CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022234Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	04-Mar-2011
From	Anthony J. Murgo, M.D., M.S.
Subject	Deputy Division Director Summary Review
NDA #	22234
Applicant Name	Hospira, Inc.
Date of Submission	Original: 11-Jul-2007 Amendments: 23-Sept-2010; 03-Nov-2010
PDUFA Goal Date	23-Mar-2011
Established (USAN) Name	Docetaxel
Dosage Forms / Strength	Docetaxel injection 20 mg/2mL (single-dose vial) Docetaxel injection 80 mg/8 mL (multi-dose vial) Docetaxel injection 160 mg/16 mL (multi-dose vial)
Proposed Indication(s)	1. Breast Cancer • Docetaxel Injection is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy. • Docetaxel Injection in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer. 2. Non-Small Cell Lung Cancer • Docetaxel Injection as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy. • Docetaxel Injection in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition. 3. Prostate Cancer • Docetaxel Injection in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.
Action	Approval

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	
Statistical Review	
Pharmacology Toxicology Review	
CMC Review/OBP Review	X
Microbiology Review	
Clinical Pharmacology Review	
DDMAC	
DSI	
CDTL Review	X

OSE/DMEPA	X
OSE/DDRE	
OSE/DRISK	
Other	

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

Signatory Authority Review

1. Introduction

This NDA provides for the use of Docetaxel Injection, 20 mg/2 mL single-dose vial, 80 mg/8 mL multi-dose vial, and 160 mg/16 mL multi-dose vial for locally advanced or metastatic breast cancer after failure of prior chemotherapy, in combination with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive breast cancer, for locally advanced or metastatic non-small lung cancer after failure of prior platinum-based chemotherapy, in combination with cisplatin for unresectable, locally advanced or metastatic untreated non-small cell lung cancer, and in combination with prednisone for androgen independent (hormone refractory) metastatic prostate cancer. Of note, the NDA does not request two additional indications that are in the RLD labeling, which are for the treatment of gastric cancer and cancer of the head and neck.

The NDA was initially received July 11, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. The reference listed drug (RLD) is Taxotere (sanofi-aventis). There were multiple subsequent submissions, including one received April 28, 2008. FDA granted Tentative Approval on August 11, 2008. The Tentative Approval Letter stated that final approval cannot be granted until:

1. *a. expiration of the 30-month period provided for in Section 505(c)(3)(C) beginning on the date of receipt of the 45-day notice required under Section 505(b)(3), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or*
   b. the date the court decides that the patent(s) is/are invalid or not infringed a described in section 505(c)(3)(C)(i), (ii), (iii,) or (iv) of the Act, or,
   c. the listed patent(s) has/have expired, and
2. *we are assured there is no new information that would affect whether final approval should be granted.*

In addition, the listed reference drug product upon which you base your application is subject to a period of patent protection and exclusivity protection and therefore, final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired, i.e., September 28, 2010.

There was a subsequent amendment dated September 23, 2010 (b) (4) . This proposal was withdrawn by the applicant on November 3, 2010. The only item that was remaining in the amendment is updated Hospira labeling to comply with the latest revision of the reference listed drug labeling. However, DMEPA noted an additional safety concern of the concentration of the Hospira's Docetaxel product (10 mg/mL) differs from the recently approved Taxotere 1-vial product which is 20 mg/mL. This was considered a safety concern because the inconsistency between the concentrations of the 1-vial Docetaxel products could lead to confusion and medication errors (see Section 12, below).

2. Background

Please see above. The Deputy Division Director review dated August 11, 2008 contains more details on the application, but those additional details are not directly relevant to the current action.

3. CMC/Device

Please refer to the CMC review signed on November 12th and December 15th by the primary reviewer and team leader, respectively. Also see Section 12 regarding carton and container labeling. I concur with the recommendation of the CMC reviewers that the application is approvable with respect to chemistry, manufacturing, and controls.

4. Nonclinical Pharmacology/Toxicology

NA this cycle

5. Clinical Pharmacology/Biopharmaceutics

NA this cycle

6. Clinical Microbiology

NA

7. Clinical/Statistical-Efficacy

NA

8. Safety

No safety data other than that of RLD

9. Advisory Committee Meeting

NA

10. Pediatrics

New pediatric information in the RLD labeling is carved out of the labeling of this product, consistent with the handling of other 505(b)(2) docetaxel labels.

11. Other Relevant Regulatory Issues

None

12. Labeling

On November 17, 2010, the Division of Medication Error Prevention and Analysis (DMEPA) notified the review division by email of a potential safety problem concerning the Hospira's Docetaxel Injection container and carton labeling. DMEPA compared these labels and labeling to the labels and labeling of Taxotere's 1-vial product in an effort to maintain

consistency across the 1-vial Docetaxel products. Upon comparison, DMEPA noted the concentration of Hospira's Docetaxel product is 10 mg/mL which differs from the recently approved Taxotere 1-vial product which is 20 mg/mL. This was considered a safety concern because the inconsistency between the concentrations of the 1-vial Docetaxel products could lead to confusion and medication errors. In order to prevent these errors DMEPA believed the Hospira Docetaxel product should be reformulated to a 20 mg/mL concentration to match Taxotere's 1-vial product. DMEPA recognized that the review team intended to take an action on November 22, 2010 but felt that this issue should be fully vetted before action is taken. An internal meeting was held on November 18, 2010 involving DMEPA, CMC, pharmacology/toxicology and clinical members of the review team to discuss this matter. While all recognized that there was the potential for medication errors, the concerns with requiring a formulation change in the Hospira Docetaxel product discussed at that meeting were that doing so would not eliminate the medication errors and a formulation change would delay the approval of the product for at least 6 months; it could also affect actions on other 505(b)(2) docetaxel applications tentatively approved or under review. The group discussed alternatives to changing the formulation, including ways to enhance product recognition, such as modifying the appearance of the vial cap and/or ferrule and applying a "stop sign". The review team discussed the concerns and potential solutions in a teleconference with the applicant on November 23. The applicant submitted a revised Dear Health Care Profession Professional letter on December 2, 2010 and revised container and carton labels on December 24, 2010 for FDA review. The revised Dear HCP letter and container and carton labeling were considered acceptable by the review team including DMEPA. See the DMEPA review signed by the primary and secondary reviewers on January 28, 2011 and the CDTL review signed March 2, 2011. I concur with the review team that the potential for medication errors is minimized and that there are no outstanding deficiencies precluding approval.

13. Decision/Action/Risk Benefit Assessment

- Regulatory Action: Approval

- Risk Benefit Assessment

Consistent with the RLD

- Recommendation for Postmarketing Risk Management Activities
  None

- Recommendation for other Postmarketing Study Commitments

None

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/s/

ANTHONY J MURGO
03/04/2011