CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203049Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Ann. T. Farrell, M.D., Acting Division Director
Subject	Division Director Summary Review and CDTL memo
NDA/BLA # Supplement #	203049
Applicant Name	Hikma Pharmaceutical Co. LTD
Date of Submission	March 21, 2011
PDUFA Goal Date	January 28, 2012
Proprietary Name / Established (USAN) Name	Argatroban Injection
Dosage Forms / Strength	Injection 100mg/mL; Each vial contains 250 mg Argatroban
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:	**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	Li-Shan Hsieh, Ph.D./Janice Brown, Ph.D./ D.A. Lakhani, Ph.D./Angelica Dorantes, Ph.D.
Microbiology Review	Denise A. Miller/Bryan S. Riley, Ph.D.
Clinical Pharmacology Review	Young J. Moon, Ph.D./ Julie Bullock, Pharm.D.
DDMAC	James Dvorsky
DSI	N/A
CDTL Review	Janice Brown, Ph.D.
OSE/DMEPA	Jibril Abdus-Samad, PharmD/Todd Bridges, RPh./ Carol Holquist, RPh.
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 203049 is a 505 b2 application for argatroban which was submitted to the Agency on March 21, 2011.

2. Background

The Reference Listed Drug (RLD) for this submission is Argatroban Injection (NDA 20-883), which is currently marketed by Pfizer. This NDA was approved on June 30, 2000.

The Pfizer product and the Hikma product have the same active ingredient, dosage form, strength, and route of administration. The products differ by quantity of dehydrated alcohol and one excipent: Hikma replaces Pfizer's D-Sorbitol with Propylene Glycol.

In support of in vivo bioequivalence waiver, the sponsor submitted an *in vitro* bridging study to compare Hikma's product's pharmacodynamic activity (anticoagulant) with Pfizer's product.

3. CMC/Device

There were no issues identified that preclude approval. Both the primary reviewer and the CDTL noted that the product should not be kept in the freezer.

Based on the stability data provided, a 24-month expiration dating period is granted for room temperature storage conditions.

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.

5. Clinical Pharmacology/Biopharmaceutics

The in vitro bridging study was reviewed by Clinical Pharmacology. Additionally the Office of New Drugs Quality Assessment (ONDQA)-Biopharmaceutics reviewed the information included in NDA 203-049 for Argatroban Injection in Propylene Glycol, 100 mg/ml and granted the applicant's request for a waiver of the CFR's requirement

to provide in vivo BA/BE data to support the approval. No issues that would preclude approval were identified.

6. Clinical Microbiology

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

- 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
01/04/2012