

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205383Orig1s000

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 and Evaluation Clinical Studies - NAI

NDA/BLA NDA 205-383
Serial Number: Sequence 18
Drug Name: Iohexol (b) (4) Oral Solution (Oraltag)
Indication(s): Oraltag is an iodinated contrast agent indicated for **oral** use in adults and children for opacification of the gastrointestinal tract during computed tomography of the abdomen and pelvis.
Applicant: Interpharma Praha, a.s. (US agent: Otsuka Pharmaceutical Development & Commercialization)
Date(s): NDA re-submission: September 26, 2014
PDUFA Date:, July 25, 2015
Review Priority: Standard

Biometrics Division:
Statistical Reviewer: Satish C. Misra, Ph. D.
Concurring Reviewers: Jyoti Zalkikar, Ph. D., Team Leader
Thomas Gwise, Ph. D., Deputy Division Director

Medical Division: Division of Medical Imaging Products (DMIP)
Clinical Team: Clinical: Harris E. Orzach, M.D.
Clinical TL: Alex Gorovets, M. D.
Project Manager: Thuy M Nguyen

EXECUTIVE SUMMARY

OralTag is an iodine-based oral contrast agent, which is used to opacify the gastrointestinal tract, for abdominal and pelvic CT scanning. The drug, contains the same active ingredient as prepared solutions of Omnipaque 300 (iohexol), which is the reference listed drug (RLD) for oral use.

NDA 205-383 was submitted to FDA on behalf of Interpharma Praha, a.s., by the US agent, Otsuka Pharmaceutical Development & Commercialization, Inc. on March 11, 2013 (Sequence 00). The clinical reviewer, Barbara Stinson recommended approval from the clinical perspective of the 505(b)(2) NDA for the product, which at that time was called [REDACTED]^{(b) (4)}. This was based on the FDA's previous finding of safety and effectiveness of Omnipaque, which was approved under NDAs 18-956 and 20-608 and literature search. However, this NDA was not approved due to lack of meeting the CMC regulatory requirement and other deficiencies.

The sponsor resubmitted a complete response to all deficiencies outlined in the Complete Response letter of January 8, 2014, consistent with the proposal that was deemed acceptable by FDA on August 8, 2014 and this NDA was resubmitted on September 26, 2014. The CMC issues have been addressed in this submission.

Any new clinical/efficacy data were not required and were not submitted. Therefore, it is NAI from statistical perspective.

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/s/

SATISH C MISRA
03/02/2015

JYOTI ZALKIKAR
03/02/2015
I concur with the primary reviewer.

THOMAS E GWISE
03/02/2015

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: NDA 205-383 **Applicant:** Interpharma Praha a. s. **U.S. Agent:** Otsuka Novel Products; **Stamp Date:** March 11, 2013

Drug Name: Iohexol (b) (4) Oral solution **NDA/BLA Type:** NDA

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			No clinical studies conducted or submitted.
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		No data sets submitted

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE?

No Action Intended (NAI)

Remarks:

This 505(b)(2) NDA was submitted on behalf of Interpharma Praha, a.s., by the US agent, Otsuka Pharmaceutical Development & Commercialization, Inc. It is a new formulation of a marketed product (NDA 18-956, Omnipaque-Original Applicant Holder-General Electric Health Care and in accordance with the agreements reached at the pre-NDA meeting held on March 20, 2012. No clinical studies have been conducted in support of this application. The NDA relies on the pharmacokinetic (PK) data supporting the approval of OMNIPAQUE. Available summaries of the individual publications are provided. Methods to combine information using Meta Analyses etc. are not explored. There are no statistical contents in this NDA. Therefore it is NAI from statistical point of view.

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

If the NDA/BLA is not fileable from the statistical perspective, state the reasons and provide comments to be sent to the Applicant.

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	Comment
Designs utilized are appropriate for the indications requested.	X			
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.			X	limited to published reports
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	Safety data limited to published reports
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			X	

Satish C. Misra, Ph. D.

April 25, 2013

Reviewing Statistician

Date

Jyoti Zalkikar, Ph. D.

April 25, 2013

Supervisor/Team Leader

Date

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/s/

SATISH C MISRA
04/26/2013

JYOTI ZALKIKAR
04/30/2013