CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022150Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

JUNE 2, 2011

NDA: 22-150 [Re-submission]

Drug Product Name
Proprietary: Firazyr® (b) (4)
Non-proprietary: Icatibant acetate

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
February 25, 2011	February 25, 2011	March 4, 2011	March 10, 2011

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
October 22, 2007	1	March 11, 2008

Applicant/Sponsor
Name: Shire Pharmaceuticals Inc. (see remarks)
Address: 700 Main Street, Cambridge, MA 02139
Representative: Thomas Class, RAC, Group Director
Telephone: Joel Alvarez, Assoc Dir., 781-482-9370.

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

Conclusion: The application is recommended for approval from product quality microbiology standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: New product, new molecular entity

3. MANUFACTURING SITE: (b) (4)

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Sterile solution in a pre-filled syringe (3 mL)
- Subcutaneous injection
- 30 mg (10 mg/mL)

5. METHOD(S) OF STERILIZATION: (b) (4) (b) (4) (b) (4) (b) (4)

6. PHARMACOLOGICAL CATEGORY: The product is indicated for the treatment of hereditary angioedema.

B. SUPPORTING/RELATED DOCUMENTS:
1. IND 68,214
2. Type III DMF (b) (4) for the (b) (4) syringe system

C. REMARKS: Reference is made to NDA 22-150 for Firazyr® (icatibant) submitted on 22 October 2007 and to the "Not Approvable" Action Letter issued by FDA on 23 April 2008. The purpose of this submission was to provide a Complete Response to the deficiencies outlined in the Action Letter.
This is an electronic submission in CTD format. An Initial Quality Assessment was provided on 21-DEC-2007 and identified the sterility and endotoxin content of the final drug product as critical issues for review. The original sponsor, Jerini AG, became a wholly owned subsidiary of Shire Human Genetic Therapies (HGT) who assumed responsibility for the NDA and all FDA communications under the name Jerini US, Inc. Shire Pharmaceuticals plans to change the Jerini US, Inc. company name immediately following approval of the NDA.
DMF (b) (4) was not reviewed during the original review cycle as a specific letter of authorization was needed which identified the facilities that perform the (b) (4) of the syringe barrels and plunger stoppers used for this product.

Filename: **N022150R1**

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

P.┌.┐ Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – Firazyr® is (b) (4) (b) (4) (b) (4) (b) (4) is responsible for production of icatibant 30 mg solution for filling, sealing, sterilization of the drug product in syringes, assembly of syringes/needles, packaging and labeling.

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., NDMS, OPS, CDER

B. Endorsement Block _____
Bryan S. Riley, Ph.D., NDMS, OPS, CDER

P.┌.┐ CC Block
N/A

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/s/

VINAYAK B PAWAR
06/03/2011

BRYAN S RILEY
06/03/2011
I concur.

Product Quality Microbiology Review

11 MAR 2008

NDA: 22-150

Drug Product Name
Proprietary: Firaz [redacted] (b) (4)
Non-proprietary: Icatibant acetate
Drug Product Priority Classification: 1P

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
22-OCT-2007	26-OCT-2007	21-DEC-2007	03-JAN-2008

Submission History (for amendments only) – N/A

Applicant/Sponsor
Name: Jerini US Inc.
Address: 55 Madison Ave
Morristown, NJ 07960

Representative: Glenn D. Park, PharmD
Target Health Inc., NY (US Agent)
Telephone: 212-681-2100

Name of Reviewer: Anastasia G. Lolas

Conclusion: Approvable pending the resolution of product quality microbiology deficiencies (see Section 3 of review)

Product Quality Microbiology Data Sheet

A. **1.** **TYPE OF SUBMISSION:** Original new drug application

2. **SUBMISSION PROVIDES FOR:** New product, new molecular entity

3. **MANUFACTURING SITE:** (b) (4)

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

- Sterile solution in a pre-filled syringe (3 mL)
- Subcutaneous injection
- 30 mg (10 mg/mL)

5. **METHOD(S) OF STERILIZATION:** (b) (4)

6. **PHARMACOLOGICAL CATEGORY:** A pharmacological class has not been assigned to the active ingredient but it is proposed that it is classified as a bradykinin receptor antagonist. The product is indicated for the treatment of hereditary angioedema.

B. **SUPPORTING/RELATED DOCUMENTS:**

- IND 68,214
- Type III DMF (b) (4) for the (b) (4) syringe system

C. **REMARKS:** This is an electronic submission in CTD format. An Initial Quality Assessment was conducted on 21-DEC-2007 and identified the sterility and endotoxin content of the final drug product as critical issues for review.

There was one pre-IND meeting, one end-of-phase-2 meeting and two pre-NDA meetings. However, it does not appear from the meeting minutes provided in the submission and internal records that NDMS was consulted.

DMF (b) (4) was not reviewed. A request will be made to the applicant to provide an updated letter of authorization identifying the facilities that perform the (b) (4) of the syringe barrels and plunger stoppers used for this product.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability – Approvable pending the resolution of product quality microbiology deficiencies (see Section 3)

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 – Firazyr® is (b) (4) is reviewed along with drug product microbiological specifications and container-closure integrity.

B. Brief Description of Microbiology Deficiencies – The applicant does not provide a container-closure integrity study for the (b) (4) (b) (4) Sterility assurance information on the 25G needle to be included in the final packaging is not included in the submission. The requalification program for the (b) (4) is not provided. In addition, a description of the microbiological environmental monitoring program and (b) (4) (b) (4) are not provided.

C. Assessment of Risk Due to Microbiology Deficiencies – High risk to the patient if the integrity of the container-closure system is compromised and the sterility of the 25G needle is not assured.

III. Administrative

A. Reviewer's Signature _____
Anastasia G. Lolas

B. Endorsement Block
Stephen E. Langille, Ph.D.

C. CC Block
N/A

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/s/

Anastasia Lolas
3/11/2008 10:50:24 AM
MICROBIOLOGIST

Stephen Langille
3/11/2008 12:37:34 PM
MICROBIOLOGIST