APPLICATION NUMBER:
21-738

CHEMISTRY REVIEW(S)
NDA 21-738

Extina (ketoconazole) Foam

Stiefel Laboratories, Inc.

Jane L. Chang, Ph.D.

Review Chemist

Division of Dermatologic and Dental Drug Products
HFD-540

Appears This Way
On Original
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1. NDA 21-738

2. REVIEW #: 2

3. REVIEW DATE: 06-JUN-2007

4. REVIEWER: Jane L. Chang

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7. NAME & ADDRESS OF APPLICANT:

Name: Stiefel Laboratories, Inc.
Address: 20 TW Alexander Drive
          Research Triangle Park, NC 27709
Representative: Marcia Gaido, Ph.D., R.A.C.
               Director, Regulatory Affairs
Telephone: Phone (919) 990-6202
           Fax (919) 990-6978

8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: Extina
   b) Non-Proprietary Name: Ketoconazole
   c) Code Name/# (ONDQA only): N/A
   d) Chem. Type/Submission Priority (ONDQA only):
      - Chem. Type: 3 (new dosage form per MAPP 7500.3)
      - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(2)

10. PHARMACOL. CATEGORY: Antifungal

11. DOSAGE FORM: Aerosol, Foam

12. STRENGTH/POTENCY: 2%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: _X_ Rx ___OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
   \( \square \) SPOTS product – Form Completed
   \( \times \) Not a SPOTS product

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

   \[
   \text{Ketoconazole}
   \]

   \[
   \text{C}_{26}\text{H}_{28}\text{Cl}_2\text{N}_4\text{O}_4 \quad \text{M.W.: 531.43} \quad \text{CAS-65277-42-1}
   \]

   or

   \[
   \text{Appears This Way}
   \]

   \[
   \text{On Original}
   \]
CMC REVIEW OF NDA 21-738

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

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\(^1\) Action codes for DMF Table:
- 1 – DMF Reviewed.
- Other codes indicate why the DMF was not reviewed, as follows:
  - 2 – Type 1 DMF
  - 3 – Reviewed previously and no revision since last review
  - 4 – Sufficient information in application
  - 5 – Authority to reference not granted
  - 6 – DMF not available
  - 7 – Other (explain under “Comments”)

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

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The Chemistry Review for NDA 21-738

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From a chemistry, manufacturing, and controls review perspective, this NDA may be approved.

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

The applicant is committed to address

II. Summary of Chemistry Assessments

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

(1) Drug Product

Ketoconazole Foam, 2\% is delivered in a quick-breaking, temperature-sensitive, patented foam vehicle platform. The manufacture of drug product involves

The proposed drug product specifications are acceptable to ensure product quality. The drug product specifications include testing for appearance, absorbance at minimum fill pressure, leakage, ketoconazole identity (release only), content of ketoconazole and related substances, microbial limits, apparent pH, ethanol content, weight loss (stability
only), product/packaging interactions (stability only), dispensing rate, and delivered amount. Acceptable acceptance criteria have been established for these tests except those for dispensing rate and delivered amount. The acceptance criteria for dispensing rate and delivered amount will be established when sufficient data become available (from commercial lots or within one year of NDA approval).

The proposed acceptance criterion of \( \text{b}(4) \) has not been adequately justified. As the correlation between the absorbance and quantity has not been established, it is unclear whether the \( \text{b}(4) \) the ICH Q3B qualification threshold. In order to resolve these issues, this reviewer recommended based on data from the clinical batches. However, the applicant maintained their proposal based on their manufacturing capability.

The concern with \( \text{b}(4) \) has been brought to the attention of the Pharm/tox reviewer, Dr. K. Mainigi and the Pharm/tox team leader, Dr. P. Brown. Since neither Dr. Mainigi nor Dr. Brown expressed any safety concern (see Dr. Brown’s review on 6/1/2007), the \( \text{b}(4) \) is not deemed to be a safety concern. It is believed that the \( \text{b}(4) \) would have little impact on the safety and efficacy of the drug product unless either the toxicology team or the clinical team has any reservation. Therefore, from the CMC perspective, the \( \text{b}(4) \) is considered to be acceptable based on the manufacturing capability.

The drug product will be packaged in two commercial package sizes, 50 g and 100 g cans, and a physician’s sample, 10 g cans. The CMC information for the 10 g and 100 g cans, provided in the 11/1/2000 amendment, was adequate to support the addition of these two packaging sizes.

Stability data on \( \text{b}(4) \) of each fill size of Ketoconazole Foam, 2% were provided, ranging from months of long-term and of accelerated conditions. The data showed increasing trends for absorbance at 490 nm and total related substances. The stability data support the proposed 12 months expiry for the 10 g professional sample size and 24 months for the 50 g and 100 g fill sizes when stored at controlled room temperature.

(2) Drug Substance

Ketoconazole is currently approved in the United States for use in three different prescription topical dosage forms (all at a concentration of 2%): Xolegel (NDA 21-
B. Description of How the Drug Product is Intended to be Used

Ketoconazole Foam, 2% is intended to be applied to the affected area(s) twice daily for four weeks, or as directed by a physician for topical treatment of seborrheic dermatitis in immunocompetent patients 12 years of age and older. Seborrheic dermatitis is a common, inflammatory skin condition that causes flaky, white to yellowish scales to form on oily or greasy areas such as the scalp, creases of the nose, or inside the ear.

Ketoconazole Foam, 2% is to be stored at controlled room temperature 68-77°F (20-25°C). When stored under the specified conditions, an expiration dating period of 12, 24, and 24 months can be supported for the 10 g, 50 g, and 100 g cans, respectively. The drug product should not be exposed to heat or stored at temperature above 120°F (49 °C), or stored under refrigerated conditions. The contents are flammable. Cautions should be taken to avoid fire, flame, and/or smoking during and immediately following application.

C. Basis for Approvability or Not-Approval Recommendation

From the CMC perspective, all the CMC issues were resolved adequately to ensure the drug product’s identity, strength, quality, purity, potency, and stability. All manufacturing and testing facilities were found to be acceptable by the Office of Compliance. Therefore, from a CMC standpoint, this new drug application may be approved.

III. Administrative

A. Reviewer’s Signature: electronically signed in DFS

B. Endorsement Block: electronically signed in DFS

C. CC Block: entered electronically in DFS
Page(s) Withheld

☑ Trade Secret / Confidential (b4)

☐ Draft Labeling (b4)

☐ Draft Labeling (b5)

☐ Deliberative Process (b5)
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
--------------------
Jane Chang
6/6/2007 03:27:40 PM
CHEMIST

Moo-Jhong Rhee
6/6/2007 03:31:23 PM
CHEMIST
Chief, Branch III
NDA 21-738

EXTINA™
(ketoconazole)
Foam, 2%

Connetics Corporation

Allan Fenselau, Ph.D.
Division of Dermatologic and Dental Drug Products
(HFD-540)
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    - **P.2.1.2 Excipients**
  - **P.2.2 Drug Product**
    - **P.2.2.1 Formulation Development**
    - **P.2.2.2 Overages**
    - **P.2.2.3 Physicochemical and Biological Properties**
  - **P.2.3 Manufacturing Process Development**
  - **P.2.4 Container Closure System**
  - **P.2.5 Microbiological Attributes**
  - **P.2.6 Compatibility**
- **P.3 Manufacture**
  - **P.3.1 Manufacturers**
  - **P.3.2 Batch Formula**
  - **P.3.3 Description of Manufacturing Process and Process Controls**
  - **P.3.4 Controls of Critical Steps and Intermediates**
  - **P.3.5 Process Validation and/or Evaluation**
- **P.4 Control of Excipients**
  - **P.4.1 Specifications**
  - **P.4.2 Analytical Procedures**
  - **P.4.3 Validation of Analytical Procedures**
  - **P.4.4 Justification of Specifications**
  - **P.4.5 Excipients of Human or Animal Origin**
  - **P.4.6 Novel Excipients**
- **P.5 Control of Drug Product**
  - **P.5.1 Specification(s)**
  - **P.5.2 Analytical Procedures**
  - **P.5.3 Validation of Analytical Procedures**
  - **P.5.4 Batch Analyses**
  - **P.5.5 Characterization of Impurities**
  - **P.5.5.1 Inquiry into Product Discoloration**
  - **P.5.6 Justification of Specification(s)**
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  - **P.7.1 Specifications and Analytical Methods**
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  - **P.8.1 Stability Summary and Conclusion**
    - **P.8.1.1 Stress Testing**
  - **P.8.2 Post-approval Stability Protocol and Stability Commitment**
  - **P.8.3 Stability Data**
Chemistry Review Data Sheet

1. NDA 21-738
2. REVIEW: # 1
3. REVIEW DATE: 19-OCT-2004
4. REVIEWER: Allan Fenselau
5. PREVIOUS DOCUMENTS: None

6. SUBMISSION(S) BEING REVIEWED:

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<tr>
<td></td>
<td>Palo Alto, CA 94303</td>
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<td>Representative:</td>
<td>Charles Democko,</td>
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<td>Telephone:</td>
<td>VP, Regulatory Affairs</td>
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8. DRUG PRODUCT NAME/ CODE/ TYPE:
   a) Proprietary Name: EXTINA™ Foam
   b) Non-Proprietary Name (USAN): Ketoconazole
   c) Code Name/# (ONDC only): NA

NDA 21-738 EXTINA (ketoconazole) Foam, 2% Connetics Corp.
d) Chem. Type/Submission Priority:  3/S

9. LEGAL BASIS FOR SUBMISSION: Not Applicable

10. PHARMACOLOGICAL CATEGORY: Antifungal

11. DOSAGE FORM: Foam

12. STRENGTH/POTENCY: 2% w/w

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: X Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
   ___ SPOTS product – Form Completed
   X  Not a SPOTS product

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

   ![Chemical Structure](image)

   KETOCONAZOLE

   C_{26}H_{28}Cl_2N_4O_4  M.W.: 531.43  CAS-65277-42-1
17. RELATED/SUPPORTING DOCUMENTS:

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1 Action codes for DMF Table:

1 – DMF Reviewed.
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2 – Type 1 DMF
3 – No revision since last review
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5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under “Comments”)

2 Adequate, Inadequate, or NA (i.e., there is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

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18. STATUS: ONDC

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NDA 21-738       EXTINA (ketoconazole) Foam, 2%       Page 7 of 100

Connetics Corp.
EXECUTIVE SUMMARY
Chemistry Review for NDA 21-738

I. Recommendations
   A. Recommendation and Conclusion on Approvability

   NDA 21-738 for EXTINA (ketoconazole) Foam, 2% is Approvable and will require satisfactory resolution of the safety issues that relate to before receiving a recommendation for Approval.

   B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable
   Not Applicable

II. Summary of Chemistry Assessments
   A. Description of the Drug Product(s) and Drug Substance(s)

   Drug Substance: Ketoconazole is currently approved in the US for use in six products [NDAs 18-533, 19-084, 19-576, 19-648, 19-927, and 20-310]. Detailed CMC information pertaining to the drug substance is provided by reference in the Drug Master File of the DMF, which is considered Adequate to support the subject NDA.

   The structure of ketoconazole, as drawn in the Package Insert for the various approved products, indicates, which will be revised by the sponsor in the product labeling.

   Drug Product: Ketoconazole Foam, 2% is delivered in a quick-breaking, temperature-sensitive, patented foam vehicle platform. This topical drug product contains ketoconazole, USP, specially denatured alcohol, cetyl alcohol, citric acid, polysorbate 60, potassium citrate, propylene glycol, purified water, and stearyl alcohol pressurized in a hydrocarbon (propane/butane) propellant. With the exception of the denatured alcohol, all of the excipients are USP or NF grade. Control of these latter excipients is established adequately. Acceptance testing of the propane/butane propellant also indicates adequate control. However, use of the denatured alcohol posed several problems.

   The denatured alcohol consists of absolute alcohol plus the additives tert-butyl alcohol and brucine sulfate, a potentially toxic alkaloid of the strychnine class. The absolute alcohol is manufactured formulation for each 50g can of Ketoconazole Foam, 2% should contain approximately orucine sulfate. The opinion of the Pharmacology/Toxicology reviewer is that this level presents no safety concerns. Two CMC actions have been taken to better assure safe use of the product: 1) revising the specification for the denatured alcohol and 2) stating the composition of the denatured alcohol in the Package Insert. The revised specification will list the content of brucine sulfate as determined by.
(based on a content of mg brucine sulfate/mL alcohol calculated from the formation). The Package Insert will specify the two additives in the absolute alcohol—tert-butyl alcohol and brucine sulfate—as opposed to merely stating that is present in the formulation.

The manufacture of drug product involves the

The manufacturing operations are well described in the batch record; adequate in-process testing is performed to assure batch-to-batch uniformity and product quality.

The container closure system is designed to dispense foam from an upright canister (unlike the firm’s other approved foam products OLUX and Luxiq). The specifications for the canister and its component parts are presented in sufficient detail.

The container closure was subjected to thorough extractable/leachable testing. Extraction conditions for the can and valve assemblies were in accord with those described by the current USP/NF Physicochemical Testing of Extracts and 21 CFR §175.300 Testing. The results of these tests on cans from the proposed suppliers were well within the established limits. Based on these results, no additional analyses were applied to obtain further information as to the chemical nature of certain sets of extractables.

The drug product specification includes testing for Appearance, Minimum Fill, Pressure, Leakage, Ketoconazole Identity (Release only), Content of Ketoconazole and Related Substances, Microbial Limits, Apparent pH, Ethanol Content, Weight Loss (Stability only), and Product/Packaging Interactions (Stability only). With the exceptions of the determination of ketoconazole content and Product/Packaging Interactions test, the listed tests and acceptance criteria were acceptable. The method for determining ethanol content has been satisfactorily validated.

The acceptance criteria were set using data from testing of the product for related substances, an adjustment to the 99% confidence interval, and consideration of the drug substance specification (see above). The related substances with RRT values of have been included as well as any single unidentified or unspecified related substance. The total related substances cannot exceed of the ketoconazole label claim. The acceptance criteria for ketoconazole and its related substances were revised to reflect the capabilities of the test methods for obtaining data to three significant figures. The proposed testing and acceptance criteria for the specified related substances are acceptable.

Deficiencies, however, were found in testing for ketoconazole-related substances and product/packaging interactions. These problems were associated with the sponsor’s finding that all registration lots showed
Consequently, a test for absorbance has been included in the product specification, and an acceptance criterion of absorbance unit [AU] has been established based on analysis of limited data. Another test missing in the specification is a determination of spray rate, which would assure dispensation of a uniform amount of foam from the can. The sponsor will include this test in the product specification in order to comply with USP <601> for pressurized topical aerosols. An acceptance criterion will be set when sufficient data become available (from commercial lots or within one year of NDA approval).

become issues of concern.

These revised procedures for testing product/packaging interactions have been incorporated into the product specification.

Possibly relevant information on the biological safety of product containing the ketoconazole-related substance may be found in the results from the studies on irritation/sensitization, comparative bioavailability, and Phase 3 safety and efficacy.

These findings permit a tentative conclusion

batches of Ketoconazole Foam, 2% have been manufactured in the 50-gram product size: of these lots (SCFC-C and SCFH-C) had a batch size of and were used in clinical studies and stability testing. Lot SCFL-C had a batch size of

NDA 21-738
EXTINA (ketoconazole) Foam, 2%
Connetics Corp.
and was used for stability testing. The batch analyses demonstrated that the chemical, physical, and microbiological characteristics of all batches met their respective product release specifications.

The results of the stability studies were reported for storage at 40°C/75% RH for and at 25°C/60% RH for . The data show little or no change over time and little or no variability when the lots of 50 gram product are stored under either long-term or accelerated conditions or in an orientation. All test parameters comply with the specification after of recommended storage with no apparent of the ketoconazole. Consequently, Connetics has proposed an expiration dating period of for the 50-gram product size of Ketoconazole Foam, 2%. A shelflife of is unacceptable based on the data contained in the submission and subsequent amendments.

These stability data do not permit full evaluation of product stability and expiry dating. Limitations in testing and analysis are responsible for the lack of information on the content of the product's most apparent

Drug product stress testing was carried out using standard conditions (treatment with acid, base, peroxide, heat, and light exposure). Unlike the results of the standard stability studies, the study established the utility of the HPLC method as a stability-indicating method.

The proposed post-approval stability protocol and stability commitment are standard statements and are acceptable with modification (based on revisions to be made to the product specification). Product labeling is acceptable with incorporation of the changes cited earlier (regarding representation of the ketoconazole structure and inclusion of the components of the denatured alcohol). The claim for the environmental impact indicates the amount of ketoconazole introduced into the aquatic environment falls within acceptable limits; the amount, however, appears to be miscalculated. All manufacturing and testing sites for drug substance and drug product have been recommended for Approval by the Office of Compliance [OC].

**B. Intended Use of the Drug Product**
Connetics developed Ketoconazole Foam, 2% as a convenient-to-use formulation of the established active pharmaceutical ingredient ketoconazole for topical use in the treatment of seborrheic dermatitis. Seborrheic dermatitis is an extremely common and recurrent dermatosis, which occurs primarily on the face and scalp. This disease is characterized by redness and scaling, with occasional papule and plaque formation. The yeasts *Pityrosporon ovale* or *Pityrosporon orbiculare* (*Malassezia furfur*) are believed to play a role in the pathogenesis of seborrheic
dermatitis and are susceptible to treatment with antifungal agents. Ketoconazole is a broadspectrum, synthetic antifungal drug, whose therapeutic effect has been postulated to be due to its ability to impair fungal synthesis of ergosterol, producing deficient fungal cell membranes.

The treatment of relapsing seborrheic dermatitis requires a safe topical preparation. Ketoconazole is currently approved for prescription use in the United States in two different prescription topical dosage forms (both at a concentration of 2%): Nizoral Cream and Ketoconazole shampoo. Nizoral Cream was first approved in 1985 initially for the treatment of tinea corporis, tinea cruris, and tinea pedis, but subsequently for the treatment of seborrheic dermatitis, cutaneous candidiasis, and tinea versicolor. Ketoconazole shampoo, 2% was approved in 1990 and is currently indicated for the treatment of tinea versicolor. [A nonprescription formulation of 1% ketoconazole shampoo for flaking, scaling, and itching associated with dandruff was also approved for marketing in the United States in 1997.] Over topical treatment courses of ketoconazole have been prescribed worldwide, the majority using a 2% formulation. Connetics Ketoconazole Foam, 2% differs from these approved products in that it employs VersaFoam—a quick-breaking, temperature-sensitive patented foam vehicle platform that, when applied to the skin, breaks down due to body heat and deposits the active ingredient directly on the lesion. Better patient compliance is expected with the foam formulation because of the localized application, longer contact time (compared to the shampoo), and the improved cosmetic aspects (compared to the cream).

### C. Justification of Recommendation

Three serious concerns about the possible effects of ketoconazole foam discoloration on product safety and quality were identified: 1) _______ , 2) _______ and 3) _______.

The sponsor needs to address these issues in order to provide greater assurance on product quality and safety.

### III. Administrative

#### A. Reviewer’s Signature

#### B. Endorsement Block

A.FENSELAU/08-OCT-2004: Same date as draft review

N.SCHMUFF/Date:

V.GIROUX/Date:

#### C. CC Block

HFD-830

D.LIN/Date:

N.SCHMUFF/Date:

NDA 21-738 EXTINA (ketoconazole) Foam, 2% Connetics Corp.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
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Allan Fenselau
10/19/04 10:54:15 AM
CHEMIST

Norman Schmuff
10/20/04 03:09:07 PM
CHEMIST

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**NDA FILEABILITY CHECKLIST**

**NDA Number:** 21-738  
**Applicant:** Connetics Corp.  
**Drug Name:** EXTINA™ (ketoconazole) Foam, 2%  
**Stamp Date:** 28-JAN-2004  
**Letter Date:** 26-JAN-2004

**IS THE CMC SECTION OF THE APPLICATION FILEABLE? (Yes or No) YES**

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

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<th>Parameter</th>
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<td>Y</td>
<td></td>
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<tr>
<td>2. Is the section indexed and paginated adequately?</td>
<td>Y</td>
<td>CMC Pagination is non-sequential. Location is given as pg.no. in subsection, e.g., &quot;General Information.&quot; Referencing in review the location of data in the submission is difficult/awkward.</td>
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<td>3. On its face, is the section legible?</td>
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| 4. Are all of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs? | Y      | DS: OK  
DP: OK                                                                                      |
| 5. Is a statement provided that all facilities are ready for GMP inspection? | Y      | DS: Yes  
DP: Yes                                                                                      |
| 6. Has an environmental assessment report or categorical exclusion been provided? | Y      | Module 1.3.6: “Environmental Impact”                                                              |
| 7. Does the section contain controls for the drug substance [DS]?          | NA     | DS information is contained in DMF — for which a Letter of Authorization has been received.      |
| 8. Does the section contain controls for the drug product [DP]?           | Y      | Modules 3.2.P.4 and 3.2.P.5.                                                                    |
| 9. Has stability data and analysis been provided to support the requested expiration date? | N      | DP: Module 3.2.P.8. Only — data have been submitted to support a — expiration date.               |
| 10. Has all information requested during the IND phase, and at the pre-NDA meetings been included? | Y      | The sponsor appears to discuss all relevant FDA guidance in Module 2.3 (“Quality Overall Summary”) |
| 11. Have draft container labels been provided?                            | Y      | Module 1.3.2.2: “Draft Immediate and Carton Label”                                               |
| 12. Has the draft package insert been provided?                           | Y      | Module 1.3.2.1: “Draft Package Insert”                                                            |
| 13. Has an Investigational Formulations section been provided?            | Y      | Module 3.2.P.2.                                                                                 |
| 14. Is there a Methods Validation package?                                | Y      | Submitted separately                                                                           |
| 15. Is a separate microbiological section included?                       | NA     | DP Specification includes appropriate Microbial Limit Tests.                                    |

If the NDA is not fileable from a manufacturing and controls perspective, state on a separate page why it is not.

**Reviewing Chemist:** Allan Fenselau  
**Date:**  
**Team Leader (Acting):** Norman Schmuff  
**Date:**

**cc:**  
Original NDA 21-738  
HFD-540/Chem/A.Fenselau  
HFD-540/PM/L.Carrington  
HFD-540/Division File  
HFD-830/DivDir(Acting)/D.Lin
CHEMISTRY REVIEW

Chemistry Assessment Section

NDA Number: 21-738  Applicant: Connetics Corp.
Drug Name: EXTINA™ (ketoconazole) Foam, 2%

KETOCONAZOLE  CAS-65277-42-1
C_{20}H_{26}Cl_{12}N_{12}O_{12}
M.W.: 531.43

LISTING of MANUFACTURING and TESTING SITES USED in the MANUFACTURE of the DRUG PRODUCT, EXTINA FOAM

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Abbreviations used: DS, Drug Substance; DP, Drug Product; AC, Acceptable; PN, Pending.
1 The CFN nos. provided by the sponsor do not agree with the CFN nos. of the sites reviewed by the Office of Compliance.

SUPPORTING DOCUMENTS:

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1 LOA = Letter of Authorization; Included Yes/No [Y/N]; LOA Date
2
3 No review listed in “DMFReviews”
4 NA = Not Applicable
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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/

Allan Fenselau
6/15/04 03:42:48 PM
CHEMIST
For some reason this list did not get placed in DFS at the time of the Fileability Meeting. Everything was OK for filing.

Norman Schmuff
6/18/04 09:51:20 AM
CHEMIST

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