

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-998**

**OTHER ACTION LETTER(s)**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

Duramed Research, Inc.  
Attention: Joseph A. Carrado, M.Sc., R.Ph  
Vice President, Clinical Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your new drug application (NDA) dated and received on January 24, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel tablets, 1.5 mg.

We acknowledge receipt of your presubmissions dated December 2, 2005, January 11 and 12, 2006.

We also acknowledge receipt of your submissions dated January 24, February 23, March 2 and 20, June 20 and 29, July 14, August 16, September 26 and 27, October 13, and 19, November 3(2), 8(2), 9, and 21, 2006.

This application proposes the use of a levonorgestrel tablet for emergency contraception that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure.

We have completed our review of this application, as amended, and it is approvable. As you are aware, levonorgestrel tablets consisting of two 0.75 mg doses taken 12 hours apart are approved, with the same total dosage, for prescription-only (Rx) use for emergency contraception in women 17 years of age and younger and for nonprescription (over-the-counter or OTC) use in women 18 years of age and older. Your application proposed marketing a 1.5 mg levonorgestrel tablet as a prescription-only product for women of all ages. FDA has evaluated the data incorporated by reference into your application concerning actual use and labeling comprehension in relation to levonorgestrel for emergency contraceptive use. These data establish that the 1.5 mg levonorgestrel product can safely and effectively be used as an OTC product for women ages 18 and over. Therefore, before this application may be approved, you will need to submit revised labeling that meets the requirements of marketing of levonorgestrel tablets, 1.5 mg, as a prescription product for women 17 years of age and younger, and as a nonprescription product for women 18 years of age and older. You will also need to submit your plan regarding distribution of both the Rx and OTC versions of your product.

Further comments on labeling are deferred until the above deficiency is addressed.

When you respond to the above deficiency, 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.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Reproductive and Urologic Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file 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.

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Under 21 CFR 314.102(d), you may request a meeting or telephone conference with the Division of Reproductive and Urologic Products to discuss what steps need to be taken before the application may be approved.

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

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at (301) 796-0875.

Sincerely,

*{See appended electronic signature page}*

**Scott Monroe, M.D.**  
**Acting Director**  
**Division of Reproductive and Urologic Products**  
**Office of Drug Evaluation III**  
**Center for Drug Evaluation and Research**

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

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Scott Monroe

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