Product Quality Microbiology Review

2/24/2014

NDA: 206289

Drug Product Name
  Proprietary:
  Non-proprietary: Atropine Sulfate Ophthalmic Solution USP, 1%

Review Number: 1

Dates of Submission(s) Covered by this Review

<table>
<thead>
<tr>
<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/10/2014</td>
<td>1/10/2014</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>2/14/2014</td>
<td>2/14/2014</td>
<td>N/A</td>
<td>N/A</td>
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</table>

Submission History (for 2\textsuperscript{nd} Reviews or higher)
None

Applicant/Sponsor
  Name: Akorn, Inc.
  Address: 1925 West Field Ct., Suite 300, Lake Forest, IL 60045
  Representative: Sam Bodapaddi
  Telephone: (847) 353-4909

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Recommended for Approval
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: Manufacture and marketing of a sterile drug product

3. MANUFACTURING SITE: Akorn, Inc., 1222 West Grand Avenue, Decatur, IL 62522

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
   - Dosage Form: Solution, Drops
   - Route of Administration: Topical, Ocular
   - Strength/Potency: 1%
   - Container: plastic dropper bottle; 2 mL and 5 mL/6 mL and 15 mL/15mL

5. METHOD(S) OF STERILIZATION:

6. PHARMACOLOGICAL CATEGORY:

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: An information request was sent to the sponsor on 12/18/2014 and a response was received on 1/10/2014. Another IR was sent to the sponsor on 2/03/2014 and a response was received on 2/14/2014.

filename: N206289r1.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 –

B. Brief Description of Microbiology Deficiencies –
No product quality microbiology deficiencies were identified based upon the information provided.

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

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

III. Administrative

A. Reviewer's Signature ________________________________
   Steven P. Donald, M.S.
   Microbiology Reviewer

B. Endorsement Block ________________________________
   Stephen Langille, Ph.D.
   Senior Microbiology Reviewer

C. CC Block
   N/A

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

STEVEN P DONALD
02/24/2014

STEPHEN E LANGILLE
02/24/2014
The following are necessary to initiate a review of the NDA application:

<table>
<thead>
<tr>
<th>Content Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is the product quality microbiology information described in the NDA and</td>
<td></td>
<td>x</td>
<td>CTD Format</td>
</tr>
<tr>
<td>organized in a manner to allow substantive review to begin? Is it legible,</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>indexed, and/or paginated adequately?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. Has the applicant submitted an overall description of the manufacturing</td>
<td></td>
<td>x</td>
<td>See P.3.3 for all fill sizes.</td>
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<tr>
<td>processes and microbiological controls used in the manufacture of the drug</td>
<td></td>
<td></td>
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<td>product?</td>
<td></td>
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<tr>
<td>3. Has the applicant submitted protocols and results of validation studies</td>
<td></td>
<td>x</td>
<td>Yes. See P.3.5 for validation of the largest batch. Additional information provided for sterility assurance, PET,</td>
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<td>concerning microbiological control processes used in the manufacture of the drug</td>
<td></td>
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<td>media fill, etc.</td>
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<td>product?</td>
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<td>4. Are any study reports or published articles in a foreign language? If yes,</td>
<td></td>
<td>x</td>
<td></td>
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<td>has the translated version been included in the submission for review?</td>
<td></td>
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<tr>
<td>5. Has the applicant submitted preservative effectiveness studies (if applicable)</td>
<td></td>
<td>x</td>
<td>BAC identity and concentrations tests for release and stability. PET testing for stability on selected samples at</td>
</tr>
<tr>
<td>and container-closure integrity studies?</td>
<td></td>
<td></td>
<td>(b)(6) months and expiry; PET testing performed at the lowest preservative concentration (b)(4). CCI test</td>
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<td></td>
<td></td>
<td></td>
<td>protocol provided in P.3.5. Results of CCI testing are not found within the submission.</td>
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<td>6. Has the applicant submitted microbiological specifications</td>
<td></td>
<td>x</td>
<td>Sections P.3.5 and</td>
</tr>
<tr>
<td>Content Parameter</td>
<td>Yes</td>
<td>No</td>
<td>Comments</td>
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<td>for the drug product and a description of the test methods?</td>
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<td>P.5.3</td>
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<tr>
<td>Has the applicant submitted the results of analytical method verification studies?</td>
<td>x</td>
<td></td>
<td>Sections P.3.5 and P.5.3</td>
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<tr>
<td>Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?</td>
<td></td>
<td></td>
<td>N/A</td>
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<tr>
<td>If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?</td>
<td></td>
<td></td>
<td>N/A. This is a preserved ophthalmic product</td>
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<tr>
<td>Is this NDA fileable? If not, then describe why.</td>
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Additional Comments:
The results of container closure integrity testing will be requested after the initial review of the application.

Steven Donald, MS 11/12/2013
Reviewing Microbiologist

Stephen Langille, Ph.D. 11/12/2013
Microbiology Secondary Reviewer
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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STEVEN P DONALD
11/15/2013

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STEPHEN E LANGILLE
11/15/2013