CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206316Orig1Orig2s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

4/03/2014

NDA: 206316

Drug Product Name
Proprietary: Savaysa
Non-proprietary: edoxaban tosylate

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
1/08/2014	1/08/2014	1/13/2014	1/15/2014
3/21/2014	3/21/2014	N/A	N/A

Submission History (for 2nd Reviews or higher)
None

Applicant/Sponsor
Name: Daiichi Sankyo, Inc.
Address: 399 Thornall St., Edison, NJ 08837
Representative: Doreen Morgan, Regulatory Affairs
Telephone: 732 590-5198

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original New Drug Application

2. SUBMISSION PROVIDES FOR: The manufacture and marketing of an oral, tableted drug product.

3. MANUFACTURING SITE: Daiichi Sankyo Propharma Co., Ltd. (DSPP), Hiratsuka Plant, 1-12-1 Shinomiya, Hiratsuka, Kanagawa 254-0014

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

- Dosage Form: Tablet
- Route of Administration: Oral
- Strength/Potency: 15 mg, 30 mg, 60 mg
- Container

5. METHOD(S) OF STERILIZATION: N/A

6. PHARMACOLOGICAL CATEGORY: For the treatment of venous thromboembolism; to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: An information request was sent to the sponsor on 3/7/2014 and a response was received on 3/21/2014.

filename: N206316r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for 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 -

(b) (4)

[redacted]

B. Brief Description of Microbiology Deficiencies –
No product quality microbiology deficiencies were identified based upon the information provided.

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

D. Contains Potential Precedent Decision(s)- ☐ Yes ☒ No

III. Administrative

A. Reviewer's Signature _____
Steven P. Donald, M.S.
Microbiology Reviewer

B. Endorsement Block _____
Stephen Langille, Ph.D.
Senior Microbiology Reviewer

C. CC Block
N/A

[redacted]

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/s/

STEVEN P DONALD
04/03/2014

STEPHEN E LANGILLE
04/03/2014

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206316 **Applicant:** Daiichi Sankyo, Inc **Letter Date:** 1/08/2014

Drug Name: Edoexaban Tosylate **NDA Type:**505 (b)(1) **Stamp Date**: 1/08/2014

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		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	x		QbD Approach; (b) (4)
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	x		Reference is made to USP <61> and <62>
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?			N/A
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	x		(b) (4) is proposed for release; however, the stability protocol/commitment is acceptable
7	Has the applicant submitted the results of analytical method verification studies?	x		Only reference to the USP methods (above) are made
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			N/A
10	Is this NDA fileable? If not, then describe why.	X		Adequate information appears to be available to qualify this submission for

	Content Parameter	Yes	No	Comments
				reduced microbial limits testing.

Additional Comments:
Supplemental data are provided that could support reduced microbial limits testing, such as historical microbial limits test results, (b) (4) activity testing results and microbial limits specifications for some excipients. The applicant would have to modify the release specification and provide additional commentary on how potential microbial contamination would be controlled in the manufacturing process. An information request will be sent to the sponsor under separate cover.

Steven P. Donald	2/12/2014
Reviewing Microbiologist	Date
Stephen A. Langille	2/12/2014
Microbiology Secondary Reviewer	Date

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/s/

STEVEN P DONALD
02/27/2014

STEPHEN E LANGILLE
02/27/2014