

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204781Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

February 6, 2013

NDA: 204781

Drug Product Name

Proprietary: Dotarem

Non-proprietary: Gadoterate Meglumine Injection 376.9 mg/mL

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
September 20, 2012	September 20, 2012	September 21, 2012	September 27, 2012

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: Guerbet LLC

Address: 1185 W 2nd street, Bloomington, IN 47403

Representative: Corina Harper, RAC, Head N American RA

Telephone: 812-333-0059 x 211

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: Recommend Approval.

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA
 - 2. SUBMISSION PROVIDES FOR:** Dotarem®, a Gadolinium based contrast agent.
 - 3. MANUFACTURING SITE:** The drug product will be manufactured in Vials at [REDACTED]^{(b) (4)} and in Syringes at [REDACTED]^{(b) (4)}
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Single dose vials in 10, 15 and 20 mL presentations per vial. Single dose syringes in 10, 15 and 20 mL presentations per syringe. Bulk pack is manufactured in 100 mL/vial presentation.
 - 5. METHOD(S) OF STERILIZATION:** [REDACTED]^{(b) (4)}
Sterilization
 - 6. PHARMACOLOGICAL CATEGORY:** Contrast agent for intravenous use with MRI.
- B. SUPPORTING/RELATED DOCUMENTS:** None
- C. REMARKS:** The subject original NDA submission has been granted a priority review cycle. The drug has been approved for European Market. This is an electronic submission. The IQA was provided by Eldon Leutzinger on October 11, 2012.

filename: N204781R1

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** – The drug product in both vial and syringe presentations are (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** _____
Vinayak B. Pawar, Ph.D., Senior Reviewer, NDMS, OPS, CDER
- B. Endorsement Block** _____
Brian S. Riley, Ph.D., Acting Team Leader, NDMS, OPS, CDER
- C. CC Block**
N/A

14 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

VINAYAK B PAWAR
02/11/2013

BRYAN S RILEY
02/11/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204781 **Applicant: Guerbet LLC** **Letter Date: September 20, 2012**
Drug Name: Dotarem® **NDA Type: Original** **Stamp Date: September 20, 2012**
 (gadoterate meglumine)

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		Section 3.2.P.3.3 & Section 3.2.P.3.4 for Control Critical steps
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		Container closure Integrity provided in Section 3.2.P.3.5.3
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section 3.2.P.5.2 Report 2_11_000505
7	Has the applicant submitted the results of analytical method verification studies?	X		Section 3.2.P.5.3. See Additional Comments.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	
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		

Additional Comments: The drug product is (b) (4) sterilized by (b) (4) Validation reports for Sterility [2_12_00091] and Bacterial Endotoxins [2_12_00092] provided.

 Vinayak B. Pawar, Ph.D., Senior Review Microbiologist Date

 Bryan S. Riley, Ph.D., Senior Review Microbiologist Date

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/s/

VINAYAK B PAWAR
10/16/2012

BRYAN S RILEY
10/16/2012
I concur.