CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201195Orig1s000

SUMMARY REVIEW

DD Summary Review for Regulatory Action

Date	(electronic stamp)
From	Anthony J. Murgo, M.D., M.S. Acting Deputy Division Director
Subject	NDA 505(b)(2) review
NDA #	201195
Applicant Name	Accord Healthcare, Inc.
Date of Submission	21-DEC-2009 (orig.); 10-DEC-2010 (resubmission)
PDUFA Goal Date	10-June-2011
Proprietary Name / Established (USAN) Name	Docetaxel Injection Docetaxel
Dosage Forms / Strength	20 mg/0.5 mL and 80 mg/2 mL (and diluent)
Proposed Indication(s)	1. Breast cancer 2. Non-small cell lung cancer 3. Prostate cancer 4. Gastric adenocarcinoma 5. Squamous cell carcinoma of the head and neck cancer
Action:	**Approval**

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	X
Statistical Review	
Pharmacology Toxicology Review	X
CMC Review/OBP Review	X
Microbiology Review	
Clinical Pharmacology Review	X (this cycle labeling only)
DDMAC	X
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

Accord submitted a 505(b)(2) New Drug Application (NDA 201195) for Docetaxel Injection on December 21, 2009. The reference listed drug (RLD) is Taxotere® for Injection (docetaxel; Sanofi-Aventis), initially approved by the FDA on May 14, 1996 (NDA 20-449). Taxotere® for Injection is indicated for the treatment of breast cancer (as a single-agent for metastatic disease and in combination as adjuvant treatment), non-small cell lung cancer (as a single-agent and in combination), hormone refractory prostate cancer, gastric adenocarcinoma, and squamous cell carcinoma of the head and neck (SCCHN). Accord is seeking approval for all five of these indications.

A CR action was taken on 22-OCT-2010 mainly due to nonclinical/product quality deficiencies. This summary review pertains mainly to the class 2 resubmission dated 10-DEC-2010.

2. Background

This Docetaxel Injection 505(b)(2) NDA application was originally submitted by Accord Healthcare, Inc. on 21-DEC-2009. The applicant is seeking the same indications as the RLD Taxotere. A CR action was taken on 22-OCT-2010 mainly due to the nonclinical/product quality deficiencies as conveyed in the CR letter as follows:

1. Revise the drug product release specification to include a single criterion for purity and related substances to be used both at release and on stability. Include a justification for the proposed criteria.

2. In section 3.2.P.2 Table 18, Comparator Comparison Stability Study, the levels of impurity (b) (4) at 3 and 6 months are lower at 40±2°C/75±5% RH than at 25±2°C/60±5% RH. However, other impurity levels are generally higher at the higher temperature than at the lower temperature. Explain this apparent discrepancy.

3. Either provide additional stability data and information to support the proposed storage condition (b) (4) in the absence of light) or revise the proposed label storage statement to indicate a condition supported by the submitted long-term stability studies. The current stability information is not sufficient to support storage (b) (4)

4. Provide additional long term stability data to support the proposed initial drug product expiry period. The submitted 6 month data is not sufficient to support approval of (b) (4)

5. Using the analytical method in your NDA, there are two new impurity peaks identified as RRT (b) (4) and RRT (b) (4) The acceptance criteria for these two compounds are set at NMT (b) (4). This acceptance criterion is above the threshold of 0.2% set by ICH Q3B (R2) based on the maximum daily dose of 180 mg/person. Please identify these two impurity peaks.

   If the impurity peaks at RRT (b) (4) and RRT (b) (4) cannot be identified, their levels should be adequately justified (e.g., based on nonclinical studies), or reduced to meet the ICHQ3B (R2) threshold. If the impurity peaks at RRT (b) (4) and RRT (b) (4) are identified to be an impurity in the RLD, their levels should be reduced to less than the levels observed in the RLD; levels above the RLD should be adequately justified based on nonclinical or clinical studies.

This review pertains mainly to the applicant's class 2 resubmission (10-DEC-2010) addressing the above deficiencies.

3. CMC/Product Quality and PQ Microbiology

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 recommended a "Complete Response" from a CMC perspective, based on eight (8) remaining CMC deficiencies (see above).

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 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 (b) (4) 25°C ((b) (4) 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), 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.

I concur with the conclusions reached by the review of CMC and of the CDTL (review signed 07-June-2011) that the application is acceptable from a CMC perspective.

The Product Quality Microbiology review was signed 05-OCT-2010. I concur with the conclusion of the reviewers that the application is approvable on the basis of issues pertaining to product quality microbiology.

4. Nonclinical Pharmacology/Toxicology

The impurity deficiencies noted in the Nonclinical Pharmacology/Toxicology review that was signed on 9-SEPT-2010 are resolved according to the final review of this resubmission signed on 02-June-2011.

I concur with the Nonclinical Pharmacology/Toxicology reviewers that this NDA is approvable from a nonclinical pharmacology/toxicology perspective.

5. Clinical Pharmacology/Biopharmaceutics

As noted in Clinical Pharmacology review of the original submission and reiterated more recently in the review of this resubmission (signed 08-APR-2011), the application is acceptable from a Clinical Pharmacology/Biopharmaceutics perspective. I concur with this recommendation.

6. Clinical Microbiology

N/A

7. Clinical/Statistical-Efficacy

As noted in the Clinical Reviews signed on 27-May-2011 and 28-May-2011 by the primary reviewer and team leader, respectively, no new clinical data were submitted for this NDA. The RLD Taxotere (NDA 20449) has been previously reviewed for efficacy and safety. I concur with the conclusions of the clinical reviewers that there are no outstanding clinical deficiencies.

8. Safety

NA

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. For a more detailed explanation, please refer to the Clinical Review signed on 27-May-2011 and 28-May-2011 by the primary reviewer and team leader, respectively.

11. Other Relevant Regulatory Issues

None

12. Labeling

Review of the labeling will be completed during the next cycle or when the application is otherwise approvable. The FDA and applicant agreed upon the final PI labeling (received on 06-JUN-2011) with the exception of the following change to be conveyed in the action letter:

Store at 25°C (77°F); excursions permitted ~~to~~ <u>from</u> 15°C - 30°C (59°-86°F) [see USP Controlled Room Temperature]. Protect from bright light.

DMEPA finds the final Carton/Container labeling acceptable (see review signed 03-June-2011).

13. Decision/Action/Risk Benefit Assessment

- Regulatory Action: **Approval**
- Risk Benefit Assessment

  Similar to the RLD

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

/s/

ANTHONY J MURGO
06/08/2011