

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022460Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

December 22, 2009

NDA: 22-460 Amendment

Drug Product Name

Proprietary: Flodart

Non-proprietary: dutasteride and tamsulosin

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
December 15, 2009	December 16, 2009	December 16, 2009	December 16, 2009

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
March 20, 2009	1	September 29, 2009

Applicant/Sponsor

Name: GlaxoSmithKline

Address: P.O. Box 13398, Research Triangle Park,
NC 27709

Representative: Michele M. Hardy, Senior Director, USRA

Telephone: 919-483-5098, Fax: 919-315-0033

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

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

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** An amended original NDA
 - 2. SUBMISSION PROVIDES FOR:** Agreement to add Microbial Limits test criteria to the drug product specification.
 - 3. MANUFACTURING SITE:**
 1. Manufacture (encapsulation) of the DTC product at:
Catalent Germany Schorndorf GmbH (formerly Cardinal Health Germany 405 GmbH) Steinbeisstrasse 2
73614 Schorndorf, Germany
 2. Manufacture of Tamsulosin HCl Product Intermediate at:
Rottendorf Pharma GmbH
Ostenfelder Strasse 51-61
59320 Ennigerloh, Germany
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** [REDACTED] (b) (4)
 - 5. METHOD(S) OF STERILIZATION:** Oral capsule
 - 6. PHARMACOLOGICAL CATEGORY:** Treatment of benign prostate hyperplasia.
- B. SUPPORTING/RELATED DOCUMENTS:** N/A
- C. REMARKS:** The drug substances, dutasteride and tamsulosin hydrochloride, are the same active components used for commercial supply of AVODART® (NDA 21-319) and generic Tamsulosin Hydrochloride Capsules. The drug product described in the subject NDA is a combination of dutasteride (0.5 mg) and tamsulosin hydrochloride (0.4 mg). The combination capsule is intended for the treatment of benign prostate hyperplasia. Based on the antimicrobial properties of dutasteride and the stability history of the approved products, [REDACTED] (b) (4) on the commercial combination product. This resulted in a deficiency which was conveyed to the sponsor. In a letter dated November 17, 2009 the sponsor was given an opportunity to discuss this deficiency in a teleconference. During the teleconference between FDA and GSK on November 19, the sponsor agreed to add Microbial Limits test to the drug product specification (letter is copied on page 4 of this review). The original application and the letter can also be viewed in EDR.

filename: C:\my documents\review\NDA\N022460R2

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – The amended original NDA is 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** – The manufacturing process involves the over-encapsulation of two approved intermediate products. Both intermediates are filled into (b) (4) hard shell capsule to deliver 0.5 mg and 0.4 mg doses of dutasteride and tamsulosin.
- 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.
CDER/OPS/NDMS
- B. Endorsement Block** _____
Stephen langille, Ph.D.
CDER/OPS/NDMS
- C. CC Block**
N/A

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

VINAYAK B PAWAR
12/23/2009

STEPHEN E LANGILLE
12/23/2009

Product Quality Microbiology Review

September 29, 2009

NDA: 22-460

Drug Product Name

Proprietary: Flodart

Non-proprietary: dutasteride and tamsulosin

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
March 20, 2009	March 20, 2009	May 7, 2009	May 22, 2009

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: GlaxoSmithKline

Address: P.O. Box 13398, Research Triangle Park,
NC 27709

Representative: Michele M. Hardy, Senior Director, USRA

Telephone: 919-483-5098, Fax: 919-315-0033

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

Conclusion: The NDA is approvable pending resolution of the deficiency listed in section 3 of this review.

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA
 - 2. SUBMISSION PROVIDES FOR:** Combination capsule (dutasteride and tamsulosin hydrochloride)
 - 3. MANUFACTURING SITE:**
 1. Manufacture (encapsulation) of the DTC product at:
Catalent Germany Schorndorf GmbH (formerly Cardinal Health Germany 405 GmbH) Steinbeisstrasse 2
73614 Schorndorf, Germany
 2. Manufacture of Tamsulosin HCl Product Intermediate at:
Rottendorf Pharma GmbH
Ostenfelder Strasse 51-61
59320 Ennigerloh, Germany
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** [REDACTED] (b) (4)
 - 5. METHOD(S) OF STERILIZATION:** Oral capsule
 - 6. PHARMACOLOGICAL CATEGORY:** Treatment of benign prostate hyperplasia.
- B. SUPPORTING/RELATED DOCUMENTS:** N/A
- C. REMARKS:** The drug substances, dutasteride and tamsulosin hydrochloride, are the same active components used for commercial supply of AVODART® (NDA 21-319) and generic Tamsulosin Hydrochloride Capsules. The drug product described in the subject NDA is a combination of dutasteride (0.5 mg) and tamsulosin hydrochloride (0.4 mg). The combination capsule is intended for the treatment of benign prostate hyperplasia. Based on the antimicrobial properties of dutasteride and the stability history of the approved products, [REDACTED] (b) (4) [REDACTED] on the commercial combination product. The submission is electronic and can be viewed in EDR.

filename: C:\my documents\review\NDA\N022460R1

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – The NDA is approvable pending resolution of the deficiency listed in section 3 of this review.
- 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 manufacturing process involves the over-encapsulation of two approved intermediate products. Both intermediates are filled into (b) (4) hard shell capsule to deliver 0.5 mg and 0.4 mg doses of dutasteride and tamsulosin.
- 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.
CDER/OPS/NDMS
- B. Endorsement Block** _____
Stephen langille, Ph.D.
CDER/OPS/NDMS
- C. CC Block**
N/A

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

VINAYAK B PAWAR
09/30/2009

STEPHEN E LANGILLE
10/01/2009