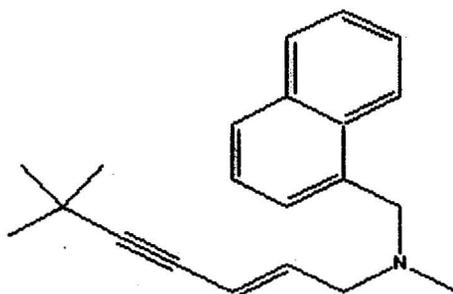


Chemistry Review Data Sheet

TRANS-N-(6,6-DIMETHYL-2-HEPTEN-4-YNYL)-N-METHYL-; Lamisil (free base);
 Lamosil; 1-Naphthalenemethanamine, N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-, (E)-,
 monohydrochloride;

Molecular Formula: $C_{21}H_{26}ClN$

Molecular Weight: 327.90



HCL

17. RELATED/SUPPORTING DOCUMENTS: None

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCE D	CODE1	STATUS2	DATE REVIEW COMPLETED	COMMENTS
(b) (4)				1	Adequate	9/23/05 K. Woodland	
							(b) (4) WITHDRAWN
				4			
				4			
				4			
				4			
				4			
				4			

*ANDA is a 1A'ed application. No new chemistry related amendments as of June 26, 2007



CHEMISTRY REVIEW



Chemistry Review Data Sheet

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	7/6/06	S.Adams
Methods Validation	Not Required		
Labeling	Acceptable	7/13/05	Ruby Wu
Bioequivalence	Acceptable	1/6/06	C. Kim
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:



The Chemistry Review for ANDA 77-511

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This product is a FIRST GENERIC. Approvable. The product was Tentatively approved on March 22, 2006.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Substance:

Terbinafine Hydrochloride drug substance is a white to off-white crystalline powder. The drug substance is soluble in methylene chloride and methanol; sparingly soluble in acetone, ethanol, 2-propanol; slightly soluble in water; practically insoluble in toluene.

Drug Product:

The product is

(b) (4)

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g). The IT is (b) (4)%, the QT is (b) (4)%.

B. Description of How the Drug Product is Intended to be Used

The drug product Terbinafine Hydrochloride Cream, 1% is an OTC product used for the treatment of Athlete's Foot (tinea pedis), jock itch (tinea cruris), and body ringworm (tinea corporis) (antifungal).

The treatment is one week for Athlete's Foot between the toes, jock itch, and body ringworm, and two weeks for Athlete's Foot on the bottoms or sides of the foot.

The market sizes are (b) (4), 12 gram, 15 gram, 24 gram, and 30 gram (b) (4) tubes.

The MDD is 40 mg/day. (30 g/7days x 1% x 1000mg/g) The IT is (b) (4)%, the QT is (b) (4)%.



C. Basis for Approvability or Not-Approval Recommendation

Approvable

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**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Kathy P. Woodland
6/27/2007 01:58:44 PM
CHEMIST

Gururaj Bykadi
6/27/2007 02:02:00 PM
CHEMIST

Benjamin Danso
7/2/2007 09:01:13 AM
CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-511

BIOEQUIVALENCE REVIEWS

Review of

A Bioequivalence Study

with

Clinical Endpoints

ANDA # 77-511

Taro Pharmaceuticals USA

Terbinafine Hydrochloride Cream,

1%

Carol Kim, Pharm.D.
Clinical Review Team
Submission date reviewed: 12/30/04

Date of Review: 12/28/05
V:\FIRMSnz\taro\ltrs&rev\77511A1204.mor

Clinical Review Section

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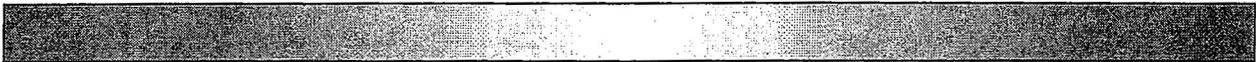
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Review of A BE Study with Clinical Endpoints for ANDA 77-511

Executive Summary

This double-blind, randomized, single-center, parallel-group study demonstrates that Taro's Terbinafine Hydrochloride Cream, 1%, is safe and bioequivalent to the approved Over the Counter (OTC) product, Lamisil^{AT} 1% Cream, for the treatment of tinea pedis. The FDA statistical review confirms that the 90% Confidence Interval (CI) of the difference in therapeutic cure rates between the test and reference products at the 5 weeks follow-up visit (Visit 3, Week 6) is (-0.108, 0.054), which is within the bioequivalence limits of -0.20 and 0.20. A total of 500 patients with mycologically confirmed tinea pedis were randomized and treated with test, reference, or vehicle. Based on the FDA statistical review, 491 patients were included in the Intent-to-Treat (ITT)¹ population, and 485 were included in the Per Protocol (PP) Population².

I. Recommendation on Approval

The data submitted to ANDA 77-511, using the primary endpoint of therapeutic cure rate at Week 6 (Visit 3, 5 weeks post treatment visit), are adequate to demonstrate bioequivalence of Taro's Terbinafine Hydrochloride Cream, 1%, with the reference listed drug, Novartis' Lamisil^{AT} 1% Cream. Therefore, the test product is recommended for approval.

II. Summary of Clinical Findings

The data presented in this ANDA 77-511 demonstrate that Taro Pharmaceuticals USA, Inc.'s Terbinafine Hydrochloride Cream, 1%, is bioequivalent to the reference listed drug, Lamisil^{AT} (terbinafine hydrochloride) Cream, 1%.

A. Brief Overview of Clinical Program

The study #TRB 0401 was a randomized, double-blind, comparative study of Taro's Terbinafine Hydrochloride Cream, 1%, versus the reference listed drug, Lamisil^{AT} (terbinafine hydrochloride) Cream, 1%, in the treatment of tinea pedis. Five hundred (500) patients with

¹ Included all randomized patients who met inclusion/exclusion criteria, mycologically confirmed tinea pedis, received at least one dose of study medication and completed one post-baseline assessment.

² Included all randomized patients who met inclusion/exclusion criteria, mycologically confirmed with tinea pedis, complied with the minimum treatment course, returned to the study site within the specified window and did not have any protocol violations.

Clinical Review Section

tinea pedis confirmed by fungal culture were randomized in a 2:2:1 ratio to receive the test, reference, or placebo/vehicle cream twice daily for 7 days.

B. Comparative Efficacy

The primary endpoint of this study is a therapeutic cure at the week 6 visit (Visit 3, 5 weeks follow-up after completion of 1 week of treatment). Therapeutic cure was defined by the sponsor as a combination of clinical cure and mycological cure. The sponsor defined a clinical cure as erythema score ≤ 2 and sum of all other symptom scores < 2 at the 6-week visit. Mycological cure was defined by the sponsor based on a negative KOH wet mount for pseudohyphae and a negative culture for tinea pedis species at the 6-week visit (visit 3).

According to the FDA statistical analysis, therapeutic cure rates in the Per Protocol (PP) Population at Visit 3 were 70% in the test group and 72% in the reference group. The 90% CI for the difference in therapeutic cure rates between the two active products was (-0.108, 0.054), which is within the bioequivalence limits of (-0.20 and +0.20).

C. Comparative Safety

The safety data submitted in this ANDA confirms that the test product is not causing any worse adverse events compared to the reference product in the treatment of tinea pedis. A total of 164 adverse events occurred in the study (66 in the test, 58 in the reference and 40 in the vehicle group). The most frequent adverse event reported in the active treatment groups was headache (9/66 Test and 16/58 Reference). In the vehicle group, burning was the most frequently reported adverse event.

Burning (3.7% test, 3.3% reference, and 7.5% vehicle) at the application site was the most frequent skin related adverse event reported in all treatment groups.

Two patients (469 test, 362 vehicle) reported adverse events (hospitalized due to a fracture of the femur and a severe asthma attack) that were considered serious but not related to the study treatment by the investigator.

Clinical Review

I. Introduction and Background

Tinea Pedis is a dermatophytic infection of the feet, characterized by erythema, chronic diffuse desquamation, and /or bulla formation. *T. rubrum* is the most common cause of chronic tinea pedis and *T. mentagrophytes* causes more inflammatory lesions. Once established, the individual becomes a carrier and is more susceptible to recurrences³. The demonstration of hyphae on direct microscopy and isolation of dermatophyte on fungal culture confirm the diagnosis.

³ Habif, Thomas. Clinical Dermatology: A Color Guide to Diagnosis and Therapy (3rd edition, 1996), p. 366.

Clinical Review Section

A. Drug Established Name, Drug Class,

Drug Established Name: Terbinafine Hydrochloride Cream, 1%
Drug Class: Antifungal agent

B. Trade Name of Reference Drug, NDA number, Date of approval, Approved Indication(s), Dose, Regimens

Reference Drug (NDA number): Lamisil^{AT} Cream (NDA 20980, OTC), Novartis
Date of approval: 3/9/99
Approved indication(s): Non-prescription topical treatment for athlete's foot (*tinea pedis*), jock itch (*tinea cruris*) and ringworm (*tinea corporis*).

Recommended dosing regimens: For treatment of athlete's foot, apply twice a day for 1 week (between the toes only) or 2 weeks (bottom or sides of the foot). For treatment of jock itch and ringworm, apply once a day for 1 week.

C. Regulatory Background

The following submissions have been reviewed by the OGD for Terbinafine Hydrochloride Cream:

1. INDs, Protocols, and/or Control Documents submitted by Taro

<u>Submission</u>	<u>Submission date</u>	<u>Name of the Product</u>
CD# 04-499	5/25/04	terbinafine hydrochloride

2. INDs, Protocols, and/or Control Documents submitted by other sponsors

<u>Submission</u>	<u>Submission date</u>	<u>Name of the Product/Sponsor</u>
(b) (4)		

3. Previous ANDA submissions for same or related product

none

D. Other Relevant Information

Terbinafine was approved for a prescription use under NDA 20-192 (Lamisil[®] Cream 1%) in 1992 for the treatment of interdigital tinea pedis, tinea cruris and tinea corporis caused by *Epidermophyton floccosum*, *Trichophyton mentagrophytes*, or *Trichophyton rubrum*. In 1997, supplemental NDA was approved for the treatment of plantar tinea pedis (moccasin type) due to *Trichophyton mentagrophytes* or *Trichophyton rubrum*. In 1998, Novatis proposed to switch

Clinical Review Section

terbinafine hydrochloride 1% cream from the prescription product to the over the counter product. Novartis initially proposed to [REDACTED] (b) (4) but on March 9, 1999, NDA 20-980 (Lamisil^{AA} Cream 1%) was approved for the non-prescription topical treatment of tinea pedis (athlete's foot), tinea cruris (jock itch) and tinea corporis (ringworm). The Lamisil[®] interdigital and plantar tinea pedis indications were combined into an "athlete's foot" indication for OTC product and the directions were split with regard to duration of treatment and anatomic location of the disease on the foot.

II. Description of Clinical Data and Sources

Study Centers/Investigators: The study was performed by a single investigator.

Site	Investigator	Address	Number of patients eligible for randomization
1	Howard Yanofsky, M.D.	5885 Cote Des Neiges #609, Montreal, Quebec	535

Study Period: September 4, 2004 to November 18, 2004

Enrollment: A total of 968 patients were initially screened and 433 patients failed to meet the randomization criteria. Of 535 patients eligible for randomization, thirty five (35) patients were discontinued after randomization due to negative baseline culture specimen (33 patients) and negative baseline KOH result (2 patients).

III. Clinical Review Methods

A. Overview of Materials Consulted in Review

Original Submission: ANDA 75-711, Vol. 1.1-1.6, submitted on 12/30/04

Study Amendment: none

B. Overview of Methods Used to Evaluate Data Quality and Integrity

Division of Scientific Investigations (DSI) Report:

The DSI inspection was not requested for this study due to previous satisfactory inspection history on the same clinical site (ANDAs 75-883, review dated 2/26/03 and 75-953, review dated 1/20/04).

C. Were Trials Conducted in Accordance with Accepted Ethical Standards

The sponsor declared that the study was conducted under the guiding principals of the Declaration of Helsinki. The sponsor's original protocol and consent forms were reviewed and approved by the Ethics Review Committee prior to initiation of the study.

Clinical Review Section

Reviewer's Comment: *The sponsor's study appears to be in compliance with the accepted ethical standards.*

D. Evaluation of Financial Disclosure: The sponsor submitted a signed financial disclosure document certifying that the principal investigator (Dr. Yanofsky) has not entered into any financial arrangement with the sponsor that could be affected by the outcome of the study and declared that he has not received significant payment of other sorts as defined in 21 CFR 54.2 (f).

IV. Review of Bioequivalence Study with Clinical Endpoints

A. Brief Statement of Conclusions

The sponsor's study demonstrates the bioequivalence of the test product with the reference product.

B. General Approach to Review of the Comparative Efficacy of the Drug

The sponsor's study (protocol #TRB 0401) was reviewed to determine bioequivalence of the test product and the reference product. The primary endpoint of this product is a therapeutic cure (both clinical and mycological cure) at the week 6 visit (5 weeks post treatment). The sponsor's proposed primary parameter was evaluated for bioequivalence and secondary parameters were considered as supportive information.

C. Detailed Review of Bioequivalence Studies with Clinical Endpoints

Protocol Review (TRB 0401):

1. The sponsor's protocol was amended two times prior to this submission.
2. Taro submitted the original protocol on May 25, 2004 (CD #04-499) and the OGD provided the following comments related to the primary endpoint analysis:
 - Patients should apply the study drug twice daily for 7 days and should be evaluated for therapeutic cure at study week 6 (5 weeks after the end of treatment).
 - To be included in the study, patients should have clinical diagnosis of tinea pedis with lesions localized to the interdigital spaces or predominantly interdigital but may extend to other areas of the foot; clinical diagnosis of tinea pedis confirmed by both positive KOH and culture results at baseline; and total sum of the scores of the clinical signs and symptoms of the target lesion should be at least 6, including a minimum score of at least 2 for erythema and a minimum score of 2 for either scaling or pruritis at the baseline target test site.
 - The recommended primary endpoint of this product is a therapeutic cure, which is both clinical and mycological cure. Clinical cure is defined as a total score of ≤ 2 for erythema and < 2 for all other signs and symptoms. Mycological cure is defined as a negative KOH and a negative fungal culture results.

Clinical Review Section

- A Physician's Global Assessment may be used as a secondary endpoint.
3. After receiving the FDA comments dated August 18, 2004, the sponsor's protocol was revised (Amendment 1, 8/26/04) to incorporate the following changes:
 - Entry criteria: only KOH positive patients were enrolled and randomized to treatment. Patients must also have moderate erythema and moderate scaling or pruritus at baseline to meet entry criteria. Two symptoms, maceration and exudation, were added for clinical evaluation.
 - Modified exclusion criteria to include peripheral vascular disease, neuropathy of the feet, history of atopic dermatitis, contact dermatitis, or psoriasis involving the feet, onychomycosis, and previous enrollment in the study.
 - The definition of cure was evaluated only at the 6-week visit, eliminating the 4-week visit. The proposed primary endpoint was the therapeutic cure at the 6-week visit.
 - Patients were permitted to miss 3 doses in the 7-day period or use an additional 3 doses to be considered evaluable.
 - Reduced the wash-out period of topical corticosteroid or antifungal therapy to 2 weeks (instead of 1 month).
 4. The first patient was enrolled on September 4, 2004.
 5. Protocol Amendment #2 was issued on 9/22/04. This amendment changed the visit window for the 1-week return visit from +1 day to +3 days and made minor administrative changes into the protocol.

Sponsor's protocol#: TRB 0401

Title: A 3-Way, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Therapeutic Equivalence of Terbinafine Hydrochloride Cream, 1%, Manufactured by Taro Pharmaceuticals Inc. and Lamisil[®] ^{AT} Cream Manufactured by Novartis in the Treatment of Clinically Diagnosed and Mycologically Confirmed Interdigital Tinea Pedis

Objective: The primary purpose of this study was to demonstrate comparable safety and efficacy of Taro Pharmaceuticals Inc.'s terbinafine hydrochloride cream 1% (test product) and Lamisil[®] ^{AT} Cream (reference listed drug) in the treatment of interdigital tinea pedis, and to show the superiority of the active treatments over that of the placebo (vehicle).

Study Design: This was a randomized, double-blind, parallel-group, placebo-controlled study design comparing the following products:

1. Test: Terbinafine Hydrochloride Cream, 1%, Taro Pharmaceuticals USA Inc., applied topically twice daily for 7 days; lot # (L) S182-54787
2. Reference: Lamisil[®] ^{AT} Cream (terbinafine hydrochloride), 1%, Novartis, applied topically twice daily for 7 days; lot #(L)326706
3. Vehicle/Placebo: Taro's vehicle, applied topically twice daily for 7 days; lot #S182-54786

Clinical Review Section

Blinding:

The study medications were supplied by the sponsor in individual patient kits, each containing one tube of study drug (Taro, Novartis, or vehicle). The Novartis product was used in its commercial form covered by an opaque label and a study label. Tubes were placed in identical cartons that were labeled as described below. Each tube and carton (patient kit) was covered with identical labels (in English and French) with the following information: protocol number, treatment identification number (treatment ID), reference to directions for use, a note that drug is for investigational use only, and storage conditions.

Neither the patient nor the investigator knew the origin of the terbinafine hydrochloride cream 1% in the patient kit. Blinding and labeling were performed by Taro. The randomization code was retained by the Clinical Pharmacy Associate at Taro.

In the event that it was necessary to break the blind (e.g., for patient safety), the investigator was to contact the study manager who would obtain the necessary information.

Study Population: Patients at least 18 years of age or older with clinical signs and symptoms of tinea pedis. Patients who met the following criteria were eligible for the study:

Inclusion Criteria

1. At least 18 years of age; no upper age limit was established.
2. Males and non-pregnant, non-nursing female patients.
3. Clinical diagnosis of interdigital tinea pedis provisionally confirmed by presence of segmented fungal hyphae on KOH mount.
4. A minimum severity score of 2 for erythema and 2 for either scaling or pruritus on the same target lesion, and a total sum of the scores of the clinical signs and symptoms of the target lesion of at least 6.
5. Positive culture for *T. rubrum*, *T. mentagrophytes*, *Epidermophyton floccosum*, or other causative dermatophytes.
6. Signed informed consent after the study had been fully explained and before any procedures dictated by the protocol were performed.
7. Women of childbearing potential had to have a negative urine pregnancy test result prior to entry into the study and had to agree to use a medically accepted form of birth control.
8. Patients able to comply with all requirements of the protocol.

Exclusion Criteria

1. Received systemic corticosteroid, anti-fungal, or other anti-infective therapy within one month prior to enrollment.
2. Received topical corticosteroid or anti-fungal therapy to the feet within 2 weeks prior to enrollment.
3. Received immunosuppressive medication or radiation therapy within 3 months prior to enrollment.
4. Concomitant yeast infection or bacterial infection that is systemic or localized to the foot.

Clinical Review Section

5. Confluent, diffuse moccasin-type tinea pedis of the entire plantar surface.
6. Concurrent onychomycosis of the toenails of the foot.
7. Signs of systemic fungal disease.
8. Pregnancy or breast-feeding.
9. Uncontrolled diabetes mellitus, peripheral vascular disease, neuropathy of the feet, or any significant medical conditions likely to compromise participation of the study or place the patient at risk.
10. History of atopic dermatitis, contact dermatitis, or psoriasis involving the feet.
11. Known allergy or sensitivity to any of the study medications or inactive ingredients.
12. Previously enrolled in the study.
13. Participated in another clinical study within the previous month.
14. Delayed exclusion if the culture taken at baseline proves to be negative for dermatophyte or shows evidence of a significant concomitant yeast or bacterial infection.

Criteria for discontinuation of study:

Patients were discontinued from the study after randomization for any of the following reasons:

- Patient's decision to leave the study for any reason.
- Development of an intercurrent condition or complication which could have affected the safety of the patient or the validity of evaluation of the patient's clinical state to an extent considered significant by the investigator.
- Pregnancy.
- Ingestion or topical application of any interdicted medication (oral antibiotics or antifungal agents, or topical application of any other medications to the affected areas for the entire time of the study).
- Failure to comply with the protocol.

Use of any of the following medications prior to randomization (enrollment) was considered non-eligible and use during the study was considered a protocol violation resulting in discontinuation from the study.

- Systemic corticosteroid, antifungal, or other anti-infective therapy within 1 month prior to entry into the study.
- Topical corticosteroid or anti-fungal therapy to the feet within 2 weeks prior to entry into the study.
- Immunosuppressive medication or radiation therapy within 3 months of entry into the study.
- Participation in another clinical study within the previous month.
- Ingestion or topical application of any interdicted medication.
- Any oral antibiotics or antifungal agents, or application of any other medications to the affected areas for entire time of the study.

Treatment Compliance

Treatment compliance (>75% and <125% of scheduled doses) was encouraged by

Clinical Review Section

instructing the patient in use of the daily diary. Compliance with the protocol requirements was assessed by the principal investigator at each visit by questioning the patient regarding the study drug and other medication use.

Based on the FDA comments issued on 8/18/04, the final protocol allowed patients to miss 3 doses in the 7 day period, or use an additional 3 doses to be considered treatment compliance.

Reviewer's Comments: *No patient in the sponsor's per protocol population received an additional dose in the 7 day study period. One patient (146) who received the study drug 4 times a day was excluded from the sponsor's per protocol population due to protocol violation.*

Procedures/Observations, and safety measures:

Visit 1(Day 1); Enrollment and Treatment day

The medical history and foot assessments were completed. Patients underwent laboratory testing. Female patients with childbearing potential performed urine pregnancy tests. A 10% KOH smear was taken from an area of active lesion (study foot).

Mycological and Clinical assessments were performed as follows:

1) Mycological Assessment

- a. 10% potassium hydroxide (KOH) smear was examined microscopically for evidence of fungus.
- b. Mycological cultures were obtained for *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum* or other causative dermatophyte (the majority of patients should have cultures positive for *T. rubrum*). Other organisms were identified but the culture results were listed as "negative" for the purpose of the study.

2) Clinical Assessment

During the examination of the foot, the signs and symptoms were graded on a 4-point scale. Patients recorded the severity of symptoms of itching and burning and the investigator evaluated the severity of erythema, fissuring, maceration, vesiculation, desquamation (scaling), and exudation using the same 4-point scale as follows:

<u>Investigator's evaluation</u>	<u>Patient's evaluation</u>	<u>Scale</u>
• erythema	Itching	0=none
• scaling (desquamation)	Burning	1=mild
• fissuring		2=moderate
• maceration		3=Severe
• vesiculation		
• exudation		

Clinical Review Section

Patients were given a package of study medication and instructed to follow all instructions provided.

Visit 2 (Day 7 +3 days); End of treatment (Week 1) visit

One week (+ 3 days) after initiating of study treatment, patients were instructed to return the study medication and diary. Patients were questioned concerning possible adverse events and compliance with the protocol. Any adverse events or changes to concomitant medications were documented. Women of child-bearing potential repeated urine pregnancy tests.

Visit 3 (Day 42 +/3 days); follow-up Week 6 visit, Primary Endpoint Visit

Five weeks after completion of 1 week study treatment, patients repeated clinical and mycological assessments on the study foot. Clinical signs and symptoms of tinea pedis were recorded, and specimens of the lesions were obtained for evaluation by 10% potassium hydroxide smear and by mycological culture. These assessments were repeated using the same scale as proposed at Visit 1.

Endpoints:

The primary endpoint is a therapeutic (both clinical and mycological) cure.

Definitions:

- Clinical Cure: an erythema score ≤ 2 with the sum of all other symptom scores < 2 at the 6-week visit.
- Mycological Cure: a negative KOH smear and a negative mycological culture at the 6-week visit. If the KOH was not available, the cure was based solely on the mycological culture.
- Therapeutic cure: Both a clinical and mycological cure.

Patients who were discontinued early from the study due to protocol violations or missed the 6-week visit were excluded from the per protocol (PP) analysis and were classified as treatment failures in the intent-to-treat (ITT) population analysis.

Reviewer's Comments: *Patients dropped due to protocol violations should be excluded from the PP population analysis but included in the ITT population analysis using the LOCF method.*

Statistical analysis plan

Primary Endpoint: The primary endpoint is the therapeutic cure at the 6-week visit. Secondary endpoint evaluation was performed on clinical and mycological cure rates at the 6-week visit.

Sample Size: At least five hundred patients were proposed to allow 200 patients per active treatment group and 100 patients in the vehicle/placebo group to complete the study. This

Clinical Review Section

sample size was proposed based on the sponsor's estimated calculation of cure rate of 66% for the Taro and the RLD groups.

Analysis: For the bioequivalence analysis, the 90% confidence interval was constructed for the difference in therapeutic cure rates between the test and the reference products at the 6-week visit. If the 90% Wald confidence limits, using Yate's continuity correction, were within -0.20 and +0.20, the test was considered therapeutically equivalent to the RLD. Superiority of each active treatment over the placebo was evaluated in the ITT population at the 6-week visit by independent, two-sided, $\alpha=0.05$, continuity-corrected Z-tests on the differences between active treatment and placebo therapeutic cure rates.

Demographic characteristics were summarized with descriptive statistics to assess the comparability of the treatment groups.

Study Conduct

Discussion of ITT and PP populations:

Two patient populations were defined by the sponsor as follows:

Intent-to-treat (ITT): all patients who had mycologically confirmed tinea pedis and received at least one dose of study medication. For the ITT population analysis, patients missing the 6-week visit were classified as treatment failures.

Reviewer's Comment: *Patients with no post baseline data should be excluded from both ITT and PP populations.*

Per-protocol (PP): Patients who had mycologically confirmed tinea pedis (positive mycological culture at the baseline visit), had clinical and mycological data at the 6-week visit, had completed the visit 3 within the visit window of 39-45 days, and had not violated protocol. Any patient missing either follow-up visit because of early declared treatment failure was included as a clinical, mycological, and therapeutic failure.

Retention of Reserve Samples:

The sponsor's protocol proposes to ship the blinded and labeled study drug to the investigator who then was instructed to remove samples in a random fashion and ship them to an independent 3rd party facility for storage.

Reviewer's Comment: *The detailed explanation of retention sample procedure was not provided in the study report.*

Clinical Review Section

Demographics

Of the 500 treated patients, 351 (70%) were Caucasian, 39 (8%) were Black, 87 (17%) were Hispanic, and 23 (5%) were classified as "other". Baseline demographics, age, and race in the ITT population were similar in all treatment groups. The mean age was 38.3 (18-75), 40.2 (18-80) and 38.8 (19-77) years for the test, reference and vehicle groups, respectively. The demographic characteristics for all treated patients are tabulated by the sponsor in Table I.

Table I: Demographic Characteristics for 500 treated patients (per sponsor)

Characteristic		TARO (N=199)	RLD (N=199)	Vehicle (N=102)	Total (N=500)
Race	Caucasian	144 (72%)	135 (68%)	72 (71%)	351 (70%)
	Black	12 (6%)	16 (8%)	11 (11%)	39 (8%)
	Hispanic	30 (15%)	40 (20%)	17 (17%)	87 (17%)
	Other	13 (7%)	8 (4%)	2 (2%)	23 (5%)
Age (years)	Mean (Std)	38.3 (12.2)	40.2 (12.1)	38.8 (11.9)	39.2 (12.1)
	Min - Max	18 - 75	18 - 80	19-77	18-80
Gender	Male	149 (75%)	164 (82%)	75 (74%)	388 (78%)
	Female	50 (25%)	35 (18%)	27 (26%)	112 (22%)

Baseline disease severity

The sponsor tabulated mean severity scores for each sign and symptom of tinea pedis at baseline for the ITT population in Table II. The mean severity scores were similar in all treatment groups for the ITT population. The sponsor did not provide baseline disease severity scores for the PP population.

Table II: Mean Severity Scores for Signs and Symptoms of T. Pedis at Baseline for Treatment Groups: ITT population (per sponsor)

TREATMENT	N	Fissuring		Erythema		Maceration		Vesiculation		Desquamation		Exudation		Pruritus		Burning/ Stinging		Total*	
		mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
TARO	199	0.56	0.55	2.22	0.41	0.35	0.62	0.00	0.00	2.20	0.53	0.01	0.10	2.51	0.59	0.88	0.87	8.72	1.99
RLD	199	0.61	0.65	2.23	0.42	0.34	0.59	0.00	0.00	2.25	0.56	0.00	0.00	2.44	0.64	0.75	0.84	8.63	1.74
VEHICLE	102	0.50	0.54	2.25	0.43	0.37	0.64	0.02	0.14	2.17	0.51	0.01	0.10	2.46	0.64	0.80	0.86	8.58	1.86
For difference between treatment groups p=		0.29		0.84		0.91		0.02		0.37		0.37		0.57		0.31		0.79	

* Sum of individual sign/symptom scores for each patient

Reviewer's Comment: Except for the sign of vesiculation, there was no statistically significant difference between treatment groups for individual mean baseline clinical sign and symptom scores or total signs and symptoms scores at baseline in the sponsor's defined ITT population.

Clinical Review Section

Baseline Fungal Culture

The majority of patients had the baseline fungal culture positive for *Trichophyton rubrum* (81.6%) in the sponsor's ITT population. The other dermatophytes isolated were *T. Mentagrophytes* (10.8%) and *Epidermophyton Floccosum* (7%). Three patients (0.6%) in the test group had baseline fungal culture positive for *T. raubitschekii* and *T. violaceum*. According to the sponsor's analysis, the percentage of patients with baseline fungal culture positive for *Trichophyton rubrum* was comparable in all treatment groups (p=0.13).

Reviewer's Comments: *Three patients (patient ID # 70, 271, and 607) in the test group had baseline fungal culture positive for T. raubitschekii and T. violaceum and were included in the PP population analysis by the sponsor.*

T. raubitschekii is a dermatophyte that belongs to the T. rubrum complex and is more commonly associated with tinea corporis. T. violaceum is a dermatophyte known to be associated with tinea capitis. Since these microorganism species were identified with clinical symptoms of tinea pedis and the majority of infections were caused by T. rubrum in this study, this reviewer agrees with the sponsor's decision to include these patients in the PP population analysis.

Results

Of 968 patients initially screened for the study, 433 patients were considered as screening failures (negative KOH, does not meet inclusion/exclusion criteria) at baseline. Of 535 patients randomized, 35 patients were excluded at baseline due to negative baseline KOH or culture results. A total of 500 patients (199 test, 199 reference, 102 vehicle) were treated and included in the ITT population by the sponsor.

The distribution of patients per treatment arm for each analysis population is shown in Table III. Table IV shows the sponsor's efficacy outcome analysis for the per protocol (PP) population.

Table III: Patient Disposition (per sponsor)

	TARO	RLD	VEHICLE	ALL
Safety Population	214	214	107	535
All randomized patients				
Exclusions:				
Negative KOH	1	0	1	2
Negative culture	14	15	4	33
Intent-to-Treat Population	199	199	102	500
(all eligible randomized patients)				
Exclusions:				
Missing visits 2 and 3	1	1	2	4
Missing visit 3	3	1	0	4
Other protocol violations	4	2	1	7
Outside window for visit 3	0	0	0	0
Per Protocol Population	191	195	99	485
Visit 3: 39-45 days				

Clinical Review Section

Table IV: Primary Efficacy Analysis: Therapeutic Cure¹ Rate at Visit 3 (per sponsor)

Parameter	TARO	RLD	90% C.I. for Bioequivalence of Taro's product to Lamisil ^{AT} Cream 1% (OTC)		
Per-Protocol Patients					
Visit 3	(N=191)	(N=195)			
Therapeutic Cure	133 (70%)	141 (72%)	(-10.8%, 5.4%)		
Clinical Cure	142 (74%)	155 (79%)	(-12.7%, 2.4%)		
Mycological Cure	177 (93%)	176 (90%)	(-2.8%, 7.6%)		
Intent-to-Treat Patients					
	TARO	RLD	Vehicle	P-Value (2-sided cc Z-test)	
Visit 3	(N=199)	(N=199)	(N=102)	T vs. Vehicle	Ref vs. Vehicle
Therapeutic Cure	136 (68%)	142 (71%)	3 (3%)	<0.0001	<0.0001
Clinical Cure	145 (73%)	156 (78%)	41 (40%)	<0.0001	<0.0001
Mycological Cure	181 (91%)	177 (89%)	8 (8%)	<0.0001	<0.0001

¹ Mycological cure defined as culture and KOH negative at the 6-week visit.

Clinical cure defined as erythema score ≤ 2 and sum of all other symptom scores < 2 at the 6-week visit.

Therapeutic cure defined as having both a clinical and mycological cure.

Patients missing the 6-week visit designated as mycological, clinical, and therapeutic failures for the ITT population analysis only.

Reviewer's Comments:

- *The sponsor included patient #462 (reference) who used prohibited medication in the per protocol analysis. This patient received Lamisil for treatment of fungus infection in the groin area 1 week prior to the study treatment day. Although Lamisil use is considered a protocol violation, since it was not applied to the study site, this reviewer agrees with the sponsor's decision to include this patient in the per protocol analysis.*
- *No patient discontinued the study due to lack of treatment effect.*

D. Bioequivalence Conclusion

Based on the FDA statistical analyses, the study demonstrates that the 90% CI of the difference in therapeutic cure rates between the test and the reference products at visit 3 (Week 6) is (-0.108, 0.054), which is within the bioequivalence limits of (-.20, +.20). A patient was considered a clinical cure by the sponsor if erythema score is ≤ 2 and sum of all other symptom scores are < 2 at the 6-week visit. A patient was considered a mycological cure if he or she had negative KOH and negative fungal culture at the 6-week visit.

V. Comparative Review of Safety

A. Brief Statement of Conclusions

This study showed no significant difference between the generic and reference products with regard to the adverse events reported.

Clinical Review Section

B. Description of Adverse Events

A total of 164 adverse events (66 in the test, 58 in the reference, and 40 in the vehicle group) occurred in 535 randomized patients. Seventy (70) of the 164 adverse events were skin related adverse events (25 test, 24 reference, and 21 vehicle). Fifty-three (53) of the 164 adverse events [19(8.9%) test, 19(8.9%) reference, and 15 (10.3%) vehicle] were thought to be treatment related adverse events by the investigator. Burning (3.7% test, 3.3% reference, and 7.5% vehicle) at the application site was the most frequent skin related adverse event reported in all treatment groups.

No death occurred in the study. Two patients reported adverse events that were considered serious by the investigator. Patient 469 (test) was hospitalized and underwent surgery to repair a fracture of the femur caused by a sports injury. Patient 362 (vehicle) was hospitalized for a severe asthma attack. None of these events were considered study treatment related.

The sponsor's summary of frequency of adverse events is listed below.

Summary of Adverse Events (per sponsor)

Treatment Group:									
Test (N=214)									
Event	Mild	Mild	Moderate	Moderate	Severe	Severe	Total	Total	Total
	Related	Not related	Related	Not related	Related	Not related	Related	Not related	
Allergy		1 (0.5%)						1	1
Arthritis		1 (0.5%)						1	1
Back pain		2 (0.9%)						2	2
Burning	8 (3.7%)	1 (0.5%)					8	1	9
Cold		8 (3.7%)		2 (0.9%)				10	10
Cold sores		1 (0.5%)						1	1
Fatigue		1 (0.5%)						1	1
Fissuring		1 (0.5%)						1	1
Fracture						1 (0.5%)		1	1
Headache	1 (0.5%)	8 (3.7%)					1	8	9
Injury		3 (1.4%)		2 (0.9%)				5	5
Insomnia		1 (0.5%)						1	1
Irritation	2 (0.9%)	1 (0.5%)					2	1	3
Itching	3 (1.4%)	3 (1.4%)					3	3	6
Muscle pain		1 (0.5%)						1	1
Numbness		1 (0.5%)						1	1
Renal colic				1 (0.5%)				1	1
Sore cheek		1 (0.5%)						1	1
Sore throat		1 (0.5%)						1	1
Surgery						1 (0.5%)		1	1
Swelling	2 (0.9%)						2		2
Swollen lymph node	1 (0.5%)						1		1
Tingling	2 (0.9%)						2		2
Toothache		2 (0.9%)		1 (0.5%)				3	3
Vaginal infection				1 (0.5%)				1	1
Total	19 (8.9%)	38 (17.8%)		7 (3.3%)		2 (0.9%)	19	47	66

(%) denotes the percent of total subjects within treatment groups

Clinical Review Section

Treatment Group: Reference (N=214)									
Event	Mild Related	Mild Not related	Moderate Related	Moderate Not related	Severe Related	Severe Not related	Total Related	Total Not related	Total
Bleeding		1 (0.5%)						1	1
Burning	7 (3.3%)						7		7
Cold		7 (3.3%)		1 (0.5%)				8	8
Ear infection				1 (0.5%)				1	1
Fissuring	2 (0.9%)	2 (0.9%)					2	2	4
Fracture		1 (0.5%)						1	1
Gastroenteritis		1 (0.5%)						1	1
Headache		14 (6.5%)		2 (0.9%)				16	16
Irritable bowel syndrome				1 (0.5%)				1	1
Irritation	4 (1.9%)						4		4
Itching	2 (0.9%)						2		2
Muscle pain		3 (1.4%)						3	3
Rash		1 (0.5%)						1	1
Surgery		1 (0.5%)						1	1
Swelling	1 (0.5%)						1		1
Tingling	3 (1.4%)	1 (0.5%)					3	1	4
Tonsillitis		1 (0.5%)						1	1
Urinary tract infection		1 (0.5%)						1	1
Total	19 (8.9%)	34 (15.9%)		5 (2.3%)			19	39	58

(%) denotes the percent of total subjects within treatment groups

Treatment Group: Vehicle (N=107)									
Event	Mild Related	Mild Not related	Moderate Related	Moderate Not related	Severe Related	Severe Not related	Total Related	Total Not related	Total
Arthritis		1 (0.9%)						1	1
Asthma						1 (0.9%)		1	1
Burning	4 (3.7%)	1 (0.9%)	4 (3.7%)				8	1	9
Cold		7 (6.5%)						7	7
Desquamation		2 (1.9%)						2	2
Fracture				1 (0.9%)				1	1
Headache		4 (3.7%)						4	4
Injury				1 (0.9%)				1	1
Irritation	2 (1.9%)	1 (0.9%)					2	1	3
Itching	1 (0.9%)	1 (0.9%)					1	1	2
Menstrual pain		1 (0.9%)						1	1
Muscle pain		1 (0.9%)						1	1
Sore throat		1 (0.9%)						1	1
Tendonitis				1 (0.9%)				1	1
Tingling	4 (3.7%)	1 (0.9%)					4	1	5
Total	11 (10.3%)	21 (19.6%)	4 (3.7%)	3 (2.8%)		1 (0.9%)	15	25	40

(%) denotes the percent of total subjects within treatment groups

Reviewer's Comments: The reported frequency of skin related adverse events in this study is comparable between the test and reference groups. Although the approved labeling notes a smaller percentage of patients reported burning/tingling (0.9%) with use of the reference product than the proportion noted in this study, the medical officer's review of the original NDA 20-980 (review dated 1/29/99) noted that in 550 patients treated with terbinafine HCl cream 1% in 9 clinical studies, up to 29.8% of patients reported burning.

Clinical Review Section

VI. Relevant Findings From Division of Scientific Investigations, Statistics and/or Other Consultant Reviews

A. Review of the Division of Scientific Investigation (DSI) Report

Dr. Yanofsky's office was previously inspected by the DSI for ANDA 75-883 (Ammonium Lactate Cream, 12%). Based on the final report issued on February 26, 2003, a Form FDA-483 was issued because the investigator did not comply with the requirement for retention of study drugs as per 21 CFR 320.38 and 320.63 at this site. Other than retention sample issue, the study was acceptable for the review.

A subsequent inspection (1/20/04) for 75-953 (terconazole vaginal cream) did not find any deficiency related to retention samples, and no Form FDA-483 was issued although the sponsor had not provided a sealed copy of the randomization code to the site.

Reviewer's Comment: Based on acceptable previous inspection history of Dr. Yanofsky's clinical site, no DSI inspection was requested for this study.

B. Review of the FDA Statistical Report (12/21/05)

The conclusion of the FDA statistical analysis confirms the bioequivalence of the test and the reference products. The 90% CI of the difference in therapeutic cure rates for the per protocol population at the primary endpoint (Visit 3, Week 6) is (-0.108, 0.054), which is within the bioequivalence limits of (-.20 and +.20). Both the test and the reference products showed superiority over the placebo group at Visit 3.

Based on this reviewer's comments above, nine patients (27, 407, 638, 674, 693, 776, 855, 912, and 955) were excluded from the sponsor's ITT population. These patients did not return after visit 1 (enrollment visit) and/or missed visit 3.

The FDA statistician provided the summary of the equivalence test for the per protocol population and efficacy analyses for the ITT population as follows:

Primary Endpoint: Therapeutic cure rates at visit 3 (Week 6)

Population	Test* % successes (No. of successes /total)	Reference* % successes (No. of successes /total)	Placebo* % successes (No. of successes /total)	p-value# for Test vs. Placebo	p-value# for Reference vs. Placebo	90% Confidence interval for Test vs. Ref. (%)	90% CI is within (-20%, 20%)
FITT	69.7 (136/195)	72.5 (142/196)	3.0 (3/100)	<0.001	<0.001		
PP	69.6 (133/191)	72.3 (141/195)	3.0 (3/99)			-10.8, 5.4	Yes

*: The rate of success equals the number of successes divided by the total number, then multiplied by 100.

#: The p-values were from Fisher's exact test (2-sided).

FITT: All subjects randomized to treatment, treated, and who had an assessment at visit 3/week 6 (follow-up visit).

Clinical Review Section

Efficacy and equivalence analyses for secondary endpoints

Population /endpoint	Test % successes (No. of successes /total)	Reference % successes (No. of successes /total)	Placebo % successes (No. of successes /total)	p-value for Test vs. Placebo	p-value for Reference vs. Placebo	90% Confidence interval for Test vs. Ref. (%)	90% CI is within (-20%, 20%)
FITT							
Mycological response	92.8 (181/195)	90.3 (177/196)	8.0 (8/100)	<0.001	<0.001		
Clinical response	74.4 (145/195)	79.6 (156/196)	41.0 (41/100)	<0.001	<0.001		
PP							
Mycological response	92.7 (177/191)	90.3 (176/195)	8.1 (8/99)	<0.001	<0.001	-2.8, 7.6	Yes
Clinical response	74.4 (142/191)	79.5 (155/195)	40.4 (40/99)	<0.001	<0.001	-12.7, 2.4	Yes

Reviewer's Comment: *The conclusion of the FDA statistical analysis confirms the bioequivalence of the test and the reference products.*

VII. Formulation

Taro's formulation

Component	Taro formulation Quantity per unit (mg/g); 1% strength, 10 mg/g	RLD formulation* Per gram
Terbinafine hydrochloride	10	10.0
Purified water, USP	(b) (4)	(b) (4)
Polysorbate 60, NF		
Cetyl alcohol, NF		
Stearyl alcohol, NF		
Cetyl palmitate, NF		
Isopropyl myristate, NF		
Sorbitan monostearate, NF		
Sodium hydroxide, NF		
Benzyl alcohol, NF		
Total weight/volume		1000 mg

*Per medical officer's review of the 1% prescription Lamisil[®] Cream, NDA 20-192 (9/25/92). The RLD, OTC formulation (Lamisil^{AT} 1% Cream, NDA 20-980) is identical to the 1% prescription cream.

Reviewer's Comment: *The test product is qualitatively the same but quantitatively different from the reference product. It contains significantly lower amounts of (b) (4). The results of this study suggest that these quantitative differences in inactive ingredients will not result in any differences in safety or efficacy of the product.*

VIII. Conclusion and Recommendation

A. Conclusion

The data presented in this ANDA 77-511 demonstrate that Taro Pharmaceuticals Inc.'s Terbinafine Hydrochloride Cream, 1%, is bioequivalent to the reference listed drug, Lamisil^{AT} Cream, 1%. The FDA statistical review confirms that the 90% CI of the difference in therapeutic cure rates between the test and reference products at the 5 weeks follow-up visit (Visit 3, Week 6) is within the bioequivalence limits of (-.20,+20). The test and reference products also demonstrate superiority over Placebo arm at Visit 3.

B. Recommendations to be conveyed to Sponsor

The data submitted to ANDA 77-511, using the primary endpoint of therapeutic cure rate at the 5 weeks follow-up visit (Visit 3, Week 6), are adequate to demonstrate bioequivalence of Taro Pharmaceuticals USA, Inc.'s Terbinafine Hydrochloride Cream, 1%, with the reference listed drug, Novartis' Lamisil^{AT} 1% Cream.



Carol Y. Kim, Pharm.D.
Clinical Reviewer
Office of Generic Drugs

12/28/05
Date



Dena Hixon, M.D.
Associate Director for Medical Affairs
Office of Generic Drugs

1/03/06
Date



Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence
Office of Generic Drugs

1/6/06
Date

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:77-511

APPLICANT: Taro Pharmaceuticals USA, Inc.

DRUG PRODUCT: Terbinafine Hydrochloride Cream, 1%

The Division of Bioequivalence has completed its review and has no further questions at this time.

The data submitted to ANDA 77-511, using the primary endpoint of therapeutic cure rate at the 5 weeks follow-up visit (Visit 3, Week 6), are adequate to demonstrate bioequivalence of Taro Pharmaceuticals USA, Inc.'s Terbinafine Hydrochloride Cream, 1%, with the reference listed drug, Novartis' Lamisil^{AT} 1% Cream.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,



Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-511
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-600/ C.Kim
HGD-600/ D. Hixon

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Endorsements: (Final with Dates)

HFD-600/C. Kim *CW 1/28/05*
HFD-600/D. Hixon *DRH 1/03/06*
HFD-650/D. Conner *DRH 1/6/06*

BIOEQUIVALENCY - ACCEPTABLE

submission date:
December 30, 2004

1. Bioequivalence Study (STU); 12/30/04
(new study)

Strengths: 1%
Outcome: AC

Please note: This review should close the BCE and BST assignments.

Outcome Decisions: **AC** - Acceptable
WC - Without charge
IC - Incomplete
UC - Unacceptable

OFFICE OF GENERIC DRUGS

DIVISION OF BIOEQUIVALENCE

ANDA #: 77-511

SPONSOR : Taro Pharmaceuticals USA, Inc.

DRUG AND DOSAGE FORM : Terbinafine Hydrochloride Cream, 1%

STRENGTH(S) : 1%

TYPES OF STUDIES : Clinical Endpoints

CLINICAL STUDY SITE(S) : Dr. Yanofsky office (Montreal, Quebec)

STUDY SUMMARY: Study is acceptable.

DSI INSPECTION STATUS

Inspection needed: YES / <input checked="" type="checkbox"/> NO	Inspection report: N/A	Inspection results: N/A
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
other _____		

PRIMARY REVIEWER : Carol Y. Kim, Pharm. D.

INITIAL : Cal Y Kim DATE : 12/28/05

ASSOCIATE DIRECTOR FOR MEDICAL AFFAIRS: Dena R. Hixon, M.D.

INITIAL : DRH DATE : 1/3/06

DIRECTOR, DIVISION OF BIOEQUIVALENCE : Dale P. Conner, Pharm. D.

INITIAL : APC DATE : 1/6/06

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-511

STATISTICAL REVIEWS

ANDA 77-511**Drug Product: Terbinafine hydrochloride cream, 1%****Sponsor: Taro Pharmaceuticals****Reference Listed Drug: Lamisil[®] Cream (terbinafine hydrochloride), 1%, Novartis****Submission date: 12/30/2004****V:/firmsnz/taro/ltrs&rev/77511st.doc****Reviewer: Huaixiang Li, Ph.D., QMRS/OB/CDER****Requestor: Dena Hixon, MD, Carol Kim, Pharm.D., OGD/CDER, 10/21/2005****Objectives of the study**

The primary objective of the study was to establish the bioequivalence of the test product, Taro Pharmaceuticals, Terbinafine Hydrochloride Cream, and the reference product, Novartis Pharmaceutical Corporation, Lamisil[®] Cream, and to show superiority of the two active treatments to the placebo, a cream vehicle, in the treatment of tinea pedis.

Remarks

The sponsor submitted SAS datasets and programs to the Electronic Document Room (EDR), CDER on December 30, 2004. The statistical analyses used information from one dataset: 'data.xpt'.

The following adjustment to this submitted dataset was made in accordance with recommendations of the FDA medical and statistical reviewers¹.

Exclusion from the FDA's Intent-to-treat population (FITT)

Nine patients, 27, 674, 912, and 955 in the test treatment group, 407, 693, and 776 in the reference treatment group, 638 and 855 in the placebo group, did not return after visit 1 (enrollment visit) and/or missed visit 3². These patients were originally excluded from the sponsor's PP population, but not the Sponsor's ITT population.

Study Design

This was a 3 arm parallel double-blind study in patients with signs and symptoms of tinea pedis. The three creams were the test product, Taro Pharmaceuticals, Terbinafine Hydrochloride Cream, the reference product, Novartis Pharmaceutical Corporation, Lamisil[®] Cream, and the placebo, a cream vehicle.

535 patients were enrolled and randomly assigned to three treatment groups in a 2:2:1 ratio (test:reference:placebo) in the study.

¹ Please see the details on page 4 in this report and the FDA medical reviewer's report.

² This study had three visits, visit 1 (enrollment), visit 2 (end of treatment), and visit 3 (follow-up). Patients returned study medicine and diary, were questioned about AE, etc. with no measurement for signs/symptoms and test for KOH/culture at visit 2. The efficacy and equivalence analyses could not be carried out when the patient(s) missed visit 3.

At the enrollment visit (visit 1), patients with clinical signs and symptoms of tinea pedis had a skin scraping taken from an area of active lesions for KOH mount and fungal culture. Signs and symptoms - erythema, scaling, fissuring, maceration, vesiculation, exudation, pruritus/itching, and burning - were measured by using a score (0-3, none to severe). Eligible subjects, who had a positive KOH result and met the eligibility criteria, were instructed to apply the cream to the clean, dry study foot twice a day for 7 days.

At visit 2/week 1 (end of treatment visit), patients were instructed to return the study medication and diary, were questioned about possible adverse events and compliance with the protocol, and repeated urine pregnancy test if of childbearing potential.

At visit 3/week 6 (follow-up visit), the mycological evaluations (both KOH and fungal culture test) were performed and the signs/symptoms were measured.

Outcome Variables at Visit 3

The sponsor provided the mycological cure rate, clinical cure rate, and therapeutic cure rate at visit 3.

The FDA medical reviewer requested analysis of the Primary endpoint – Therapeutic cure rate, and the secondary endpoints – Mycological cure rate and clinical cure rate at visit 3/week 6 (Follow-up visit).

Definitions:

Mycological cure: negative KOH and culture.

Clinical cure: an erythema score ≤ 2 with the sum of all other signs/symptoms scores < 2 .

Therapeutic cure: both a mycological cure and a clinical cure.

Statistical Analysis Methods

Efficacy Analysis

All treatment arms should be similar for signs/symptoms scores at the enrollment visit.

The efficacy analyses for the therapeutic cure rate were carried out by using Fisher's exact test (two-sided) for each active treatment versus placebo with a two-sided significance level of $\alpha=0.05$.

The active treatments should have been more distinguishable from placebo as the study progressed.

Equivalence Analysis

Based on the usual method used in the Office of Generic Drugs (OGD) for binary outcomes, the 90% confidence interval for the difference in proportions between the test and reference treatments should be contained within $-.20$ to $.20$ in order to establish equivalence.

The compound hypothesis to be tested is:

$$H_0: \quad p_T - p_R < -.20$$

$$\text{or} \quad p_T - p_R > .20$$

versus

$$H_A: \quad -.20 \leq p_T - p_R \leq .20$$

where p_T = cure rate of test treatment p_R = cure rate of reference treatment

Let n_T = sample size of test treatment n_R = sample size of reference treatment

$$\text{and} \quad se = \left(\hat{p}_T (1 - \hat{p}_T) / n_T + \hat{p}_R (1 - \hat{p}_R) / n_R \right)^{1/2}$$

The 90% confidence interval for the difference in proportions between test and reference was calculated as follows, using Yates' correction:

$$L = (\hat{p}_T - \hat{p}_R) - 1.645 se - (1/n_T + 1/n_R)/2$$

$$U = (\hat{p}_T - \hat{p}_R) + 1.645 se + (1/n_T + 1/n_R)/2$$

We reject H_0 if $L \geq -.20$ and $U \leq .20$.

Rejection of the null hypothesis H_0 supports the conclusion of equivalence of the two products.

Analysis Populations

Two analysis populations were used in this statistical reviewer's report:

FDA's Intent-to-treat population (FITT) – All subjects randomized to treatment, treated, and who had an assessment at visit 3/week 6 (follow-up visit).

Per protocol population (PP) – All subjects in the FITT population who were evaluable for the analyses based on the protocol and FDA medical and statistical reviewer's best judgment. The sponsor's PP population met the requirement in this study.

According to the FDA medical reviewers, the determination of clinical equivalence of the two active treatments was to be assessed using the sponsor's per protocol population (PP), while the superiority comparison of the two active treatments to placebo was to be assessed using the FDA's intent-to-treat population (FITT).

Statistical Analysis Results

535 patients were enrolled. The FITT population included 491 patients and the PP population included 485 patients.

This table shows the number of patients in each population per treatment arm[&]

	Terbinafine	Lamisil [®]	Placebo	Total
Enrollment	214	214	107	535
<i>Negative baseline KOH</i>	1	0	1	2
<i>Negative baseline culture</i>	14	15	4	33
Sponsor's ITT population	199	199	102	500
Exclusion from the FITT population				
Did not return after visit 1 (enrollment visit)*	4	3	2	9
FDA's FITT population	195	196	100	491
Exclusion from the PP population				
Protocol violation	4	1	1	6
Sponsor's and FDA's PP population	191	195	99	485

&: Patient(s) may have multiple reasons to be excluded from ITT, FITT, and PP populations.

*: Patient 407 in the reference treatment group was excluded from the sponsor's PP population due to protocol violation. This patient should be excluded from FITT due to not returning after visit 1.

Demographics and baseline

The mean age was 39.1 years and the age ranged from 18 to 80 years old in the FITT population. The table below shows the sex and race distribution for the FITT population. The age, gender, and race of patients were comparably distributed among the three treatment groups for the FITT and PP populations³.

	Terbinafine	Lamisil [®]	Placebo	Total
Gender				
Female	48	34	27	109
Male	147	162	73	382
Race				
White	142	133	71	346
Black	12	16	10	38
Hispanic	28	40	17	85
Others	13	7	2	22

An analysis of the frequencies and chi-square tests for homogeneity of signs/symptoms scores for the FITT and PP populations at the enrollment visit was performed. There were no significant differences between treatment arms for all the signs/symptoms scores for both populations at the enrollment visit.

Efficacy and equivalence Analyses

Primary endpoint: Therapeutic cure rate at visit 3/week 6.

³ Age was analyzed using a general linear model with treatment as a factor. Gender and race were analyzed using Chi-square tests.

Efficacy and equivalence analyses for primary endpoint – Therapeutic cure rate at visit 3

Population	Test* % successes (No. of successes /total)	Reference* % successes (No. of successes /total)	Placebo* % successes (No. of successes /total)	p-value# for Test vs. Placebo	p-value# for Reference vs. Placebo	90% Confidence interval for Test vs. Ref. (%)	90% CI is within (-20%, 20%)
FITT	69.7 (136/195)	72.5 (142/196)	3.0 (3/100)	<0.001	<0.001		
PP	69.6 (133/191)	72.3 (141/195)	3.0 (3/99)			-10.8, 5.4	Yes

*: The rate of success equals the number of successes divided by the total number, then multiplied by 100.
#: The p-values were from Fisher’s exact test (2-sided).

The two active treatments were statistically significantly better than placebo for the FITT population and the equivalence test was passed for the PP population for the therapeutic cure rate at visit 3.

Secondary endpoints: Mycological cure rate and clinical cure rate at visit 3/week 6.

Efficacy and equivalence analyses for secondary endpoints

Population /endpoint	Test % successes (No. of successes /total)	Reference % successes (No. of successes /total)	Placebo % successes (No. of successes /total)	p-value for Test vs. Placebo	p-value for Reference vs. Placebo	90% Confidence interval for Test vs. Ref. (%)	90% CI is within (-20%, 20%)
FITT							
Mycological response	92.8 (181/195)	90.3 (177/196)	8.0 (8/100)	<0.001	<0.001		
Clinical response	74.4 (145/195)	79.6 (156/196)	41.0 (41/100)	<0.001	<0.001		
PP							
Mycological response	92.7 (177/191)	90.3 (176/195)	8.1 (8/99)	<0.001	<0.001	-2.8, 7.6	Yes
Clinical response	74.4 (142/191)	79.5 (155/195)	40.4 (40/99)	<0.001	<0.001	-12.7, 2.4	Yes

The two active treatments were statistically significantly better than placebo for the FITT population and the equivalence test was passed for the PP population for the mycological cure rate and clinical cure rate at visit 3.

Comments on the Sponsor’s Analysis

The sponsor’s analysis results using their ITT and PP populations for the therapeutic cure rate, mycological cure rate, and clinical cure rate were summarized in the FDA medical reviewer’s report (page 18). The two active treatments were statistically significantly better than placebo for the ITT population and the equivalence test was passed for the PP population for the three cure rates at visit 3.

The differences between our results and the sponsor’s were due to the adjustment of the ITT population to the FITT population in accordance with recommendations of the medical and statistical reviewers.

Safety

Please see the details in the OGD medical reviewer's report.

Conclusion

The two active treatments were statistically significantly better than placebo for the FITT population and the equivalence test was passed for the PP population for the **Therapeutic cure rate (both clinical cure and mycological cure)**, mycological cure rate, and clinical cure rate, at visit 3/week 6 (Follow-up visit).

Huaixiang Li 12/22/05
Huaixiang Li, Ph.D.
Mathematical Statistician, QMR

Donald J. Schuirmann 12/21/05
Donald J. Schuirmann
Expert Mathematical Statistician, QMR

AMT - for stella 12/21/05
Stella G. Machado, Ph.D.
Director, QMR

cc:
HFD-600 Dena R Hixon, Carol Y Kim, Debra M Catterson
HFD-705 Stella G. Machado, Donald J. Schuirmann, Huaixiang Li, QMR Chron

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-511

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

December 30, 2004

Handwritten notes:
D. J. K. (K)
M. (M)
77-511
25 Feb 2005



Taro Pharmaceuticals U.S.A., Inc.

Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
MPN II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

re: **Abbreviated New Drug Application**
Terbinafine Hydrochloride Cream, 1%

RECEIVED
JAN 03 2005
OGD / CDER

Dear Sir/Madam:

Taro Pharmaceuticals U.S.A., Inc. (Taro) submits today an original abbreviated new drug application (ANDA) seeking approval to market Terbinafine Hydrochloride Cream, 1% which is bioequivalent to the reference listed drug, Lamisil® (Terbinafine Hydrochloride) Cream, 1% manufactured by Novartis Consumer Health Inc. pursuant to NDA 20-980.

This ANDA is prepared in the ICH-CTD format, following the recommendations of the following guidance documents:

- Submitting Marketing Applications According to the ICH-CTD Format – General Considerations
- M4: Organization of the CTD
- M4E: The CTD – Efficacy
- M4Q: The CTD – Quality
- M4S: The CTD – Safety

This ANDA is comprised of 9 volumes. The volumes are distributed as follows:

- Module 1: Administrative and Prescribing Information (1 volume)
- Module 2: Common Technical Document Summaries (1 volume)
- Module 3: Quality (3 volumes)
- Module 4: Non-clinical study reports (not applicable)
- Module 5: Clinical safety reports (4 volumes)

Taro Pharmaceuticals U.S.A., Inc., is filing archival, review and field copies as follows:

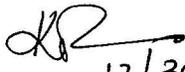
Archival Copy (9 copies)	Blue Jackets: Modules 1-5
Review Copy	
Quality (5 volumes)	Red Jackets: Modules 1, 2, and 3
Clinical – Bioequivalency (4 volumes)	Orange Jackets: Modules 1, 2, and 5
Clinical – Safety and Efficacy, Clinical	Not Applicable

Review	
Clinical – Safety and Efficacy, Statistical Review	Not Applicable
Field Copy (4 volumes)	Burgundy Jackets: Modules 1 and 3
Method Validation Package (1 volume, 3 copies)	Separately bound folders: Module 3.2.R.2

Taro hereby certifies that the 'field copy' is a true copy of the technical sections of the ANDA (copy: this letter, 356h form, 'true copy' certification). This 'field copy' is contained in burgundy folders. An additional three (3) copies of the method validation reports are included in a separate folder.

If you have any questions regarding this application, please contact the undersigned at 914-345-9001, ext 6298.

Sincerely,


12/30/04

Kalpana Rao
Vice President, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

**BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS**

ANDA# 77-511 FIRM NAME Taro Pharmaceuticals USA, Inc.

DRUG NAME Terbinafine HCl Cream, 1%

DOSAGE FORM Cream

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

Summary of Findings by Division of Bioequivalence	
<input checked="" type="checkbox"/>	Study meets statutory requirements
<input type="checkbox"/>	Study does NOT meet statutory requirements
	Reason:
<input type="checkbox"/>	Waiver meets statutory requirements
<input type="checkbox"/>	Waiver does NOT meet statutory requirements
	Reason:

RECOMMENDATION: COMPLETE INCOMPLETE

Reviewed by:

Krista M. Sordan Date: 2/4/05
Reviewer

Dena R. Hixon MD Date: 2/4/05
Dena R. Hixon, M.D.
Associate Director for Medical Affairs

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments
Protocol	X				
Summary of Study	X				
Clinical Site (s)	X				
Study Investigator (s)	X				
List of subjects included in PP/ (M)ITT populations per treatments	X				
List of subjects excluded/ from PP/ (M)ITT per treatments	X				
Reasons for discontinuation from the study if discontinued	X				
Adverse Events	X				
Concomitant Medications	X				
Individual subject's scores/data per visit	X				
Pre-screening of Patients	X				
IRB Approval	X				
Consent Forms	X				
Randomization Schedule	X				
Protocol Deviations	X				
Case Report Forms	X				
PD Data Disk (or Elec Subm)	X				EDR
Study Results	X				
Clinical Raw Data/ Medical Records	X				
Composition	NA				In Chemistry Section

BioStudy Lot Numbers	UA				} In Chemistry Section.
Date of Manufacture	UA				
Exp. Date of RLD	UA				
Statistical Reports	X				
Defined BE endpoints	X				
Summary results provided by the firm indicate studies pass BE criteria	X				Primary Endpoint is Therapeutic Cure at Week 6. CI: -10.8, 5.4
Summary results provided by the firm indicate superiority of the active treatments over the vehicle/placebo	X				p < 0.001 for both test and reference compared to placebo.
Waiver requests for other strengths / supporting data	N/A				

Additional Comments regarding the ANDA:

OGD provided protocol comments to Taro on August 18, 2004. The firm stated that after they received comments from OGD, they significantly changed their protocol. The first patient was not enrolled into the protocol was finalized.

This ANDA meets bioequivalence confidence intervals for the primary endpoint and is acceptable from a clinical standpoint.

ANDA 77-511

Taro Pharmaceuticals U.S.A. Inc.
Attention: Kalpana Rao
5 Skyline Drive
Hawthorne, NY 10532

FEB 25 2005

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Terbinafine Hydrochloride Cream, 1%

DATE OF APPLICATION: December 30, 2004

DATE (RECEIVED) ACCEPTABLE FOR FILING: January 3, 2005

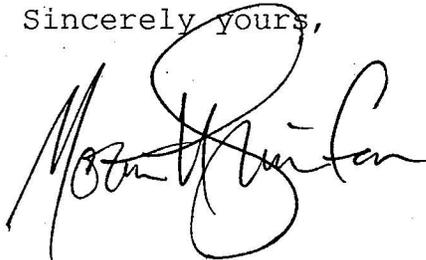
We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Benjamin Danso
Project Manager
(301) 827-5848

Sincerely yours,



Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-511

cc: DUP/Jackets

HFD-600/Division File

Field Copy

HFD-92

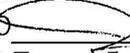
Endorsement:

HFD-615/MShimer, Chief, RSB



date 25 Feb 05

HFD-615/IMargand, CSO



date 2/25/05

Word File V:\Firmsnz\Taro\Ltrs&rev\7751.ack

F/T 2/24/05

ANDA Acknowledgment Letter!

ANDA 77-511 Final Check List for Branch Chief

- 1) Check letter date and stamp date of ANDA vs. drafted letter.
- 2) Check for any NC arriving post stamp date but prior to Reg. Review.
- 3) Check for gross errors in letter.
- 4) Check that correct letter format is used. (PIV vs. Other acknowledgment)
- 5) Check address and contact person on letter vs. 356h.
- 6) Check for any t-cons and verify date and correspondence date.
- 7) Check Patent Certification information in entered in COMIS (by Eda) vs. Actual certification. If multiple patent certifications, should be based on PIV if applicable or latest expiring patent.
- 8) Check for any comments or problems raised by reviewer on Check List.
- 9) If first generic, copy BE review and file.
- 10) Sign Check List.
- 11) Check electronic Orange Book to verify current patent information and correct RLD. *Lamisil Cream*
- 12) Check for MOU patents
- 13) Review 356h. Check NDA number and RLD for correct reference. If proprietary name proposed, notify Labeling reviewer.
- 14) Review Basis for Submission. *Lamisil 20-980*
- 15) Review Patent Certifications and Exclusivity Statement. (If an expiration of an exclusivity has occurred make a note to the Labeling reviewer. *PIV → 534 app 12/30/06*)
- 16) Review Comparison between Generic Drug and RLD for: condition of use, active ingredients, route of administration, dosage form and strength. Check Components and Composition.
- 17) Sign cover letter 505 (j)(2)(A) OK, date, and full signature.
- 18) Pull USP information. (USP yes no)
- 19) Final Grammar review on letter.
- 20) Verify information in OGD Patent Tracking System.
- 21) EES slip.
- 22) Document in record book.

Signature

Martin H. [Signature]

date

25 Feb 2005

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 77-511 FIRM NAME: TARO PHARMACEUTICALS U.S.A., INC.

RELATED APPLICATION(S): SEE 77-423 FOR
 TERBINAFINE HYDROCHLORIDE TABLETS 250 MG FROM
 TARO PHARMACEUTICALS (PN 12/6/04) RLD LAMISIL

First Generic Product Received? YES

Bio Assignments:		<input type="checkbox"/> Micro Review
<input checked="" type="checkbox"/> BPH	<input checked="" type="checkbox"/> BCE	
<input checked="" type="checkbox"/> BST	<input type="checkbox"/> BDI	

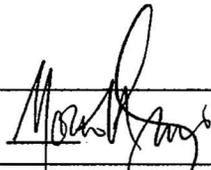
DRUG NAME: TERBINAFINE HYDROCHLORIDE

DOSAGE FORM: CREAM, 1 %

Random Queue: 5

Chem Team Leader: Liu, Shing PM: Benjamin Danso Labeling Reviewer: Ruby Wu

Letter Date: DECEMBER 30, 2004	Received Date: JANUARY 3, 2005
Comments: EC - 1 YES	On Cards: YES
Therapeutic Code:	
Archival Format: PAPER	Sections I (356H Sections per EDR Email)
Review copy: YES	E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections	
Field Copy Certification (Original Signature)	
Methods Validation Package (3 copies PAPER archive)	YES
(Required for Non-USP drugs)	
Cover Letter YES	Table of Contents YES
PART 3 Combination Product Category N Not a Part3 Combo Product	
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm	

Reviewing CSO/CST Iain Margand 	Recommendation:
Date 2/24/05	<input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE to RECEIVE
Supervisory Concurrence/Date: 	Date: 25 Feb 2005
ADDITIONAL COMMENTS REGARDING THE ANDA:	
Top 200 Drug Product:	

Sec. I	Signed and Completed Application Form (356h) (Statement regarding Rx/OTC Status)	<input checked="" type="checkbox"/>
Sec. II	Basis for Submission NDA# : 20-980 Ref Listed Drug: LAMISIL Firm: NOVARTIS CONSUMER HEALTH INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	<input checked="" type="checkbox"/>
Sec. III	Patent Certification 1. Paragraph: III patent '534 2. Expiration of Patent: 12/30/2006 A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? Exclusivity Statement: YES	<input checked="" type="checkbox"/>
Sec. IV	Comparison between Generic Drug and RLD-505(j)(2)(A) 1. Conditions of use OK 2. Active ingredients OK 3. Route of administration OK 4. Dosage Form OK 5. Strength OK	<input checked="" type="checkbox"/>
Sec. V	Labeling (Mult Copies N/A for E-Submissions) 1. 4 copies of draft (each strength and container) or 12 copies of FPL Y 2. 1 RLD label and 1 RLD container label Y 3. 1 side by side labeling comparison with all differences annotated and explained Y 4. Was a proprietary name request submitted? NO (If yes, send email to Labeling Rvwr indicating such.)	<input checked="" type="checkbox"/>
Sec. VI	Bioavailability/Bioequivalence 1. Financial Certification (Form FDA 3454) and Disclosure Statement (Form 3455) YES 2. Request for Waiver of In-Vivo Study(ies): NA 3. Formulation data same? (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) N/A 4. Lot Numbers of Products used in BE Study(ies): S182-54787 5. Study Type: IN-VIVO BE STUDY WITH C/EndPts (Continue with the appropriate study type box below)	<input checked="" type="checkbox"/>
Study Type	IN-VIVO PK STUDY(IES) (i.e., fasting/fed/sprinkle) NA a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted: NA c. In-Vitro Dissolution: NA	<input type="checkbox"/>

<p>Sec. VIII</p>	<p>Raw Materials Controls</p> <p>1. Active Ingredients</p> <p>a. Addresses of bulk manufacturers Y</p> <p>b. Type II DMF authorization letters or synthesis DMF# (b) (4)</p> <p>c. COA(s) specifications and test results from drug substance mfg(s) Y</p> <p>d. Applicant certificate of analysis Y</p> <p>e. Testing specifications and data from drug product manufacturer(s) Y</p> <p>f. Spectra and chromatograms for reference standards and test samples Y</p> <p>g. CFN numbers</p> <p>2. Inactive Ingredients</p> <p>a. Source of inactive ingredients identified 3.2.P.4.1</p> <p>b. Testing specifications (including identification and characterization) Y</p> <p>c. Suppliers' COA (specifications and test results) Y</p> <p>d. Applicant certificate of analysis Y</p>	<p><input checked="" type="checkbox"/></p>
<p>Sec. IX</p>	<p>Description of Manufacturing Facility</p> <p>1. Full Address(es) of the Facility(ies) YES</p> <p>2. CGMP Certification: YES</p> <p>3. CFN numbers</p>	<p><input checked="" type="checkbox"/></p>
<p>Sec. X</p>	<p>Outside Firms Including Contract Testing Laboratories</p> <p>1. Full Address Y</p> <p>2. Functions Y</p> <p>3. CGMP Certification/GLP Y</p> <p>4. CFN numbers</p>	<p><input checked="" type="checkbox"/></p>
<p>Sec. XI</p>	<p>Manufacturing and Processing Instructions</p> <p>1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) 3.2.P.3.3</p> <p>2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) kg</p> <p>3. If sterile product: Aseptic fill / Terminal sterilization N/A</p> <p>4. Filter validation (if aseptic fill) N/A</p> <p>5. Reprocessing Statement Y</p>	<p><input checked="" type="checkbox"/></p>
<p>Sec. XII</p>	<p>In-Process Controls</p> <p>1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation Ty: (b) (4) kg</p> <p>2. In-process Controls - Specifications and data Y Ay: (b) (4) kg</p> <p>packaged: (b) (4)</p>	<p><input checked="" type="checkbox"/></p>
<p>Sec. XIII</p>	<p>Container</p> <p>1. Summary of Container/Closure System (if new resin, provide data) (b) (4)</p> <p>2. Components Specification and Test Data (Type III DMF References) Y</p> <p>3. Packaging Configuration and Sizes (b) (4) 12g, 15g, 24g and 30g tubes</p> <p>4. Container/Closure Testing Y</p> <p>5. Source of supply and suppliers address Y</p>	<p><input checked="" type="checkbox"/></p>

Sec. XIV	Controls for the Finished Dosage Form 1. Testing Specifications and Data Y 2. Certificate of Analysis for Finished Dosage Form Y	<input checked="" type="checkbox"/>
Sec. XV	Stability of Finished Dosage Form 1. Protocol submitted Y 2. Post Approval Commitments Y 3. Expiration Dating Period 24 months 4. Stability Data Submitted a. 3 month accelerated stability data Y b. Batch numbers on stability records the same as the test batch S182-54787	<input checked="" type="checkbox"/>
Sec. XVI	Samples - Statement of Availability and Identification of: 1. Drug Substance 2. Finished Dosage Form 3. Same lot numbers	<input checked="" type="checkbox"/>
Sec. XVII	Environmental Impact Analysis Statement	<input checked="" type="checkbox"/>
Sec. XVIII	GDEA (Generic Drug Enforcement Act)/Other: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) N/A 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) N/A 4. Field Copy Certification (original signature) YES	<input checked="" type="checkbox"/>



Taro Pharmaceuticals U.S.A., Inc.

March 9, 2005

Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

W/AC

RE: Terbinafine Hydrochloride Cream, 1%
Amendment to Abbreviated New Drug Application
ANDA 77-511

Dear Sir/Madam:

Taro Pharmaceuticals U.S.A., Inc. (Taro) submits today an amendment to our original abbreviated new drug application (ANDA) seeking approval to market Terbinafine Hydrochloride Cream, 1% using the active drug substance, Terbinafine Hydrochloride from the alternate manufacturer, (b) (4)

(b) (4)

This amendment is prepared in the ICH-CTD format, following the recommendations of the following guidance documents:

- Submitting Marketing Applications According to the ICH-CTD Format – General Considerations
- M4: Organization of the CTD
- M4Q: The CTD – Quality

RECEIVED

MAR 10 2005

OGD / CDER

This amendment is comprised of 1 volume. The volume consists of the following modules:

- Module 1: Administrative and Prescribing Information
- Module 2: Common Technical Document Summaries
- Module 3: Quality

Taro Pharmaceuticals U.S.A., Inc., is filing archival, review and field copies as follows:

Archival Copy (1 volume)	Blue Jackets: Modules 1-3
Review Copy	
Quality (1 volume)	Red Jackets: Modules 1- 3
Field Copy (1 volume)	Burgundy Jackets: Module 3

Taro hereby certifies that the 'field copy' is a true copy of the technical sections of the amendment to the ANDA. This 'field copy' is contained in burgundy folders.

If you have any questions regarding this application, please contact the undersigned at 914-345-9001, ext 6298.

Sincerely,



JK
Kalpana Rao
Vice President, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

May 25, 2005

ORIG AMENDMENT

NIAP



Taro Pharmaceuticals U.S.A., Inc.

Ruby Wu
Office of Generic Drugs
CDER, Food & Drug Administration
Metro Park North
7500 Standish Place, Room 150
Rockville, MD 20855

**Re: ANDA #77-511
Terbinafine Hydrochloride Cream, 1% (OTC)
Labeling Amendment**

Dear Ms. Dillahunt:

Reference is made to Taro Pharmaceuticals U.S.A., Inc.'s Abbreviated New Drug Application (ANDA), submitted on December 30, 2004, under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Terbinafine Hydrochloride Cream, 1% (OTC). Reference is also made to the labeling deficiency letter dated May 11, 2005, in which the following was noted:

1. GENERAL COMMENTS

- a. Revise "Terbinafine Hydrochloride 1% Cream" to read "Terbinafine Hydrochloride Cream 1%".
- b. In order for us to verify your compliance with the labeling format requirements of 21CFR 201.66, please submit a format legend for each size of your container and carton labels.

2. CONTAINER ^(b)₍₄₎ 12 g, 15 g, 24 g, and 30 g tubes)

Refer to GENERAL COMMENTS

3. CARTON (one tube)

- a. Refer to GENERAL COMMENTS
- b. 12 g and 15 g Cartons: In the electronic submission, text is cut-off. Please realign the horizontal barlines (refer to attachment).

4. CONSUMER EDUCATIONAL BROCHURE:

- a. Refer to GENERAL COMMENT 1.a
- b. Picture #1: add the caption "1 week between the toes"

Please revise your labels and labeling, as instructed above, and submit final printed labels and labeling.

To facilitate review of your next submission, please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

RECEIVED

MAY 26 2005

OGD / CDER

Response

We have made the requested changes and enclosed please find:

- **12 Final Printed tube and carton labels ^{(b) (4)} 12 g, 15 g, 24 g, and 30 g)**
- **12 Final Printed Consumer Educational Brochures**

In addition, and in accordance with 21CFR 314.94(a)(8)(iv), we are providing a side-by-side comparison of one size of our previously submitted tube and carton with our current tube and carton and of our previously submitted Consumer Educational Brochures with our current Consumer Educational Brochure. We are also submitting electronically a Word document containing the text of the Consumer Educational Brochure and a CD with PDF files of each of the labels and labeling.

This concludes our response to the Agency's labeling deficiency letter of May 11, 2005. If you should have any questions regarding this submission, please do not hesitate to contact the undersigned at (914) 345-9001 x6298.

Sincerely,



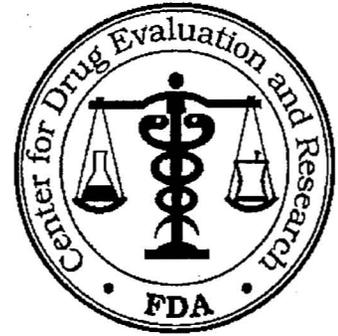
For Kalpana Rao
Vice President, Regulatory Affairs (Global)

MINOR AMENDMENT

ANDA 77-511

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

JUN 30 2005



APPLICANT: Taro Pharmaceuticals U.S.A, Inc.

TEL: 914-345-9001

ATTN: Kalpana Rao

FAX: 914-593-0078

FROM: Benjamin Danso

PROJECT MANAGER: 301-827-5848

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated December 30, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Terbinafine Hydrochloride Cream, 1%.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (2 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Please include in response.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

9/20/05
[Handwritten signature]



Taro Pharmaceuticals U.S.A., Inc.

August 23, 2005

ORIG AMENDMENT

NIAM

Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2773

RE: Terbinafine Hydrochloride Cream, 1%
ANDA 77-511
Response to **Minor Amendment** dated June 30, 2005

Dear Sir/Madam:

Reference is made to our Abbreviated New Drug Application (ANDA) for the above referenced product submitted on December 30, 2004 pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act.

Reference is also made to the Minor Amendment letter dated June 30, 2005, stating that the application was deficient and, therefore not approvable under Section 505 of the Food, Drug and Cosmetic Act. Listed below are the comments raised in the Minor Amendment letter followed by our responses.

Comment 1.

The DMF [REDACTED] ^{(b) (4)}, is currently inadequate. The DMF holder has been notified. Please do not respond to this letter until the DMF holder has informed you that a complete response to the DMF deficiencies has been submitted to the agency.

Response

[REDACTED] ^{(b) (4)}
A copy of the cover letter is provided.

RECEIVED

AUG 24 2005

OGD/CDER

Comment 2.

Regarding the drug substance specifications, we have the following comments:

- a) **Please revise the specification to include (b) (4) content and submit the method.**
- b) **Please revise the specification to include Clarity of Solution.**
- c) **Please revise the specification for ‘any individual unknown impurities’ from NMT (b) (4)% to NMT (b) (4)%.**
- d) **Please revise the specification to include particle size.**
- e) **Please submit a revised drug substance certificate of analysis with aforementioned revisions.**

Response

- a) *The specification has been revised to include a (b) (4) Content’ test.*

With the addition of the (b) (4) Content test, the (b) (4) Identification test has been replaced with an HPLC Identification test. A copy of the revised specification is provided in Appendix 1. The (b) (4) content method used was adapted from Taro Pharmaceutical Laboratories Inc. A copy of the method is provided in Appendix 2.

- b) *The specification has been revised to include ‘Clarity of Solution’. A copy of the revised specification is provided in Appendix 1. A copy of the Clarity of Solution test method is provided in Appendix 2.*
- c) *The specification for ‘any individual unknown impurities’ has been revised from ‘NMT (b) (4)% to NMT (b) (4)%’. A copy of the revised specification is provided in Appendix 1.*
- d) *A specification for particle size will not be proposed. The particle size does not impact the manufacture of the Terbinafine HCl Cream, 1% as the terbinafine HCl drug substance is (b) (4)*
- e) *A revised drug substance certificate of analysis with the aforementioned revisions is provided in Appendix 3.*

Please note that the Assay specification was tightened from (b) (4)% to (b) (4)% to be consistent with the revised Taro Pharmaceutical Laboratories Inc.’s specification for the Assay of Terbinafine HCl.

Comment 3.

(b) (4) is listed as a residual solvent in your drug substance specifications. In Section 3.2.S.4.1 the results were not reported on the CoA for drug substance manufactured by Taro. Please explain.

Response

(b) (4) is not present in Terbinafine HCl manufactured by Taro Pharmaceutical Laboratories Inc., but is present in the (b) (4). The specification provided in Appendix 1 was revised to identify the applicable drug substance manufacturer for each solvent listed.

Comment 4.

Regarding your drug product release and stability, please set the impurity specifications based on ICH Q3(B). Please set the individual unidentified degradation products as NMT the identification threshold ((b) (4) %).

Response

The following proposed impurity specification for the release and stability of the drug product has been revised based on the ICH Q3(B).

Using a Total Daily Intake (TDI) of 34 mg/day of terbinafine HCl, the ICH Q3(B) presents the following thresholds:

	Maximum daily dose	ICH Q3(B) recommended limits	Proposed limit		
			Degradation products	For Release	For Stability
<u>Reporting Thresholds:</u>	≤ 1 g	0.1%			
<u>Identification Thresholds:</u>	> 10 mg – 2 g	0.2% or 2 mg TDI (equivalent to 5.9%)	Individual unknown	NMT (b) (4)	NMT %
<u>Qualification Thresholds:</u>	10 mg – 100 mg	0.5% or 200 µg TDI (equivalent to 0.59%)	Known degradants	NMT (b) (4) %	NMT (b) (4) %

The proposed limit for release of the finished product is tighter than that recommended by the ICH Q3(B), the proposed limit for stability of the finished product is as per the ICH Q3(B).

The original specifications provided in the ANDA were as follows:

Degradation products	For Release	For Stability
Individual unknown	NMT (b) (4) %	NMT (b) (4) %
Known degradants	NMT (b) (4) %	NMT (b) (4) %

The TDI was calculated as follows:

The recommended treatment period for Lamisil AT is 7 days.

If a patient used the entire tube of the largest size (24 g tube) for a 7 day treatment, TDI of cream = 24g/7days = 3.4g/day of the cream. Since the concentration of active in the cream is 1%, each 1g of cream has 10 mg of API. Hence, TDI of API = 3.4g/day of cream x 10 mg API/ g of cream = 34 mg/day of terbinafine API.

In addition to the revision of the impurity specification, the in-process, release, and stability specifications were revised to finalize the limit for viscosity. The tentative limit [REDACTED] (b) (4) cps is now the established limit.

Provided in Appendix 4 are the revised in-process, finished product release and stability specifications.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response.

1. Your bioequivalence information is pending review. Deficiencies, if any, will be communicated separately.
2. Please provide all available long-term stability data to update your studies.
3. Your labeling responses, dated May 26, 2005, are under review and any deficiencies will be communicated to you.
4. All facilities referenced in your application should have a satisfactory compliance evaluation by our Division of Compliance at the time of approval.

Response to B. above

1. *We acknowledge that the bioequivalence information is pending review and be there any deficiencies, it will be communicated separately.*
2. *All available long-term stability data has been provided in Appendix 5. The following data is available:*
 - *9 month RT data for Lot S182-55236 (manufactured with Taro Israel API)*
 - *12 month RT data for Lot S182-54787 (manufactured with [REDACTED] (b) (4))*
3. *We acknowledge that our labeling responses, dated May 26, 2005 is under review.*
4. *We acknowledge that all facilities referenced in our application need to have a satisfactory compliance evaluation by the Division of Compliance at the time of approval.*

This Minor Amendment is being submitted in two copies. A third (Field copy) is also enclosed. Taro hereby certifies that the 'field copy' is a true copy of the technical sections of the amendment to the ANDA.

We trust that the deficiencies raised have been addressed in a complete and satisfactory manner. If you have any questions regarding this application, please contact us at:

Taro Pharmaceuticals U.S.A., Inc.
Attn: Kalpana Rao, VP, Regulatory Affairs (Global)
3 Skyline Drive
Hawthorne, New York 10532
Tel: 914-345-9001, ext 6298
Fax: 914-593-0078

Sincerely,



for Kalpana Rao
Vice President, Regulatory Affairs (Global)

ANDA APPROVAL SUMMARY

ANDA: 77-511	CHEMIST: Kathy P. Woodland	DATE: September 23, 2005
DRUG PRODUCT: Terbinafine Hydrochloride Cream, 1%		
FIRM: Taro Pharmaceuticals U.S.A., Inc.		
DOSAGE FORM: Cream	STRENGTH: 1%	
cGMP: Satisfactory, February 28, 2005, S. Adams		
BIO: PENDING		
VALIDATION - (Description of dosage form same as firm's): Not required		
STABILITY: The containers in the stability studies are identical to those in the container section.		
LABELING: Acceptable, Ruby Wu, July 13, 2005		
STERILIZATION VALIDATION (If applicable): N/A		
SIZE OF BIO BATCH (Firm's source of NDS ok?): (b) (4) is the source of drug substance		
SIZE OF STABILITY BATCHES (If different from bio batch, were they Manufactured via the same process?): The exhibit batches were (b) (4) kg each, made from Taro (b) (4) drug substance.		
PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?: The proposed production batch is (b) (4) kg		
Signature of chemist: 	Signature of supervisor:  10-26-05	

V:\FIRMS\NZ\TARO\LTRS&REV\77511.APSUM.DOC

Danso, Benjamin

From: Grace, John F
Sent: Tuesday, January 24, 2006 9:19 AM
To: Wu, Ruby (Chi-Ann); Danso, Benjamin
Subject: RE: ANDA 77-511 FPL sign off

I concur.

-----Original Message-----

From: Wu, Ruby (Chi-Ann)
Sent: Monday, January 23, 2006 1:35 PM
To: Danso, Benjamin; Grace, John F
Subject: ANDA 77-511 FPL sign off

John,

Sorry! I was in a hurry to go to a meeting and didn't check my facts. The product is OTC and I forgot to click the OTC box when I checked the orange book.

I checked the OB (OTC section), USP, and DSS. The labeling approval summary signed off 7/15/2005 remains acceptable.

Ruby

-----Original Message-----

From: Wu, Ruby (Chi-Ann)
Sent: Monday, January 23, 2006 11:03 AM
To: Danso, Benjamin; Grace, John F
Subject: FW: ANDA 77-511 FPL sign off

John,

The RLD is now in the DISCONTINUED section of the orange book. Do we need to know if it was discontinued for safety/efficacy reasons?

There is no other terbinafine hcl cream applications approved.

Drug product not subject to USP monograph.

Ruby

-----Original Message-----

From: Danso, Benjamin
Sent: Friday, January 20, 2006 3:26 PM
To: Wu, Ruby (Chi-Ann); Grace, John F
Subject: ANDA 77-511 FPL sign off

Ruby/ John,

Is the attached fpl sign off doc still in good standing for TA to move fwd? Your response to this e-mail will represent your final signatures on the TA letter.

Thanks

<< File: 77511.fpl.pdf >>

LT Benjamin Danso, Pharm. D.
7500 Standish Pl
OGD/HFD-617/MPN2
Rockville, MD 20855
DansoB@CDER.FDA.GOV

OGD APPROVAL ROUTING SUMMARY

ANDA # 77-511 Applicant Taro Pharmaceuticals U.S.A. Inc.
Drug Terbinafine Hydrochloride Cream Strength(s) 1%

APPROVAL [] TENTATIVE APPROVAL [X] SUPPLEMENTAL APPROVAL (NEW STRENGTH) [] OTHER []

REVIEWER:

DRAFT Package

FINAL Package

1. Martin Shimer
Chief, Reg. Support Branch

Date 20 Jan 2006
Initials MS

Date
Initials

Contains GDEA certification: Yes [X] No [] Determ. of Involvement? Yes [] No []
Pediatric Exclusivity System
RLD = NDA#

Patent/Exclusivity Certification: Yes [X] No [] Date Checked
Nothing Submitted []

If Para. IV Certification- did applicant Notify patent holder/NDA holder Yes [] No [] Written request issued []

Was applicant sued w/in 45 days: Yes [] No [] Study Submitted []

Has case been settled: Yes [] No [] Date settled:

Is applicant eligible for 180 day

Generic Drugs Exclusivity for each strength: Yes [] No []

Date of latest Labeling Review/Approval Summary 7/15/05

Any filing status changes requiring addition Labeling Review Yes [] No [X]

Type of Letter:

Comments: PIII to 1534 app 12/30/06 :. eligible for TA only

2. Project Manager, Ben Danso Team 5
Review Support Branch

Date 1-19-06
Initials BD

Date
Initials

Original Rec'd date 12-30-04 EER Status Pending [X] Acceptable [] OAI []

Date Acceptable for Filing 1-03-05 Date of EER Status

Patent Certification (type) P III Date of Office Bio Review 1-06-06

Date Patent/Exclus. expires 12-30-06 Date of Labeling Approv. Sum 7-15-05

Citizens' Petition/Legal Case Yes [] No [X] Labeling Acceptable Email Rec'd Yes [X] No []

(If YES, attach email from PM to CP coord) Labeling Acceptable Email filed Yes [X] No []

First Generic Yes [X] No [] Date of Sterility Assur. App.

Methods Val. Samples Pending Yes [] No []

MV Commitment Rcd. from Firm Yes [] No []

Acceptable Bio reviews tabbed Yes [X] No [] Modified-release dosage form: Yes [] No [X]

Suitability Petition/Pediatric Waiver Interim Dissol. Specs in AP Ltr: Yes []

Pediatric Waiver Request Accepted [] Rejected [] Pending []

Previously reviewed and tentatively approved [] Date

Previously reviewed and CGMP def. /NA Minor issued [] Date

Comments:

3. David Read (PP IVs Only) Pre-MMA Language included []

Date

OGD Regulatory Counsel, Post-MMA Language Included []

Initials

Comments:

4. Div. Dir./Deputy Dir.
Chemistry Div. I II OR III

Date 1/31/05
Initials PS

Comments:

CAC is OK

REVIEWER:

FINAL ACTION

5. Frank Holcombe First Generics Only
Assoc. Dir. For Chemistry
Comments: (First generic drug review)

Date 2-14-06
Initials lh

Joe Frank

cme ok - Radhika Rajagopalan

6. Vacant
Deputy Dir., DLPS

Date _____
Initials _____

7. Peter Rickman
Director, DLPS

Date 2/14/06
Initials WR

Para.IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No

Comments:
IP III to the '534 patent TA only expires 12/30/2006
No exclusivity issues

OR
Labeling acceptable per TA summary 7/15/2005

Bio acceptable per office stud sign off 1/6/2006 (clinical endpoint study)
Applicant w/D alternate API manufacturer on 3/21/2006
EE R now acceptable 2/28/2005
No DSI needed

8. Robert L. West
Deputy Director, OGD

TA only

Date _____
Initials _____

Para.IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No

9. Gary Buehler
Director, OGD
Comments:

Date 3/22/06
Initials GB

First Generic Approval PD or Clinical for BE Special Scientific or Reg. Issue

10. Project Manager, Team Ben Danso
Review Support Branch

Date 3/22/06
Initials BD

Date PETS checked for first generic drug (just prior to notification to CDM)

Applicant notification:

140 Time notified of approval by phone 1:50 Time approval letter faxed

FDA Notification:

3/22/06 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.

Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

Search results from the "OB_OTC" table for query on "020980."

Active Ingredient:	TERBINAFINE HYDROCHLORIDE
Dosage Form;Route:	CREAM; TOPICAL
Proprietary Name:	LAMISIL
Applicant:	NOVARTIS
Strength:	1%
Application Number:	020980
Product Number:	001
Approval Date:	Mar 9, 1999
Reference Listed Drug	Yes
RX/OTC/DISCN:	OTC
Patent and Exclusivity Info for this product:	View

[Return to Electronic Orange Book Home Page](#)

FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through December, 2005

Patent and Generic Drug Product Data Last Updated: January 18, 2006

Patent and Exclusivity Search Results from query on Appl No 020980 Product 001 in the OB_OTC list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code
<u>020980</u>	001	4755534	DEC 30,2006			<u>U-73</u>

Exclusivity Data

There is no unexpired exclusivity for this product.

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
 2. Patents submitted on FDA Form 3542 and listed after August 18, 2003 will have one to three patent codes indicating specific patent claims as submitted by the sponsor and are detailed in the above table.
 3. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
 4. *PED and PED represent pediatric exclusivity. Patents with pediatric exclusivity granted after August 18, 2003 will be indicated with *PED as was done prior to August 18, 2003. Patents with *PED added after August 18, 2003 will not contain any information relative to the patent itself other than the *PED extension. Information related specifically to the patent will be conveyed on the original patent only.
-

[View a list of all patent use codes](#)

[View a list of all exclusivity codes](#)

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FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

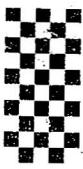
Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through December, 2005

Patent and Generic Drug Product Data Last Updated: January 18, 2006



MAR. 21. 2006 3:49PM

TARO PHARMACEUTICAL

Taro Pharmaceuticals U.S.A., Inc.
NO. 390
3 Skyline Drive
Hawthorne, NY 10532

Tel (914)345-9001
Fax (914)593-0078

facsimile transmittal

To: Benjamin Danso, Project Manager, OGD, CDER, FDA **Fax:** 301-594-0180

From: Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals USA, Inc. **Date:** 03/21/06

Re: **Gratuitous Amendment**
ANDA 77-511
Terbinafine Hydrochloride Cream, 1%
Request for (b) (4)
[Redacted]

Pages: 6 (including cover page)

CC:

- Urgent For Review Please Comment Please Reply Please Recycle

Taro Pharmaceuticals USA Inc. has submitted a Gratuitous amendment for the Abbreviated New Drug Application (ANDA 78-511) for Terbinafine Hydrochloride Cream, 1% requesting (b) (4) [Redacted]

Copy of the amendment is enclosed. The Gratuitous amendment has been mailed to the Agency via courier.

Should there be any questions or need for additional documents, please do not hesitate to contact the undersigned (914)345-9001x6298.

Sincerely,

Kavita Srivastava
for Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

Enclosures





Taro Pharmaceuticals U.S.A., Inc.

March 21, 2006

Attn: Benjamin Danso,
Project Manager
Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
MPN II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: **ANDA # 77-511, Terbinafine Hydrochloride Cream, 1%**
Gratuitous Amendment
Request for [REDACTED] (b) (4)

Dear Sir,

This is in reference to our Abbreviated New Drug Application for the above mentioned product submitted to the Agency on December 30, 2004. Reference is also made to the amendment dated March 9, 2005 and subsequent correspondence from the FDA dated June 30, 2005 followed by amendment dated August 12, 2005.

At this time, Taro Pharmaceuticals U.S.A., Inc. hereby submits a gratuitous amendment requesting [REDACTED] (b) (4)

[REDACTED] for this product without prejudice for further filing.

If there are any questions with regards to this amendment, please do not hesitate to contact us at:

Taro Pharmaceuticals U.S.A., Inc.
Attn: Kalpana Rao
Group Vice President, Regulatory Affairs (Global)
3 Skyline Drive
Hawthorne, NY 10532
Tel.: (914) 345-9001X6298
Fax: (914) 593-0078

Sincerely,

Kavita Srivastava

for

Kalpana Rao
Group Vice President, Regulatory Affairs (Global)

cc: FDA, Office of International Programs

<p>DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION</p> <p>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE <i>(Title 21, Code of Federal Regulations, Parts 314 & 601)</i></p>	<p><i>Form Approved: OMB No. 0910-0338 Expiration Date: September 30, 2008 See OMB Statement on page 2.</i></p>
<p>FOR FDA USE ONLY</p>	
<p>APPLICATION NUMBER</p>	

APPLICANT INFORMATION	
NAME OF APPLICANT Taro Pharmaceuticals USA, Inc.	DATE OF SUBMISSION 3/21/06
TELEPHONE NO. (Include Area Code) 914-345-9001	FACSIMILE (FAX) Number (Include Area Code) 914-593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3 Skyline Drive Hawthorne, NY 10532	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION		
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) <u>77-511</u>		
ESTABLISHED NAME (e.g., Proper name, USPI/USAN name) Terbinafine Hydrochloride Cream, 1%	PROPRIETARY NAME (trade name) IF ANY	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalenemethanamine hydrochloride		CODE NAME (If any)
DOSAGE FORM: Cream	STRENGTHS: 10 mg/g (1%)	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Treatment of athlete's foot.		

APPLICATION DESCRIPTION		
APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)		
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug <u>Lamisil</u> Holder of Approved Application <u>Novartis consumer Health Inc.</u>		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: <u>N/A</u>		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)		
REASON FOR SUBMISSION Gratuitous Amendment-Request for (b) (4)		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC		
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
Man/Pack/Controls: Taro Pharmaceuticals Inc., 130 East Dr., Brampton, ON, Canada (Establishment no. FCCA133); Controls: (b) (4)		

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application) See Attachment

This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input checked="" type="checkbox"/>	4. Chemistry section
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense. U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>Kavita Srivastava for Kalpana Rao</i>	TYPED NAME AND TITLE Kalpana Rao, GVP Regulatory Affairs (Global)	DATE: 3/21/06
ADDRESS (Street, City, State, and ZIP Code) 3 Skyline Drive, Hawthorne, NY 10532		Telephone Number (914) 345-9001

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research Central Document Room 5901-B Ammendale Road Beltville, MD 20705-1266	Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research (HFM-99) 1401 Rockville Pike Rockville, MD 20852-1448	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
--	---	--

Attachment to Form FDA 356h

Cross References

DMF List

Name	DMF No.	Function
(b) (4)		



Taro Pharmaceuticals U.S.A., Inc.

March 21, 2006

N/AA

Attn: Benjamin Danso,
Project Manager
Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
MPN II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: **ANDA # 77-511, Terbinafine Hydrochloride Cream, 1%
Gratuitous Amendment
Request for** [REDACTED] (b) (4)

Dear Sir,

This is in reference to our Abbreviated New Drug Application for the above mentioned product submitted to the Agency on December 30, 2004. Reference is also made to the amendment dated March 9, 2005 and subsequent correspondence from the FDA dated June 30, 2005 followed by amendment dated August 12, 2005.

At this time, Taro Pharmaceuticals U.S.A., Inc. hereby submits a gratuitous amendment requesting [REDACTED] (b) (4)

[REDACTED] for this product without prejudice for further filing.

RECEIVED
MAR 22 2006
OGD / CDER

If there are any questions with regards to this amendment, please do not hesitate to contact us at:

Taro Pharmaceuticals U.S.A., Inc.
Attn: Kalpana Rao
Group Vice President, Regulatory Affairs (Global)
3 Skyline Drive
Hawthorne, NY 10532
Tel.: (914) 345-9001X6298
Fax: (914) 593-0078

Sincerely,

Kavita Srivastava

for

Kalpana Rao
Group Vice President, Regulatory Affairs (Global)

cc: FDA, Office of International Programs

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Taro Pharmaceuticals USA, Inc.	DATE OF SUBMISSION 3/21/06
TELEPHONE NO. (Include Area Code) 914-345-9001	FACSIMILE (FAX) Number (Include Area Code) 914-593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3 Skyline Drive Hawthorne, NY 10532	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 77-511		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Terbinafine Hydrochloride Cream, 1%	PROPRIETARY NAME (trade name) IF ANY	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalenemethanamine hydrochloride	CODE NAME (If any)	
DOSAGE FORM: Cream	STRENGTHS: 10 mg/g (1%)	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Treatment of athlete's foot.		

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug <u>Lamisil</u> Holder of Approved Application <u>Novartis consumer Health Inc.</u>
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: <u>N/A</u>
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION Gratuitous Amendment-Request for (b) (4)
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready. Man/Pack/Controls: Taro Pharmaceuticals Inc., 130 East Dr., Brampton, ON, Canada (Establishment no. FCCA133); Controls: (b) (4)

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

See Attachment

RECEIVED

MAR 22 2006

OGD / CDER

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<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
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<input checked="" type="checkbox"/>	4. Chemistry section
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
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<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>Kavita Divastava for Kalpana Rao</i>	TYPED NAME AND TITLE Kalpana Rao, GVP Regulatory Affairs (Global)	DATE: 3/21/06
ADDRESS (Street, City, State, and ZIP Code) 3 Skyline Drive, Hawthorne, NY 10532		Telephone Number (914) 345-9001

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Attachment to Form FDA 356h

Cross References

DMF List

Name	DMF No.	Function
(b) (4)		



Taro Pharmaceuticals U.S.A., Inc.

October 4, 2006

Office of Generic Drugs, CDER
Food and Drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773
USA

ORIG AMENDMENT
N/AM

RE: **ANDA 77-511**
Terbinafine Hydrochloride Cream, 1%
Minor Amendment – Final Approval Requested

Dear Sir or Madam,

Reference is made to our Abbreviated New Drug Application (ANDA) for the above referenced product, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, submitted on December 30, 2004 and tentatively approved on March 22, 2006.

At this time Taro would like to request that a final approval be granted for the above mentioned ANDA. Taro submitted the above-referenced ANDA containing a paragraph III certification to the Patent No. 4755534 which will expire on December 30, 2006. The Certification stated that Taro Pharmaceuticals USA Inc. will not market its Terbinafine HCl Cream, 1% prior to the expiration of the patent.

As recommended in the Tentative Approval Letter, in order to reactivate our application prior to the final approval, we are hereby submitting a "Minor Amendment – Final Approval Requested" 90 days prior to the date that our application will be approved, i.e., December 30, 2006.

In addition to requesting final approval of this ANDA, we would also like to inform the Agency of the following minor changes made to the analytical method SOP A-1164-2 "HPLC Assay Method for the Quantitation of Terbinafine HCl and Its Related Impurities in Terbinafine HCl Drug Substance and Terbinafine HCl Cream, 1%" (copy attached):

a.

(b) (4)

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OCT 05 2006
OGD / CDER

b.

(b) (4)

With the exception of the above mentioned changes, there are no other revisions to the labeling or Chemistry, Manufacturing and Controls information approved in the ANDA.

This concludes our request for final approval. If there are any questions, with regards to this amendment, please contact the undersigned at 914-345-9001, Ext. 6298.

Sincerely,



for Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

cc. FDA, Office of International Programs



Taro Pharmaceuticals U.S.A., Inc.

October 4, 2006

Center for Drug Evaluation and Research
Central Document Room
12420 Parklawn Drive
Room 2-14
Rockville, Maryland
U.S.A. 20852

Attention: FDA, Office of International Programs

Ref: **ANDA 77-511**
Terbinafine Hydrochloride Cream, 1%
Minor Amendment – Final Approval Requested

Dear Sir/Madam:

Taro Pharmaceuticals U.S.A., Inc. hereby submits and certifies that the enclosed field copy is a true copy of the technical information provided in the above referenced Minor Amendment – Final Approval Requested.

If there are any questions in regards to this documentation, please do not hesitate to contact the undersigned at 914-345-9001, Ext. 6298.

Sincerely,

for 

Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

RECEIVED
OCT 05 2006
OGD / CDER

March 30, 2007

Food and Drug Administration
Office of Generic Drugs,
Metro Park North II,
Room # 150,
7500 Standish Place,
Rockville, MD 20855



Taro Pharmaceuticals U.S.A., Inc.

RE: **ANDA 77-511**
Terbinafine Hydrochloride Cream, 1%
Minor Amendment – Final Approval Requested

ORIG AMENDMENT
N-AM

Dear Sir or Madam,

Reference is made to our Abbreviated New Drug Application (ANDA) for the above referenced product, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, submitted on December 30, 2004 and tentatively approved on March 22, 2006. Reference is also made to the Minor Amendment – Final Approval Requested dated October 4, 2006.

At this time Taro Pharmaceuticals U.S.A., Inc., (Taro) would like to request that a final approval be granted for the above mentioned ANDA. Taro submitted the above-referenced ANDA containing a paragraph III certification to the Patent No. 4755534 which expired on December 30, 2006. Pediatric exclusivity was granted to patent No. 4755534*PED which will expire June 30, 2007.

As recommended in the Tentative Approval Letter, in order to reactivate our application prior to the final approval, we are hereby submitting a "Minor Amendment – Final Approval Requested" 90 days prior to the date that our application will be approved, i.e., June 30, 2007.

Please note that there are no revisions to the labeling or Chemistry, Manufacturing and Controls information approved in the ANDA and subsequent amendments.

This concludes our request for final approval. If there are any questions, with regard to this amendment, please contact the undersigned at 914-345-9001, Ext. 6298.

Sincerely,

Kalpana Rao
for Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

RECEIVED
APR 02 2007
REGISTRATION

cc. FDA, Office of International Programs



Taro Pharmaceuticals U.S.A., Inc.

March 30, 2007

Food and Drug Administration
Office of Generic Drugs,
Metro Park North II,
Room # 150,
7500 Standish Place,
Rockville, MD 20855

Attention: FDA, Office of International Programs

RE: **ANDA 77-511**
Terbinafine Hydrochloride Cream, 1%
Minor Amendment – Final Approval Requested

Dear Sir/Madam:

Taro Pharmaceuticals U.S.A., Inc. hereby submits and certifies that the enclosed field copy is a true copy of the technical information provided in the above referenced Minor Amendment – Final Approval Requested.

If there are any questions in regards to this documentation, please do not hesitate to contact the undersigned at 914-345-9001, Ext. 6298.

Sincerely,

A handwritten signature in cursive script, appearing to read "Kalpana Rao".

for Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Application : ANDA 77511/000 Sponsor: TARO PHARMS (US)
Org Code : 600 5 SKYLINE DR
Priority : HAWTHORNE, NY 10532

Stamp Date : 03-JAN-2005 Brand Name :
PDUFA Date : Estab. Name: TERBINAFINE HYDROCHLORI
Action Goal : Generic Name:
District Goal: 03-DEC-2005 Dosage Form: (CREAM)
Strength : 10 MG/G (1%)

FDA Contacts: B. DANSO Project Manager (HFD-617) 301-8
27-5763
A. MUELLER Team Leader (HFD-623) 301-8
27-5848

Overall Recommendation: ACCEPTABLE on 28-FEB-2005 by S. ADAMS (HFD-322) 3
01-827-9051

Establishment : CFN : FEI :



DMF No: (b)(4) AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 28-FEB-05
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Profile : CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-FEB-05
Decision : ACCEPTABLE
Reason : BASED ON PROFILE

Establishment : CFN : 9614240 FEI : 3002808384
TARO PHARMACEUTICALS INC
130 EAST DRIVE
BRAMPTON, ONTARIO, CA

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

Profile : OIN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-FEB-05
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

Establishment : CFN : (b) (4) FEI : (b) (4)

(b) (4)

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Profile : CTL OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 25-FEB-05

Decision : ACCEPTABLE

Reason : BASED ON PROFILE

Establishment : CFN : (b) (4) FEI : (b) (4)

(b) (4)

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Application : ANDA 77511/000 Sponsor: TARO PHARMS (US)
Org Code : 600 5 SKYLINE DR
Priority : HAWTHORNE, NY 10532

Stamp Date : 03-JAN-2005 Brand Name :
PDUFA Date : Estab. Name: TERBINAFINE HYDROCHLO
IDE
Action Goal : Generic Name:
District Goal : 03-DEC-2005 Dosage Form: (CREAM)
Strength : 10 MG/G (1%)

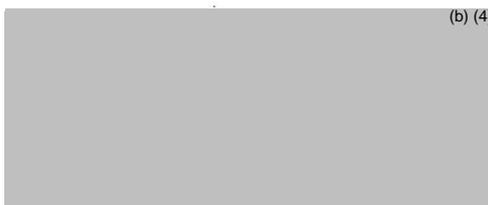
FDA Contacts: B. DANSO Project Manager (HFD-617) 301
-827-5763
 A. MUELLER Team Leader (HFD-623) 301
-827-5848

Overall Recommendation: ACCEPTABLE on 28-FEB-2005 by S. ADAMS (HFD-322)
301-827-9051

One site is still Pending

*2/16/06
ll*

Establishment : CFN : FEI :



DMF No: (b) (4)

AADA:

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Profile : CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-FEB-05
Decision : ACCEPTABLE
Reason : BASED ON PROFILE

Establishment : CFN : (b) (4) FEI : (b) (4)

(b) (4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE
Last Milestone: ASSIGNED INSPECTION TO (b) (4)
Milestone Date: 28-JUN-05
:
:

Establishment : CFN : 9614240 FEI : 3002808384
TARO PHARMACEUTICALS INC
130 EAST DRIVE
BRAMPTON, ONTARIO, CA

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 28-FEB-05

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

Establishment : CFN : (b) (4) FEI : (b) (4)

(b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Profile : CTL OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 25-FEB-05

Decision : ACCEPTABLE

Reason : BASED ON PROFILE

Establishment : CFN : (b) (4) FEI : (b) (4)

(b) (4)

DMF No: AADA:

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

Profile : OIN OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 25-FEB-05

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

Establishment : CFN : (b) (4) FEI : (b) (4)



DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Profile : CTL OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 25-FEB-05

Decision : ACCEPTABLE

Reason : BASED ON PROFILE

Establishment : CFN : (b) (4) FEI : (b) (4)



DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Profile : CTL OAI Status: NONE
 Last Milestone: OC RECOMMENDATION
 Milestone Date: 25-FEB-05
 Decision : ACCEPTABLE
 Reason : BASED ON PROFILE

Establishment : CFN : (b) (4) FEI : (b) (4)



DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile : CSN OAI Status: NONE
 Last Milestone: ASSIGNED INSPECTION TO (b) (4)
 Milestone Date: 28-JUN-05

Establishment : CFN : 9614240 FEI : 3002808384

✓ TARO PHARMACEUTICALS INC
 130 EAST DRIVE
 BRAMPTON, ONTARIO, CA

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

Profile : OIN OAI Status: NONE
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 Milestone Date: 25-FEB-05

Decision : ~~ACCEPTABLE~~
Reason : DISTRICT RECOMMENDATION

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Profile : CSN OAI Status: NONE

Last Milestone: SUBMITTED TO OC

Milestone Date: 25-FEB-05

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Establishment : CFN : (b) (4) FEI : (b) (4)

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Last Milestone: SUBMITTED TO OC
Milestone Date: 25-FEB-05
:
:

17511
TARD

Terbinafine ~~TABLETS~~
CREAM

20 JAN 06

Orig strength: 1% (OTC)

Basis (RLD): Lamisil 20-980

patent/cats: PIII → '534 exp 12/30/2006

NO unexpired exclusives

AKC for filing 1/3/2005 (L.O dated 2/25/05)

Labatory Review complete 5/11/05

7/15/05

Strength (Label claim):	(1%) 10 mg/g	
Component and Quality Standard	Quantity per unit (mg/g)	%
Terbinafine hydrochloride	10	1.00 <small>(b) (4)</small>
Purified water, USP		
Polysorbate 60, NF		
Cetyl alcohol, NF		
Stearyl alcohol, NF		
Cetyl palmitate, NF		
Isopropyl myristate, NF		
Sorbitan monostearate, NF		
Sodium hydroxide, NF		
Benzyl alcohol, NF		
Total Weight / Volume	1000 mg	100.00

ii) Functions of components:

Component	Intended Functions
Purified water, USP	<small>(b) (4)</small>
Polysorbate 60, NF	
Cetyl alcohol, NF	
Stearyl alcohol, NF	
Cetyl palmitate, NF	
Isopropyl myristate, NF	
Sorbitan monostearate, NF	
Sodium hydroxide, NF	
Benzyl alcohol, NF	

c) Description of accompanying reconstitution diluent(s), if applicable:

Not applicable

d) Type of container closure system used for the dosage form and accompanying reconstitution diluent, if applicable:

The container-closure system is manufactured using commercially available materials, suitable for use in the packaging of semi solid dosage form pharmaceuticals.

Inactive Ingredients for ANDA 77-511

POLYSORBATE 60 [REDACTED] (b) (4)

CETYL ALCOHOL [REDACTED] (b) (4)

STEARYL ALCOHOL [REDACTED] (b) (4)

CETYL PALMITATE [REDACTED] (b) (4)

ISOPROPYL MYRISTATE [REDACTED] (b) (4)

SORBITAN MONOSTEARATE [REDACTED] (b) (4)

SODIUM HYDROXIDE [REDACTED] (b) (4)

BENZYL ALCOHOL [REDACTED] (b) (4)

Excipients are acceptable per IIG



Taro Pharmaceuticals U.S.A., Inc.

October 4, 2006

Center for Drug Evaluation and Research
Central Document Room
12420 Parklawn Drive
Room 2-14
Rockville, Maryland
U.S.A. 20852

Attention: FDA, Office of International Programs

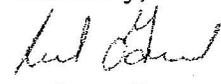
Ref: **ANDA 77-511**
Terbinafine Hydrochloride Cream, 1%
Minor Amendment – Final Approval Requested

Dear Sir/Madam:

Taro Pharmaceuticals U.S.A., Inc. hereby submits and certifies that the enclosed field copy is a true copy of the technical information provided in the above referenced Minor Amendment – Final Approval Requested.

If there are any questions in regards to this documentation, please do not hesitate to contact the undersigned at 914-345-9001, Ext. 6298.

Sincerely,

for 

Kalpana Rao
GVP, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Taro Pharmaceuticals U.S.A. Inc.	DATE OF SUBMISSION October 4, 2006
TELEPHONE NO. (Include Area Code) 914-345-9001	FACSIMILE (FAX) Number (Include Area Code) 914-593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3 Skyline Drive Hawthorne, N.Y., 10532 USA	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 77-511		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Terbinafine Hydrochloride Cream, 1%	PROPRIETARY NAME (trade name) IF ANY N/A	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalene methanamine hydrochloride	CODE NAME (If any)	
DOSAGE FORM: Cream	STRENGTHS: 1% (10 mg/g)	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Treatment of athlete's foot.		

APPLICATION INFORMATION

APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug <u>Lamisil</u> Holder of Approved Application <u>Novartis Consumer Health Inc.</u>
TYPE OF SUBMISSION (check one) <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: <u>N/A</u>
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION Minor Amendment - Request for Final Approval.
PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

RECEIVED
OCT 05 2006
OGD / CDER

This application contains the following items: <i>(Check all that apply)</i>	
<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (<i>check one</i>) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
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<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER (<i>Specify</i>) Request for final approval and a revised analytical method.

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>Rud Akhmet</i>	TYPED NAME AND TITLE for Kalpana Rao, G.V.P. Regulatory Affairs (Global)	DATE: Oct 4, 2006
ADDRESS (<i>Street, City, State, and ZIP Code</i>) 3 Skyline Dr. Hawthorne, NY 10532		Telephone Number (914) 345-9001

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Taro Pharmaceuticals U.S.A. Inc.	DATE OF SUBMISSION March 30, 2006
TELEPHONE NO. (Include Area Code) 914-345-9001	FACSIMILE (FAX) Number (Include Area Code) 914-593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3 Skyline Drive Hawthorne, N.Y., 10532 USA	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

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CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalene methanamine hydrochloride	CODE NAME (If any)	
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<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT	
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APR 02 2007
USDA/ODER

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<input checked="" type="checkbox"/>	20. OTHER (Specify) Request for final approval of ANDA

CERTIFICATION

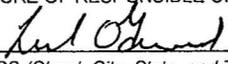
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SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE for Kalpana Rao, G.V.P. Regulatory Affairs (Global)	DATE: Mar 30, 2007
ADDRESS (Street, City, State, and ZIP Code) 3 Skyline Dr. Hawthorne, NY 10532	Telephone Number (914) 345-9001	

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Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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(PROPOSED) INDICATION(S) FOR USE: Treatment of athlete's foot.		

APPLICATION INFORMATION

APPLICATION TYPE (check one) NEW DRUG APPLICATION (21 CFR 314.50) ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE 505 (b)(1) 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Lamisil Holder of Approved Application Novartis Consumer Health Inc.

TYPE OF SUBMISSION (check one) ORIGINAL APPLICATION AMENDMENT TO APENDING APPLICATION RESUBMISSION
 PRESUBMISSION ANNUAL REPORT ESTABLISHMENT DESCRIPTION SUPPLEMENT EFFICACY SUPPLEMENT
 LABELING SUPPLEMENT CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: N/A

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY CBE CBE-30 Prior Approval (PA)

REASON FOR SUBMISSION
Minor Amendment – Request for Final Approval.

PROPOSED MARKETING STATUS (check one) PRESCRIPTION PRODUCT (Rx) OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS PAPER PAPER AND ELECTRONIC ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

RECEIVED

OCT 05 2006

OGD / CDER

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<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling <i>(check one)</i> <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
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<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
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<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER <i>(Specify)</i> Request for final approval and a revised analytical method.

CERTIFICATION

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SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>Kalpana Rao</i>	TYPED NAME AND TITLE for Kalpana Rao, G.V.P. Regulatory Affairs (Global)	DATE: <i>Oct 4, 2006</i>
ADDRESS <i>(Street, City, State, and ZIP Code)</i> 3 Skyline Dr. Hawthorne, NY 10532		Telephone Number (914) 345-9001

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Taro Pharmaceuticals U.S.A. Inc.	DATE OF SUBMISSION August 23, 2005
TELEPHONE NO. (Include Area Code) 914-345-9001	FACSIMILE (FAX) Number (Include Area Code) 914-593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3 Skyline Drive Hawthorne, N.Y., 10532 USA	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 77-511		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Terbinafine Hydrochloride Cream, 1%	PROPRIETARY NAME (trade name) IF ANY N/A	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalene methanamine hydrochloride	CODE NAME (If any)	
DOSAGE FORM: Cream	STRENGTHS: 10 mg/g (1%)	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Treatment of athlete's foot.		

APPLICATION INFORMATION

APPLICATION TYPE (check one)	<input type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50)	<input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)	<input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE	<input type="checkbox"/> 505 (b)(1)	<input type="checkbox"/> 505 (b)(2)	
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION			
Name of Drug	<u>Lamisil</u>	Holder of Approved Application	<u>Novartis Consumer Health Inc.</u>
TYPE OF SUBMISSION (check one)	<input type="checkbox"/> ORIGINAL APPLICATION	<input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION	<input type="checkbox"/> RESUBMISSION
	<input type="checkbox"/> PRESUBMISSION	<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT
	<input type="checkbox"/> LABELING SUPPLEMENT	<input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT	<input type="checkbox"/> EFFICACY SUPPLEMENT
		<input type="checkbox"/> OTHER	
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: <u>N/A</u>			
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)			
REASON FOR SUBMISSION Response to Minor Amendment dated June 30, 2005			
PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)			
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC			

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
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Man/Pack/Controls: Taro Pharmaceuticals Inc., 130 East Dr., Brampton, ON, Canada (Establishment No. FCCA133); Controls: (b) (4)

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

(b) (4)

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AUG 24 2005

OGD/CDER

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<input type="checkbox"/>	20. OTHER <i>(Specify)</i>

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SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>N. Rajic</i>	TYPED NAME AND TITLE for Kalpana Rao, V.P. Regulatory Affairs (Global)	DATE: Aug. 23, 2005
ADDRESS <i>(Street, City, State, and ZIP Code)</i> 3 Skyline Dr. Hawthorne, NY 10532		Telephone Number (914) 345-9001

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FOOD AND DRUG ADMINISTRATION

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OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Taro Pharmaceuticals U.S.A., Inc.	DATE OF SUBMISSION May 25, 2005
TELEPHONE NO. (Include Area Code) (914) 345-9001	FACSIMILE (FAX) Number (Include Area Code) (914) 593-0078
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Taro Pharmaceuticals U.S.A., Inc. 3 Skyline Drive, Hawthorne, NY 10532 (914) 345-9001 phone (914) 593-0078	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE N/A

PRODUCT DESCRIPTION

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CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) (E)-N-(6,6-dimethyl-2-hepten-4-ynyl)-N-methyl-1-naphthalene methanamine hydrochloride	CODE NAME (If any) 51672-2080	
DOSAGE FORM: Cream	STRENGTHS: 1%	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Cures most athlete's foot (tinea pedis), jock itch (tinea cruris) and ringworm (tinea corporis). Relieves itching, burning, cracking and scaling which accompany these conditions.		

APPLICATION INFORMATION

APPLICATION TYPE (check one) <input type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input checked="" type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
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TYPE OF SUBMISSION (check one) <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> OTHER
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MAY 26 2005

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SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE FOR Kalpana Rao Vice President, Regulatory Affairs (Global)	DATE: 05/25/05
ADDRESS (Street, City, State, and ZIP Code) 3 Skyline Drive, Hawthorne, NY 10532		Telephone Number (914) 345-9001

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