CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201525Orig1s000

CROSS DISCIPLINE TEAM LEADER REVIEW

Cross-Discipline Team Leader Review

Date	24-JUN-2011
From	Sarah Pope Miksinski, Ph.D.
Subject	Cross-Discipline Team Leader Review
NDA/BLA # Supplement#	201525
Applicant	Sandoz, Inc.
Dates of Submissions	17-SEP-2010
PDUFA Goal Date	17-JUL-2011
Proprietary Name / Established (USAN) names	Docetaxel Injection
Dosage forms / Strength	10 mg/mL (20 mg/2 mL, 80 mg/8 mL, 160 mg/16 mL)
Proposed Indication(s)	1. Breast cancer 2. Non-small cell lung cancer 3. Prostate cancer 4. Gastric adenocarcinoma 5. Head and neck cancer
Recommended:	**Approval**

1. Introduction

Sandoz, Inc. submitted NDA 201525 for Docetaxel Injection on 17-SEP-2010. The NDA was subsequently filed on 30-NOV-2010, and the PDUFA date is 17-JUL-2011.

This CDTL memo serves to highlight the critical approvability issues discussed in all review disciplines and recommends an "Approval" action for this application. All individual discipline reviews may be found in DARRTS. Final container labels were provided on 01-JUN-2011. Final PI labeling was also received on 01-JUN-2011. This labeling was confirmed as acceptable for all disciplines.

2. Background

The Reference Listed Drug for this submission is the one-vial formulation of Taxotere® (docetaxel) Injection Concentrate (NDA 20-449), which is currently marketed by Sanofi Aventis. The proposed drug product is a "ready to use" product containing the drug substance (in solution) in one vial. The solution is intended for reconstitution and subsequent intravenous injection. Docetaxel Injection is supplied in three presentations (20 mg/2 mL, 80 mg/8 mL, 160 mg/16 mL). All three presentations utilize the same concentration of 10 mg/mL. With the exception of two added excipients (polyethylene glycol 300 and citric acid), the proposed drug product contains the same active and inactive ingredients as the RLD. Variations are present relative to the innovator product, including small variations in concentration for both polysorbate 80 and ethanol.

Dosing Regimen and Administration
There are various indications and dosing regimens associated with this NDA. Please refer to the Medical Officer's 09-JUN-2011 review for additional details.

3. CMC

Summarized below are the major issues identified and resolved in the Quality (CMC) review:

- The current CMC reviewer (Sue-Ching Lin, M.S.) identified no outstanding deficiencies in her review dated 12-MAY-2011. The CMC reviewer recommends approval of this NDA. **The granted expiration dating period should be captured in the action letter with the following language:**

  "Based on the stability data provided, an 18-month expiration dating period is granted for the drug product, when stored at the proposed conditions (between 2°C and 25°C)"

- Reference is made to the review filed in DARRTS (see review dated 26-APR-2011, by Dr. A. Dorantes), which confirms the Applicant's requested biowaiver.

- Facilities review/inspection
  An overall "acceptable" recommendation was issued by the Office of Compliance on 26-APR-2011. The summary report for this recommendation can be located in the 12-MAY-2011 CMC review.

- Microbiology
  The Microbiology reviewer (Dr. B. Riley) conducted a review of this submission and recommended approval in a 08-APR-2011 review.

- Other notable issues (resolved or outstanding)
  None

4. Nonclinical Pharmacology/Toxicology

Reference is made to the 09-JUN-2011 Pharmacology/Toxicology review (Dr. S. Khasar) which states the following:

Although the specification for (b) (4) *in the proposed Sandoz docetaxel formulation exceeds that in the RLD,* (b) (4) *is a metabolite of docetaxel. Considering the extensive clinical experience with taxotere,* (b) (4) *is considered qualified from a toxicological perspective. Similarly,* (b) (4) *is not expected to pose a significant risk to humans. Labeling of the non-clinical sections is the same as the RLD. Therefore, there are no pharmacology/toxicology issues which*

preclude approval of Docetaxel Injection as a 505(b)(2).

Labeling recommendations for the proposed PI are also captured in the review. The Pharmacology/Toxicology recommendation for approval is further confirmed in the 08-JUN-2011 memorandum (Dr. W. Helms).

5. Clinical Pharmacology

There was no clinical pharmacology data submitted to this NDA. The clinical pharmacology reviewer (Dr. J. Fourie) recommends approval of this NDA in her review dated 08-APR-2011. The review also captures related revisions to the PI.

6. Clinical Microbiology

Not applicable.

7. Clinical/Statistical- Efficacy

There are no new clinical data provided in the current submission. The clinical reviewer (Dr. K. Snyder) recommends approval of this NDA in her 09-JUN-2011 memo.

8. Safety

No new clinical data were provided for this submission.

9. Advisory Committee Meeting

Not applicable

10. Pediatrics, Geriatrics, and Special Populations

Not applicable

11. Other Relevant Regulatory Issues

- Application Integrity Policy (AIP): This was not raised during the pre-approval inspections for this NDA.
- Exclusivity or patent issues of concern: No issues were noted for this NDA.
- Financial disclosures: Not applicable
- Other GCP issues: None
- DSI audits: Not applicable
- Other discipline consults: None
- Any other outstanding regulatory issues: None

12. Labeling

General:
All disciplines participated in internal labeling meetings held throughout the review clock. Specific labeling recommendations are captured in each discipline-specific review.

Proprietary name:
There is no proprietary name proposed for this product.

DMEPA/DDMAC comments:
Reference is made to the review dated 06-APR-2011 (L. Holmes) which details several areas of concern applicable to the proposed container/carton labeling. This review also outlines a comprehensive list of updated deficiencies related to DMEPA's review of the currently proposed container/carton and PI labeling. Following internal team discussion, these comments were issued to the Applicant. In a 27-MAY-2011 updated review, the DMEPA reviewer (L. Holmes) also confirmed that the Applicant's proposed container/carton labeling (received 24-MAY-2011) was acceptable.

A review was filed on 14-APR-2011 by the Division of Drug Marketing, Advertising, and Communications (DDMAC). The identified recommendations were discussed internally and incorporated into the labeling accordingly.

Carton and immediate container labels:
See above section titled "DMEPA/DDMAC comments."

Patient labeling/Medication guide:
This is not required for this product.

13. Recommendations/Risk Benefit Assessment

- Recommended Regulatory Action
  This reviewer recommends approval of this NDA. There are no outstanding deficiencies for any disciplines involved in the review of this submission. All disciplines were involved in labeling discussions. The final proposed labeling reflects the recommended revisions from all disciplines and is acceptable.

- Risk Benefit Assessment
  The review of this NDA is based primarily on chemistry, manufacturing and controls data. However, the NDA is recommended for approval from all disciplines.

- Recommendation for Postmarketing Risk Management Activities
  This does not apply to this NDA.

- Recommendation for other Postmarketing Study Commitments
  None

- Recommended Comments to Applicant
  The following language confirming the granted expiration dating period should be placed in the action letter:

  "Based on the stability data provided, an 18-month expiration dating period is granted for the drug product, when stored at the proposed conditions (between 2^{o}C and 25^{o}C)"

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

/s/

SARAH P MIKSINSKI
06/24/2011