CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205879Orig1s000

STATISTICAL REVIEW(S)

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

STATISTICAL REVIEW MEMORANDUM

NDA/BLA #:	NDA 205879 (CANA/MET XR FDC)
Supplement #:	
Drug Name:	Canagliflozin and Metformin Hydrochloride extended release
Indication(s):	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin is appropriate
Applicant:	Janssen
Date(s):	Submitted: 11/20/15
	Review due: 8/16/2016
Review Priority:	Standard
Biometrics Division:	II
Statistical Reviewer:	Roberto C. Crackel, PhD
Concurring Reviewers:	Mark Rothmann, PhD, Team leader
Medical Division:	Metabolism and Endocrinology Products
Clinical Team:	Hyon Kwon, Medical reviewer Lisa Yanoff, Clinical team leader
Project Manager:	Elizabeth Godwin

MEMORANDUM

The applicant is seeking approval of INVOKAMET XR tablets, an extended release form of INVOKAMET tablets (which consists of canagliflozin and metformin) for the indication:

> Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin is appropriate.

INVOKAMET XR is a fixed dose combination.

INVOKAMET tablets were originally approved August 8, 2014 and are currently indicated as an adjunct to diet and exercise to improve glycemic control in adult with T2DM when treatment with both canagliflozin and metformin is appropriate. Reference is made to the statistical reviews of INVOKAMET by Dr. Wei Liu signed 9/5/2013 and by Dr. Roberto Crackel signed April 7, 2016.

The clinical trials section of the proposed product label for INVOKAMET XR tablets is identical to the clinical studies section of the approved product label for INVOKAMET tablets. All clinical data have been previously reviewed by the FDA (see aforementioned prior statistical reviews). There are no statistical issues.

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/s/

ROBERTO C CRACKEL
08/12/2016

MARK D ROTHMANN
08/12/2016
I concur

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA/BLA Number: 205879 **Applicant:** Janssen Research and Development **Stamp Date:** 11/20/15

Drug Name: Canagliflozin **NDA/BLA Type:** Standard Review

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

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

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE?

Yes, the statistical section is fileable

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comments
Designs utilized are appropriate for the indications requested.	X			
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.	X			
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			X	
Appropriate references for novel statistical methodology (if present) are included.	X			
Safety data organized to permit analyses across clinical trials in the NDA/BLA.	X			
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.	X			

Comments: This submission is for the marketing of CANA/MET XR FDC oral tablets. The evidence for marketing is derived from previous phase 3 studies. Most, if not all of these studies have been reviewed.

Comments for the Applicant: No comments at this time.

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/s/

ROBERTO C CRACKEL
01/13/2016

MARK D ROTHMANN
01/14/2016
I concur