

**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**

<b>Submit</b>	<b>Received</b>	<b>Review Request</b>	<b>Assigned to Reviewer</b>
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.

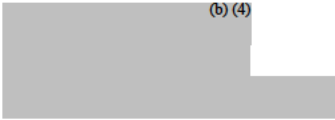

**Telephone:** 609-359-3020

**Name of Reviewer:** Erika Pfeiler, Ph.D.

**Conclusion:** Recommended for Approval

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## 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

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**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/  
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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:

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comments</b>
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.

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Erika Pfeiler, Ph.D.

Date

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Stephen Langille, Ph.D.  
Senior Microbiology Reviewer

Date

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/s/  
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ERIKA A PFEILER  
02/11/2013

STEPHEN E LANGILLE  
02/11/2013