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APPLICATION NUMBER:

200582Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	2/2/2011
From	Amna Ibrahim MD
Subject	(Deputy) Division Director Summary Review
NDA/BLA # **Supplement #**	200582
Applicant Name	Hospira Inc
Date of Submission	12/03/2010
PDUFA Goal Date	2/3/2011
Proprietary Name / **Established (USAN) Name**	Topotecan Injection
Dosage Forms / Strength	Intravenous/4 mg/ml
Proposed Indication(s)	Small cell lung cancer sensitive disease after failure of first-line chemotherapy
Action/Recommended Action for NME:	Approval

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Medical Officer Review	Michael Brave MD/Ke Liu MD
Statistical Review	Not applicable
Pharmacology Toxicology Review	Not applicable
CMC Review/OBP Review	Not applicable
Microbiology Review	Not applicable
Clinical Pharmacology Review	Not applicable
DDMAC	George Adams/ Karen Rulli
DSI	Not applicable
CDTL Review	Sarah Pope Miksinski PhD
OSE/DMEPA	Irene Z. Chan, PharmD, BCPS/Denise Toyer PharmD
OSE/DDRE	Not applicable
OSE/DRISK	Not applicable
Biopharmaceutics, OND Quality Assessment	Angelica Dorantes, Ph. D./ Patrick J. Marroum, Ph. D

OND Office of New Drugs
DDMAC Division of Drug Marketing, Advertising and Communication
OSE Office of Surveillance and Epidemiology
DMEPA Division of Medication Error Prevention and Analysis
DSI Division of Scientific Investigations
DDRE Division of Drug Risk Evaluation
DRISK Division of Risk Management
CDTL Cross Discipline Team Leader

1. Introduction

Please see my DDD summary review and other pertinent reviews from the previous submission for this NDA, on which action was taken on 11/26/2010.

This class 1 NDA submission is in response to the CR letter sent to the sponsor on 11/26/2010. Sarah Pope Miksinski PhD states in her CDTL memo that with the exception of the updated proposed PI, the resubmission did not include any new and/or updated Clinical, Pharmacology/Toxicology, Clinical Pharmacology, or Biopharmaceutics information.

2. Background

Dr Miksinski states in her CDTL memo that NDA 200582 was initially submitted on 10/29/2009 as a 505(b)(2) application. During the initial review cycle, DMF deficiencies were noted by the Chemistry reviewer. The Applicant's response to these deficiencies were submitted on 8/18/2010, and the Agency subsequently extended the PDUFA date by three months. In November 2010, the Agency took a "Complete Response" action for NDA 200582 based on an overall withhold recommendation from the Office of Compliance. Dr. Miksinski also notes that with the exception of the updated proposed PI, the resubmission did not include any new and/or updated Clinical, Pharmacology/Toxicology, Clinical Pharmacology, or Biopharmaceutics information. All disciplines were included in the negotiation and internal discussion of final PI labeling, and all disciplines concur with the final PI and container/carton labeling. Out of the three indications approved for the Reference Listed Drug (RLD) Hycamtin, the indication for ovarian cancer is still under patent. The applicant has proposed the SCLC indication only for this application.

3. CMC/Device

Per CMC review signed by Debasis Ghosh PhD on 1/25/2011, and cosigned by Dr Miksinski on 1/25/2011, "From the perspective of Chemistry, Manufacturing and Controls (CMC), this NDA is recommended for approval pending satisfactory resolution of labeling (PI) issues". A review by Angelica Dorantes PhD signed on 1/29/2011 states that the resubmission does not include any Biopharmaceutics information and that ONDQA-Biopharmaceutics does not have any comments.

In her memo, Dr Miksinski states "In a 03-DEC-2010 submission, the Applicant responded to the Agency's 26-NOV-2010 letter. The submission was classified as a Class 1 resubmission. In order to address the overall withhold recommendation from the Office of Compliance, the Applicant withdrew the non-cGMP-compliant site (Hospira Worldwide, Inc., Rocky Mount, NC) from the application. All listed sites were re-submitted to the Office of Compliance for an updated recommendation during the current review clock, and an updated overall "acceptable" recommendation was received on 04-JAN-2011. This updated recommendation resolves the cGMP deficiency issued in the previous action letter." Dr Miksinski in an amendment dated

2/2/2011 states that the expiration dating period granted for this NDA is 18 months, when the drug product is stored at 2°C-8°C (36°F-46°F) and protected from light.

I concur with the conclusions reached by the chemistry reviewer regarding the acceptability of the manufacturing of the drug product and drug substance. Manufacturing site inspections were acceptable. Stability testing supports an expiry of 18 months. There are no outstanding issues.

4. Nonclinical Pharmacology/Toxicology

Not applicable to this submission.

5. Clinical Pharmacology/Biopharmaceutics

Not applicable to this submission.

6. Clinical Microbiology

Not applicable.

7. Clinical/Statistical-Efficacy

According to Michael Brave MD, this application contains no new clinical data and relies for approval on the FDA's findings of safety and effectiveness for Hycamtin®. There were some issues with the proposed indication but they were resolved. The proposed indication was acceptable (see amended review by Dr. Brave cosigned by Dr Liu).

8. Safety

Not applicable to this submission.

9. Advisory Committee Meeting

Not applicable to this submission.

10. Pediatrics

Not applicable to this submission.

11. Other Relevant Regulatory Issues

Not applicable to this submission.

12. Labeling

DDMAC reviewer George Adams recommended that the use of the term (b) (4)

(b) (4) be changed to "combined experience" because the studies for the (b) (4).

DMEPA review by Irene Chan PharmD recommends that inconsistencies between the proposed label and other topotecan labels be streamlined. For specifics, please see the review of Irene Z. Chan, PharmD, BCPS.

13. Decision/Action/Risk Benefit Assessment

- Regulatory Action

An approval action is recommended based on the risk-assessment assessment below.

- Risk Benefit Assessment

This is a 505b2 application based on the RLD Hycamtin. The only deficiency communicated to the applicant in the previous cycle was an unsatisfactory rating of facility inspections of Hospira worldwide Inc. (Rocky Mount, NC) by the Office of Compliance and this issue was resolved. The application received an updated overall acceptable recommendation from the Office of Compliance on 1/04/2011. No review reported any deficiencies. The labeling has been reviewed by all disciplines and found acceptable.

- Recommendation for Postmarketing Risk Evaluation and Mitigation Strategies

Not applicable

- Recommendation for other Postmarketing Requirements and Commitments

Not applicable.

Amna Ibrahim MD
Deputy Director
Division of Drug Oncology Products

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/s/

AMNA IBRAHIM
02/02/2011