

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-690

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-690

3/23/04

Ortho-McNeil Pharmaceutical, Inc.
Johnson & Johnson Pharmaceutical Research & Development, L.L.C., US Agent
Attention: Tracy Healy, RN, MBA
Manager, Regulatory Affairs, Global Marketed Products
920 Route 202 South, P.O. Box 300
Raritan, New Jersey 08869-0602

Dear Ms. Healy:

Please refer to your new drug application (NDA) dated September 24, 2003, received September 25, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ortho Tri-Cyclen[®] (norgestimate/ethinyl estradiol) Tablets.

We acknowledge receipt of your submissions dated November 18 and December 8, 11 and 22, 2003, and January 13, February 2 and 25(fax), 2004.

We completed our review of this application and it is approvable. Before the application may be approved, however, submission and review of the final results from the 12-month study, CAPSS-169, will be necessary.

The labeling for this product will be discussed after we have reviewed the final results of CAPSS-169.

During a recent inspection of the manufacturing facilities for this application, our field investigator conveyed deficiencies to one facility's representative. Satisfactory resolution to these deficiencies is required before this application may be approved.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.
 - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.
 4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
 5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
 6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
 7. Provide English translations of current approved foreign labeling not previously submitted.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, call Pat Madara, Regulatory Project Manager, at (301) 827-6416.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Mary Parks
3/23/04 01:57:31 PM
for Dr. Orloff