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RESEARCH**

APPLICATION NUMBER:

21-946

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

19 MAY 2006

NDA: 21-946

Drug Product Name

Proprietary:

N/A.

Non-proprietary:

Ketoconazole USP 2%
Topical Gel

Drug Product Priority Classification:

S

Review Number:

1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
28 SEP 2005	28 SEP 2005	23 JAN 2006	27 JAN 2006

Applicant/Sponsor

Name:

Barrier Therapeutics, Inc.

Address:

600 College Rd. East
Suite 3200
Princeton, NJ 08540

Representative:

Isabel Drzewiecki

Telephone:

609-945-1247

Name of Reviewer:

John W. Metcalfe, Ph.D.

Conclusion:

Recommend Approval.

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Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** New Drug Application.
 2. **SUBMISSION PROVIDES FOR:** A new drug.
 3. **MANUFACTURING SITE:**
DPT Laboratories, Ltd.
307 E. Josephine St.
San Antonio, TX. 78215
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Gel.
 - Topical.
 - 20 mg/g.
 5. **METHOD(S) OF STERILIZATION:** Not a sterile product.
 6. **PHARMACOLOGICAL CATEGORY:** Antifungal agent.
- B. **SUPPORTING/RELATED DOCUMENTS:** None.
- C. **REMARKS:**
The subject drug product is a non-sterile, topical antifungal agent. The consult request made to the New Drug Microbiology Staff by ONDQA seeks verification that the microbial limit assay validation report is acceptable in accordance with the USP microbial limit test.

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Executive Summary**I. Recommendations**

- A. Recommendation on Approvability** – NDA 21-946 is recommended for approval on the basis of product quality microbiology.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – Not applicable.

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – The processes used to manufacture the subject drug product are contained in type II DMF _____ This DMF was not required (nor requested by this reviewer) for the assessment of the microbiological quality of the subject drug product.
- B. Brief Description of Microbiology Deficiencies** – There are no microbiology deficiencies.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Not applicable.

III. Administrative

- A. Reviewer's Signature** _____
- B. Endorsement Block**
Bryan Riley, Ph.D.
- C. CC Block**
N/A

2 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

Withheld Track Number: Microbiology-

1/1

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/s/

John Metcalfe
5/22/2006 01:23:27 PM
MICROBIOLOGIST

Bryan Riley
5/22/2006 01:32:13 PM
MICROBIOLOGIST

DIVISION OF ANTI-INFECTIVE AND OPHTHALMOLOGY PRODUCTS
CONSULTATION FOR DIVISION OF DERMATOLOGIC AND DENTAL PRODUCTS
CLINICAL MICROBIOLOGY REVIEW COMMENTS

03/21/06

eNDA: 21-946

Proposed New Drug: Sebazole (ketoconazole USP 2%) Topical Gel

Applicant: Barrier Therapeutics, Inc., 600 College Road East, Suite 3200, Princeton, N.J.

Letter Dates: 09/28/05 (original), 01/09/06, and 01/18/06 (labeling).

Proposed Indication: Treating patients with seborrheic dermatitis.

The following Clinical Microbiology comments are to be communicated to the Applicant:

"The proposed microbiology section of the mycology labeling for NDA 21-946 is unacceptable.

1. Only pathogens relevant to the "approved" indication are allowed in the labeling. For seborrheic dermatitis, *Malassezia furfur* (formerly known as *Pityrosporum ovale*) can be allowed.

The following is recommended in order for the Agency to consider putting mycology information in the "Microbiology" portion of the package insert:

Methods of the Clinical and Laboratory Standards Institute (CLSI), formerly the National Committee for Clinical Laboratory Standards (NCCLS), for performing susceptibility (MICs) testing are the methods recognized by the FDA for generating susceptibility data. Data referenced to CLSI methods need not be accompanied by the details of the methodology. However, if susceptibility data are obtained by modifying the CLSI methods, or by other methods, a detailed description of the method, including the justification for the modification of the NCCLS method and the impact on susceptibility results, is included.

Note: Recent data from published literature can be submitted in lieu of performing susceptibility testing. The susceptibility data are to be 3 years old or less. The information provided should contain the method by which the susceptibility testing was performed and include quality control information for the susceptibility testing.

3. Quality Control organisms and ranges / parameters are to be determined and validated for ketoconazole before initiating susceptibility testing. The Applicant is referred to reference 1 for information on how quality control parameters can be established.
4. It is suggested that the aforementioned recommendations and mycology testing and protocols be submitted in writing (or electronically) to the Agency for review prior to initiating any mycology studies.

REFERENCE

- ¹ CLSI (formerly NCCLS). Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters: Approved Guideline. NCCLS document M23-A2. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898, 2001.

Harold V. Silver
Clinical Microbiology Reviewer
DAIOP
March 21, 2006

Fred Marsik, Ph.D.
Team Leader Microbiology HFD-520
FIN FJM 22 Mar 06
DAIOP

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/s/

Harold Silver
3/22/2006 12:50:36 PM
MICROBIOLOGIST

Please sign off. Proj Mgr: Please communicate Clinical Microbiology
comments to the Sponsor. Thanks.

Frederic Marsik
3/22/2006 04:37:52 PM
MICROBIOLOGIST