DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-992-024

Duramed Pharmaceuticals, Inc.
Subsidiary of Barr Laboratories, Inc.
Attention: Christine Mundkur, Senior Vice president,
Quality and Regulatory Counsel
5040 Lester Road
Cincinnati, Ohio 45213

Dear Ms. Mundkur:

Please refer to your supplemental new drug application dated February 21, 2003, received February 24, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cenestin® (synthetic conjugated estrogens, A) Tablets.

This supplemental application, submitted as "Changes Being Effected," provides for the addition of risk information from the Women's Health Initiative (WHI) study in postmenopausal women. The supplement was submitted in response to our requested dated January 8, 2003.

We have completed our review of this application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted (February 21, 2003) patient package insert and package (professional) insert with the following revisions agreed upon in the telephone conversations on January 22 and 23, 2004 between your representative, Mr. Sal Peritore, Manager Regulatory Affairs, and Ms. Bronwyn Collier, Associate Director for Regulatory Affairs in the Office of Drug Evaluation III:

1. The boxed warning will describe the product used in the WHI as "conjugated equine estrogens (CE 0.625 mg) and medroxyprogesterone (MPA 2.5 mg)."
2. The first sentence only, under the CLINICAL PHARMACOLOGY section, subsection for Clinical Studies, sub-subsection for WHI, will describe the estrogen component of the product used in the WHI as "conjugated equine estrogens (CE)."
3. All other descriptions, throughout the labeling, of the estrogen component of the product used in the WHI will be "CE."
4. The indication for postmenopausal vulvar and vaginal atrophy in the INDICATIONS AND USAGE section will be revised to the following:

   Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When used solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.
   - 0.3 mg Cenestin

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-992/S-024." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

If you have any questions, call George Lyght, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel A. 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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