CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-262

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	July 30, 2008
To:	Scott Monroe, M.D., Director Division of Reproductive & Urologic Products
Through:	Jodi Duckhorn, M.A. Team Leader Patient Labeling and Education Team Division of Risk Management
From:	Nancy Carothers Patient Product Information Specialist Patient Labeling and Education Team Division of Risk Management
Subject:	Review of Patient Package Insert
Drug Name(s):	Lo Seasonique (levonorgestrel/ethinyl estradiol) 0.1 mg/0.02 mg and (ethinyl estradiol) 0.01 mg.
Application Type/Number:	NDA 22-262
Applicant/sponsor:	Duramed Pharmaceuticals, Inc.
OSE RCM #:	2008-289

Summary and *Patient Detailed Labeling* is inconsistent with the *2004 Guidance for Industry Labeling for Combined Oral Contraceptives*.

Although, regulation 21 CFR 310.501 (c) (2) states that a "summary" concerning the 1) effectiveness, 2) contraindications, and 3) risks and benefits associated with the use of oral contraceptives should be included in the PPI, it does not suggest that the directions on how to use the product be included in the summary. In order to follow this regulation more accurately, the summary should include only the information listed in the regulation.

To simplify the format of the PPI, the summary should follow the first topic listed in the Guidance, "What is an oral contraceptive?" We recommend placing the summary under a new topic heading, "What is the most important information I should know about this product?" With a shortened summary, containing information on effectiveness, contraindications, and risks and benefits, the PPI would be less confusing and the regulation -- to summarize the most important information -- would be followed.

As we understand it, the *Brief Summary* and *Detailed Patient Labeling* leaflet are provided to patients as one long document. This could mean that patients must search for the important information, and this could reduce the safe use of this product.

- Avoid presenting data in tables unless careful explanations are presented at a low reading comprehension level. Many readers have trouble comprehending information presented in tables. Remove the table that describes the number of birth-related or method-related deaths associated birth control, age, and smoking that appears under the heading, "ESTIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY." We suggest retaining some of the information from that table as a bulleted list.

- Titles and statements appearing in all UPPER CASE should be changed to an upper case first letter and lower case for the rest of the word. Upper case lettering is difficult to read. Use bold or underline for word or statement emphasis. The tradename is the exception to this recommendation and may be in upper case letters.

- Add the following statement to the end of the section, "What are the common side effects of birth control pills?

  "Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

  This verbatim statement is required for all Medication Guides effective January 2008 (see 21 CFR 208.20 (b)(7)(iii); also see Interim Final Rule, Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products in Federal Register Vol. 73, No.2, p.402-404, 1/3/2008). Although not required for PPIs, like Lo Seasonique, we recommend that this statement be included in all patient labeling for consistency.

Please let us know if you have any questions.