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APPLICATION NUMBER:

21-261

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-261

Personal Products Company
Attention: Barbara Popek
Manager, Regulatory Affairs
199 Grandview Road
Skillman, New Jersey 08558

Dear Ms. Popek:

Please refer to your new drug application (NDA) dated March 31, 2000, received April 3, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Monistat®3 Combination Pack (miconazole nitrate cream, 4% and miconazole nitrate external cream, 2%).

We acknowledge receipt of your submissions dated May 2, August 2 and 25, September 7 and 19, 2000 and January 4, 12, 25 and 29, 2001.

This new drug application provides for the use of Monistat®3 Combination Pack for the treatment of vaginal yeast infections and the relief of external itching and irritation due to a vaginal yeast infection.

We have completed the review of this application, as amended, 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 draft labeling submitted January 4, 2001, with the revisions listed below. Accordingly, the application is approved effective on the date of this letter.

As stated in your letters of commitment dated January 25 and 29, 2001, the following revisions to the labeling will be made:

Carton Label

1. Remove the word "New" in the phrase "New Combo Pack!" after the first 6 months of OTC marketing.

2. Change the PDP so that the declaration of net quantity of contents statement clearly indicates that the statement refers to 2 products. You will either separate the two phrases with the word "and" or place each phrase on a separate line.

3. Revise the warning in the Drug Facts box to read **"Ask a doctor or pharmacist before use if you are** taking the prescription blood thinning medicine warfarin, because bleeding or bruising may occur."

Consumer Information Leaflet

1. Revise the heading "**Use**" to "**Uses**".

2. Revise the **Warnings** section, 5th bulleted warning to read: **"Ask a doctor or pharmacist before use if you are** taking the prescription blood thinning medicine warfarin (Coumadin), because bleeding or bruising may occur."

3. Under the heading "**Side effects,**" revise the third sentence to read "Stop using MONISTAT® 3 Vaginal Cream Combination Pack and consult your doctor if you have abdominal pain, hives, or skin rash, or if you have severe vaginal burning, itching, or irritation."

4. In the 4th direction, first sentence, under the heading " **Directions for Use MONISTAT® 3 Vaginal Cream,**" add the word "back" as follows: "Gently insert the applicator into the vagina as far back as it will go comfortably."

We agree that you may use the current tube and current overwrap labeling for the product launch and incorporate new labeling within 180 days or at the next printing. We also agree that your use of a picture of a hand (instead of an arrow) to show where the applicator is inserted is acceptable.

We remind you of your post marketing commitments in your submission dated January 29, 2001:

1. To provide a 1-800 telephone number with information to address questions in reference to the warfarin warning. This commitment will be completed by April 1, 2001.

2. To train your detail force to respond to this question when asked. This commitment will be completed by April 1, 2001.

3. To include the warfarin statement as it is in the labeling on your next Physician/Pharmacist Detail piece. This commitment will be completed at the time of your next printing.

In addition, under 21 CFR314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. All submissions, including supplements, relating to these postmarketing commitments must be prominently labeled **"Postmarketing Protocol", "Postmarketing Final Report", or "Postmarketing Study Correspondence."**

The final printed labeling (FPL) must be identical, and include the revisions indicated, to the submitted draft labeling submitted January 4, 2001 (consumer information leaflet, tube overwrap and carton labels) and must be formatted in accordance with the requirements of 21 CFR 201.66. These revisions are terms of the NDA approval. Marketing the product with FPL that is not identical to the approved labeling and "Drug Facts" format may render the product misbranded and an unapproved new drug.

Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-261." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). The submitted over-the -counter product labeling provides directions for use by children 12 years or older. We are waiving the pediatric study requirement for children under 12 years old on the basis that vaginal yeast infection in the pre-pubertal child does not lend itself to self-diagnosis and over-the-counter treatment.

In addition, please submit one copy of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. For administrative purposes, this submission should be sent to the NDA and should be identified as new correspondence to the approved NDA 21-261.

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 regarding this application, please contact Daniel P. Keravich, R.Ph., M.S., M.B.A., Regulatory Project Manager, at (301) 827-2222.

Sincerely,

{See appended electronic signature page}

Charles Ganley, M.D.
Director
Division of Over-the-Counter
Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

{See appended electronic signature page}

Mark Goldberger, M.D., M.P.H.
Director
Division of Special Pathogen and Immunologic
Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research