CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201195Orig1s000

CROSS DISCIPLINE TEAM LEADER REVIEW

Cross-Discipline Team Leader Review

Date	07-JUN-2011
From	Sarah Pope Miksinski, Ph.D.
Subject	Cross-Discipline Team Leader Review
NDA/BLA # Supplement#	201195
Applicant	Accord Healthcare, Inc.
Dates of Submissions	10-DEC-2010
PDUFA Goal Date	10-JUN-2011
Proprietary Name / Established (USAN) names	Docetaxel Injection
Dosage forms / Strength	20 mg/0.5 mL vial and 80 mg/2 mL vial (both with diluent)
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

Accord Healthcare, Inc. submitted NDA 201195 for Docetaxel Injection on 21-DEC-2009. The NDA was subsequently filed on 05-MAR-2010 and was issued a "Complete Response" action on 22-OCT-2010. The Applicant submitted a response on 07-DEC-2010, and in a 02-FEB-2011 letter, the Agency deemed the submission a Class 2 resubmission. The PDUFA date is 10-JUN-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 received on 06-JUN-2011. This labeling was confirmed as acceptable for all disciplines.

2. Background

The Reference Listed Drug for this submission is Taxotere® (docetaxel) Injection Concentrate (NDA 20-449), which is currently marketed by Sanofi Aventis. The proposed drug product is a co-packaged product containing the drug substance (in solution) in one vial, and a product-specific diluent in a second vial. The active solution is intended for reconstitution with the supplied diluent, followed by intravenous injection. Docetaxel Injection is supplied in two presentations (20 mg/0.5 mL and 80 mg/2 mL, based on the free base). Both presentations utilize the same concentration of 40 mg/mL. With the

exception of two additional excipients, the proposed drug product contains the same active and inactive ingredients in the same final concentrations as the RLD. Variations are present relative to the innovator product, including the presence of both citric acid and dehydrated alcohol in the active solution (absent in the innovator's active vial) and polyethylene glycol 400 in the diluent (present in the innovator's active vial).

Dosing Regimen and Administration
There are various indications and dosing regimens associated with this NDA. Please refer to the Medical Officer's 18-MAY-2011 review for additional details.

3. CMC

NDA 201195 was initially submitted on 21-DEC-2009 as a 505(b)(2) application. The NDA included a full dossier of CMC information, along with proposed container/carton and PI labeling. In a review dated 19-OCT-2010, the Chemistry Reviewer (Dr. H. Chang) recommended a "Complete Response" from a CMC perspective, based on eight (8) remaining CMC deficiencies.

The current submission contained responses to seven of the eight identified CMC deficiencies. The final deficiency regarding the previously-proposed Comparability Protocol was not issued in the 22-OCT-2010 action letter, but was addressed in a 12-MAY-2011 teleconference with the Applicant. Briefly, the CMC assessment of the submitted information is summarized as follows:

- The current CMC reviewer (Dr. J. Crich) identified no new deficiencies in her review dated 31-MAY-2011. Additionally, she confirmed that the previously-issued CMC deficiencies have been adequately resolved. 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, a 12-month expiration dating period is granted for the drug product, when stored at 25°C (77°F); excursions permitted from 15°C - 30°C (59°F - 86°F)."

- This resubmission did not include any new Biopharmaceutics data. Reference is made to a previous review filed in DARRTS (see review dated 22-APR-2011, by Dr. A. Dorantes), which confirmed the Applicant's previous request for a biowaiver.

- Facilities review/inspection
  An Establishment Evaluation Request (EER) was submitted to the Office of Compliance in a previous review cycle. As stated in the 31-MAY-2011 CMC review, an overall acceptable recommendation has not been reissued for the application in this review cycle. This is because the overall recommendation from the previous review cycle is still valid, and therefore it was not necessary to submit an EER for this cycle. No new sites were added, and the overall recommendation date from the previous cycle

was within two years of the PDUFA date for this review cycle. This is not a remaining CMC deficiency.

- Microbiology
  The Microbiology reviewer (Dr. J. Metcalfe) conducted an updated review of this submission and recommended approval in a 05-OCT-2010 review.

- Other notable issues (resolved or outstanding)
  None

4. Nonclinical Pharmacology/Toxicology

Reference is made to the 09-SEP-2010 Pharmacology/Toxicology review (Dr. M. Brower) which identifies two deficiencies related to impurity qualification (ICH Q3B(R2)). The Applicant responded to these deficiencies in the current submission. The final Pharmacology/Toxicology memo for this resubmission was finalized (Dr. M. Brower) in DARRTS on 02-JUN-2011 and captures a recommendation of "Approval" for the NDA. Both previous deficiencies have been adequately resolved. Labeling recommendations for the proposed PI are also captured in the review.

5. Clinical Pharmacology

There was no clinical pharmacology data submitted to this NDA. The clinical pharmacology reviewer (Dr. Y. Moon) previously recommended approval of this NDA in her review dated 10-SEP-2010. An updated review (Dr. J. Fourie, 08-APR-2011) confirms the acceptability of the current submission to support approval and 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 28-MAY-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 05-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 03-JUN-2011 updated review, the DMEPA reviewer (L. Holmes) also confirmed that the Applicant's proposed container/carton labeling (received 01-JUN-2011) was acceptable.

A review was filed on 22-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, a 12-month expiration dating period is granted for the drug product, when stored at 25^{o}C (77^{o}F); excursions permitted from 15^{o}C - 30^{o}C (59^{o}F - 86^{o}F)."

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/s/

SARAH P MIKSINSKI
06/07/2011