CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-210

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 21, 2009

To: Donna Griebel, M.D., Director
Division of Gastroenterology Products (DGP)

Through: Claudia Karwoski, PharmD, Director
Division of Risk Management (DRISK)

Jodi Duckhorn, MA, Team Leader
Division of Risk Management

From: Jessica M. Diaz, BSN, RN
Patient Labeling Reviewer
Division of Risk Management

Subject: DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)

Drug Name(s): ZENPEP (pancrelipase)

Application Type/Number: NDA 22-210

Applicant/sponsor: Eurand Pharmaceuticals, Inc.

OSE RCM #: 2009-947

1 INTRODUCTION

This memorandum is in response to a request by the Division of Gastroenterology Products for the Division of Risk Management (DRISK) to review the proposed Risk Evaluation and Mitigation Strategy (REMS) for ZENPEP (pancrelipase). Please send these comments to the Applicant and request a response within two weeks of receipt. Please let us know if you would like a meeting to discuss these comments before sending to the Applicant. DRISK's review of the Medication Guide is being reviewed and will be provided under separate cover.

2 MATERIAL REVIEWED

- ZENPEP (pancrelipase) Risk Evaluation and Mitigation Strategy (REMS) Notification Letter dated March 19, 2009
- Proposed ZENPEP (pancrelipase) Risk Evaluation and Mitigation Strategy (REMS), submitted in EDR on May 14, 2009

3 CONCLUSIONS AND RECOMMENDATIONS

We have the following comments and recommendations for the Applicant with regard to the proposed REMS.

Comments to Eurand Pharmaceuticals, Inc:

See the appended ZENPEP (pancrelipase) REMS proposal (Appendix A) for track changes corresponding to comments in this review.

a. GOAL(S)

Revise your goal as follows:

The goal of this REMS is to inform patients about the serious risk associated with the use of Zenpep.

b. The Medication Guide distribution procedure does not provide sufficient details to determine whether it is in accordance with 21 CFR 208.24. Sufficient numbers of Medication Guides should be provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription. We recommend that each packaging configuration contain enough Medication Guides so that one is provided for each "usual" or average dose. For example:

- A minimum of 4 Medication Guides would be provided with a bottle of 100 for a product where the usual or average dose is 1 capsule/tablet daily, thus a monthly supply is 30 tablets.
- A minimum of 1 Medication Guide would be provided with unit of use where it is expected that all tablets/capsules would be supplied to the patient.

Some content and format in your submission in the section "Medication Guide" is more appropriate for a REMS Supporting Document. The format

and content of the REMS should be revised as indicated in the appended REMS.

c. We remind you of the requirement to comply with 21 CFR 208.24:

- A required statement alerting the dispenser to provide the Medication Guide with the product must be on the carton and container of all strengths and formulations. We recommend the following language dependent upon whether the Medication Guide accompanies the product or is enclosed in the carton (for example, unit of use):
  "Dispense the enclosed Medication Guide to each patient." or
  "Dispense the accompanying Medication Guide to each patient."

d. Your proposed timetable for submission of assessments (18 months, 3 years, and 7 years) is acceptable.

- You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

Please submit for review a detailed plan to evaluate patients' understanding about the safe use of Zenpep (pancrelipase). Your detailed plan should be submitted as part of the REMS supporting document. This information **does not** need to be submitted for FDA review prior to approval of your REMS, however it should be submitted at least 90 days before you plan to conduct the evaluation. The submission should be coded "REMS-Other." If you plan to conduct this assessment using a survey, your submission should include:

- All methodology and instruments that will be used to evaluate the patients' understanding about the safe use of Zenpep (pancrelipase). This should include, but not be limited to:
  - Sample size and confidence associated with that sample size
  - How the sample will be determined (selection criteria)
  - The expected number of patients to be surveyed
  - How the participants will be recruited
  - How and how often the surveys will be administered
  - Explain controls used to minimize bias
  - Explain controls used to compensate for the limitations associated with the methodology
- The survey instruments (questionnaires and/or moderator's guide).

- Any background information on testing survey questions and correlation to the messages in the Medication Guide.

Please let us know if you have any questions.

3 PP WITHHELD IN FULL IMMED. AFTER THIS PAGE AS (B)(4) DRAFT LABELING

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/s/

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7/21/2009 04:31:56 PM
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