CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204427Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 204427 SUPPL # HFD # 540

Trade Name Kerydin

Generic Name (tavaborole) Topical Solution, 5%

Applicant Name Anacor Pharmaceuticals, Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☒ NO ☐

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☐ NO ☒

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If

the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☐ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently

demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
!
IND # YES ☐ ! NO ☐
! Explain:

Investigation #2 !
!
IND # YES ☐ ! NO ☐
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in

interest provided substantial support for the study?

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☐

If yes, explain:

==========

Name of person completing form: Cristina Attinello, MPH
Title: Sr. RPM, DDDP
Date: June 19, 2014

Name of Division Director signing form: Tatiana Oussova, MD, MPH
Title: Deputy Director for Safety, DDDP

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

CRISTINA Petruccelli Attinello
06/19/2014

TATIANA OUSSOVA
06/19/2014

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 204427 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: Kerydin Established/Proper Name: (tavaborole) Dosage Form: topical solution, 5%		Applicant: Anacor Pharmaceuticals, Inc. Agent for Applicant (if applicable): n/a
RPM: Cristina Attinello		Division: DDDP

NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

BLA Application Type: ☐ 351(k) ☐ 351(a)
Efficacy Supplement: ☐ 351(k) ☐ 351(a)

For ALL 505(b)(2) applications, two months prior to EVERY action:

- **Review the information in the 505(b)(2) Assessment and submit the draft[2] to CDER OND IO for clearance.**
- **Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)**

☐ No changes
☐ New patent/exclusivity *(notify CDER OND IO)*
Date of check:

Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

❖ Actions	
• Proposed action • User Fee Goal Date is 7-29-14	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics[3]	

[1] The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.
[2] For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).
[3] Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): oxaborole antifungal
(confirm chemical classification at time of approval)

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Breakthrough Therapy designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ MedGuide w/o REMS
☐ REMS not required

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information were issued	☐ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☒ Other: Approval Page Weekly FDA News & Notes
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	☒ No ☐ Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☒ Verified ☐ Not applicable because drug is an old antibiotic.

CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	AP 7-7-14
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling *(if it is division-proposed labeling, it should be in track-changes format)*	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☒ Patient Package Insert ☒ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling *(if it is division-proposed labeling, it should be in track-changes format)*	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s)*	1-23-14 1-17-14
❖ Labeling reviews *(indicate dates of reviews)*	RPM: 9-10-13 DMEPA: 6-17-14, 3-11-14 DMPP/PLT (DRISK): 3-14-14, 3-7-14 OPDP: 3-4-14 SEALD: ☒ None CSS: ☒ None Other: ☒ None
Administrative / Regulatory Documents	
❖ RPM Filing Review[4]/Memo of Filing Meeting *(indicate date of each review)* ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	9-11-13 ☒ Not a (b)(2)
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included

[4] Filing reviews for scientific disciplines are NOT required to be included in the action package.

Version: 5/14/2014

❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC 2-5-14 If PeRC review not necessary, explain: _____	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) *(do not include previous action letters, as these are located elsewhere in package)*	4-4-14, 3-19-14, 1-23-14, 1-23-14, 12-24-13, 12-20-13, 10-10-13, 9-22-13, 8-16-13, 8-6-13
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	6-6-14, 5-5-14, 1-14-14
❖ Minutes of Meetings	
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	5-29-13
• EOP2 meeting *(indicate date of mtg)*	10-28-09
• Mid-cycle Communication *(indicate date of mtg)*	1-15-14
• Late-cycle Meeting *(indicate date of mtg)*	4-1-14
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	7-7-14
Division Director Summary Review *(indicate date for each review)*	6-19-14
Cross-Discipline Team Leader Review *(indicate date for each review)*	5-6-14
PMR/PMC Development Templates *(indicate total number)*	1
Clinical	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	5-6-14
• Clinical review(s) *(indicate date for each review)*	3-27-14, 9-5-13
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	3-27-14, p. 27

❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	11-12-13 (Qt-IRT)
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ N/A
❖ Risk Management • REMS Documents and REMS Supporting Document *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	4-7-14
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	4-23-14, 4-23-14, 4-14-14, 4-3-14
Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Microbiology Review(s) *(indicate date for each review)*	3-6-14, 12-13-13, 9-5-13
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☒ No separate review
Statistical Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Statistical Review(s) *(indicate date for each review)*	3-7-14, 9-5-13
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Pharmacology review(s) *(indicate date for each review)*	3-6-14, 9-6-13
❖ OSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☒ None requested
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	1-27-14
• Supervisory Review(s) *(indicate date for each review)*	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	2-6-14, 1-17-13, 8-30-10, 8-19-10, 11-25-09, 6-8-09, 3-9-09, 6-13-07, 11-2-06, 11-2-06, 10-30-06, 8-15-06, 6-15-06, 6-15-06, 4-17-06, 2-6-06
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	1-27-14
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	1-8-14
❖ ECAC/CAC report/memo of meeting	12-11-13
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ No separate review
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	6-16-14, 3-7-14, 9-6-13, 9-5-13
❖ Microbiology Reviews ☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	11-26-13, 8-27-13
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	3-7-14
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within **2 years** of action date) *(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[5])*	Date completed: 12-27-13 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER (date of most recent TB-EER must be within **30 days** of action date) *(original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☒ Completed ☐ Requested ☐ Not yet requested ☐ Not needed (per review)

[5] i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Day of Approval Activities	
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	☐ Done

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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/

CRISTINA Petruccelli Attinello
07/07/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

MID-CYCLE COMMUNICATION

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (tavaborole) topical solution, 5%.

We also refer to the teleconference between representatives of your firm and the FDA on January 15, 2014. The purpose of the teleconference was to provide you an update on the status of the review of your application.

A record of the teleconference is enclosed for your information.

If you have any questions, call Cristina Attinello, Regulatory Project Manager at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

David Kettl, M.D.
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure:
Mid-Cycle Communication

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MID-CYCLE COMMUNICATION

Meeting Date and Time: January 15, 2014, 10am EST

Application Number: NDA 204427
Product Name: (tavaborole) Topical Solution, 5%
Proposed Indication: Treatment of onychomycosis [redacted] (b) (4)
Applicant Name: Anacor Pharmaceuticals, Inc.

Meeting Chair: David Kettl, MD
Meeting Recorder: Cristina Attinello

FDA ATTENDEES
Julie Beitz, MD, Director, ODE III
Amy Egan, MD, Deputy Director (acting), ODE III
Susan J. Walker, MD, FAAD, Director, DDDP
David Kettl, MD, Clinical Team Leader, DDDP
Doanh Tran, PhD, Clinical Pharmacology Team Leader, DCP3
An-Chi Lu, MS, PharmD, Clinical Pharmacology Reviewer, DCP3
Maria R. Walsh, RN, MS, Associate Director for Regulatory Affairs, ODE III
Cristina Attinello, MPH, Regulatory Health Project Manager, DDDP
Stacy Blake, Regulatory Health Project Manager, DDDP

EASTERN RESEARCH GROUP ATTENDEES
[redacted] (b) (6)

APPLICANT ATTENDEES
Carmen Rodriguez, Sr. VP, Regulatory Affairs and Quality Assurance
Le-Van Nguyen, Sr. Director, Regulatory Affairs
Amy Wang, Sr. Manager, Regulatory Affairs
Lee Zane, Sr. VP, Clinical and Chief Medical Officer
Xiaoming Lin, VP, Clinical Research and Development

1.0 INTRODUCTION

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we

may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may or may not be able to consider your response before we take an action on your application during this review cycle.

2.0 SIGNIFICANT ISSUES

Chemistry, Manufacturing and Controls (CMC)

No substantial review issues; pending review of final facility inspection reports

Clinical

Proposed indication
- (b) (4) onychomycosis of toenails
- age

Pediatric Study Plan (PSP)
- necessity of studies for 6-12 years of age
- Pediatric Review Committee (PeRC) meeting pending

Meeting Discussion:
The Agency discussed that no significant review issues have been identified to date and no information requests were expected to be sent to the applicant. There are no major safety concerns at this stage of the application review.

The Agency noted that the application did not contain supportive safety and efficacy data for (b) (4) beyond onychomycosis of the toenail, and that this would likely be the indication recommended when labeling negotiations ensue later in the spring.

There was discussion related to the applicant's Pediatric Study Plan, which proposed including (b) (4) The Agency inquired about the interpretation of literature submitted to characterize the incidence and prevalence of onychomycosis in pediatric age groups. The applicant stated that it was not their intention to seek an indication down to six years of age with the proposed trial. The applicant also contended that the disease was similar enough in adults that additional efficacy data in adolescents should not be required.

Following discussion with the applicant, the Agency concurred that a waiver under age 12 would appear reasonable based on the determination that the product would be unlikely to be used by a substantial number of pediatric patients below age 12 years. A small safety trial in adolescents might be recommended, likely as a post marketing trial after Agency action, but this would not be decided until later in the review cycle and would be discussed with the applicant at the Late Cycle Meeting.

While a final determination regarding the PSP would be made later in the review cycle following discussion with the Pediatric Review Committee, the Agency stated that they would support such a waiver less than 12 years of age, with deferral of the 12-17 year age group following the action date of the application. The applicant agreed to amend their PSP and submit to the NDA by January 21, 2014.

3.0 INFORMATION REQUESTS

No information requests have been identified at this time.

4.0 MAJOR SAFETY CONCERNS/RISK MANAGEMENT

No major safety concerns have been identified at this stage of review and therefore there was no discussion related to risk management plans.

5.0 ADVISORY COMMITTEE MEETING

This product presents no novel or complex regulatory issues which might warrant advisory committee discussion and therefore there was no discussion of this topic.

6.0 LATE-CYCLE MEETING/OTHER PROJECTED MILESTONES

Late Cycle Meeting date proposed: April 4, 2014

Meeting Discussion:
The applicant requested that a date earlier in April be considered. The Agency stated their flexibility in scheduling the Late Cycle Meeting and agreed to dialogue further offline.

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/s/

DAVID L KETTL
01/23/2014

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 204427

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Anacor Pharmaceuticals, Inc.
1020 East Meadow Circle
Palo Alto, CA 94303-4230

ATTENTION: Carmen R. Rodriquez, M.Sc.
Vice President, Regulatory Affairs and Quality

Dear Ms. Rodriquez:

Please refer to your New Drug Application (NDA) dated July 26, 2013, received July 29, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tavaborole Topical Solution, 5%.

We also refer to your correspondence, dated and received October 30, 2013, requesting review of your proposed proprietary name, Kerydin. We have completed our review of the proposed proprietary name, Kerydin and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your October 30, 2013 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet Anderson, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application, contact Cristina Attinello, Regulatory Project Manager, in the Office of New Drugs at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
01/23/2014

For Internal Use Only

MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEETING DATE: January 9, 2014
TIME: 3:00 PM - 3:30 PM
LOCATION: WO Bldg 22, Rm 4322
APPLICATION: NDA 204427
DRUG NAME: Kerydin (tavaborole) Topical Solution 5%
TYPE OF MEETING: Proprietary Name Review Teleconference

APPLICANT: Anacor Pharmaceuticals Inc.

MEETING CHAIR: Lubna Merchant, Team Leader, DMEPA, OSE

MEETING RECORDER: Janet Anderson, Safety Regulatory Project Manager, OSE

FDA ATTENDEES:
Office of Surveillance and Epidemiology (OSE) Project Management
Janet Anderson (Safety Regulatory Project Manager)

Division of Medication Errors Prevention &Analysis (DMEPA-OSE)
Lubna Merchant (Team Leader)
Carlos Mena-Grillasca (Safety Evaluator)

SPONSOR ATTENDEES:
Regulatory
Carmen Rodriguez, Senior VP of Regulatory Affairs & Quality
Le-Van Nguyen, Senior Director of Regulatory Affairs
Amy Wang, Senior Manager of Regulatory Affairs

Background
DMEPA requested this teleconference to discuss our concerns with the proposed proprietary name, Kerydin.

Introduction
We appreciate you meeting with us. We asked for this tcon to provide you with comments from our preliminary assessment of the proposed proprietary name, Kerydin. We identified a name of which we are concerned about, Varidin. We will explain our concerns and then discuss your options after that.

Issues
- Kerydin is vulnerable to name confusion with the product Varidin. The name Varidin was identified by the (b) (4) in their study as a look-alike and sound-alike

name. However, we note that (b) (4) did not consider the names to have enough phonetic, orthographic or product characteristics similarities to perform a full FMEA analysis. We used POCA (Phonetic and Orthographic Computer Analysis) to determine a similarity index between the names Kerydin and Varidin. The combined POCA score for this name pair is 69 (phonetic 76; orthographic 62), which is deemed as a high score and of concern to DMEPA.

Orthographic similarities: Both names share 4 out of 7 letters in the same position ('r' and 'din') and the letters 'Ke' may look like the letters 'Ve' when scripted.
Phonetic similarities:
Both names have 3 syllables: Ker I din vs. Var I din
The first syllable has the same consonant ending sound 'r'; the middle vowel sound 'e' vs. 'a' may sound similar when spoken (voice study showed that 15/21 participants confused these sounds).
Identical 2nd and 3rd syllables

- In addition to the orthographic similarities and phonetic similarities, these products share similar product characteristics such as:

  Single strength; therefore, a strength is not required on a prescription.

  Kerydin is a topical solution applied to the affected nail(s) once daily for 48 weeks and Varidin is a vitamin supplement given once daily.

We note that we were only able to locate Varidin in two drug databases (Red Book online and Facts and Comparisons [Varidin Forte]) and the trademark was cancelled with USPTO as of June 20, 2008. All this seems to indicate that the product is no longer manufactured and/or marketed. However, we are concerned that due to the high phonetic and orthographic similarities between the names and the fact that Varidin is still listed in 2 common drug references that this could result in drug name confusion.

DMEPA would like to give you the opportunity to provide data indicating that the product Varidin is no longer manufactured and/or marketed. In addition, to have the name removed from the Red Book online and Facts and Comparisons databases, if possible.

Comments from the Applicant:

Anacor understood DMEPA's concerns and agreed to provide information indicating that Varidin was discontinued and not marketed. Anacor also agreed to send FDA their request to have the name Varidin removed from the Red Book, Facts and Comparisons, and other pertinent databases. Anacor mentioned that removal from the databases could take time but they would send to FDA their request for removal from the databases and evidence of Varidin's discontinued/non-marketed status by January 16, 2014. DMEPA agreed that evidence from Anacor showing the request for removal of the name Varidin from the databases was acceptable.

The call ended at 3:10 PM EST.

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/s/

JANET L ANDERSON
01/14/2014

Attinello, Cristina

From: Attinello, Cristina
Sent: Friday, June 20, 2014 2:42 PM
To: 'Carmen Rodriguez'
Cc: Gould, Barbara
Subject: RE: Kerydin
Attachments: PI 6-20-14.docx

Follow Up Flag: Follow up
Flag Status: Flagged

Hello,

Please see the attached draft PI for Kerydin. Please review and return to the Agency, with any applicable revisions in track changes, by COB Monday, June 23, 2014.

Thanks,

Cristina

From: Carmen Rodriguez [mailto:crodriguez@anacor.com]
Sent: Thursday, June 19, 2014 2:02 PM
To: Attinello, Cristina
Subject: RE: Kerydin

Thanks you so much Cristina!
Let me know when you have any news to share on the NDA application status that would help us to further assess printing risks.
Best
Carmen

From: Attinello, Cristina [mailto:Cristina.Attinello@fda.hhs.gov]
Sent: Thursday, June 19, 2014 10:34 AM
To: Carmen Rodriguez
Subject: Kerydin

Hello,

We are in receipt of the draft PI and note your editorial changes. The draft PI, and NDA application, remain under review.

If you opt to move forward with printing, as you reference in your voice mail message of 6-19-14, that would be at your own risk.

Thanks,

Cristina Attinello, MPH
Senior Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
06/20/2014

Attinello, Cristina

From: Attinello, Cristina
Sent: Friday, June 06, 2014 8:08 AM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Gould, Barbara
Subject: NDA 204427 Draft Kerydin PI

Hello Carmen,

Please see the attached draft PI for Kerydin. Please review and return to the Agency, with any applicable revisions in track changes, **by COB Wednesday, June 11, 2014.**

Thanks,

Cristina Attinello, MPH
Senior Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
06/06/2014

MEMORANDUM OF TELECONFERENCE

MEETING DATE: June 4, 2014
TIME: 3:00 PM
LOCATION: Teleconference
APPLICATION: NDA 204427
DRUG NAME: Kerydin (tavaborole) topical solution, 5%

FDA ATTENDEES:
Tatiana Oussova, MD, MPH, Deputy Safety Director, DDDP
David Kettl, MD, Clinical Team Leader, DDDP
Milena Lolic, MD, Clinical Reviewer, DDDP
Doanh Tran, PhD, Clinical Pharmacology Team Leader, DCP3
An-Chi Lu, MS, PharmD, Clinical Pharmacology Reviewer, DCP3
Mohamed Alosh, PhD, Biostatistics Team Leader, DB III
Barbara Gould, MBAHCM, Chief, Project Management Staff, DDDP
Cristina Attinello, MPH, Senior Regulatory Health Project Manager, DDDP

SPONSOR ATTENDEES:
Carmen Rodriguez, MSc., Sr. VP, Regulatory Affairs and Quality
Amy Walker (Wang), Sr. Manager, Regulatory Affairs
Lee Zane, MD, MAS, FAAD, Sr. VP and Chief Medical Officer
Xiaoming Lin, VP, Clinical Research and Development

BACKGROUND:
The Agency and the applicant have engaged in labeling discussions since March 25, 2014. A teleconference to discuss disagreements on components of the draft PI was previously held on May 2, 2014. Following this 15 minute teleconference, the applicant requested to speak with the Agency once again. On May 13, 2014, the applicant submitted to the NDA an outline of talking points for the call.

DISCUSSION POINTS:
The Agency and the applicant shared their positions regarding the areas of discrepancy (Table 2 and nail penetration information in section 12.1) in the draft PI.

Ultimately, the Agency proposed that:
-information regarding (b) (4) be removed from section 12.1
-the Agency version of Table 2 be used in the draft PI

ACTION ITEMS:
The Agency will revise the draft PI per the outcome of the teleconference and provide to the applicant for review.

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/s/

CRISTINA Petruccelli Attinello
06/06/2014

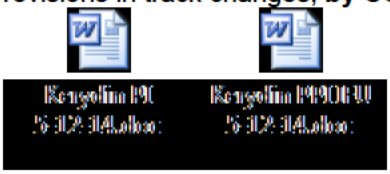
Attinello, Cristina

From: Attinello, Cristina
Sent: Monday, May 12, 2014 7:41 AM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Gould, Barbara
Subject: NDA 204427 Draft Kerydin PI, PPI, IFU

Follow Up Flag: Follow up
Flag Status: Flagged

Hello Carmen,

Please see the attached draft PI, PPI, and IFU for Kerydin. Please review and return to the Agency, with any applicable revisions in track changes, **by COB Tuesday, May 13, 2014.**



Thanks,

Cristina Attinello, MPH
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
05/12/2014

MEMORANDUM OF TELECONFERENCE

MEETING DATE: May 2, 2014
TIME: 2:15 PM
LOCATION: Teleconference
APPLICATION: NDA 204427
DRUG NAME: Kerydin (tavaborole) topical solution, 5%

FDA ATTENDEES:
Tatiana Oussova, MD, MPH, Deputy Safety Director, DDDP
David Kettl, MD, Clinical Team Leader, DDDP
Milena Lolic, MD, Clinical Reviewer, DDDP
Doanh Tran, PhD, Clinical Pharmacology Team Leader, DCP3
An-Chi Lu, MS, PharmD, Clinical Pharmacology Reviewer, DCP3
Mohamed Alosh, PhD, Biostatistics Team Leader, DB III
Kathleen Fritsch, PhD, Biostatistics Reviewer, DB III
Barbara Gould, MBAHCM, Chief, Project Management Staff, DDDP
Cristina Attinello, MPH, Regulatory Health Project Manager, DDDP

SPONSOR ATTENDEES:
Carmen Rodriguez, MSc., Sr. VP, Regulatory Affairs and Quality
Amy Walker (Wang), Sr. Manager, Regulatory Affairs
Lee Zane, MD, MAS, FAAD, Sr. VP and Chief Medical Officer

BACKGROUND:
The Agency and the applicant have engaged in labeling discussions since March 25, 2014. Following a recent exchange of draft labels and labeling, the applicant requested a teleconference with the Agency to discuss two pending concerns in the draft PI. This teleconference was scheduled to explain the Agency's position regarding these items in the draft PI.

DISCUSSION POINTS:
The Agency and the applicant shared their positions regarding the areas of discrepancy in the draft PI.

Ultimately, the Agency proposed that:
-information regarding (b) (4) be removed from section 12.1
-the Agency version of Table 2 be used in the draft PI

ACTION ITEMS:
The Agency will revise the PI per the outcome of the teleconference and provide to the applicant by May 9, 2014.

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/s/

CRISTINA Petruccelli Attinello
05/05/2014

Attinello, Cristina

From: Attinello, Cristina
Sent: Thursday, April 24, 2014 2:34 PM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Gould, Barbara
Subject: NDA 204427 Kerydin

Hello,

Thank you for your latest submission dated April 18, containing draft labels and labeling. Your submission included a request to have a teleconference with the Agency regarding the draft PI for Kerydin. We do not see the need for a teleconference to discuss labeling. Our labeling recommendations are based on objectives for consistent presentations of efficacy results across antifungal products and are consistent with comments to other applicants. With respect to the two areas of concern within the PI that you identify:

- We still recommend deleting the (b) (4) claim, as this type of study is generally not included in product labeling. The true measure of efficacy for this product is the results obtained in the Phase 3 clinical studies. The applicability of the (b) (4) is not known.

- For Table 2, our recommendation is to only include the primary endpoints (b) (4)

We refer back to the track changed PI that was sent to you on April 14. We have agreement on the PPI/IFU and carton and container labels that you returned to us on April 18. Please provide a response **by COB Monday, April 28, 2014** containing the draft PI.

Thanks,

Cristina Attinello, MPH
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
04/25/2014

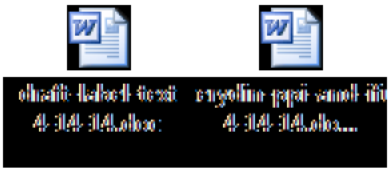
Attinello, Cristina

From: Attinello, Cristina
Sent: Monday, April 14, 2014 2:51 PM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Gould, Barbara
Subject: RE: NDA 204427 Kerydin (tavaborole) topical solution, 5%: Draft Labeling and PMR Discussion

Follow Up Flag: Follow up
Flag Status: Flagged

Hello,

Please review the attached draft labeling files and return them with track changes **by COB Friday, April 18, 2014.**



We have the following comments for your draft carton and container labels. Please apply the below edits and submit new proposed labels by the above date.

A. Container Label and Carton Labeling
1. The net quantity statement (i.e. 10 mL) is more prominent than more relevant information (i.e. the dosage form and strength). Increase the prominence of the dosage form and strength statements to the same size font as the established name.

B. Container Label
1. To implement the above mentioned recommendation on this small label without crowding the label we recommend that you either delete or reduce the size of the graphic that appears above the proprietary name.
2. The net quantity statement is in close proximity to the strength statement and highlighted in purple color; therefore, after implementing the previous recommendations, ensure that the size of the net quantity statement uses a smaller font than the strength statement and black color font.

Please confirm receipt of this email. Please let me know if you have any questions.

Thanks,

Cristina

From: Attinello, Cristina
Sent: Tuesday, March 25, 2014 2:33 PM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Amy Wang (awang@anacor.com)
Subject: NDA 204427 Kerydin (tavaborole) topical solution, 5%: Draft Labeling and PMR Discussion

Hello,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kerydin (tavaborole) topical solution, 5%.

The Agency has identified the following postmarketing requirement (PMR) study to be conducted post approval:

PMR for a pharmacokinetic/safety trial of tavaborole topical solution, 5% in 40 pediatric subjects age 12-17 years and 11 months with onychomycosis of toenails (b) (4). Pharmacokinetic assessments will be done in at least 16 evaluable subjects under maximal use conditions.

Final Protocol Submission:	12/31/2014
Study/Trial Completion:	12/31/2016
Final Report Submission:	06/30/2017

Submit to your NDA **by Tuesday, April 1, 2014,** concurrence with the above proposed dates for final protocol submission, study/trial completion, and final report submission for the required postmarketing study. Contact me if you have any questions.

Please see the attached draft Agency proposed labeling for Kerydin (tavaborole) topical solution, 5%. Please review the attached files and return them with track changes **by Tuesday, April 1, 2014.**

<< File: Kerydin PI.doc >> << File: Kerydin PPI.doc >> << File: Kerydin IFU.doc >>
As a reminder, you are responsible for submitting prescribing information that meet the SRPI requirements. You may use the SRPI resources available at
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm to guide you.

We have the following comments for your draft carton and container labels. Please apply the below edits and submit new proposed labels **by Tuesday, April 1, 2014.**

A. Proposed Container Label and Carton Labeling
1. As currently presented the established name is not commensurate in prominence to the proprietary name. Revise the presentation of the established name to ensure that it is at least ½ the size of the proprietary name and commensurate in prominence to the proprietary name taking into account all pertinent factors, including typography, layout, contrast, and other printing features per CFR 201.10(g)(2).
2. The proposed packaging configuration (with a glass pointed-tip dropper) is similar to ophthalmic solutions and may be a source of wrong route of administration errors. To reinforce the correct route of administration, increase the size of the route of administration statement “For Topical Use Only” and add the statement “Nor for oral, ophthalmic, or intravaginal use” below it using a smaller font.

B. Proposed Carton Labeling
1. The use of (b) (4) makes the route of administration statement “For Topical Use Only” difficult to read. Relocate the route of administration statements “For Topical Use Only” and “Not for oral, ophthalmic, or intravaginal use” (from comment A.2. above) to a white background area and use color font. You may achieve this by (b) (4).
2. Replace the placeholder “tradename” with the proprietary name “Kerydin” on the description statement “Each mL of Kerydin…” and on the statement “Use only supplied dropper to apply Kerydin”.
3. Change the Dosage statement to read: “Use only as prescribed by your physician. See package insert for dosage information.”

Please confirm receipt of this email and inform me if you have any questions.

Thanks,

Cristina Petruccelli Attinello, MPH
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
04/16/2014

Attinello, Cristina

From: Attinello, Cristina
Sent: Tuesday, March 25, 2014 2:33 PM
To: Carmen Rodriguez (crodriguez@anacor.com)
Cc: Amy Wang (awang@anacor.com)
Subject: NDA 204427 Kerydin (tavaborole) topical solution, 5%: Draft Labeling and PMR Discussion

Hello,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kerydin (tavaborole) topical solution, 5%.

The Agency has identified the following postmarketing requirement (PMR) study to be conducted post approval:

PMR for a pharmacokinetic/safety trial of tavaborole topical solution, 5% in 40 pediatric subjects age 12-17 years and 11 months with onychomycosis of toenails (b) (4). Pharmacokinetic assessments will be done in at least 16 evaluable subjects under maximal use conditions.

Final Protocol Submission:	12/31/2014
Study/Trial Completion:	12/31/2016
Final Report Submission:	06/30/2017

Submit to your NDA **by Tuesday, April 1, 2014,** concurrence with the above proposed dates for final protocol submission, study/trial completion, and final report submission for the required postmarketing study. Contact me if you have any questions.

Please see the attached draft Agency proposed labeling for Kerydin (tavaborole) topical solution, 5%. Please review the attached files and return them with track changes **by Tuesday, April 1, 2014.**

As a reminder, you are responsible for submitting prescribing information that meet the SRPI requirements. You may use the SRPI resources available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm to guide you.

We have the following comments for your draft carton and container labels. Please apply the below edits and submit new proposed labels **by Tuesday, April 1, 2014.**

A. Proposed Container Label and Carton Labeling
1. As currently presented the established name is not commensurate in prominence to the proprietary name. Revise the presentation of the established name to ensure that it is at least ½ the size of the proprietary name and commensurate in prominence to the proprietary name taking into account all pertinent factors, including typography, layout, contrast, and other printing features per CFR 201.10(g)(2).
2. The proposed packaging configuration (with a glass pointed-tip dropper) is similar to ophthalmic solutions and may be a source of wrong route of administration errors. To reinforce the correct route of administration, increase the size of the route of administration statement "For Topical Use Only" and add the statement "Nor for oral, ophthalmic, or intravaginal use" below it using a smaller font.

B. Proposed Carton Labeling
1. The use of (b) (4) makes the route of administration statement "For Topical Use Only" difficult to read. Relocate the route of administration statements "For Topical Use Only" and "Not for oral, ophthalmic, or

intravaginal use" (from comment A.2. above) to a white background area and use color font. You may achieve this by (b) (4).
2. Replace the placeholder "tradename" with the proprietary name "Kerydin" on the description statement "Each mL of Kerydin…" and on the statement "Use only supplied dropper to apply Kerydin".
3. Change the Dosage statement to read: "Use only as prescribed by your physician. See package insert for dosage information."

Please confirm receipt of this email and inform me if you have any questions.

Thanks,

Cristina Petruccelli Attinello, MPH
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology & Dental Products
White Oak, Bldg. 22, Room 5350
Phone: 301-796-3986
Fax: 301-796-9895

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/s/

CRISTINA Petruccelli Attinello
03/25/2014

PeRC PREA Subcommittee Meeting Minutes
February 5, 2014

PeRC Members Attending:
Lynne Yao
Rosemary Addy
George Greeley
Jane Inglese
Hari Cheryl Sachs
Wiley Chambers
Tom Smith
Peter Starke
Julia Pinto
Lily Mulugeta
Dianne Murphy

Agenda

NDA	204427	Tavaborole (kerydin) Partial Waiver/Deferral	Onychomycosis (b) (4)

(b) (4)

Tavaborole (kerydin) Partial Waiver/Deferral

- NDA 204427 seeks marketing approval for Tavaborole (kerydin) for the treatment of onychomycosis (b) (4)
- The application has a PDUFA goal date of July 29, 2014.
- The application triggers PREA as directed to a new active ingredient.
- *PeRC Recommendations:*
    - The PeRC disagreed with a partial waiver in pediatric patients aged birth to less than 12 years because studies would be impossible or highly impracticable. The PeRC noted that several publications describe treatment of onychomycosis in patients less than 12 years of age. The PeRC chair requested a vote on this issue. Eight PeRC members agreed with lowering the waiver down to 6 years of age, and one PeRC member disagreed. Therefore, the PeRC recommended that studies should be conducted in pediatric patients down to 6 years of age, but a waiver for pediatric patients less than 6 years of age may be acceptable. The number of pediatric patients having onychomycosis due to dermatophytes is far fewer than the number of adults having this condition, but there appears to be sufficient pediatric patients to study. Use data from Penlac may be useful to inform the age cut-off.
    - The PeRC recommended utilizing extrapolation of efficacy be considered to address the recommended requirement to study pediatric patients aged 6 to 11.
    - The PeRC agreed with a deferral in pediatric patients aged 12 to less than 18 years because adult studies have been completed and the product is ready for approval. The PeRC recommended including pediatric patients down to 6 years of age in the deferred study.

(b) (4)


(b) (4)

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/s/

JANE E INGLESE
02/18/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

(E) CAC – FINAL REPORT

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (tavaborole) topical solution, 5%.

Our Executive Carcinogenicity Assessment Committee (ECAC) reviewed your oral rat study report and dermal mouse study report on December 10, 2013. As requested in your July 26, 2013 submission, a copy of the final report of the ECAC regarding (tavaborole) topical solution, 5% is enclosed.

The recommendations made by the ECAC are advisory in nature and should not be interpreted as a measure of the approvability of any application for this product.

If you have any questions, call Cristina Attinello, Regulatory Project Manager, at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

Barbara Hill, PhD
Pharmacology Supervisor
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure:
ECAC Meeting Minutes

Executive CAC
Date of Meeting: December 10, 2014

Committee: David Jacobson Kram, Ph.D., OND IO, Chair
Abby Jacobs, Ph.D., OND IO, Member
Paul Brown, Ph.D., OND IO, Member
David Joseph, Ph.D., DGIEP, Alternate Member
Barbara Hill, Ph.D., DDDP, Presenting Reviewer /Supervisor

Author of Minutes: Barbara Hill, Ph.D.

The following information reflects a brief summary of the Committee discussion and its recommendations.

NDA #: 204-427
Drug Name: Tavaborole solution, 5%
Sponsor: Anacor Pharmaceuticals Inc.

Background:

Tavaborole is a (b) (4) borinic acid complex that exhibits anti-fungal activity. Tavaborole solution is being developed for the topical treatment of onychomycosis. An oral rat carcinogenicity study report and a dermal mouse carcinogenicity study report were submitted to the original NDA to support approval.

Oral Rat Carcinogenicity Study:

Oral (gavage) doses of 0 (vehicle), 12.5, 25 and 50 mg/kg/day tavaborole were administered to Sprague-Dawley rats (65/sex/dose) once daily for 104 weeks. The vehicle used in this study was 1% carboxymethylcellulose and the dose volume was 10 ml/kg/day.

A treatment related increased incidence of hyperplasia of the non-glandular stomach was noted in high dose animals. However, the clinical significance of this finding is unclear since the nonglandular stomach is absent in humans. No statistically significant differences in tumor incidence were observed in rats of either gender according to the statistical criteria used by the Executive CAC.

Dermal Mouse Carcinogenicity Study:

Topical doses of 0 (vehicle), 5, 10 and 15% tavaborole solution were administered to CD-1 mice (65/sex/dose) once daily for 104 weeks. The vehicle used in this study was propylene glycol/ethanol (20/80, v/v). The dose volume was 5 µl/cm^2 through day 14 and 1 µl/g thereafter.

A treatment related increased incidence/severity of epidermal hyperplasia, hyperkeratosis and inflammation was noted in treated skin which correlated with treatment related dermal irritation

noted at the treatment site. No statistically significant differences in tumor incidence were observed in mice of either gender according to the statistical criteria used by the Executive CAC.

Executive CAC Recommendations and Conclusions:

Oral Rat Carcinogenicity Study

- The Committee agreed that the study was adequate, noting prior Executive CAC concurrence with the protocol.

- The Committee concurred that the study was negative for drug related neoplasms.

Dermal Mouse Carcinogenicity Study

- The Committee agreed that the study was adequate, noting prior Executive CAC concurrence with the protocol.

- The Committee concurred that the study was negative for drug related neoplasms.

David Jacobson Kram, Ph.D.
Chair, Executive CAC

cc:\
/Division File, DDDP
/BHill/Reviewer/Supervisor, DDDP
/CAttinello/PM, DDDP
/ASeifried, OND IO

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/s/

ADELE S SEIFRIED
12/11/2013

ABIGAIL C JACOBS
12/11/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427 **INFORMATION REQUEST**

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (tavaborole) topical solution, 5%.

We are reviewing the Clinical section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide representative photographs taken at Week 52 from subjects enrolled in studies 301 and 302 as follows:
   - 8 subjects from each study who achieved a "clear target nail" at Week 52 (select qualifying subjects with the smallest USUBJID)
   - 8 subjects from each study who achieved an "almost clear nail" (<10% involvement) (select qualifying subjects with the smallest USUBJID)
2. Provide photographs representative of AE "ingrown toenail" if available. Include photos from all available visits for these subjects.

Respond to the above requests by December 27, 2013.

If you have any questions, call Cristina Attinello, Regulatory Project Manager, at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

David Kettl, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

ADELE S SEIFRIED
12/11/2013

ABIGAIL C JACOBS
12/11/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

METHODS VALIDATION
MATERIALS RECEIVED

Anacor Pharmaceuticals, Inc.
Attention: Carmen R. Rodriguez, M. Sc.
1020 East Meadow Circle
Palo Alto, CA 94303-4230
FAX: (650) 543-7660

Dear Carmen R. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tavaborole Topical Solution, 5% and to our September 26, 2013, letter requesting sample materials for methods validation testing.

We acknowledge receipt on October 11, 2013, of the sample materials and documentation that you sent to the Division of Pharmaceutical Analysis (DPA) in St. Louis.

If you have questions, you may contact me by telephone (314-539-3815), FAX (314-539-2113), or email (Michael.Trehy@fda.hhs.gov).

Sincerely,

{See appended electronic signature page}

Michael L. Trehy
MVP Coordinator
Division of Pharmaceutical Analysis
Office of Testing and Research
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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/s/

MICHAEL L TREHY
10/11/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427 **INFORMATION REQUEST**

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (tavaborole) topical solution, 5%.

We are reviewing the Clinical Pharmacology section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. For the analysis of [redacted] (b) (4) in 24-hour urine samples in trial P06118, provide method validation reports for these assays.
2. For the analysis of tavaborole metabolites (M5 and M6a) in plasma and urine in trail P06118, provide both the bioanalytical and method validation reports.

Respond to the above request by October 23, 2013

If you have any questions, call Barbara Gould, Chief, Project Management Staff, at (301) 796-4224.

Sincerely,

{See appended electronic signature page}

David Kettl, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

DAVID L KETTL
10/10/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

REQUEST FOR METHODS VALIDATION MATERIALS

Anacor Pharmaceuticals Inc
Attention: Carmen R. Rodriguez
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94303-4230

Dear Carmen R. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tavaborole Topical Solution, 5%.

We will be performing methods validation studies on Tavaborole Topical Solution, 5%, as described in NDA 204427.

In order to perform the necessary testing, we request the following sample materials and equipments:

Method, current version

Determination of Assay and related substances in [redacted] (by HPLC)
HPLC Identification, Assay for AN2690, Determination of Related Substances in AN2690 Drug Substances and AN2690 Topical Solution 5% w/w[redacted]

Samples and Reference Standards

[redacted] mg	[redacted] (AN2690) reference standard
[redacted] mg	[redacted] (AN2690) sample of API
8	bottles of Tavaborole Topical Solution 5%, Topical Solution 10 mL
[redacted] mL	AN2690 placebo solution
[redacted] mg	[redacted] impurity if available
[redacted] mg	[redacted] impurity if available
[redacted] mg	[redacted] impurity if available

Equipment

1 [redacted]

Please include the MSDSs and the Certificates of Analysis for the sample and reference materials.

Forward these materials via express or overnight mail to:

Food and Drug Administration
Division of Pharmaceutical Analysis
Attn: Sample Custodian
645 S Newstead
St. Louis, MO 63110

Please notify me upon receipt of this letter. You may contact me by telephone (314-539-3815), FAX (314-539-2113), or email (michael.trehy@fda.hhs.gov).

Sincerely,

{See appended electronic signature page}

Michael L. Trehy, Ph.D.
MVP coordinator
Division of Pharmaceutical Analysis
Office of Testing and Research
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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/s/

MICHAEL L TREHY
09/26/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

FILING COMMUNICATION -
FILING REVIEW ISSUES IDENTIFIED

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms Rodriguez:

Please refer to your New Drug Application (NDA) dated July 26, 2013, received July 29, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for (tavaborole) topical solution, 5%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. This application is also subject to the provisions of "the Program" under the Prescription Drug User Fee Act (PDUFA) V (refer to http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm . Therefore, the user fee goal date is July 29, 2014.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by April 04, 2014. In addition, the planned date for our internal mid-cycle review meeting is December 27, 2013. We are not currently planning to hold an advisory committee meeting to discuss this application.

During our filing review of your application, we identified the following potential review issues:

CHEMISTRY, MANUFACTURING AND CONTROLS

1. The mass spectra submitted in section 3.2.S.3.1 [redacted] (b) (4) and section 3.2.S.5 Reference Standards do not correspond. Explain the differences and provide details of the experimental conditions under which each spectrum was obtained.

2. You propose to [redacted] (b) (4) testing for the Microbial Limits test for drug product release. [redacted] (b) (4) However, due to the nature of your product and microbiological data that you have provided in your application, you may waive microbial limits testing for product release. If you choose to omit microbial limits testing for release, then remove the microbial limits tests and acceptance criteria from the drug product release specification. Alternatively, you may retain a microbial limits specification for product release, but testing must be performed on every lot of drug product produced. Submit a revised drug product release specification for whichever microbial limits testing alternative that you select.

3. You describe microbial limits testing performed according to methods described in USP <61> and USP <62>. Verify the suitability of these testing methods for your drug product.

4. Submit a representative sample for the evaluation of dosage form. The sample should be accompanied with corresponding certificate of analysis.

5. Submit quantitative analytical data for fluorine and boron in tavaborole drug substance to support the presence of one fluorine and one boron molecule in the structure of tavaborole.

6. Submit suppliers' certificates of analysis for the starting material, reagents and solvents used in the manufacture of tavaborole drug substance.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

We request that you submit the following information:

CLINICAL MICROBIOLOGY

7. Submit all nonclinical study reports that pertain to clinical microbiology for review including 002-NCL-PP-003-01 and 002-NCL-015-01.

CLINICAL PHARMACOLOGY

8. For the Thorough QTc Trial AN2690-ONYC-102, provide the duration of pharmacokinetic plasma samples storage, from sample collection to sample analysis, to ensure that it is within the available long-term stability of [redacted] (b) (4)

CLINICAL

9. Submit your rationale for assuming the applicability of foreign data to U.S. population/practice of medicine.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

HIGHLIGHTS (HL)

GENERAL FORMAT

Each summarized statement in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contains more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each information summary (e.g. end of each bullet).

Comment: *References to the specific section or subsection in the FPI needs to added for all items in "DOSAGE AND ADMINISTRATION" and "DOSAGE FORMS AND STRENGTHS" in the Highlights.*

HIGHLIGHTS DETAILS

Highlights Limitation Statement

The **bolded** HL Limitation Statement must be on the line immediately beneath the HL heading and must state: "**These highlights do not include all the information needed to use (insert name of drug product in UPPER CASE) safely and effectively. See full prescribing information for (insert name of drug product in UPPER CASE)**."

Comment: *The name of the drug product should be in "UPPER CASE".*

FULL PRESCRIBING INFORMATION (FPI)

GENERAL FORMAT

The **bolded** section and subsection headings must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. If a section/subsection is omitted, the numbering does not change.

Comment: *The title of section 17 should be "PATIENT COUNSELING INFORMATION" without the word* (b) (4) *inserted. This should be corrected in both TOC of and FPI.*

The preferred presentation for cross-references in the FPI is the section heading (not subsection heading) followed by the numerical identifier in italics. For example, [*see Warnings and Precautions (5.2)*].

Comment: *The cross reference in section 12.1 should be corrected to read [see CLINICAL PHARMACOLOGY (12.4)].*

FULL PRESCRIBING INFORMATION DETAILS

Adverse Reactions
When clinical trials adverse reactions data is included (typically in the "Clinical Trials Experience" subsection of Adverse Reactions), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

> *"Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice."*

Comment: *The statement should be modified to refer to "clinical trials" instead of* (b) (4)

Patient Counseling Information
Must reference any FDA-approved patient labeling, include the type of patient labeling, and use one of the following statements at the beginning of Section 17:

- "See FDA-approved patient labeling (Medication Guide)"
- "See FDA-approved patient labeling (Medication Guide and Instructions for Use)"
- "See FDA-approved patient labeling (Patient Information)"
- "See FDA-approved patient labeling (Instructions for Use)"
- "See FDA-approved patient labeling (Patient Information and Instructions for Use)"

Comment: *The words "approved patient labeling" should not be capitalized in the labeling, and the overall statement should not be italicized.*

We request that you resubmit labeling that addresses these issues by September 30, 2013. The resubmitted labeling will be used for further labeling discussions.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI), Medication Guide, and patient PI (as applicable). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), Medication Guide, and patient PI (as applicable), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a partial waiver and for a partical waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

If you have any questions, call Barbara Gould, Chief, Project Management Staff, at (301) 796-4224.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, MD, FAAD
Director
Division of Division of Dermatology and Dental Product
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

SUSAN J WALKER
09/22/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427 **INFORMATION REQUEST**

Anacor Pharmaceuticals, Inc.
Attention: Carmen R. Rodriguez, M.Sc.,
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94303-4230

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (tavaborole) Topical Solution, 5%.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following information request. We request a prompt written response by August 20, 2013 in order to continue our evaluation of your NDA.

> Resubmit the file "Description of the Manufacturing Process and Process Controls" to section 3.2.S.2.2.

If you have any questions, call Barbara Gould, MBAHCM, Chief, Project Management Staff, at (301) 796-4224.

Sincerely,

{See appended electronic signature page}

Gary Chiang, MD
Acting Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

GARY T CHIANG
08/16/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

NDA ACKNOWLEDGMENT

Anacor Pharmaceuticals, Inc.
Attention: Carmen R. Rodriguez, M.Sc.
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94303-4230

Dear Ms. Rodriguez:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: (tavaborole) Topical Solution, 5%

Date of Application: July 26, 2013

Date of Receipt: July 29, 2013

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on September 27, 2013, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology and Dental Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me at (301) 796-4224.

Sincerely,

{See appended electronic signature page}

Barbara Gould, MBAHCM
Chief, Project Management Staff
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

BARBARA J GOULD
08/06/2013

LATE-CYCLE COMMUNICATION DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

LATE-CYCLE MEETING MINUTES

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, MSc
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) dated July 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kerydin (tavaborole) topical solution, 5%.

We also refer to the Late-Cycle Meeting (LCM) between representatives of your firm and the FDA on April 1, 2014.

A copy of the official minutes of the LCM is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Cristina Attinello, Regulatory Project Manager, at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

David Kettl, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure:
Late-Cycle Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF LATE-CYCLE MEETING MINUTES

Meeting Date and Time: April 1, 2014, 11 AM (EST)
Meeting Location: Teleconference

Application Number: NDA 204427
Product Name: Kerydin (tavaborole) topical solution, 5%
Applicant Name: Anacor Pharmaceuticals, Inc.

Meeting Chair: David Kettl, MD
Meeting Recorder: Cristina Attinello

FDA ATTENDEES
Julie Beitz, MD, Director, ODE III
Amy Egan, MD, Deputy Director (acting), ODE III
LCDR, Richard Ishihara, Regulatory Scientist (acting), ODE III
Stanka Kukich, MD, Deputy Director, DDDP
David Kettl, MD, Clinical Team Leader, DDDP
Milena Lolic, MD, Clinical Reviewer, DDDP
Doanh Tran, PhD, Clinical Pharmacology Team Leader, DCP3
An-Chi Lu, MS, PharmD, Clinical Pharmacology Reviewer, DCP3
Barbara Gould, MBAHCM, Chief, Project Management Staff, DDDP
Cristina Attinello, MPH, Regulatory Health Project Manager, DDDP
Stacy Blake, Regulatory Health Project Manager, DDDP
Belainesh Robnett, MS, Regulatory Health Project Manager, DDDP
Laya Keyvan, Regulatory Health Project Manager, DDDP
Jennifer Dao, Regulatory Health Project Manager, DDDP
Kimberly Taylor, Operations Research Analyst, CDER

EASTERN RESEARCH GROUP ATTENDEES
(b) (6)

APPLICANT ATTENDEES
Carmen Rodriguez, MSc, Sr. VP, Regulatory Affairs and Quality Assurance
Amy Wang, Sr. Manager, Regulatory Affairs
Lee Zane, MD, MAS, FAAD, Sr. VP, Clinical and Chief Medical Officer
Xiaoming Lin, VP, Clinical Research and Development

1.0 BACKGROUND

NDA 204427 was submitted on July 26, 2013 for Kerydin (tavaborole) topical solution, 5%.

Proposed indication: for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*

PDUFA goal date: July 29, 2014

FDA issued a Background Package in preparation for this meeting on March 19, 2014.

2.0 DISCUSSION

1. Introductory Comments
   - Welcome, Introductions, Ground rules, Objectives of the meeting

2. Discussion of Minor Review Issues
   - Labeling discussions pending

3. Postmarketing Requirements/Postmarketing Commitments
   - Post Marketing Requirement (PMR) for a pharmacokinetic/safety trial of tavaborole topical solution, 5% in 40 pediatric subjects age 12-17 years and 11 months with onychomycosis of the toenails. Pharmacokinetic assessments will be done in at least 16 evaluable subjects under maximal use conditions.

     PMR/PMC Schedule Milestones:

Final Protocol Submission:	12/31/2014
Study/Trial Completion:	12/31/2016
Final Report Submission:	06/30/2017

4. Review Plans
   - At this time there are no significant review issues.
   - The Office of Compliance has given an overall recommendation of acceptable for the manufacturing sites.
   - The Office of Scientific Investigation (OSI) inspection results are pending.

5. Wrap-up and Action Items

Meeting Discussion:

The applicant presented (b) (4)

(b) (4) The Agency is aware of recruitment challenges and agreed to modify the milestone dates for study completion.

The applicant agreed with the Agency recommendation to conduct this PMR. New milestone dates were proposed as follows:

Study/Trial Completion:	12/31/2018
Final Report Submission:	06/30/2019

The Agency agreed that these milestone dates appear reasonable. Further protocol comments will be provided at the time of protocol submission.

No substantive review issues have been identified to date for this application. The applicant will respond with a counterproposal to Agency proposed draft labeling by April 4, 2014.

This application has not yet been fully reviewed by the signatory authority, division director, and Cross-Discipline Team Leader (CDTL) and therefore, this meeting did not address the final regulatory decision for the application.

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/s/

DAVID L KETTL
04/04/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204427

LATE CYCLE MEETING
BACKGROUND PACKAGE

Anacor Pharmaceuticals, Inc.
Attention: Carmen Rodriguez, MSc
Vice President, Regulatory Affairs and Quality
1020 East Meadow Circle
Palo Alto, CA 94309-4320

Dear Ms. Rodriguez:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kerydin (tavaborole) topical solution, 5%.

We also refer to the Late-Cycle Meeting (LCM) scheduled for April 1, 2014. Attached are our agenda and background package for this meeting.

If you have any questions, call Cristina Attinello, Regulatory Project Manager, at (301) 796-3986.

Sincerely,

{See appended electronic signature page}

Tatiana Oussova, MD, MPH
Deputy Director for Safety
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Late-Cycle Meeting Background Package

LATE-CYCLE MEETING BACKGROUND PACKAGE

Meeting Date and Time: April 1, 2014, 11am EST
Meeting Location: TBD

Application Number: NDA 204427
Product Name: Kerydin (tavaborole) topical solution, 5%
Proposed Indication: Treatment of onychomycosis (b) (4)
Applicant Name: Anacor Pharmaceuticals, Inc.

INTRODUCTION

The purpose of a Late-Cycle Meeting (LCM) is to share information and to discuss any substantive review issues that we have identified to date, Advisory Committee (AC) meeting plans (if scheduled), and our objectives for the remainder of the review. The application has not yet been fully reviewed by the signatory authority, division director, and Cross-Discipline Team Leader (CDTL) and therefore, the meeting will not address the final regulatory decision for the application. We are sharing this material to promote a collaborative and successful discussion at the meeting.

During the meeting, we may discuss additional information that may be needed to address the identified issues and whether it would be expected to trigger an extension of the PDUFA goal date if the review team should decide, upon receipt of the information, to review it during the current review cycle. If you submit any new information in response to the issues identified in this background package prior to this LCM or the AC meeting, if an AC is planned, we may not be prepared to discuss that new information at this meeting.

BRIEF MEMORANDUM OF SUBSTANTIVE REVIEW ISSUES IDENTIFIED TO DATE

1. Discipline Review Letters

No Discipline Review letters have been issued to date.

2. Substantive Review Issues

There are no substantive review issues at this time.

ADVISORY COMMITTEE MEETING

An Advisory Committee meeting is not planned.

REMS OR OTHER RISK MANAGEMENT ACTIONS

No issues related to risk management have been identified to date.

LCM AGENDA

1. Introductory Comments – 5 minutes
   - Welcome, Introductions, Ground rules, Objectives of the meeting

2. Discussion of Minor Review Issues – 2 minutes
   - Labeling discussions pending

3. Postmarketing Requirements/Postmarketing Commitments – 5 minutes
   - Post Marketing Requirement (PMR) for a pharmacokinetic/safety trial of tavaborole topical solution, 5% in pediatric subjects age 12-17 years and 11 months with onychomycosis of toenails due to dermatophytes.

4. Review Plans – 2 minutes
   - At this time there are no significant review issues.
   - The Office of Compliance has given an overall recommendation of acceptable for the manufacturing sites.
   - The Office of Scientific Investigation (OSI) inspection results are pending.

5. Wrap-up and Action Items – 2 minutes

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/s/

TATIANA OUSSOVA
03/19/2014