CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-398

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

19 OCTOBER 2006

NDA: 21-398 AZ (re-submission)

Drug Product Name
Proprietary: COMBIGAN
Non-proprietary: brimonidine tartrate 0.2%/timolol maleate 0.5% ophthalmic solution
Drug Product Priority Classification: S

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
6/29/2006	6/30/2006	8/23/2006	8/31/2006

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
9/18/2001	1	11/16/2001

Applicant/Sponsor
Name: Allergan Inc.
Address: 2525 Dupont Drive, PO Box 19534, Irvine, CA 92623
Representative: Lewis Gryziewicx, PharmD
Telephone: 714-246-6088

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Resubmission of an original NDA in response to an approvable letter.

2. **SUBMISSION PROVIDES FOR:** An ophthalmic drug product

3. **MANUFACTURING SITE:** Allergan
Waco, TX

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile preserved aqueous solution for ophthalmic administration in plastic bottles with dropper tips, 5 mL bottle [redacted] fill volume, 10 mL bottle [redacted] 10 mL fill volume and 15 mL bottle w/ 15 mL fill volume.)

5. **METHOD(S) OF STERILIZATION:** [redacted]

6. **PHARMACOLOGICAL CATEGORY:** Control of intraocular pressure

B. **SUPPORTING/RELATED DOCUMENTS:** Product Quality Microbiology review of original submission (review dated 16 November 2001)

C. **REMARKS:** The original submission was recommended for approval on the basis of product quality microbiology. However, the submission was considered approvable based on other considerations. The applicant has submitted this application in response to two approvable letters from the agency (dated 5 June 2002 and 14 March 2005) The only changes to the original application that may impact sterility assurance are [redacted] not reviewed as part of the original submission. This review will address the sterility assurance validation [redacted]

filename: N021398R2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission is recommended for approval on the basis of product quality microbiology.

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 is [redacted] filled.

B. Brief Description of Microbiology Deficiencies – N/A

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

III. Administrative

A. Reviewer's Signature _____
Bryan S. Riley, Ph.D.

B. Endorsement Block _____
James L. McVey
(Microbiology Team Leader)

C. CC Block
N/A

2 Page(s) Withheld

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_____ Draft Labeling

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Withheld Track Number: Microbiology- 11

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/s/

Bryan Riley
10/20/2006 02:43:24 PM
MICROBIOLOGIST

James McVey
10/20/2006 03:59:03 PM
MICROBIOLOGIST

REVIEW FOR HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1
16 November 2001

A. 1. NDA 21-398

APPLICANT: Allergan, Inc.
2525 DuPont Drive
P.O. Box 19534
Irvine, CA 92623-9534

2. PRODUCT NAMES: Brimonidine Tartrate, 0.2%/Timolol, 0.5% Ophthalmic Solution

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is an ophthalmic solution for instillation into the eye.

4. METHODS OF STERILIZATION:
The product is [redacted]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is indicated for the [redacted] of intraocular pressure in-patients with [redacted] glaucoma or ocular hypertension.

B. 1. DATE OF INITIAL SUBMISSION: 18 September 2001

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: [redacted], NDA 20-490, NDA 20-613, NDA 21-262, NDA 21-275, IND 58,460, IND 32,292

4. ASSIGNED FOR REVIEW: 12 October 2001

C. REMARKS: The application provides for the manufacture of the multi-dose product at the applicant's facility in Waco, Texas. The Waco, Texas facility has been previously approved as the manufacturing site for a number of the applicant's other products. [redacted]

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

_____

Paul Stinavage, Ph.D.

cc: Original NDA 21-398
HFD-550/M. Puglisi
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 16 November 2001
R/D initialed by P. Cooney

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/s/

Paul Stinavage
11/30/01 09:42:29 AM
MICROBIOLOGIST

Peter Cooney
11/30/01 11:45:39 AM
MICROBIOLOGIST