CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204824Orig2s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

29 July 2013

NDA: 204824

Drug Product Name
Proprietary: Otrexup
Non-proprietary: methotrexate injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
14 DEC 2012	14 DEC 2012	28 JAN 2013	01 FEB 2013
14 MAR 2013	14 MAR 2013	N/A	N/A
17 MAY 2013	17 MAY 2013	N/A	N/A

Applicant/Sponsor
Name: Antares Pharma Inc.
Address: 100 Princeton South Corporate Center, Suite 300, Ewing, NJ 08628
Representative: Dave Kaushik, Ph.D.
Telephone: 609-359-3020

Name of Reviewer: Erika Pfeiler, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(2)

2. SUBMISSION PROVIDES FOR: Initial marketing of a sterile drug

3. MANUFACTURING SITE:

(b) (4)

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

10, 15, 20, and 25 mg/0.4 ml
Subcutaneous injection
Primary container closure consists of a 1 ml glass syringe

5. METHOD(S) OF STERILIZATION: Drug product is sterilized by (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment of rheumatoid arthritis and moderate to severe psoriasis

B. SUPPORTING/RELATED DOCUMENTS:

Microbiology Review 20 of DMF (b) (4) (DARRTS Date 16 March 2012)
Microbiology Review 1 of DMF (b) (4) (DARRTS Date 18 March 2013)
Microbiology Review 1 of DMF (b) (4) (DARRTS Date 29 July 2013)

C. REMARKS: This application was submitted in the eCTD format.

filename: N204824R1.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 – N/A

B. Brief Description of Microbiology Deficiencies – N/A

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

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

III. Administrative

A. Reviewer's Signature _____

Erika Pfeiler, Ph.D.
Microbiologist

B. Endorsement Block_____

John Metcalfe, Ph.D.
Senior Review Microbiologist

C. CC Block
N/A

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/s/

ERIKA A PFEILER
07/29/2013

JOHN W METCALFE
07/29/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204824 **Applicant:** Antares Pharma, Inc. **Letter Date:** 14 DEC 2012

Drug Name: Otrexup **NDA Type:** 505(b)(2) **Stamp Date:** 14 DEC 2012

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		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
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	The submission is in English.
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		Applicant has submitted container closure integrity studies, the drug product does not contain preservatives.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?	X		
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?	X		
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The drug product is a sterile solution for subcutaneous injection in a single use syringe. The product is intended for the treatment of rheumatoid arthritis and moderate to severe psoriasis.

Erika Pfeiler, Ph.D. Date

Stephen Langille, Ph.D. Date
Senior Microbiology Reviewer

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/s/

ERIKA A PFEILER
02/11/2013

STEPHEN E LANGILLE
02/11/2013