CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022434Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Ann. T. Farrell, M.D., Acting Division Director
Subject	Division Director Summary Review
NDA/BLA # **Supplement #**	22434
Applicant Name	Eagle Pharamceuticals, Inc.
Date of Submission	January 12, 2011
PDUFA Goal Date	July 12, 2011
Proprietary Name / **Established (USAN) Name**	Argatroban Injection RTU ready to use
Dosage Forms / Strength	50 mL solution in single-use, piggyback vial at a concentration of 1 mg/mL
Proposed Indication(s)	Indicated for prophylaxis or treatment of thrombosis in adult patients with heparin-induced thrombocytopenia (HIT), and as an anticoagulant in adult patients with or at risk for HIT undergoing percutaneous coronary intervention (PCI).
Action/Recommended Action for NME:	**Full Approval**

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	Firoozeh Alvandi, M.D./ Virginia Kwitkowski, RNP
Statistical Review	N/A
Pharmacology Toxicology Review	Shwu Luan Lee Ph.D./ Haleh Saber, Ph.D.
CMC Review/OBP Review	W. Michael Adams, Ph.D./Janice Brown, Ph.D. and Angelica Dorantes, Ph.D. and Patrick J. Marroum, Ph.D.
Microbiology Review	Stephen Langille, Ph.D.
Clinical Pharmacology Review	Hua Zhang, Ph.D./ Julie Bullock, Pharm.D.
DDMAC	
DSI	N/A
CDTL Review	Janice Brown, Ph.D.
OSE/DMEPA	Anne C. Tobenkin, Pharm.D./ Melina Griffis, R.Ph./ Carol Holquist, R. Ph.
OSE/DDRE	
OSE/DSRCS	
Other	

OND=Office of New Drugs
DDMAC=Division of Drug Marketing, Advertising and Communication
OSE= Office of Surveillance and Epidemiology
DMETS=Division of Medication Errors and Technical Support
DSI=Division of Scientific Investigations
DDRE= Division of Drug Risk Evaluation
DSRCS=Division of Surveillance, Research, and Communication Support
CDTL=Cross-Discipline Team Leader

Signatory Authority Review Template

1. Introduction

NDA 22434 is a 505 b2 application for argatroban. The original application was submitted on September 26, 2008; however the deficiencies were such that the applicant was issued a refusal to file determination. The applicant resubmitted on March 27, 2009. During the first cycle review Chemistry, Manufacturing and Control deficiencies were identified and the applicant received a complete response (CR) letter on January 29, 2010. The applicant submitted a response to their CR letter on January 12, 2011.

2. Background

The Reference Listed Drug (RLD) for this submission is Argatroban Injection (NDA 20-883), which is currently marketed by Pfizer.

3. CMC/Device

The applicant adequately addressed previously identified CMC concerns. No new concerns arose during this review cycle. There were no issues identified that preclude approval. A biowaiver was granted.

From Dr. Brown's CDTL memo:

Sufficient stability data have been provided to support an expiry period of 24 months for the drug product stored at the recommended room temperature conditions. Agratroban Injection is light sensitive.

4. Nonclinical Pharmacology/Toxicology

The pharmacology/toxicology review team reviewed the submission and participated in labeling review. No issues that would preclude approval were identified.
From Dr. Lee's review:
Two nonclinical studies were submitted to justify the use of lactobionic acid as an excipient in the drug product. Based on the results of nonclinical studies and data available on erythromycin lactobionate (an approved FDA drug), the proposed level of

lactobionic acid in the drug product is acceptable.

5. Clinical Pharmacology/Biopharmaceutics

No issues that would preclude approval were identified. The only information submitted for review was data to support bridging between this 505 b2 product and the RLD. This information was reviewed previously during the first cycle and found to be acceptable. However, the applicant submitted another study to serve as an *in vitro* bridge.

From Dr. Zhang's review:
In this re-submission, Eagle submitted another in vitro "bridge" study report (EAG-ARG-10-CLOT) to compare the anticoagulant activity between Eagle's product and the RLD - Pfizer's ARGATROBAN Injection in support of a waiver of in vivo bioequivalence (BE). The study design and conduct of the study are similar to those indicated in the study report (0409) submitted on February 27, 2009, except that the formulation batch used in the current study was from the commercial site rather than that from the non-commercial site used in Study 0409. The results of the data analyses of the current study indicate that an acceptable in vitro bridge between Eagle's product and Pfizer's product was established.

6. Clinical Microbiology

There are no outstanding microbiology issues related to the manufacturing process and/or overall sterility assurance. No issues that would preclude approval were identified.

7. Clinical/Statistical-Efficacy

No new clinical data was submitted. Dr. Alvandi and Ms. Kwitkowski reviewed the labeling.

8. Safety

No new safety issues have been identified.

9. Advisory Committee Meeting

This product is not a NME.

10. Pediatrics

This product is not a NME.

11. Other Relevant Regulatory Issues

None

12. Labeling

All disciplines made recommendations for labeling which were incorporated.

13. Decision/Action/Risk Benefit Assessment

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- Recommended regulatory action

Full Approval

- Risk Benefit Assessment

N/A

- Recommendation for Post marketing Risk Management Activities

None

- Recommendation for other Post marketing Study Requirements/ Commitments

None

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/s/

ANN T FARRELL
06/28/2011