

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**022460Orig1s000**

**STATISTICAL REVIEW(S)**



U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Translational Science  
Office of Biostatistics

# STATISTICAL REVIEW AND EVALUATION

## CLINICAL STUDIES

**NDA/Serial Number:** 22-460

**Drug Name:** Dutasteride and tamsulosin hydrochloride capsule

**Indication(s):** Treatment of symptomatic benign prostate hyperplasia (BPH) in men with an enlarged prostate

**Applicant:** GlaxoSmithKline & Company

**Date(s):** Submission Date: 3/20/2009  
PDUFA Due Date: 11/20/2009

**Review Priority:** Standard

**Biometrics Division:** Division of Biometrics III

**Statistical Reviewer:** Kate Dwyer, Ph.D.

**Concurring Reviewers:** Mahboob Sobhan, Ph.D.

**Medical Division:** Division of Reproductive and Urologic Drug Products, HFD-580

**Clinical Team:** Christine Nguyen, M.D., Medical Reviewer  
Suresh Kaul, M.D., Team Leader

**Project Manager:** Olga Salis

**Keywords:** NDA review, clinical studies

## **BACKGROUND**

Dutasteride and tamsulosin hydrochloride capsule is an oral dosage form that combines dutasteride, a 5 $\alpha$ -reductase inhibitor and the active ingredient in Avodart (NDA 21-319, approved on November 20, 2001), and tamsulosin, an  $\alpha$ -adrenergic blocker and the active ingredient in Flomax (NDA 20-579, approved on April 15, 1997). The rationale for using this combination capsule is to reduce the pill burden.

## **CONCLUSION**

The safety and efficacy data to support dutasteride and tamsulosin hydrochloride capsule was cross-referenced from the 2-year data from Study ARI40005 in NDA 21-319/S-014, and therefore, no statistical review was necessary.

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/

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KATE L DWYER  
10/23/2009

MAHBOOB SOBHAN  
10/23/2009

## STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

**NDA:** 22-460

**Applicant:** GlaxoSmithKline

**Stamp Date:** 3/20/2009

**Drug Name:** Flodart (dutasteride/tamsulosin combination capsule) **45 day Meeting Date:** 5/04/2009

**Indication:** Treatment of symptomatic benign prostate hyperplasia (BPH) in men with an enlarged prostate

**Medical Officer:** Christine Nguyen, M.D.

**Project Manager:** Olga Salis

### A: Summary

This filing review will determine whether the format and content of the safety and efficacy database for this NDA is sufficiently complete for substantive statistical review as per study protocol. Data which support the efficacy of FLODART in BPH are provided by cross-reference from the pre-defined 2-year analyses of the pivotal 4-year co-administration study ARI40005 and from the pivotal bioequivalence study ARI109882. Efficacy data from the pre-defined 2-year analyses of Study ARI40005 were submitted and approved for the coadministration of dutasteride and tamsulosin in supplement 014 to NDA 21-319.

On **initial** overview of the NDA/BLA application for RTF:

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>NA</b>	<b>Comments</b>
1	Index is sufficient to locate necessary reports, tables, data, etc.	<b>X</b>			
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)			<b>X</b>	Cross referencing other application
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated (if applicable).			<b>X</b>	Cross referencing other application
4	Data sets in EDR are accessible and do they conform to applicable guidances (e.g., existence of define.pdf file for data sets).			<b>X</b>	Cross referencing other application

### B: Conclusion

After preliminary review of the submission of the following checklist items, this submission is fileable from statistical point of view.

Potential review issues to be forwarded to the Applicant for the 74-day letter:

<b>Content Parameter (possible review concerns for 74-day letter)</b>	<b>Yes</b>	<b>No</b>	<b>NA</b>	<b>Comment</b>
Designs utilized are appropriate for the indications requested.			<b>X</b>	Cross referencing other application
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.			<b>X</b>	Cross referencing other application
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			<b>X</b>	
Appropriate references for novel statistical methodology (if			<b>X</b>	

## STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

present) are included.				
Safety data organized to permit analyses across clinical trials in the NDA/BLA.			<b>X</b>	
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			<b>X</b>	Cross referencing other application

Kate Dwyer, Ph. D.

5/4/09

Reviewing Statistician

Date

Mahboob Sobhan, Ph. D.

5/4/09

Supervisor/Team Leader

Date

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/s/

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Kate L Dwyer  
5/5/2009 11:27:07 AM  
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Mahboob Sobhan  
5/6/2009 09:18:43 AM  
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