CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022434Orig1s000

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-434 **COMPLETE RESPONSE**

Eagle Pharmaceuticals, Inc.
Attention: Brenda Marczi, Pharm.D.
Vice President, Regulatory Affairs
Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Dear Ms. Marczi:

Please refer to your new drug application (NDA) dated March 27, 2009, received March 30, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Argatroban Injection.

We acknowledge receipt of your amendments dated June 2, 2009, June 3, 2009, July 28, 2009, September 24, 2009, October 5, 2009, October 26, 2009, November 12, 2009, December 14, 2009 and December 17, 2009.

We also acknowledge receipt of your amendment dated September 24, 2009, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

1. We were not able to adequately assess the quality of your drug product during the review of NDA 22-434. The Chemistry, Manufacturing and Control (CMC) sections (Module 3) contain numerous deficiencies and conflicting information, the magnitude of which precludes issuing an itemized list in this communication. As discussed in several telephone conferences with you, the only recourse is to begin anew being sure that the CMC sections are complete, up-to-date, and correspond to the drug product intended for commercial distribution. Please note that previously submitted material is unsuitable to be used for referenced information.

2. Please be aware that the sufficiency of other aspects of your application (such as non-clinical, clinical pharmacology and clinical data) is also contingent upon the findings from our review of your supplied CMC information.

LABELING

3. We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm.

FACILITY INSPECTIONS

Our field investigator could not complete inspection of the Cipla Limited (b) (4) manufacturing facility at Verna, Goa 403 722, India because the facility was not ready for inspection. Satisfactory inspection is required before this application may be approved. Please notify us in writing when this facility is ready for inspection.

SAFETY UPDATE

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 nonclinical and clinical studies/trials 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/clinical trials 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 trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial 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 updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

7. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

8. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA's *Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants*, May 2009 at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf.

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, call Ebla Ali Ibrahim, Regulatory Health Project Manager, at (301) 796-3691.

Sincerely,

{See appended electronic signature page}

Rafel Dwaine Rieves, M.D.
Director
Division of Medical Imaging and Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22434	ORIG-1	EAGLE PHARMACEUTICALS INC	ARGATROBAN INJECTION

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RAFEL D RIEVES
01/29/2010