NDA 20-756/S-009

Columbia Research Laboratories, Inc. 03 APR 2001
Attention: Howard Levine, Pharm. D.
Vice President
100 No. Village Avenue/Suite 32
Rockville Centre, NY 11570

Dear Dr. Levine:

Please refer to your supplemental new drug application dated August 27, 1999, received August 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Crinone® progesterone gel, 8%.

We acknowledge receipt of your submissions dated February 8, March 9 and July 4, 2000.

This supplemental new drug application provides for a change in font from CRINONE all capital letters to Crinone title case for the trademark throughout the labeling. This application also provided for labeling revisions in the Package Insert, Patient Package Insert and Carton and Container labels as follows:

Package Insert:

1. **CLINICAL PHARMACOLOGY** section
   **Pharmacokinetics** subsection
   *Distribution* subsection

2. **PRECAUTIONS** section
   **Geriatric Use** subsection

3. **HOW SUPPLIED** section to revise the storage description and add a new distributor.

Patient Package Inserts for the 8% gel and the 4% and 8% gel:

1. **PATIENT INFORMATION** introduction section

2. **About CRINONE** section

3. **When you should not use CRINONE** section

4. **Risks of CRINONE** section

5. **PRECAUTIONS** section
   SIDE EFFECTS REPORTED AT A FREQUENCY OF 5% OR GREATER
   SIDE EFFECTS REPORTED AT A FREQUENCY OF LESS THAN 1% subsection

6. **How to use CRINONE** section, #3 and #5

7. **SPECIAL INSTRUCTIONS FOR USE AT ALTITUDES ABOVE 2500 FEET** section

8. **HOW SUPPLIED** section

Carton and Container labeling

1. Change from green color to violet shades

2. Use of Rx only notation

3. Storage conditions rewording

4. New distributor

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted March 9, 2000, patient package insert submitted July 4, 2000, immediate container and carton labels submitted July 4, 2000).

Please 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 ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-756/S-009." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We also request that you submit the FPL text in an electronic format in WORD 7.0

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Diane Moore, BS, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Susan Allen, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research