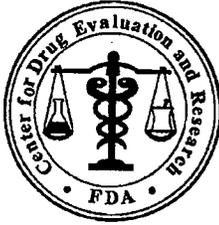


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-201

**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: December 23, 2008

To: Robert Justice, MD, Director
Division of Drug Oncology Products

Thru: Kellie Taylor, PharmD, MPH, Team Leader
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Laura Pincock, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Label and Labeling Review

Drug Name: Degarelix for Injection
80 mg, 120 mg

Application Type/Number: NDA 22-201

Applicant: Ferring Pharmaceuticals

OSE RCM #: 2008-1679

1 INTRODUCTION

The Division of Medication Error Prevention and Analysis (DMEPA) has participated in ongoing label and labeling negotiations between the Applicant and FDA. We have made various recommendations regarding the proposed vial labels and carton labeling throughout the process. Subsequently, the Applicant submitted has their latest version of the vial labels and carton labeling on December 22, 2008.

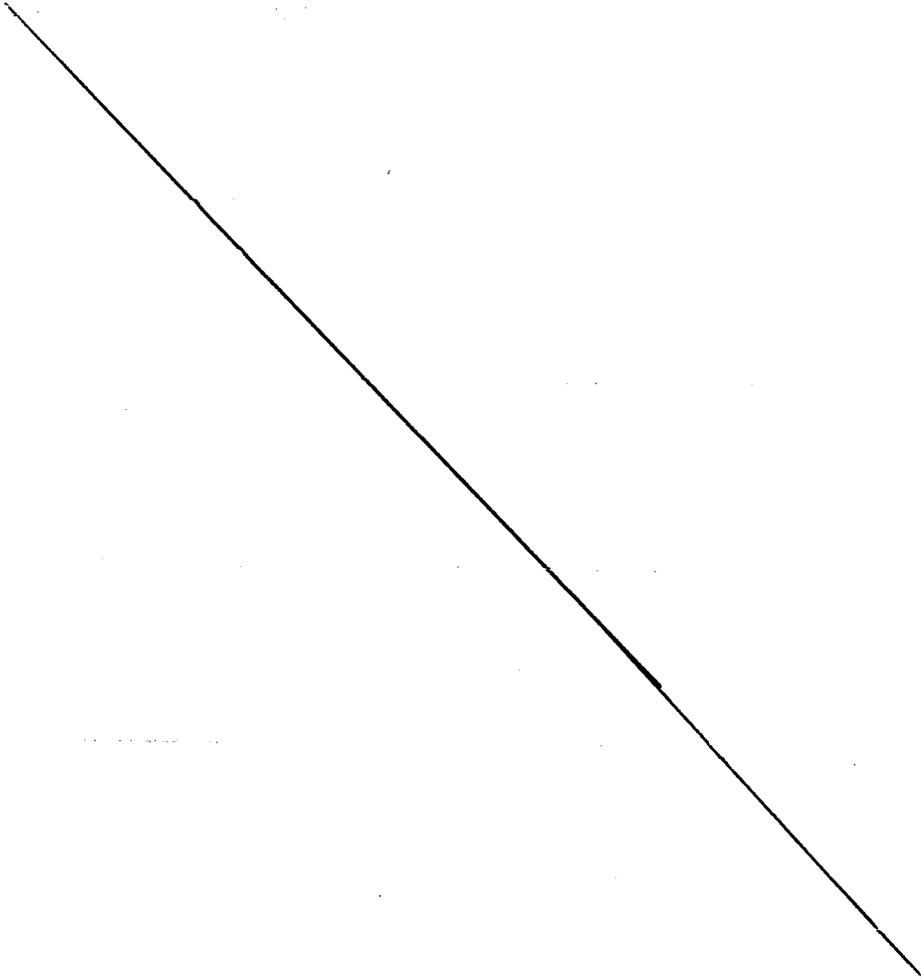
2 MATERIAL REVIEWED

DMEPA reviewed the revised labels and labeling submitted by the Applicant on December 22, 2008. See Appendices A and B for pictures of the labels and labeling.

- Vial Labels (80 mg and 120 mg)
- Carton Labeling (80 mg and 240 mg [contains two vials of 120 mg])

3 DISCUSSION

DMEPA has noted areas of concern where there is room for improvement to the carton labeling from a medication errors perspective. These issues are noted below.



b(4)

4 CONCLUSIONS AND RECOMMENDATIONS

Based on our assessment of the labels and labeling, DMEPA is satisfied with all revisions made to the vial labels. However we have identified the following areas of needed improvement to the carton labeling. To minimize the potential for errors, and to improve readability, we recommend implementation of the carton labeling revisions outlined below in section 4.1.

DMEPA would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy our division on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Sandra Griffith, OSE Project Manager, at 301-796-2445.

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✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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this page is the manifestation of the electronic signature.**

/s/

Laura Pincock
12/23/2008 11:27:15 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
12/23/2008 11:29:22 AM
DRUG SAFETY OFFICE REVIEWER



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: December 20, 2008

To: Robert Justice, MD, Director
Division of Drug Oncology Products

Through: Jodi Duckhorn, MA, Team Leader
Patient Labeling and Education Team
Division of Risk Management

From: Nancy Carothers, RN
Patient Product Information Reviewer
Patient Labeling and Education Team
Division of Risk Management

Subject: DRISK Review of Patient Labeling (Patient Package Insert)

Drug Name(s): degarelix for injectable _____ 80 mg and 120 mg

Application Type/Number: NDA 22-201

Applicant/sponsor: Ferring Pharmaceuticals, Inc.

OSE RCM #: 2008-1679

b(4)

1 INTRODUCTION

Ferring Pharmaceuticals submitted an original NDA 22-201 on February 14, 2008. In October, 2008 the sponsor responded to the Chemistry Manufacturing and Controls (CMC) reviewers' inquiries concerning sterility and other issues. In November 2008, FDA requested from the sponsor changes to the drug product — The sponsor agreed with changes to the — submitted a revised PI. After further revisions, DDOP provided a substantially complete PI to DRISK on December 11, 2008. The revisions included the addition of detailed "Instructions for Proper Use" for the healthcare provider who will reconstitute and inject the product. Since then, the CMC has added minor changes to the Highlights Section under "Dosage and Administration." The originally proposed trade name, Firmagon, was not approved and the new name, — was submitted for approval on November 25, 2008. The new trade name has not been approved as of this date so the term "[TRADENAME]" will be used for this review. The review materials for this Package Insert (PI) and Patient Package Insert (PPI) were received in DRISK on December 11, 2008. The PDUFA date is December 31, 2008.

b(4)

The Division of Drug Oncology Products requested that the Patient Labeling and Education Team review the Patient Package Insert for this product. This review was written in response to that request.

2 MATERIAL REVIEWED

- Draft [TRADENAME] (degarelix for injectable — PI submitted by the Sponsor on December 4, 2008, revised substantially by the Review Division and sent to DRISK on December 18, 2008.
- Draft [TRADENAME] (degarelix for injectable : — PPI submitted by the Sponsor on December 4 revised by the Review Division and sent to DRISK on December 18, 2008.

b(4)

3 DISCUSSION

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

The draft PPI submitted by the sponsor has a Flesch Kinkaid grade level of — and a Flesch Reading Ease score of — To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8th grade reading level). Our revised PPI has a Flesch Kinkaid grade level of 8.7 and a Flesch Reading Ease score of 54.9%.

In our review of the PPI we have:

- simplified wording and clarified concepts where possible,
- made the PPI consistent with the PI,
- removed unnecessary or redundant information
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

b(4)

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APFont to make medical information more accessible for patients with low vision. We have reformatted the PPI document using the font APFont, which was developed by the American Printing House for the Blind specifically for low vision readers.

See the attached document for our recommended revisions to the PPI. Comments to the review division are ***bolded, underlined and italicized***.

We are providing the review division a marked-up and clean copy of the revised PPI.
We recommend using the clean copy as the working document.

4 CONCLUSIONS AND RECOMMENDATIONS

- We added a statement for patients to tell their healthcare provider about any heart problems and if they are taking any heart medications. Under "Warnings and Precautions," the PI states that long term use of androgen therapy may prolong QT intervals. The PI suggests physicians assess the risks versus the benefits for patients with congenital long QT syndrome, electrolyte abnormalities, or congestive heart failure. Patients need to tell their oncologist, who is probably not the primary care physician, about any cardiac problems.
- We added a statement for patients to tell their healthcare provider about any kidney or liver problems because the PI states under "Use in Specific Populations" that data on patients with moderate to severe renal impairment is limited. Therefore, this product should be used with caution in patients with CrCl < 50 mL/min. In patients with hepatic impairment, the dose should be monitored every month until medical castration is achieved. These patients may have less exposure to the product because of liver impairment. Patients should report any kidney or liver problems before receiving this drug product.
- We added the instruction to tell your healthcare provider about all of your medicines and then added specifically "heart medicines" because in the "Warnings and Precautions," section (5.3), the PI advises that the risks versus benefits to patients taking the following medicines: quinidine, procainamide, or other antiarrhythmics, should be assessed before prescribing this product.
- Each injection site should be free of any pressure caused by belts, waistbands or other types of clothing. This advice is located in the PI under "Dosage and Administration." If this advice is to be followed by the patient during the month between injections then the patient should receive this instruction in the PPI as a reminder.
- We have added the following statement to the end of the section, "What are the possible side effects of TRADENAME?":

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

This verbatim statement is required for all Medication Guides effective January 2008. Although not required for voluntary PPIs like [TRADENAME], we recommend adding this language to all FDA-approved patient labeling for consistency.

Please let us know if you have any questions.

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 Trade Secret / Confidential (b4)

 Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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this page is the manifestation of the electronic signature.**

/s/

Nancy B Carothers
12/20/2008 04:57:33 PM
DRUG SAFETY OFFICE REVIEWER

Jodi Duckhorn
12/20/2008 09:23:46 PM
DRUG SAFETY OFFICE REVIEWER