CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204760Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

6 June 2014

NDA: 204760

Drug Product Name
Proprietary: MONVANTIK™ Tablets
Non-proprietary: naloxegol oxalate

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
16 September 2013	16 September 2013	17 September 2013	4 October 2013
10 April 2014	10 April 2014	N/A	N/A

Submission History (for 2nd Reviews or higher): Not applicable

Applicant/Sponsor
Name: AstraZeneca Pharmaceuticals LP
Address: 1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19083-8355

Representative: Lynley K. Thinnes
Telephone: 302-866-7607

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original Submission

2. SUBMISSION PROVIDES FOR: Manufacture of a solid coated tablet

3. MANUFACTURING SITE: AstraZeneca AB
Gartunavagen
SE-151 85
Sodertalje
Sweden

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

- Coated tablet
- Oral
- 12.5 and (b) (4) mg

5. METHOD(S) OF STERILIZATION: Not applicable

6. PHARMACOLOGICAL CATEGORY: Treatment for opioid-induced constipation.

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: The application was provided in eCTD format. The product is a coated tablet that does not involve any aqueous processing steps and the maximum holding time for the coating solution is adequate to prevent microbial proliferation. Because there is little microbiological risk associated with this product, the applicant has asked for a waiver of microbial limits testing at product release. The applicant will conduct microbial limits testing as part of the stability protocol.

An information request was sent to the applicant on 1 April 2014. The applicant provided a response to the deficiencies on 10 April 2014.

filename: N204760r1.doc

Reference ID: 3520443

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for Approval

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -
Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
The drug product will [redacted] (b) (4)

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies –
Not applicable

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

III. Administrative

A. Reviewer's Signature _____
Stephen E. Langille, Ph.D.
Senior Microbiology Reviewer

B. Endorsement Block
Bryan Riley, Ph.D. – Acting Team Leader

C. CC Block
N/A

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/s/

STEPHEN E LANGILLE
06/06/2014

BRYAN S RILEY
06/06/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204760 **Applicant: Astra Zeneca** **Letter Date: 9/16/13**

Drug Name: MOVANTIG™ **NDA Type: Standard** **Stamp Date: 9/16/13**

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		Sections P.2.5, P.3.3 and P.5.1
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 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	No microbiological test verification study results were provided.
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	The drug product is a solid tablet.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section P.5.1
7	Has the applicant submitted the results of analytical method verification studies?		X	Microbial limit verification studies were not provided
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	No such studies were requested
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The applicant provided little information regarding microbial limit specifications, test methods or test frequency. The applicant proposes the use of skip lot testing as described in ICH Q6A. The applicant claims that raw materials are subject to microbial limits testing according to compendial standards. A full evaluation of the application will be conducted prior to the issuance of an information request regarding the skip-lot testing proposal.

Stephen E. Langille, Ph.D. Senior Microbiology Reviewer	10/4/13
John Metcalfe, Ph.D. Senior Microbiology Reviewer	10/4/13

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/s/

STEPHEN E LANGILLE
10/07/2013

JOHN W METCALFE
10/07/2013
I concur.