CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201532

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

09 AUGUST 2010

NDA: 201-532/N-000

Drug Product Name
Proprietary: Halaven Injection
Non-proprietary: Eribulin Mesylate

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
30 MARCH 2010	30 MARCH 2010	08 APRIL 2010	10 APRIL 2010
07 JUNE 2010	07 JUNE 2010	n/a	n/a
27 JULY 2010	28 JULY 2010	n/a	n/a
09 AUGUST 2010	09 AUGUST 2010	n/a	n/a

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Eisai, Inc.
Address: 300 Tice Boulevard
Woodcliff Lake, NJ 07677
Representative: Annemarie Petraglia
Senior Director, Regulatory Affairs
Telephone: 201-949-4516

Name of Reviewer: Robert J. Mello, Ph.D.

Conclusion: The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA, 505(b)(1)

2. SUBMISSION PROVIDES FOR: Marketing Approval

3. MANUFACTURING SITE:

Drug Product:
Nerviano Medical Sciences S.r.I.
Viale Pasteur, 10
20014, Nerviano
Italy

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Injection, Intravenous, 1mg/2ml packaged in a (b) (4) vial with a (b) (4) stopper and (b) (4) seal.

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Antineoplastic agent (halichondrin class of microtubule dynamics inhibitor)

B. SUPPORTING/RELATED DOCUMENTS:

- (b) (4) DMF update submission.
- Microbiology Reviews of DMF (b) (4)
  - (b) (4)
  -
  -)

C. REMARKS:

- An ONDQA Initial Quality Assessment was filed by the Chemistry Pharmaceutical Assessment Lead (PAL), L. Zhou, on 30 April 2010. A microbiology consult was recommended in that report. It was requested that the proposed maximum level of endotoxins in DP specification be confirmed with the reviewing microbiologist.
- The submission is electronic, and is in eCTD format. It is located in the EDR system. Priority Review was granted to this submission.
- An information request related to component sterilization validation was transmitted to the Applicant on 7/29/2010. A response was received via email and as an amendment to the NDA on 08/09/2010.

filename: N201532N000R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommend Approval

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 – Following formulation, the drug product is (b) (4)

B. Brief Description of Microbiology Deficiencies - None

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature: _____

Robert J. Mello, Ph.D.
Senior Microbiology Reviewer

B. Endorsement Block: _____

John W. Metcalfe, Ph.D.
Senior Microbiology Reviewer

C. CC Block

NDA 201532

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201532	ORIG-1	EISAI INC	eribulin mesylate

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/s/

ROBERT J MELLO
08/10/2010

JOHN W METCALFE
08/10/2010
I concur.

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 03 MAY 2010

TO: Vaishali Jarrai, Consumer Safety Officer, DBOP/OODP

FROM: Robert J. Mello, Ph.D., Senior Reviewer, New Drug Microbiology Staff

THROUGH: John W. Metcalfe, Ph.D., Senior Reviewer, New Drug Microbiology Staff

cc: David Hussong, Ph.D., Director, New Drug Microbiology Staff
James McVey, Team Leader, New Drug Microbiology Staff

SUBJECT: Amendment to Filing Review for NDA 201-232, Eribulin Mesylate (Eisai, Inc.)

My original Filing Review (dated 19 APRIL 2010) for NDA 201-232, Eribulin Mesylate, contained a recommendation that the Applicant (Eisai, Inc.) include a test for bacterial endotoxin at expiry in the drug product's ongoing stability program. Upon further review within the New Drug Microbiology Staff, this requirement is no longer considered necessary and such a request need not be forwarded to the Applicant.

The second information request (repeated herein) remains. The following microbiology product quality information request should be conveyed to the Applicant: "*Please submit the protocol and final report for the microbial immersion container/closure integrity test.*"

END

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201532	ORIG-1	EISAI INC	eribulin mesylate

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/s/

ROBERT J MELLO
05/03/2010

JOHN W METCALFE
05/03/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 201,532 **Applicant: Eisai, Inc.** **Submit Date: 30 March 2010**

Drug Name: Eribulin mesylate Injection **NDA Type: 505(b)(1) (Priority review requested)** **Received Date: 30 March 2010**

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		The NDA was submitted in eCTD format.
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Section 2.3.P.3.3, Section 3.2.P.3.3
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Section 3.2.P.3.5
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?		**X**	Only a container closure integrity study summary was provided. No protocol or summary report. (b) (4)
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section 3.2.P.5.1; Section 3.2.P.5.2.1
7	Has the applicant submitted the results of analytical method verification studies?	X		Section 3.2.P.5.3.4; Section 3.2.P.5.3.5
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	-	-	Not applicable to Product Quality Microbiology
9	Is this NDA fileable? If not, then describe why.	X		**NDA is Fileable**

Additional Comments: Eribulin mesylate is a sterile, ready-to-use, clear, colorless aqueous solution for intravenous administration with 1 mg of eribulin mesylate in a 2 mL fill volume (0.5mg/ml) per vial. The drug product is formulated, (b) (4) into (b) (4) vials and sealed with a (b) (4) stopper and (b) (4) overseal. The product is to be stored at temperatures up to 25°C.
The stability program does not include a test for bacterial endotoxin at expiry. Also, no details of the microbial immersion container/closure integrity test were provided.

From a microbiological product quality perspective, the applicant appears to have submitted the requisite documentation for review of manufacturing and controls for the above described drug product. This NDA submission **is fileable** from a Microbiology Product Quality standpoint.

An information request will be submitted to the applicant requesting the following:

1. Please include a test for bacterial endotoxin at expiry in the drug product's ongoing stability program.

2. Please submit the protocol and final report for the microbial immersion container/closure integrity test.

Robert J. Mello, Ph.D., Senior Review Microbiologist Date

John W. Metcalfe, Ph.D., Senior Review Microbiologist Date

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NDA-201532	ORIG-1	EISAI INC	eribulin mesylate

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/s/

ROBERT J MELLO
04/19/2010

JOHN W METCALFE
04/19/2010
I concur.