CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-840

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-840

Duramed Pharmaceuticals, Inc.
Attention: Joseph A. Carrado, M.Sc., R.Ph.
Senior Director, Regulatory Affairs
One Belmont Ave., 11th Floor
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your new drug application (NDA) dated October 21, 2004, received October 21, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Seasonique™ (levonorgestrel/ethinyl estradiol and ethinyl estradiol) Tablets.

We also refer to your submissions dated November 11, December 1(2) and 14, 2004, March 1, April 15, June 10 and 23, July 14, 15, and 28, and August 4, 2005.

We completed our review of this application, as amended, and it is approvable. The following deficiency was noted:

> The application for the Seasonique™ extended cycle contraceptive regimen (consisting of 150 micrograms levonorgestrel and 30 micrograms ethinyl estradiol administered for 84 days and 10 micrograms ethinyl estradiol administered for days 85-91) did not provide clinical trial data that demonstrated benefit of the addition of 10 micrograms of ethinyl estradiol per day on days 85-91 to this extended cycle contraceptive regimen compared to the exact same regimen that has placebo during days 85 to 91. Because of the known risks of exogenous estrogen, replacement of placebo by ethinyl estradiol to this regimen cannot be supported without demonstration of a clinically meaningful benefit to the patient.

To address this deficiency, you should conduct a randomized controlled clinical trial that demonstrates that the addition of 10 micrograms of ethinyl estradiol to the previous hormone free period provides a meaningful clinical benefit to the patient, such as [redacted] The full details of such a trial and what clinically meaningful benefit you wish to demonstrate should be discussed with the Division prior to initiation.

We also remind you that the professional and patient labeling and the container/carton label negotiations remain outstanding.

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.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with this division 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, call Karen Kirchberg, Regulatory Project Manager, at (301) 827-4254.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug 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 this page is the manifestation of the electronic signature.

/s/

Daniel A. Shames
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