CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201023s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

08-JUN-2010

NDA 201023/N-000

Drug Product Name
Proprietary: Jevtana®
Non-proprietary: Cabazitaxel

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
08-JUN-2010	08-JUN-2010	N/A	N/A
25-MAY-2010	25-MAY-2010	N/A	N/A
21-MAY-2010	21-MAY-2010	N/A	N/A
24-FEB-2010	24-FEB-2010	15-MAR-2010	16-MAR-2010

Applicant/Sponsor
Name: Sanofi Aventis
Address: 55 Corporate Drive
Bridgewater, NJ 08807
Representative: Linda Gustavson, Ph.D.
Telephone: 908-304-6221

Name of Reviewer: Steven Fong, Ph.D.

Conclusion: CMC-Microbiology recommends APPROVE.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA.

2. SUBMISSION PROVIDES FOR: New drug product.

3. MANUFACTURING SITE:

Aventis Pharma, Dagenham
Rainham Road South
Dagenham, Essex RM 107XS
United Kingdom

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Intravenous solution for infusion.
- Provided as a kit containing two vials:
  - Cabazitaxel concentrate for solution for infusion (CCSI), 60 mg/1.5 mL.
  - Cabazitaxel solvent (CS), 5.7 mL 13% w/w alcohol. The volume includes a (b) (4) overfill. Only (b) (4) is used for dilution of CCSI.
- (b) (4) from the CS vial is mixed with the CCSI vial contents to form a 10 mg/mL intermediate premix.
- Premix is diluted with 0.9% sodium chloride or 5% dextrose in an infusion bag.

5. METHOD(S) OF STERILIZATION:

- CCSI is sterilized by (b) (4).
- CS is sterilized by (b) (4)

6. PHARMACOLOGICAL CATEGORY: Prostate cancer therapeutic.

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS:

- The application was provided in a rolling submission format. The original submission was submitted 18-DEC-2009 and contained non-clinical information only. CMC information was submitted 24-FEB-2010 (amendment 1, supporting document 2) in eCTD format.

- The application proposes a promising therapy for metastatic prostate cancer. On 09-NOV-2009 the submission was granted Fast Track status.

- On 11-MAY-2010 an IR was submitted requesting details regarding the bacterial ingress test used to assess container-closure integrity, and the method

and method validation for [redacted] of the rubber stoppers used for product closure. An amendment response (sponsor submission 14) was received on 21-MAY-2010.

- On 18-MAY-2010 a second IR was submitted requesting information regarding the [redacted], the endotoxin testing method, the environmental monitoring action limits, and [redacted] validation. An amendment response (sponsor submission 17) was received on 25-MAY-2010.

- On 04-JUN-2010 the reviewer placed a phone call to Sanofi-Aventis regulatory affairs representative Linda Gustavson regarding the stability data presented in support of the proposed CCSI shelf life. On the same day a return phone call was received from Sanofi-Aventis regulatory affairs CMC specialist Zareen Ahmed clarifying that the information was present in CCSI submission section 3.2.P.8.3, Table 1.

- On 07-JUN-2010 an IR was sent to the sponsor requesting data supporting the proposed [redacted]. On 08-JUN-2010 an amendment response was received that contained the requested data.

- The application presented the manufacturing information for CCSI and CS in two separate sections. In this review these are referred to, respectively, as the CCSI and the CS submission sections.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommended for approval from a microbiology quality standpoint.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology - CCSI is [redacted] (b) (4) 15 mL glass vials that are sealed with 13 mm grey [redacted] (b) (4) rubber stoppers and aluminum overseals. CS is [redacted] (b) (4) filled into the same container-closure system used for CCSI: 15 mL glass vials sealed with 13 mm grey [redacted] (b) (4) rubber stoppers and aluminum overseals. The CS vials are [redacted] (b) (4)

B. Brief Description of Microbiology Deficiencies – No deficiencies identified.

C. Assessment of Risk Due to Microbiology Deficiencies – Minimal risk.

III. Administrative

A. Reviewer's Signature _____
Steven Fong, Ph.D., Microbiology Reviewer

B. Endorsement Block _____
Bryan Riley, Ph.D.
Senior Microbiology Reviewer

C. CC Block N/A

26 Pages Have Been Withheld In Full As b4(CCI/TS) Immediately Following This Page

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