CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 65-184

Name: Clindamycin Phosphate Topical Solution USP, 1% (base)

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

Approval Date: March 31, 2004

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

APPROVAL LETTER

ANDA 65-184

MAR 31 2004

Taro Pharmaceuticals U.S.A, Inc.
Attention: Kalpana Rao
U.S. Agent for: Taro Pharmaceutical Industries Ltd.
5 Skyline Drive
Hawthorne, NY 10532

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated June 16, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Clindamycin Phosphate Topical Solution USP, 1% (base). We note that this product is subject to the exception provisions of Section 125(d)(2) of Title I of the Food and Drug Administration Modernization Act of 1997.

Reference is also made to your amendments dated January 22, February 13, February 23, March 16, March 26, and March 30, 2004.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Clindamycin Phosphate Topical Solution USP, 1% (base), to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Cleocin T® Topical Solution, 1% (base) of Pharmacia and Upjohn Co.).

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

Post-marketing reporting requirements for this abbreviated application 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.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print.

Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Robert Lumpkin for
3/31/2004

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

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA 65-184
Division File
Field Copy
HFD-610/R. West
HFD-330
HFD-205

Endorsements:
HFD-643/S.Zuk/3/22/04 S Zuk 3/22/04
HFD-643/R.Adams/3/22/04 R.C. adams 3/24/04
HFD-617/M.Anderson/3/22/04 M Anderson 3/30/04
HFD-613/M.Shin/3/22/04 ms. 3/24/04
HFD-613/L.Golson/3/22/04 L Golson 3/24/04

V:\firmsnz\taro\ltrs&rev\65184apd.doc
F/T by: mda/3/22/04

APPROVAL

Robert West
3/31/2004

Conc satisfactory
Wayne Bowen
3/31/04

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

APPROVED LABELING

Clindamycin Phosphate
Topical Solution, USP

PK-0000-0
000

ENLARGED TO 115% BY FOLA STAFF

Rx only

For External Use

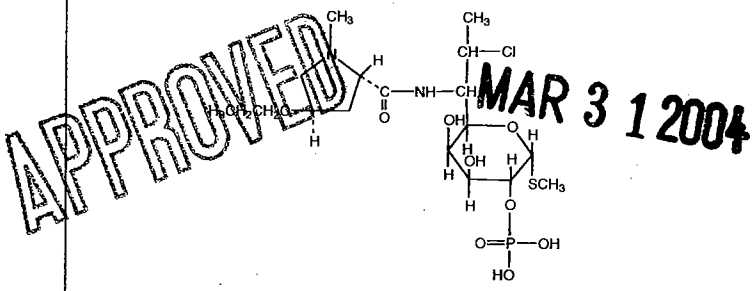
DESCRIPTION

Clindamycin Topical Solution contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per milliliter.

Clindamycin phosphate is a water-soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic lincomycin.

The solution contains isopropyl alcohol 39% w/v, propylene glycol, and purified water. May contain sodium hydroxide for pH balance.

The structural formula is represented below:



APPROVED MAR 3 1 2004

The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-(α)-D-*galacto*-octopyranoside 2-(dihydrogen phosphate).

CLINICAL PHARMACOLOGY

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Cross resistance has been demonstrated between clindamycin and lincomycin.

Antagonism has been demonstrated between clindamycin and erythromycin.

Following multiple topical applications of clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per mL in an isopropyl alcohol and water solution, very low levels of clindamycin are present in the serum (0-3 ng/mL) and less than 0.2% of the dose is recovered in urine as clindamycin.

Clindamycin activity has been demonstrated in comedones from acne patients. The mean concentration of antibiotic activity in extracted comedones after application of clindamycin topical solution for 4 weeks was 597 mcg/g of comedonal material (range 0-1490). Clindamycin *in vitro* inhibits all *Propionibacterium acnes* cultures tested (MICs 0.4 mcg/mL). Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of clindamycin.

INDICATIONS AND USAGE

Clindamycin Topical Solution is indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate. (See **CONTRAINDICATIONS**, **WARNINGS** and **ADVERSE REACTIONS**.)

CONTRAINDICATIONS

Clindamycin Topical Solution is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

10mm

ILPO II

2 | 6mm | 2

WARNINGS

Orally and parenterally administered clindamycin has been associated with severe colitis which may result in patient death. Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin.

Studies indicate a toxin(s) produced by clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

When significant diarrhea occurs, the drug should be discontinued. Large bowel endoscopy should be considered to establish a definitive diagnosis in cases of severe diarrhea.

Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. The usual adult dosage is 500 milligrams to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestyramine or colestipol resins bind vancomycin *in vitro*. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin.

10mm

EPOII

2 | 6mm | 2

PRECAUTIONS

General

Clindamycin Topical Solution contains an alcohol base which will cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin, mucous membranes), bathe with copious amounts of cool tap water. The solution has an unpleasant taste and caution should be exercised when applying medication around the mouth.

Clindamycin should be prescribed with caution in atopic individuals.

Drug Interactions

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore it should be used with caution in patients receiving such agents.

Pregnancy: Teratogenic Effects -- Pregnancy Category B

Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 100 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to clindamycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of clindamycin topical solution. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients under the age of 12 have not been established.

Geriatric Use

Clinical studies for clindamycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

In 18 clinical studies of various formulations of clindamycin using placebo vehicle and/or active comparator drugs as controls, patients experienced a number of treatment emergent adverse dermatologic events [see table below].

Number of Patients Reporting Events

Treatment Emergent Adverse Event	Solution n=553 (%)		Gel n=148 (%)		Lotion n=160 (%)	
Burning	62	(11)	15	(10)	17	(11)
Itching	36	(7)	15	(10)	17	(11)
Burning/Itching	60	(11)	#	(-)	#	(-)
Dryness	105	(19)	34	(23)	29	(18)
Erythema	86	(16)	10	(7)	22	(14)
Oiliness/Oily Skin	8	(1)	26	(18)	12*	(10)
Peeling	61	(11)	#	(-)	11	(7)

not recorded
* of 126 subjects

Orally and parenterally administered clindamycin has been associated with severe colitis which may end fatally.

Cases of diarrhea, bloody diarrhea and colitis (including pseudomembranous colitis) have been reported as adverse reactions in patients treated with oral and parenteral formulations of clindamycin and rarely with topical clindamycin (see **WARNINGS**).

Abdominal pain and gastrointestinal disturbances as well as gram-negative folliculitis have also been reported in association with the use of topical formulations of clindamycin.

OVERDOSAGE

Topically applied clindamycin can be absorbed in sufficient amounts to produce systemic effects. (See **WARNINGS.**)

DOSAGE AND ADMINISTRATION

Apply a thin film of Clindamycin Topical Solution twice daily to affected area.

Keep all liquid dosage forms in containers tightly closed.

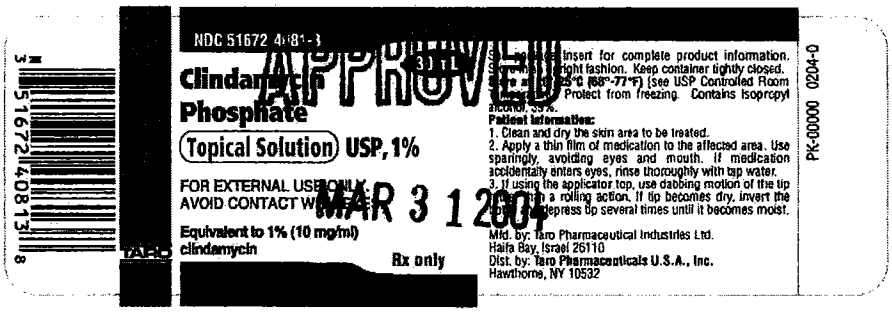
HOW SUPPLIED

Clindamycin Phosphate Topical Solution USP, 1% containing clindamycin phosphate equivalent to 10 mg clindamycin per milliliter is available in the following sizes:
1 oz (30 mL) applicator bottle.....NDC 51672-4081-3
2 oz (60 mL) applicator bottle.....NDC 51672-4081-4
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].
Protect from freezing.

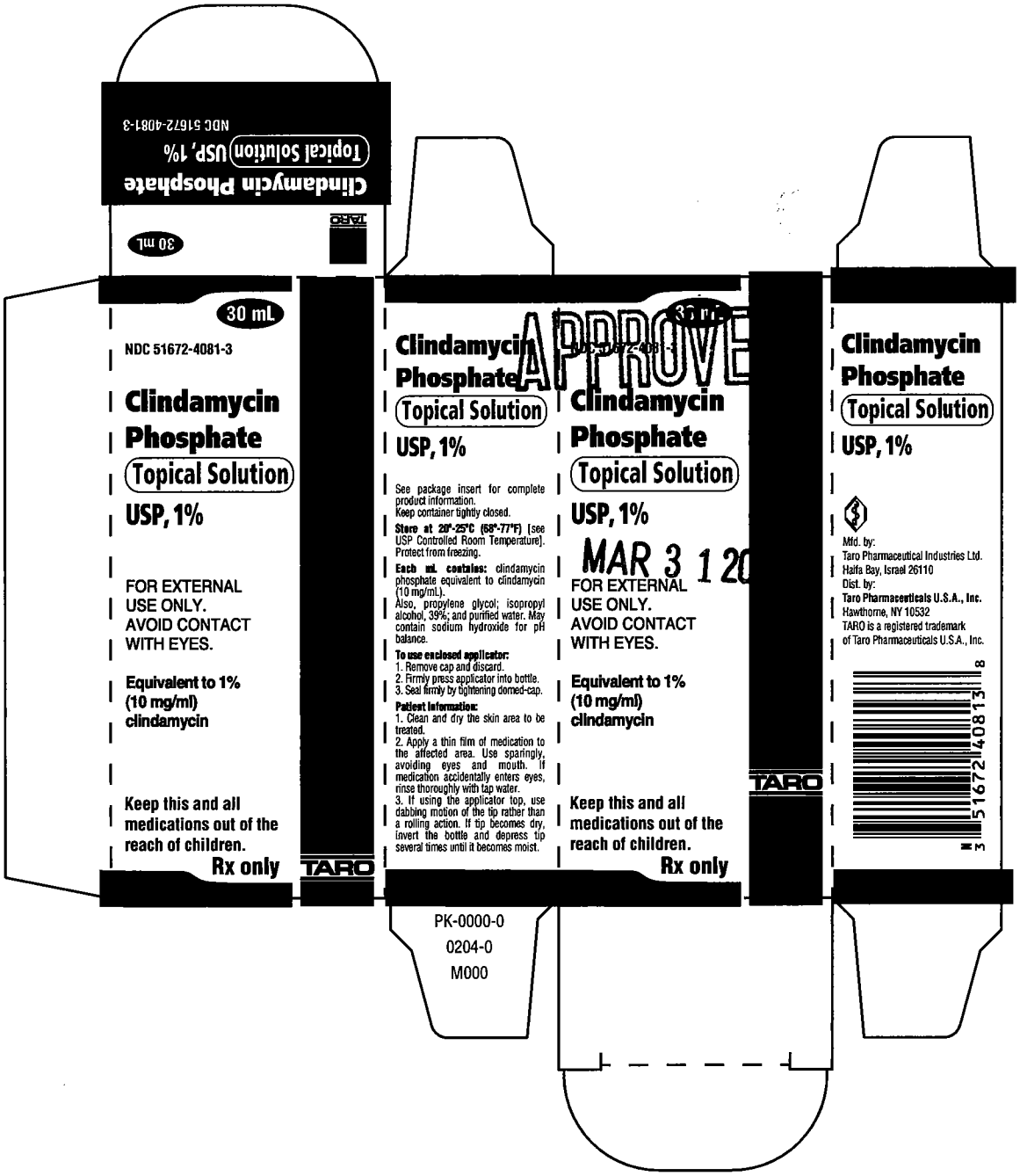
Mfd. by: Taro Pharmaceutical Industries Ltd., Haifa Bay, Israel 26110
Dist. by: **Taro Pharmaceuticals U.S.A., Inc.**, Hawthorne, NY 10532

Issued: February, 2004

BLACK MAGENTA
(template only do not print)


NDC 51672 4081-3
APPROVED
Clindamycin Phosphate
Topical Solution USP, 1%
FOR EXTERNAL USE ONLY
AVOID CONTACT WITH EYES
MAR 3 1 2004
Equivalent to 1% (10 mg/ml) clindamycin
Rx only
TARO
Patient Information:
1. Clean and dry the skin area to be treated.
2. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. If using the applicator top, use dabbing motion of the tip with a rolling action. If tip becomes dry, invert the bottle and depress tip several times until it becomes moist.
Mfd. by: Taro Pharmaceutical Industries Ltd.
Haifa Bay, Israel 26110
Dist. by: Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
PK-00000 0204-0

605184


30 mL
NDC 51672-4081-3
Clindamycin Phosphate
Topical Solution
USP, 1%
FOR EXTERNAL USE ONLY.
AVOID CONTACT WITH EYES.
Equivalent to 1% (10 mg/ml) clindamycin
Keep this and all medications out of the reach of children.
Rx only
TARO
See package insert for complete product information.
Keep container tightly closed.
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].
Protect from freezing.
Each mL contains: clindamycin phosphate equivalent to clindamycin (10 mg/mL).
Also, propylene glycol; isopropyl alcohol, 39%; and purified water. May contain sodium hydroxide for pH balance.
To use enclosed applicator:
1. Remove cap and discard.
2. Firmly press applicator into bottle.
3. Seal firmly by tightening domed-cap.
Patient Information:
1. Clean and dry the skin area to be treated.
2. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. If using the applicator top, use dabbing motion of the tip rather than a rolling action. If tip becomes dry, invert the bottle and depress tip several times until it becomes moist.
APPROVED
MAR 3 1 20
PK-0000-0
0204-0
M000
Mfd. by:
Taro Pharmaceutical Industries Ltd.
Haifa Bay, Israel 26110
Dist. by:
Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
TARO is a registered trademark of Taro Pharmaceuticals U.S.A., Inc.
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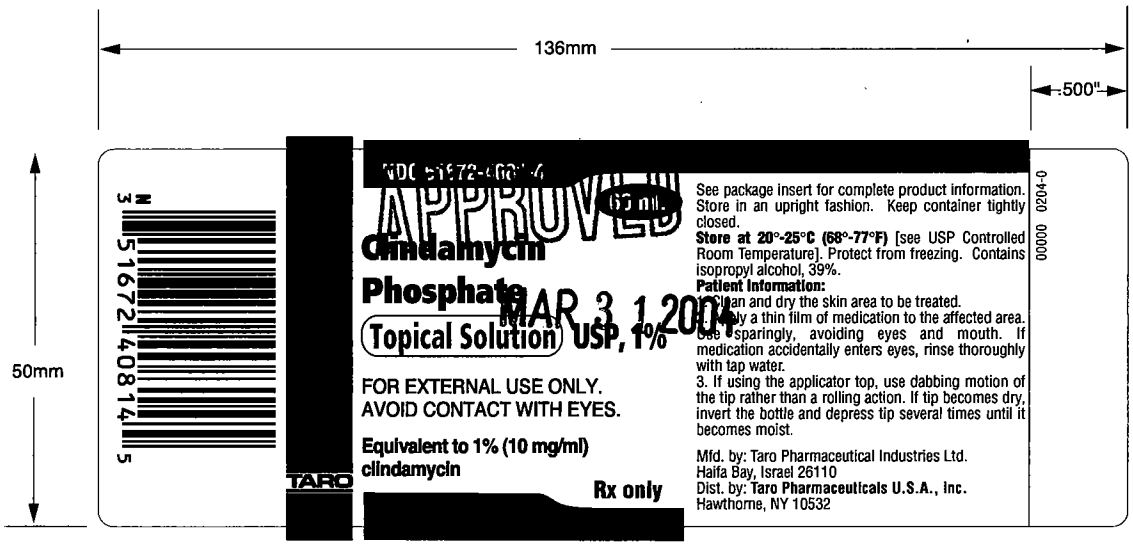
65184


136mm
.500"
50mm
NDC 51672-4081-4
APPROVED
60 mL
Clindamycin Phosphate
Topical Solution USP, 1%
MAR 3 1 2004
FOR EXTERNAL USE ONLY.
AVOID CONTACT WITH EYES.
Equivalent to 1% (10 mg/ml) clindamycin
Rx only
TARO
See package insert for complete product information. Store in an upright fashion. Keep container tightly closed.
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature]. Protect from freezing. Contains isopropyl alcohol, 39%.
Patient Information:
1. Clean and dry the skin area to be treated.
2. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. If using the applicator top, use dabbing motion of the tip rather than a rolling action. If tip becomes dry, invert the bottle and depress tip several times until it becomes moist.
Mfd. by: Taro Pharmaceutical Industries Ltd.
Haifa Bay, Israel 26110
Dist. by: Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
00000 0204-0


65-184
APPROVED
MAR 3 1 2004
60 mL
NDC 51672-4081-4
Clindamycin Phosphate
Topical Solution
USP, 1%
FOR EXTERNAL USE ONLY.
AVOID CONTACT WITH EYES.
Equivalent to 1% (10 mg/ml) clindamycin
Keep this and all medications out of the reach of children.
Rx only
TARO
See package insert for complete product information.
Keep container tightly closed.
Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature]. Protect from freezing.
Each mL contains: clindamycin phosphate equivalent to clindamycin (10 mg/mL). Also, propylene glycol; isopropyl alcohol, 39%; and purified water. May contain sodium hydroxide for pH balance.
To use enclosed applicator:
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Mfd. by:
Taro Pharmaceutical Industries Ltd.
Haifa Bay, Israel 26110
Dist. by:
Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532
TARO is a registered trademark of Taro Pharmaceuticals U.S.A., Inc.
N 3 51672 40814 5
PK-0000-0
0204-0
M000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

LABELING REVIEW(S)

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

ANDA Number:	ANDA 65-184
Date of Submission:	July 16, 2003 (Original draft labeling)
Applicant's Name:	Taro Pharmaceuticals U.S.A., Inc.
Established Name:	Clindamycin Phosphate Topical Solution, USP
Proposed Proprietary Name:	NONE

Labeling Deficiencies:

1. **GENERAL**

   Please revise your storage temperature recommendation as follows:

   "Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature]."

2. **CONTAINER**

   See comment under GENERAL

3. **CARTON**

   See comment under GENERAL

4. **PROFESSIONAL PACKAGE INSERT**

   - See comment under GENERAL
   - Add the following subsection to the PRECAUTIONS section, after the Pediatric Use subsection:

     Geriatric Use

     Clinical studies for clindamycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

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

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>

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), 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

APPEARS THIS WAY
ON ORIGINAL

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's 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 26**	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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? 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. [see FTR]		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	
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.		X	
Scoring: Describe scoring configuration of RLD and applicant (p. #) 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 p. # 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?[see FTR]		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.		X	
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. **See FTR.**			

Note to the Chemist:

The RLD, Cleocin T solution, contains Isopropyl Alcohol 50% and the generic product contains 39%. Please confirm that it's acceptable.

***** The reviewing chemist referred this question to the Biopharm Division and the bio review is still pending.**

FOR THE RECORD:

1. MODEL LABELING

   This review was based on the labeling for Cleocin T Topical Solution, USP by Pharmacia & Upjohn [NDA 50-537/S-026: Approved May 30, 2003.

2. PATENTS/EXCLUSIVITIES

   There are no unexpired patents or exclusivity for this product.

   [Vol 1.1, page 9-12]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

   Taro Pharmaceutical Industries, Ltd.
   14 Hakitor Street
   Haia Bay, 26110
   Israel

   [Vol. 1.1. page 166]

4. CONTAINER/CLOSURE

Bottles: 30 mL & 60 mL	HDPE [redacted] white [redacted]
Caps (Commercial) 24 mm White [redacted] Caps with [redacted] Sealing Disc	[redacted] Sealing Disk: [redacted]
Caps (In-use):	[redacted]

[Vol. 1.2. page 356]

5. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. [Vol. 1.1. page 73]

6. PACKAGING CONFIGURATIONS

RLD: 30 mL and 60 mL bottles
ANDA: 30 mL and 60 mL bottles

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

RLD: Store at controlled room temperature 20 to 25C (68 to 77F) [See USP]
ANDA: Store at controlled room temperature 20 to 25C (68 to 77F) [See USP]

Recommendation: Store at 20-25C (68 –77F) [See USP Controlled Room Temperature].

8. DISPENSING STATEMENTS COMPARISON

USP: Preserve in tight containers
RLD: Protect from freezing
ANDA: Protect from freezing

Date of Review: 1/9/03 **Date of Submission: July 16, 2003**

Primary Reviewer: _____ 1-22-04
Melaine Shin Date:

Team Leader: _____ 1/22/04
Lillie Golson Date:

cc:

ANDA: 65-184
DUP/DIVISION FILE
HFD-613/MShin/LGolson (no cc)
v:\firmsnz\TARO\ltrs&rev\65184NA1.Labeling.doc
Review

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

ANDA Number: **65-184** Date of Submission: **February 13, 2004**

Applicant's Name: Taro Pharmaceuticals U.S.A., Inc.

Established Name: Clindamycin Phosphate Topical Solution, USP

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

CONTAINER LABELS - 30 mL and 60 mL

Satisfactory in FPL as of 2/13/04 submission

CARTON LABELS - 30 mL and 60 mL

Satisfactory in FPL as of 2/13/04 submission

PROFESSIONAL PACKAGE INSERT LABELING:

Satisfactory in FPL as of 2/13/04 submission

REVISIONS NEEDED POST-APPROVAL: NONE

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Cleocin T Topical Solution, USP

NDA Number: 50-537

NDA Drug Name: Cleocin T Topical Solution, USP

NDA Firm: Pharmacia & Upjohn

Date of Approval of NDA Insert and supplement #: S-026 / May 30, 2003

Has this been verified by the MIS system for the NDA?
Yes

Was this approval based upon an OGD labeling guidance? No

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's 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 26**	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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? 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. [see FTR]		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	

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.		X	
Scoring: Describe scoring configuration of RLD and applicant (p. #) 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 p. # 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?[see FTR]		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.		X	
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. **See FTR.**			

FOR THE RECORD:

This submission was submitted in response to the NA letter and all the requested revisions were accurately made and it is satisfactory for approval.

1. MODEL LABELING

   This review was based on the labeling for Cleocin T Topical Solution, USP by Pharmacia & Upjohn [NDA 50-537/S-026: Approved May 30, 2003.

2. PATENTS/EXCLUSIVITIES

   There are no unexpired patents or exclusivity for this product.

   [Vol 1.1, page 9-12]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

   Taro Pharmaceutical Industries, Ltd.
   14 Hakitor Street
   Haia Bay, 26110
   Israel

   [Vol. 1.1. page 166]

4. CONTAINER/CLOSURE

Bottles: 30 mL & 60 mL	HDPE white
Caps (Commercial) 24 mm White Caps with Sealing Disc	Sealing Disk:
Caps (In-use):	

   [Vol. 1.2. page 356]

5. INACTIVE INGREDIENTS

   The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. [Vol. 1.1. page 73]

6. PACKAGING CONFIGURATIONS

   RLD: 30 mL and 60 mL bottles
   ANDA: 30 mL and 60 mL bottles

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

RLD: Store at controlled room temperature 20 to 25C (68 to 77F) [See USP]
ANDA: Store at controlled room temperature 20 to 25C (68 to 77F) [See USP]

Recommendation: Store at 20-25C (68 –77F) [See USP Controlled Room Temperature].

8. DISPENSING STATEMENTS COMPARISON

USP: Preserve in tight containers
RLD: Protect from freezing
ANDA: Protect from freezing

Date of Review: March 10, 2004 **Date of Submission: February 13, 2004**

Primary Reviewer: _____ 3-10-04
Melaine Shin Date:

Team Leader: _____ 3/12/04
Lillie Golson Date:

cc:

ANDA: 65-184
DUP/DIVISION FILE
HFD-613/MShin/LGolson (no cc)
v:\firmsnz\TARO\ltrs&rev\65184AP.Labeling.doc
Review

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

CHEMISTRY REVIEW(S)

ANDA 65-184

Clindamycin Phosphate Topical Solution USP, 1%

Taro Pharmaceutical Industries Ltd.

Susan Zuk
Chemistry Division II, OGD

Table of Contents

Chemistry Review Data Sheet

1. ANDA 65-184

2. REVIEW #: 1

3. REVIEW DATE: 10/31/03

4. REVIEWER: Susan Zuk

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original ANDA	7/16/03

7. NAME & ADDRESS OF APPLICANT:

Name:	Taro Pharmaceutical Industries, Ltd.
Address:	14 Hakitor Street Haifa Bay, Israel 26110
Representative:	Kalpana Rao
US Agent's Address	5 Skyline Drive Hawthorn, NY 10532
FAX	(914) 593-0078

Telephone: (914) 345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Clindamycin Phosphate Topical Solution , USP 1%

9. LEGAL BASIS FOR SUBMISSION: The legal basis for submission of the ANDA is the reference listed drug Cleocin T® Topical Solution manufactured by Pharmacia & Upjohn, NDA #50537.

10. PHARMACOL. CATEGORY: Antibiotic

11. DOSAGE FORM: Topical Solution

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

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __X_Rx ___OTC

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

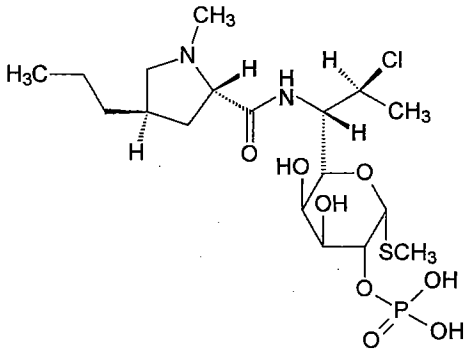
_____SPOTS product – Form Completed

___X__Not a SPOTS product

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

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97.

CAS # 24729-96-2.



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II			3	A	9/25/03	G. Kang
	III			3, 4	A	4/18/96	K. Furnkranz
	III			3, 4	A	4/29/02	R. Frankewich
	III			3, 4	A	4/3/01	P. Maturu
	III			3, 4	A	4/24/00	M. Sloan
	III			3, 4	A	8/25/99	D. Cummings
	III			3, 4	A	5/28/03	D. Klein
	III			3, 4	A	7/18/02	A. Shaw
	III			3, 4	A	7/17/02	A. Shaw

[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

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	9/12/03	S. Adams
Methods Validation	N/A		
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. ___X_ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 65-184

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability: The application is not recommended for approval.

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)

The drug substance is Clindamycin Phosphate, a water soluble ester of the semi-synthetic antibiotic produced by 7(S)-chloro substitution of the 7(R)-hydroxyl group on lincomycin. In vivo hydrolysis converts it into active Clindamycin. Clindamycin Phosphate, USP is a white, crystalline, hygroscopic powder. It is soluble in water, slightly soluble in ethanol, sparingly soluble in acetone and insoluble in chloroform, benzene and ether.

The drug product is Clindamycin Phosphate Topical Solution USP, 1%. The product contains 1% drug substance, as Clindamycin, in an alcohol-based solution. The total Isopropyl Alcohol, USP content is 39% w/v. The other inactive ingredients are Propylene Glycol, USP, Purified Water, USP and Sodium Hydroxide, NF for pH adjustment.

The maximum batch size is ———— One exhibit batch was manufactured for the ANDA to ——. This was completely packaged into 30 cc and 60 cc bottles. The batch was placed on stability study at 40°C and 25°C. The proposed expiry is — months. The product is stable at room temperature.

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

Clindamycin Phosphate Topical Solution USP, 1% is indicated for the topical treatment of acne vulgaris. The recommended usage is application of a thin film onto the affected area twice daily. The product is supplied in 1 oz and 2oz bottles with applicators.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is not approvable due to deficiencies in the following sections:

1. composition statement
2. method validation
3. container/closure
4. stability

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Susan Zuk/10/31/03 Susan Zuk 11/13/03
Richard Adams/11/12/03
Mark Anderson/11/13/03 Re. Adams 11/14/03

C. CC Block

APPEARS THIS WAY
ON ORIGINAL

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of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1

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

Provide current data from your on-going stability study.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-643/SZuk/10/31/03 11/13/03

HFD-643/RAdams/11/12/03 R C. Adams 11/14/03

HFD-617/MAnderson/11/13/03 M Anderson 11/17/03

F/T by : mda /11/13/03

V:\FIRMSNZ\TARO\LTRS&REV\65184NA.R01

TYPE OF LETTER: NOT APPROVABLE - MINOR

APPEARS THIS WAY
ON ORIGINAL

ANDA 65-184

Clindamycin Phosphate Topical Solution USP, 1%

Taro Pharmaceutical Industries Ltd.

Susan Zuk
Chemistry Division II, OGD

Table of Contents

Chemistry Review Data Sheet

1. ANDA 65-184

2. REVIEW #: 2

3. REVIEW DATE: 3/17/04

4. REVIEWER: Susan Zuk

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original ANDA	7/16/03

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	1/22/04 response to deficiency letter 11/17/03
Telephone Amendment	2/23/04 response to telephone request for correction
Telephone Amendment	3/16/04 change in unknown Impurity spec based on supplier

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceutical Industries, Ltd.

Address: 14 Hakitor Street
Haifa Bay, Israel 26110

Representative: Kalpana Rao

Chemistry Review Data Sheet

US Agent's Address	5 Skyline Drive Hawthorn, NY 10532
FAX	(914) 593-0078
Telephone:	(914) 345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Clindamycin Phosphate Topical Solution , USP 1%

9. LEGAL BASIS FOR SUBMISSION: The legal basis for submission of the ANDA is the reference listed drug Cleocin T® Topical Solution manufactured by Pharmacia & Upjohn, NDA #50537.

10. PHARMACOL. CATEGORY: Antibiotic

11. DOSAGE FORM: Topical Solution

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

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __X_Rx ___OTC

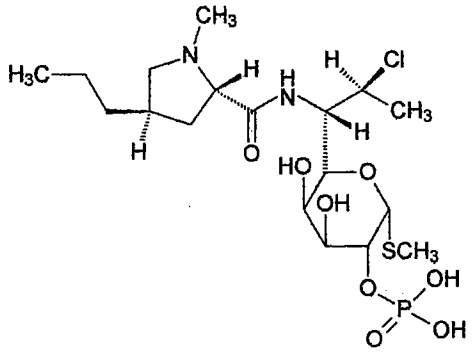
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___X__Not a SPOTS product

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

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97.
CAS # 24729-96-2.



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
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	III			3, 4	A	4/18/96	K. Furnkranz
	III			3, 4	A	4/29/02	R. Frankewich
	III			3, 4	A	4/3/01	P. Maturu
	III			3, 4	A	4/24/00	M. Sloan
	III			3, 4	A	8/25/99	D. Cummings
	III			3, 4	A	5/28/03	D. Klein
	III			3, 4	A	7/18/02	A. Shaw
	III			3, 4	A	7/17/02	A. Shaw

[1] Action codes for DMF Table:
1 – DMF Reviewed.
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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

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	9/12/03	S. Adams
Methods Validation	N/A		
Labeling	Accepable	3/12/04	M. Shin
Bioequivalence	Acceptable	3/16/04	H. Nguyen
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. ___X_ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 65-184

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability: The application is recommended for approval.

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)

The drug substance is Clindamycin Phosphate, a water soluble ester of the semi-synthetic antibiotic produced by 7(S)-chloro substitution of the 7(R)-hydroxyl group on lincomycin. In vivo hydrolysis converts it into active Clindamycin. Clindamycin Phosphate, USP is a white, crystalline, hygroscopic powder. It is soluble in water, slightly soluble in ethanol, sparingly soluble in acetone and insoluble in chloroform, benzene and ether.

The drug product is Clindamycin Phosphate Topical Solution USP, 1%. The product contains 1% drug substance, as Clindamycin, in an alcohol-based solution. The total Isopropyl Alcohol, USP content is 39% w/v. The other inactive ingredients are Propylene Glycol, USP, Purified Water, USP and Sodium Hydroxide, NF for pH adjustment.

The maximum batch size is ———————. One exhibit batch was manufactured for the ANDA to produce —— This was completely packaged into 30 cc and 60 cc bottles. The batch was placed on stability study at 40°C and 25°C. The proposed expiry is — months. The product is stable at room temperature.

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

Clindamycin Phosphate Topical Solution USP, 1% is indicated for the topical treatment of acne vulgaris. The recommended usage is application of a thin film onto the affected area twice daily. The product is supplied in 1 oz and 2oz bottles with applicators.

C. Basis for Approvability or Not-Approval Recommendation

Approval is recommended once labeling is acceptable and a bio-waiver is granted.

The following support approval:

- DMF for API is adequate
- EER acceptable
- Chemistry, manufacturing and controls are acceptable

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Susan Zuk/3/17/04 Susan Zuk 3/22/04
Richard Adams/3/19/04 R. C. Adams 3/24/04
Mark Anderson/3/19/04

C. CC Block

APPEARS THIS WAY
ON ORIGINAL

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information from

CHEMISTRY REVIEW #2

30. MICROBIOLOGY
N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
N/A

32. LABELING - Satisfactory
Labeling is acceptable per review dated 3/12/04.

33. ESTABLISHMENT INSPECTION Satisfactory
The manufacturing facility and API supplier are acceptable as of 9/12/03.

34. BIOEQUIVALENCE - Satisfactory
A waiver was requested due to topical use only. Division of Bioequivalence has granted the waiver per review dated 3/16/04.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: N/A

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-643/SZuk/3/17/04 3/22/04

HFD-643/RAdams/3/19/04 R. C. Adams 3/24/04

FT by : mda/3/19/04

V:\FIRMSNZ\TARO\LTRS&REV\65184AP.R02

TYPE OF LETTER: ANDA APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

BIOEQUIVALENCE REVIEW(S)

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	65-184
Drug Product Name	Clindamycin Phosphate Topical Solution USP
Strength	1%
Applicant Name	Taro Pharmaceutical Industries Ltd.
Address	Haifa, Israel (Agent: Taro Pharmaceuticals USA, Hawthorn, NY)
Submission Date(s)	July 16, 2003
Amendment Date(s)	
Reviewer	**Hoainhon Nguyen**
First Generic	**No**
File Location	**V:\firmsnz\taro\ltrs&rev\65184w0703.doc**

I. Executive Summary

The firm has requested a waiver of *in vivo* bioequivalence requirements for its Clindamycin Phosphate Topical Solution USP, 1%. The test formulation contains the same active and inactive ingredients as the RLD product, Cleocin T® Topical Solution, 1%, except for Propylene Glycol. The amount of Propylene Glycol in the test formulation, ——— is —— greater than that in the RLD formulation. However, the amount of Propylene Glycol has been found to exceed that of the RLD product in several approved ANDA's. The amount of Propylene Glycol in the current test product, therefore, is considered not to affect the safety of the test product. The formulation is found acceptable per 21 CFR 314.94 (a)(9)(v). The biowaiver requests for the test products are granted per CFR 320.22 (b) (3). The application is acceptable with no deficiencies.

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Clindamycin Phosphate Topical Solution USP, 1%
Reference Product	Cleocin T® Topical Solution, 1%
RLD Manufacturer	Pharmacia & Upjohn
NDA No.	50-537
RLD Approval Date	07/09/1980
Indication	Indicated in the treatment of acne vulgaris.

B. PK/PD Information (Source: csi.micromedex.com)

Bioavailability	Less than 5%. Detectable serum concentrations usually were not achieved.
Food Effect	N/A
Tmax	Not available
Metabolism	Based on PK data from oral dosage form, clindamycin is extensively metabolized in the liver to form clindamycin sulfoxide and N-dimethyl clindamycin.
Excretion	Excreted unchanged and metabolized in the urine within 24 hours.
Half-life	1.5 to 5 hours, based on PK data from oral dosage form.
Relevant OGD or DBE History (NOT TO BE RELEASED UNDER FOI)	Waiver requests have been granted in accordance with 21 CFR 320.22 (b)(3) for the following ANDA's: # ———————————————— ———, 65-049 (Clay Park Lab; 06/24/99), ——— ———————————, 64-159 (Fougera; 10/02/95). ————————————————, 64-136 (Steifel Labs; 09/06/94), 64-108 (Steifel Labs; 10/21/93), 64-050 (Clay Park Labs; 08/05/92), 63-329 (Paddock Labs; 01/27/92) and 63-304 (PBI; 02/09/90). It should be noted that several of the approved ANDA's contain the inactive ingredient of Propylene Glycol in an amount greater than that of the RLD product by more than 5%: #64-136 (————— % difference), 65-049 (————— % difference), 64-050 (————————— % difference), 64-108 (————————% difference), 63-304 (————————— % difference)

C. Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	
Single-dose fed	No	
Steady-state	No	
In vitro dissolution	No	
Waiver requests	Yes	1
BCS Waivers	No	
Vasoconstrictor Studies	No	
Clinical Endpoints	No	
Failed Studies	No	
Amendments		

D. Pre-Study Bioanalytical Method Validation N/A

E. In Vivo Studies N/A

F. Formulation

Location in appendix	SectionIV.A, Page 5
Are inactive ingredients within IIG limits?	**Yes**
If NO, list ingredients outside of limits	
If a tablet, is the product scored?	**N/A**
If yes, which strengths are scored?	
Is scoring of RLD the same as test?	
Is the formulation acceptable?	**Yes**
If not acceptable, why?	

G. In Vitro Dissolution N/A

H. Waiver Request(s)

Strengths for which waivers are requested	1%
Regulation cited	21 CFR 320.22 (b) (3)
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	Yes
If not then why?	

I. Comments

The content of Propylene Glycol in the test formulation is —% greater than that of the RLD product. However, the amount of Propylene Glycol has been found to exceed that of the RLD product in several approved ANDA's , (see Relevant OGD or DBE History on page 2 of this review). The amount of Propylene Glycol in the current test product,

therefore, is considered not to affect the safety of the proposed drug product. The formulation is found acceptable per 21 CFR 314.94 (a)(9)(v).

J. Recommendations

The Division of Bioequivalence agrees that the information submitted by Taro Pharmaceutical Industries demonstrates that its Clindamycin Phosphate Topical Solution USP, 1%, falls under 21 CFR 314.94 (a)(9)(v) of the Bioavailability/Bioequivalence Regulations. The Division of Bioequivalence recommends that the waiver of *in vivo* bioavailability study be granted per 21 CFR 320.22(b) (3). The test product, Taro's Clindamycin Phosphate Topical Solution USP, 1%, is deemed bioequivalent to the currently approved Cleocin T® Topical Solution, 1%, manufactured by Pharmacia & Upjohn.

3/16/04

Hoainhon Nguyen, Team I, Date Signed

3/16/2004

Yih Chain Huang, Ph.D., Team leader, Team I, Date Signed

for 3/16/04

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

HNguyen/02/13/04/v:\firmsnz\taro\ltrs&rev\65184w0703.doc

IV. Appendix

A. Formulation Data

	Test	Reference
Ingredients	**%v/v**	**%v/v**
Clindamycin Phosphate USP	Eq. 1.000 base	Eq. 1.0 base
Isopropyl Alcohol USP	50 (39.24%w/v*)	50
Propylene Glycol USP		
Sodium Hydroxide NF		
Hydrochloric acid		
Purified Water USP		

*Equivalent to 50% v/v (Specific gravity of 0.785)

Comments on the Test Formulation: The content of Propylene Glycol in the test formulation is — % greater than that of the RLD product. However, the amount of Propylene Glycol has been found to exceed that of the RLD product in several approved ANDA's , (see Relevant OGD or DBE History on page 2 of this review). The amount of Propylene Glycol in the current test product, therefore, is considered not to affect the safety of the proposed drug product. The formulation is found acceptable per 21 CFR 314.94 (a) (9) (v).

APPEARS THIS WAY
ON ORIGINAL

BIOEQUIVALENCE COMMENTS

ANDA: 65-184 APPLICANT: Taro Pharmaceutical Industries, Ltd.

DRUG PRODUCT: Clindamycin Phosphate Topical Solution USP, 1%

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

Please note that the bioequivalence 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 bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

for Barbara M. Davit

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

CC: ANDA 65-184
ANDA DUPLICATE
DIVISION FILE
HFD-652/ Bio Secretary - Bio Drug File
HFD-652/ HNguyen

V:\firmsnz\taro\ltrs&rev\65184w0703.doc
Printed in final on / /00

Endorsements: (Final with Dates)
HFD-652/ HNguyen
HFD-652/ YHuang 3/16/2004
HFD-617/A. Sigler
HFD-650/ D. Conner 3/16/04

BIOEQUIVALENCY - ACCEPTABLE Submission Date: 07-16-03
☐ OIC
☐
1. WAIVER (WAI) Strength: 1%
Outcome: AC

☐
☐
☐
Outcome Decisions:
AC - Acceptable

APPEARS THIS WAY
ON ORIGINAL

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 65-184 SPONSOR: Taro Pharmaceutical Industries, Ltd.
DRUG AND DOSAGE FORM: Clindamycin Phosphate Topical Solution USP
STRENGTH(S): 1%
TYPES OF STUDIES: N/A
CINICAL STUDY SITE(S): N/A
ANALYTICAL SITE(S): N/A

STUDY SUMMARY: N/A
DISSOLUTION: N/A.
WAIVER REQUEST: Acceptable

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic No New facility _____ For cause _____ Other _____	Inspection requested: (date) Inspection completed: (date)	

PRIMARY REVIEWER: Hoainhon Nguyen BRANCH: I

INITIAL : HNC DATE : 3/16/04

TEAM LEADER: Yih-Chain Huang BRANCH: I

INITIAL : YCH DATE : 3/16/2004

for DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : Barbara M Davit DATE : 3/16/04

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

Susan Zuk and I called Kalpana Rao of Teva regarding their Clindamycin Phosphate Topical Solution application. We said the 11/17/03 amendment was under review and that we had the following concern:

[redacted]

Response can be sent as a telephone amendment to 301-594-1174.

V:\firmsnz\taro\telecons\65184.001

DATE:

2/19/04

ANDA NUMBER:

65-184

PRODUCT NAME:

Clindamycin Phosphate Topical Solution USP

FIRM NAME:

TARO

FIRM REPRESENTATIVE:

Kalpana Rao

PHONE NUMBER:

914-345-9001 x 6298

FDA REPRESENTATIVES:

Susan Zuk
Mark Anderson

SIGNATURES:

Mark Anderson

RECORD OF TELEPHONE CONVERSATION

Richard Adams, Susan Zuk, and I called Kalpana Rao at Taro regarding their application for Clindamycin Phosphate Topical Solution. Ms. Rao had called previously and left a message that the firm had become aware that their API supplier had established a limit for individual unknown impurity of —%. Taro currently has a specification of —%. Ms. Rao indicated that the API supplier was unwilling to certify that the DS would meet Taro's tighter limit of —%. She asked if Taro could propose limits consistent with their API supplier.

Ms. Rao was unavailable to talk so Mr. Adams left a message stating that Taro could revise their API specification to include the unknown impurity limit of —% and submit a Telephone amendment.

V:\firmsnz\taro\telecons\65184.001

DATE:

3/15/04

ANDA NUMBER:

65-184

PRODUCT NAME:

Clindamycin Phosphate Topical Solution USP, 1%

FIRM NAME:

Taro

FIRM REPRESENTATIVE:

Kalpana Rao

PHONE NUMBER:

914-345-9001 ex 6298

FDA REPRESENTATIVES:

Richard Adams
Susan Zuk
Mark Anderson

SIGNATURES:

Mark Anderson

Mark Anderson

R.C. Adams 3/24/04

RECORD OF TELEPHONE CONVERSATION

Susan Zuk called Kalpana Rao at Taro with regard to the firm's pending application for Clindamycin Phosphate Topical Solution.

She told the firm that it would be necessary to provide for the addition of weight loss to the stability protocol. The request was made by the Division Director.

The firm may submit response as a Telephone Amendment via FAX with hard copy to the application.

3/29/04: The firm submitted revised stability protocol but did not set a specification for weight loss so Susan Zuk and I called Kalpana Rao and asked that she provide for a specification.

The submission can again be sent as a Telephone Amendment.

V:\firmsnz\taro\telecons\65184.003

DATE:

3/26/04
3/29/04

ANDA NUMBER:

65-184

PRODUCT NAME:

Clindamycin Phosphate Topical Solution 1%

FIRM NAME:

Taro Pharmaceutical Industries

FIRM REPRESENTATIVE:

Kalpana Rao

PHONE NUMBER:

914-345-9001 x 6298

FDA REPRESENTATIVES:

Susan Zuk
Mark Anderson

SIGNATURES:

Mark Anderson

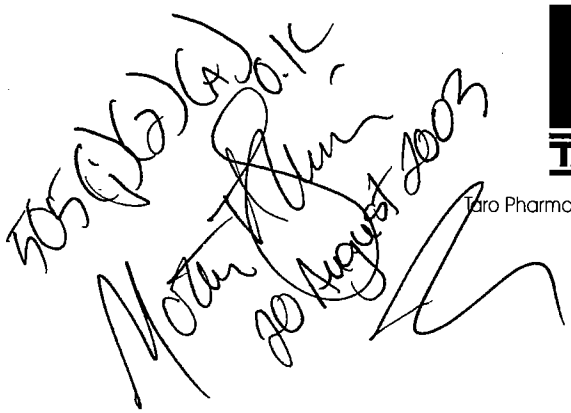
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-184

CORRESPONDENCE

July 16, 2003



Taro Pharmaceuticals U.S.A., Inc.

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

Re: ANDA for Clindamycin Phosphate Topical Solution USP, 1%

Dear Sir/Madam:

Taro Pharmaceutical Industries Ltd. ("Taro") submits today an original, abbreviated new drug application (ANDA) seeking approval to market Clindamycin Phosphate Topical Solution USP, 1% which is bioequivalent to the listed drug, Cleocin T® Topical Solution, manufactured by Pharmacia & Uphohn and pursuant to NDA 50-537.

This ANDA consists of 2 volumes. Taro is filing an archival copy (in blue folders) of the ANDA that contains all the information required in the ANDA, and a technical review copy (in red folders) which contains all the information in the archival copy with the exception of the Bioequivalence section (Section VI). A separate copy of the Bioequivalence waiver request is provided in the orange folder. In addition, a field copy for this ANDA is also submitted herewith (as Taro is located in Haifa Bay, Israel). Taro hereby certifies that the "field copy" is a true copy of the technical sections of the ANDA (also included is a copy of this letter, the 356h form and a certification that the contents are a true copy of those filed with the Office of Generic Drugs). This "field copy" is contained in burgundy folders. An additional three (3) copies of the method validation reports are included in a separate folder.

In accordance with the Patent Certification guidelines issued by the Agency, please refer to the signed Paragraph III Patent Certification (page 09).

Also, please find Taro's signed Generic Drug Enforcement Act of 1992 (page 749), and the "field copy" certification (page 751).

The Stability Commitment is located in Section XVI (page 719), and the signed certifications of compliance with current Good Manufacturing Practices is located in Section IX (page 170).

Five Skyline Drive, Hawthorne, NY 10532 Tel: 914-345-9001 1-888-TARO-USA Fax: 914-345-8728 www.taro.com

Please note, as per our authorization on page 745, that our US agent, Taro Pharmaceuticals U.S.A., Inc., can be contacted at the following address:

Taro Pharmaceuticals U.S.A., Inc.
Five Skyline Drive
Hawthorne, NY 10532
Tel.: 914-345-9001
Fax: 914-593-0078

Attn: Kalpana Rao

Thanking you for your prompt handling of this submission.

Sincerely,

7/16/03

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

ANDA 65-184

Taro Pharmaceuticals U.S.A., Inc.
U.S. Agent for: Taro Pharmaceutical Industries Ltd.
Attention: Kalpana Rao
5 Skyline Drive
Hawthorne, NY 10532

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: Clindamycin Phosphate Topical Solution USP, 1%

DATE OF APPLICATION: July 16, 2003

DATE (RECEIVED) ACCEPTABLE FOR FILING: July 17, 2003

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:

Thomas Hinchliffe
Project Manager
(301) 827-5849

Sincerely yours,

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

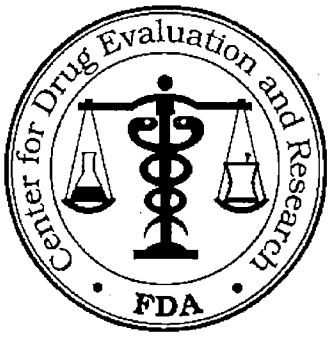
ANDA 65-184
cc: DUP/Jackets
HFD-600/Division File
Field Copy
HFD-610/G. Davis
HFD-92
Endorsement:
HFD-615/MShimer,Chief, RSB _____ date 20 Aug 2003
HFD-615/PPatel,CSO _____ date 8/20/03
Word File V:\Filesnz\Taro\ltrs&rev\65184.ACK
F/T 8/20/03 P.M.P
ANDA Acknowledgment Letter!

MINOR AMENDMENT

ANDA 65-184

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

NOV 17 2003



APPLICANT: Taro Pharmaceutical Industries Ltd. TEL: 914-345-9001 x 6298

ATTN: Kalpano Rao, U.S. Agent FAX: 914-593-0078

FROM: Mark Anderson PROJECT MANAGER: (301) 827-5737

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated July 16, 2003, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Topical Solution USP, 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 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 are provided. Labeling and bioequivalence comments will be provided when the reviews are done.

Redacted 1 page(s)

of trade secret and/or

confidential commercial

information from

11/17/2003 FDA FAX

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

Provide current data from your on-going stability study.

Sincerely yours,

R.C. Adams for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Taro Pharmaceuticals U.S.A., Inc.

January 22, 2004

ORIG AMENDMENT

N/AM

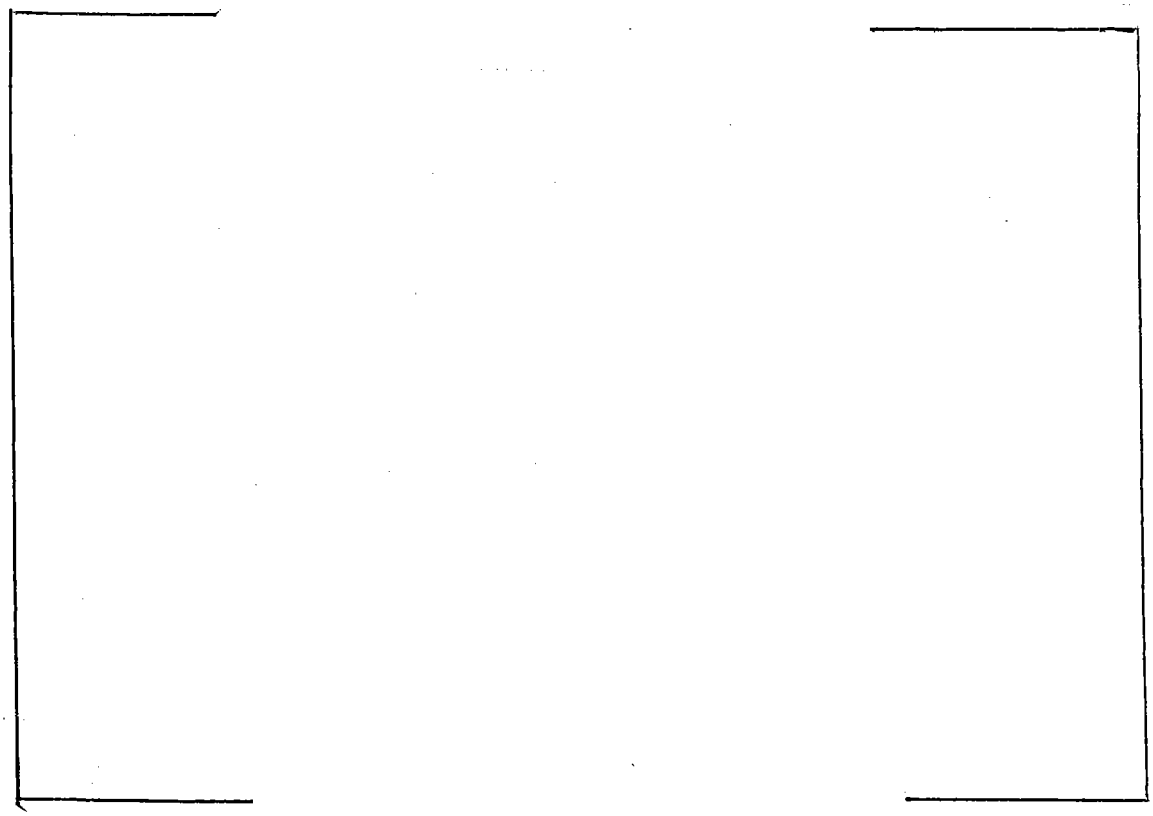
Mark Anderson, Project Manager
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20857

Re: ANDA # 65-184
Clindamycin Phosphate Topical Solution USP, 1%
Minor Amendment

Dear Mr. Anderson:

Reference is made to Taro Pharmaceutical Industries Ltd.'s Abbreviated New Drug Application (ANDA) submitted on July16, 2003 under Section 506(j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Solution USP, 1%. Reference is also made to a CMC deficiency letter dated November 17, 2003 in which the following deficiencies were provided:

Chemistry Deficiencies:



Five Skyline Drive, Hawthorne, NY 10532 Tel: 914-345-9001 1-888-TARO-USA Fax: 914-345-8728 www.taro.com

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

1/22/2004 TARO LETTER

U.S. Department of Health and Human Services
Food and Drug Administration

Fax Cover Sheet

Public Health Service
Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling & Program Support
Labeling Review Branch
Rockville, Maryland 20855

To: Kalpano Rao, U.S. agent **DATE: 1/29/04**

Fax: 914-593-0078 Phone: 914-345-9001 X6298

SUBJECT: ANDA 65-184 Clindamycin Phosphate Topical solution

From: Melaine Shin, R.Ph., Labeling Reviewer

Phone: (301) 827-5846 **Fax:** (301) 594-1174

Number of Pages:
(Including Cover Sheet)

Comments: Please send me a desk copy of your submission responding to this letter.

Attention: **Melaine Shin**
Room E124

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

ANDA Number:	ANDA 65-184
Date of Submission:	July 16, 2003 (Original draft labeling)
Applicant's Name:	Taro Pharmaceuticals U.S.A., Inc.
Established Name:	Clindamycin Phosphate Topical Solution, USP
Proposed Proprietary Name:	NONE

Labeling Deficiencies:

1. **GENERAL**

   Please revise your storage temperature recommendation as follows:

   "Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature]."

2. **CONTAINER**

   See comment under GENERAL

3. **CARTON**

   See comment under GENERAL

4. **PROFESSIONAL PACKAGE INSERT**

   - See comment under GENERAL
   - Add the following subsection to the PRECAUTIONS section, after the Pediatric Use subsection:

     Geriatric Use

     Clinical studies for clindamycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

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

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>

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), 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

APPEARS THIS WAY
ON ORIGINAL

2.1

February 13, 2004

TARO

Taro Pharmaceuticals U.S.A., Inc.

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

ORIG AMENDMENT
N/AF

FPL

Re: ANDA 65-184
Clindamycin Phosphate Topical Solution USP, 1%
Labeling Amendment

Dear Sir/Madam:

Reference is made to our Abbreviated New Drug Application (ANDA) for Clindamycin Phosphate Topical Solution USP, 1% submitted July 16, 2003, and to the labeling deficiency letter from the Agency on January 29, 2004 in which the following was noted:

1. GENERAL
Please revise your storage temperature recommendation as follows:
"Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature]."

2. CONTAINER
See comment under GENERAL

3. CARTON
See comment under GENERAL

4. PROFESSIONAL PACKAGE INSERT

- *See comment under GENERAL*
- *Add the following subsection to the PRECAUTIONS section, after the Pediatric Use subsection:*

  Geriatric Use
  Clinical studies for clindamycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

RECEIVED
FEB 17 2004
OGD/CDER

Five Skyline Drive, Hawthorne, NY 10532 Tel: 914-345-9001 1-888-TARO-USA Fax: 914-345-8728 www.taro.com

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

Enclosed please find:

- **12 - Final Printed 30 mL Bottle and Carton labels**
- **12 - Final Printed 60 mL Bottle and Carton labels**
- **12 - Final Printed Package Inserts**

In addition, and in accordance with 21CFR 314.94(a)(8)(iv), we are providing a side-by-side comparison of our Package Insert with our last submission with all differences annotated and explained.

This concludes our response to the Agency's labeling deficiency letter of January 29, 2004.

Sincerely,

FOR Kalpana Rao
Vice President, Regulatory Affairs
Taro Pharmaceuticals U.S.A., Inc.

Taro Pharmaceuticals U.S.A., Inc.

February 23, 2004

OGG AMENDMENT

N/AM

Mark Anderson, Project Manager
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20857

Re: ANDA # 65-184
Clindamycin Phosphate Topical Solution USP, 1%
Telephone Amendment

Dear Mr. Anderson:

Reference is made to Taro Pharmaceutical Industries Ltd.'s (Taro) Abbreviated Drug New Application (ANDA) submitted on July 16, 2003 under Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Solution USP, 1%. Reference is also made to a CMC deficiency letter dated November 17, 2003 and your telephone call on February 19, 2004 in which your requested the following:

Request:

[redacted]

Response:
The revised [redacted], is included in attachment 1.

This concludes our response to the Agency telephone request on February 19, 2004.

RECEIVED
FEB 2 4 2004
OGD/CDER

Five Skyline Drive, Hawthorne, NY 10532 Tel: 914-345-9001 1-888-TARO-USA Fax: 914-345-8728 www.taro.com

If you should have any questions regarding this submission, please contact the undersigned at (914) 345-9001 x 6298.

Sincerely,

2/23/04

Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs

2.1

March 16, 2004

Taro Pharmaceuticals U.S.A., Inc.

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

ORIG AMENDMENT
N/AA

Re: ANDA 65-184
Clindamycin Phosphate Topical Solution USP, 1%
Gratuitous Amendment

Dear Sir/Madam:

Reference is made to our Abbreviated New Drug Application (ANDA) for Clindamycin Phosphate Topical Solution USP, 1% submitted July 16, 2003, and to the telephone call from Mark Anderson and Richard Adams on March 15, 2004 in which he requested the following:

Comment:
Please revise your API specification to include the unknown impurity limit of NMT — %.

Response:
We have revised our API specification as indicated. Based upon the API limit for unknown impurities of NMT —% we are proposing a limit for our Finished Product Release and Stability specifications of NMT — % (our previous limit had been NMT —%). Please find these revised versions attached.

This concludes our response to the Agency's telephone call of March 15, 2004.

Sincerely,

3/16/04
Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs

RECEIVED
MAR 17 2004
OGD/CDER

Taro Pharmaceuticals U.S.A., Inc

March 26, 2004

Mark Anderson
Office of Generic Drugs
Food and Drug Administration
7500 Standish Place, Room 150
Rockville, MD 20855

RE: Clindamycin Phosphate Topical Solution USP, 1%
ANDA 65-184
Telephone Amendment

Dear Mr. Anderson:

Reference is made to Taro Pharmaceuticals Industries, Ltd., Abbreviated New Drug Application submitted under Section 505(j) of the Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Solution USP, 1%. Reference is also made to the telephone request of Susan Zuk on March 26, 2004, in which the following request was made:

"Please commit to conduct weight loss testing during stability of validation batches and also to revise your stability protocol to indicate that weight loss testing will be conducted."

A revised stability commitment protocol is enclosed and the weight loss test has been added for the first three production lots.

This concludes our response to the telephone request of March 26, 2004.

If there are any questions, please do not hesitate to contact the undersigned at (914) 345-9001, ext. 6298.

Sincerely,

3/26/04
Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs

Taro Pharmaceuticals U.S.A., Inc

March 30, 2004

Mark Anderson
Office of Generic Drugs
Food and Drug Administration
7500 Standish Place, Room 150
Rockville, MD 20855

RE: Clindamycin Phosphate Topical Solution USP, 1%
ANDA 65-184
Telephone Amendment

Dear Mr. Anderson:

Reference is made to Taro Pharmaceuticals Industries, Ltd., Abbreviated New Drug Application submitted under Section 505(j) of the Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Solution USP, 1%. Reference is also made to the telephone conversation of Mark Anderson and Susan Zuk on March 29, 2004 in which the following request was made:

"Please submit a specification for the weight loss test included in the stability commitment."

A revised stability commitment protocol was provided in a response dated March 26, 2004 and the specification for Clindamycin Phosphate Topical Solution USP, 1% including the weight loss test is enclosed. Taro's nomenclature for weight loss is the water loss rate test.

This concludes our response to the telephone request of March 30, 2004.

If there are any questions, please do not hesitate to contact the undersigned at (914) 345-9001, ext. 6298.

Sincerely,

3/30/04

Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs