CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200795Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	8/4/2011
From	Amna Ibrahim MD
Subject	Deputy Division Director Summary Review
NDA/BLA # **Supplement #**	200795 Resubmission (class 1)
Applicant Name	Hospira, Inc.
Date of Resubmission	6/10/2011
PDUFA Goal Date	8/10/2011
Proprietary Name / **Established (USAN) Name**	None Gemcitabine Injection
Dosage Forms / Strength	Sterile solution for injection/ 38 mg/mL
Proposed Indication(s)	1. In combination with carboplatin is indicated for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy. 2. In combination with paclitaxel is indicated for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated. 3. In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell lung cancer. 4. As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemcitabine injection is indicated for patients previously treated with 5-FU.
Action/Recommended Action:	Approval

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Pharmacology Toxicology Review	Brenda Gehrke/Whitney Helms
Clinical Pharmacology Review	Elimika Pfuma/Qi Liu
CMC Review/OBP Review	AKM Khairuzzaman/ Haripada Sarkar
CDTL Review	Haripada Sarkar
OSE/DMEPA	Yelena Maslov/ Carol A Holquist
OSE/DDMAC	Marybeth Toscano/ Richard A Lyght

OND=Office of New Drugs
OSE= Office of Surveillance and Epidemiology
DMEPA=Division of Medication Error Prevention and Analysis
CDTL=Cross-Discipline Team Leader

1. Introduction

NDA 200795 was originally submitted on 12/11/2009. The PDUFA date was extended due to a major amendment. Finally a CR letter was sent on 1/11/2011. Please also see my summary review dated 1/11/2011 for the original submission of this NDA. This amendment was submitted on 6/10/2011 as a complete response addressing deficiencies identified in the FDA Complete Response Letter dated January 11, 2011.

2. Background

A Class 1 review was requested and granted for this submission. Hospira provides additional impurity assay validation data, microbiological stability data to support post-dilution storage period, draft labeling, and safety update information as requested. This review covers only the deficiencies addressed by the applicant.

3. CMC/Device

The deficiencies were resolved satisfactorily. Per Akm Khairuzzaman PhD:

> "This new drug application (200-795) can be recommended for approval from the perspective of chemistry, manufacturing, and controls."
>
> "The Office of Compliance has given an acceptable recommendation for the manufacturing and testing facilities."

According to Stephen E. Langille, Ph.D., no microbiology deficiencies were identified based upon the information provided. He recommends approval from the standpoint of product quality microbiology.

Haripada Sarkar PhD states the following in his CDTL memo, cosigned by Sarah P Miksinski PhD:

> "Outstanding CMC and Pharmacology/Toxicology deficiencies are resolved in this review cycle, also Office of Compliance issued an acceptable recommendation. This application is recommended for approval from a CMC perspective, and therefore, the application is also recommended for approval overall."

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 at 3 to 8^{o} C (refrigerated storage conditions). There are no outstanding issues.

4. Nonclinical Pharmacology/Toxicology

Brenda Gehrke PhD, states the following in her review.

> "Based on the validation method, the impurity levels reported in the toxicology study appear to be accurate, and therefore, the impurities are qualified at the proposed specifications. There were no other issues requiring pharmacology/toxicology input that developed during the course of the review process for this or the previous submission. The Hospira formulation for Gemcitabine Injection is, therefore, recommended for approval."

Acting Team Lead Whitney Helms PhD agreed with these findings. I concur with the conclusions reached by the pharmacology/toxicology reviewer that there are no outstanding pharm/tox issues that preclude approval.

5. Clinical Pharmacology/Biopharmaceutics

Elimika Pfuma PhD in her review finds the NDA acceptable. No new Clinical Pharmacology information was submitted.

6. Clinical Microbiology

Not applicable.

7. Clinical/Statistical-Efficacy

Not applicable.

8. Safety

Not applicable.

9. Advisory Committee Meeting

Not applicable.

10. Pediatrics

Not applicable.

11. Other Relevant Regulatory Issues

There are no other unresolved relevant regulatory issues

12. Labeling

Labeling was based upon the package insert for the RLD. Appropriate changes were made by the reviewers to the appropriate sections and agreed upon changes will be included in the finalized label. There were no unresolved issues. There is no PPI or medication guide.

13. Decision/Action/Risk Benefit Assessment

- Regulatory Action
  This NDA should be approved. There are no remaining deficiencies.

- Risk Benefit Assessment
  The proposed drug product contains the same active ingredient as the RLD. The review of this NDA is based primarily on chemistry, manufacturing and controls data. The risk benefit profile should be the same as the RLD. There are no outstanding deficiencies for this NDA.

- Recommendation for Postmarketing Risk Evaluation and Mitigation Strategies
  None

- Recommendation for other Postmarketing Requirements and Commitments
  None

Amna Ibrahim MD
Deputy Director
Division of Drug Oncology Products

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

/s/

AMNA IBRAHIM
08/04/2011