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CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

21-663

Trade Name: Menopur For Injection

Generic Name(s): (menotropins)

Sponsor: Ferring Pharmaceuticals, Inc.

Agent:

Approval Date: October 29, 2004

Indication: Provides for use by subcutaneous injection for the indication of the development of multiple follicules and pregnancy in patients participating in assisted reproductive technologies

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-663

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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-663

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-663

Ferring Pharmaceuticals
Attention: James H. Conover, Ph.D.
Executive Director, Regulatory Affairs
400 Rella Boulevard, Suite 300
Suffern, NY 10901

Dear Dr. Conover:

Please refer to your new drug application (NDA) dated December 19, 2003, received December 29, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Menopur® (menotropins for injection, USP).

We acknowledge receipt of your submissions dated January 13, 23, and 27, February 12(3), 13, 18(2), 20, and 26, March 4, April 8, 27, and 29, May 10, June 10(2), July 2(2), 19, and 29, August 3, 5(2), 10, 13, and 17, September 1, 2, 10, 16, and 23, October 4, 22, 25(2), 2004.

This new drug application provides for the use of Menopur® (menotropins for injection, USP) by subcutaneous injection for the indication of the development of multiple follicules and pregnancy in patients participating in Assisted Reproductive Technologies.

We completed our review of this application, as amended. 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 enclosed labeling (text for the package insert) and the carton and container labeling submitted May 10, 2004. Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL 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 but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-663**." Approval of this submission by FDA is not required before the labeling is used.

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 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, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Martin Kaufman, D.P.M., M.B.A., Regulatory Health Project Manager, at (301) 827-4234.

Sincerely,

{See appended electronic signature page}

/S/

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug
Products (HFD-580)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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
10/29/04 06:10:09 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-663

Approvable Letter (S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-869

Ferring Pharmaceuticals
Attention: James H. Conover, Ph.D.
Executive Director, Regulatory Affairs
400 Rella Boulevard, Suite 300
Suffern, NY 10901

Dear Dr. Conover:

Please refer to your new drug application (NDA) dated December 19, 2003, received December 29, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Menopur® (menotropins for injection, USP).

We acknowledge receipt of your submissions dated January 13, 23, and 27, February 12(3), 13, 18(2), 20, and 26, March 4, April 8, 27, and 29, May 10, June 10(2), July 2(2), 19, and 29, August 3, 5(2), 10, 13, and 17, September 1, 2, 10, 16, and 23, October 4, 22, 25(2), 2004.

We completed our review and find the information presented is inadequate to support the indications [ ] multiple follicular development and pregnancy (intramuscular injection) in ovulatory patients participating in Assisted Reproductive Technologies. Therefore, the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies are summarized as follows:

1. [ ]

2. Efficacy for Menopur® (intramuscular injection) as determined by non-inferiority to Repronex® was not demonstrated in the submitted clinical study, 2000-02, for multiple follicular development and pregnancy in ovulatory women participating in Assisted Reproductive Technologies.

To address these deficiencies you should:

1. Conduct a clinical trial(s) which demonstrate safety and efficacy of Menopur® [

2. Conduct a clinical trial(s) which demonstrate safety and efficacy of Menopur® (intramuscular injection) for multiple follicular development and pregnancy in ovulatory women participating in Assisted Reproductive Technologies. This study (s) should be a randomized, double-blind comparator study of Menopur® vs. an approved drug product that evaluates a primary efficacy endpoint of clinical pregnancy as defined by a gestational sac with heartbeat on ultrasound obtained 6 weeks after embryo transfer. The primary efficacy analysis should be a time to event analysis.

When you respond to the above deficiencies, 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.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. 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 the Division of Reproductive and Urologic Drug 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 this application is approved.

If you have any questions, contact Martin Kaufman, D.P.M., M.B.A., Regulatory Health Project Manager, at (301) 827-4234.

Sincerely,

/S/

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

14 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

✓ § 552(b)(5) Draft Labeling

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/s/

Daniel A. Shames
10/29/04 06:00:00 PM