CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20-310

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-310

OCT 10 1997

Johnson & Johnson Consumer products Inc.
Attention: Marjorie B. McTernan
Director, Regulatory Affairs
Grandview Road
Stillman, New Jersey 08558-9418

Dear Ms. McTernan:

Please refer to your new drug application dated December 18, 1992, received December 18, 1992, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nizoral A-D (ketoconazole shampoo), 1%.

Please refer to your approvable letters dated March 13, 1996, and May 15, 1997.

We acknowledge receipt of your submission dated September 18, 1997. The User Fee goal date for this application is March 19, 1998.

This new drug application provides for control of flaking, scaling, and itching associated with dandruff.

We have completed the review of this application including the submitted final labeling and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed final labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed final labeling. Marketing the product with FPL that is not identical to this final labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-310. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

We remind you of your Phase 4 commitment specified in your submission dated March 22, 1996. This commitment, along with any completion dates agreed upon,is listed below.

Protocols, data, and final reports should be submitted to your IND for this product, and a copy of the cover letter sent to this NDA. Should an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to this NDA as correspondences. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to this application a status summary of each commitment. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements relating to these Phase 4 commitments must be clearly designated "Phase 4 commitments."

In addition please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Mary Jean Kozma-Fornaro, Supervisor, Project management Staff, at (301) 827-2020.

Sincerely yours

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and
Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ENCLOSURE

cc:
Original NDA 20-310
HFD-540/Division File
HFD-2/MEDWATCH/with labeling
HFD-002/ORM/with labeling
HFD-92/DDM-DIAB/with labeling
HFD-101/L.Carter
HFD-40/DDMAC/with labeling
HFD-613/OGD/with labeling
HFD-735/DPE/with labeling
HFD-560/OTC/Bowen/Katz/Cook/with labeling
DISTRICT OFFICE
HFD-830/ONDC/with labeling
HFI-20/Press Office/with labeling
HFD-540/Wilkin/with labeling
HFD-540/Huene/with labeling
HFD-540/DeCamp/with labeling
HFD-540/Higgins/with labeling
HFD-540/Nostrandt/with labeling
HFD-540/Jacobs/with labeling
HFD-540/Kozma-Fornaro/with labeling
HFD-105/Weintraub/with labeling

APPROVAL (AP)
PHASE 4 COMMITMENT

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-310

APPROVABLE LETTER

6.1

MAR 13 1996

NDA 20-310

Johnson & Johnson Consumer Products, Inc.
Attention: Marjorie B. McTernan
Director, Regulatory Affairs
Grandview Road
Skillman, NJ 08558-9418

Dear Ms. McTernan:

Please refer to your December 18, 1992 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nizoral A-D (ketoconazole shampoo), 1%.

We acknowledge receipt of your communications dated January 26, February 4 and 10, March 3, 22, and 23, April 2, 7, and 19, May 3, 4, and 27, June 8 (two), July 9, September 22 and 29, October 1, 25, and 29, November 8 and 12, and December 10, 1993; January 20, 21, and 31, February 25 and 28, March 11, April 13, May 5, June 28, July 14, October 6, December 14, 15, and 19, 1994; January 6 and 31, March 8 and 15, and June 21, 1995; and January 2, 1996.

We have completed the review of this application as submitted with draft labeling and it is approvable. Before the application may be approved, however, it will be necessary for you to submit the following:

1. Sixteen copies of the final printed labeling (FPL) for the drug product that are identical to the enclosed revised version of the draft labeling. Ten copies of the FPL should be individually mounted on heavy-weight paper or similar material.

   Should additional information relating to the safety or effectiveness of this drug become available, revision of the FPL may be required.

2. A safety update that includes all safety information you now have regarding your new drug, as required by the provisions of 21 CFR 314.50(d)(5)(vi)(b)

3. An Environmental Assessment (EA) suitable for release under the Freedom Of Information Act (FOI) to be revised as follows:

   A. The information included in the format items 5.a through 5.g of the confidential EA dated March 8, 1995 should be incorporated into the FOI EA. Format item 5. h (impurities) should be listed but can be identified as "confidential."

B. No information was included in the FOI EA dated March 14, 1995 for format item 6. In general the following information should be included in the EA for both the drug product and drug substance manufacturing sites, although some of the specific information may be classified as confidential.

I. For the bulk drug production site include:

a. Substances Expected to be Emitted
b. Controls exercised
c. Citation of Statement of Compliance with Applicable Emission Requirements
d. Discussion of the Effect of Approval on Compliance with Current Emission Requirements
e. Expected Introduction Concentrations (estimate of maximum yearly market volume for abbreviated EA's)

II. For the drug product manufacturing site, some information to fulfill the requirements of format item 6 has been provided in the confidential EA but there may be a discussion included in the FOI EA. The following is suggested:

a. For 6.a and 6.e, a reference to the information in the confidential EA submitted March 8, 1995 is acceptable.

b. For 6.b, 6.c, and 6.d, information should be included in the FOI EA (this should include, but not limited to the previously submitted certifications and permitting information).

For additional guidance in the preparation of a revised FOI EA and confidential EA refer to: "Guidance for Industry for the Submission of an Environmental Assessment in Human Drug Applications and Supplements" which is available from the Consumer Affairs Branch, HFD-210, Center for Drug Evaluation and Research, 7500 Standish Place, Rockville, MD 20855, 301-594-1012, FAX on Demand, 1-800-342-2722, Document # 0803; or via Internet by connecting to the CDER file transfer protocol (FTP) server (CDVS2.CDER.VDA.GOV).

4. A commitment to complete the following as Phase 4 requests:

5. Three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that a satisfactory inspection of your manufacturing facilities for conformance with current good manufacturing practices (CGMP) is required before this application may be approved.

We also acknowledge the agreement specified in your letter dated December 19, 1994, that the approval of this application (NDA 20-310) cannot be finalized until the labeling of ketoconazole shampoo, 2%, is modified in such a way as to distinguish both drug products from each other consistent with the requirements of section 503(b) of the Federal Food, Drug, and Cosmetic Act.

Within 10 days of the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of the other options under 21 CFR 314.110. In the absence of such action, the FDA may take action to withdraw the application.

The drug may not be legally marketed until you have been notified in writing that the application is approved.

Should you have any questions concerning this application, please contact:

Harold Blatt, D.D.S.
Project Manager
Telephone: (301) 827-2020

Sincerely yours,

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and
Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-310

MAY 15 1997

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Attention: Marjorie B. McTernan
Director, Regulatory Affairs
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Please refer to your approvable letter dated March 14, 1996.

We acknowledge receipt of your communications dated March 22, April 8, July 3, and November 14, 1996; April 4 and 18, 1997. The User Fee goal date for this application is May 15, 1997.

This new drug application provides for control of flaking, scaling, and itching associated with dandruff.

We have completed the review of this application, including the submitted final labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed final labeling. Accordingly, the application is approvable effective on the date of this letter.

Please note that the co-marketing of a prescription drug product and an over-the-counter drug product for the same indication is not allowed under the Durham-Humphrey Act. Therefore, an approval letter for the marketing of this over-the-counter product cannot be issued while the indication for the treatment of dandruff exists for ketoconazole shampoo, 2%.

The final printed labeling (FPL) must be identical to the enclosed final labeling. Marketing the product with FPL that is not identical to this final labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-310. Approval of this submission by FDA is not required before the labeling is used.

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We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Roy Blay, Project Manager, at (301) 827-2020.

Sincerely yours,

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ENCLOSURE

cc:
Original NDA 20-310
HFD-540/Div. files
HFD-540/Wilkin (with labeling)
NWK-DO
HFD-540/CSO/R.Blay (with labeling)
HFD-540/PHuene (with labeling)5/12/97
HFD-540/EToombs (with labeling)
HFD-540/EPappas (with labeling)5/9/97
HFD-540/Higgins (with labeling)
HFD-540/WDeCamp (with labeling)
HFD-540/ANostrandt (with labeling)5/9/97
HFD-540/AJacobs (with labeling)
HFD-725/RSrinivasan (with labeling)5/14/97
HFD-880/Bashaw (with labeling)
HFD-002/ORM (with labeling)
HFD-105/Office Director (with labeling)5/14/97
HFD-101/L.Carter (with labeling)
HFD-830/ONDC Division Director (with labeling)
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFI-20/Press Office (with labeling)
HFD-560/OTC (with labeling)

Concurrences:
HFD-540/EToombs
HFD-540/WDeCamp
HFD-540/AJacobs5/9/97
HFD-540/Kozma-Fornaro/5/7/97

APPROVABLE (AE)
PHASE 4 COMMITMENT