CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208870Orig1s000

NON-CLINICAL REVIEW(S)

Pharmacology/Toxicology Memo for 505(b)(2) NDA Application
(No Pharmacology/Toxicology data submitted)

NDA:	208-870
Drug Product:	Tc-99m Exametazime (b) (4)
Sponsor:	Jubilant DraxImage Inc., 1675 Trans-Canada Hwy, Kirkland, Quebec, Canada H9H 4J4
Submission Date:	20 July 2016
PDUFA Goal Date:	8/20/2017
Reviewer:	Olayinka A. Dina, DVM PhD
Team Leader:	Adebayo A. Laniyonu, PhD

Summary:

Jubilant DraxImage Inc. JDI) submitted NDA208-870 (PIND123604) for the development of Technetium Tc-99m Exametazime (b) (4) under 505(b)(2). Exametazime (b) (4) Hexamethylpropylene amine oxime or (b) (4) HMPAO) has been used previously in the nuclear community under the reference listed drug (RLD) name, Ceretec (99mTc-Exametazime). Ceretec was approved in 1988 under NDA 19-829 for brain imaging. In 1995, this NDA was approved for white blood cell imaging as an additional indication. According to JDI, the formulation of Tc-99m Exametazime (b) (4) is identical to the RLD and contains the same active and inactive ingredients at the same concentrations and in the same dosage form.

According to the meeting package, the proposed product, Tc-99m Exametazime is a well-established radiopharmaceutical, is not a new chemical entity and is not being submitted for a new indication. However, Jubilant DraxImage is seeking approval for only one of the two approved indications i.e., *"leukocyte labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease"*. The sponsor is therefore not including the indication for *"detection of altered regional cerebral perfusion in stroke"* in this application. The sponsor considered that the clinical and nonclinical findings of previously approved application for Ceretec and related amendments could be used in support of JDI's projected NDA 505(b)(2).

Conclusion: I concur with the Sponsor's position. There are no additional comments from Pharmacology and Toxicology perspectives.

Olayinka A. Dina
Pharmacology/Toxicology Reviewer

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/s/

OLAYINKA A DINA
08/02/2017

ADEBAYO A LANIYONU
08/02/2017

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

NDA/BLA Number: 208-870 **Applicant:** JUBILANT DRAXIMAGE INC **Stamp Date:** July 20, 2016

Drug Name: Technetium Tc 99m Exametazime (b) (4) **NDA/BLA Type:** 505(b)(2)

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

	Content Parameter	Yes	No	Comment
1	Is the pharmacology/toxicology section organized in accord with current regulations and guidelines for format and content in a manner to allow substantive review to begin?			N/A; No new Pharm/Tox data submitted for review
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?			N/A; No new Pharm/Tox data submitted for review
3	Is the pharmacology/toxicology section legible so that substantive review can begin?			N/A; No new Pharm/Tox data submitted for review
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted (carcinogenicity, mutagenicity, teratogenicity, effects on fertility, juvenile studies, acute and repeat dose adult animal studies, animal ADME studies, safety pharmacology, etc)?			This is a 505(b)(2) application and no new Pharm/Tox data was submitted for review
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).			N/A; No new Pharm/Tox data submitted for review
6	Does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the applicant submitted a rationale to justify the alternative route?			N/A; No new Pharm/Tox data submitted for review
7	Has the applicant submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?			N/A; No new Pharm/Tox data submitted for review

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	Comment
8	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?			N/A; No new Pharm/Tox data submitted for review
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate (including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?			N/A; No new Pharm/Tox data submitted for review
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)			N/A; No new Pharm/Tox data submitted for review
11	Has the applicant addressed any abuse potential issues in the submission?			N/A
12	If this NDA/BLA is to support a Rx to OTC switch, have all relevant studies been submitted?			N/A

IS THE PHARMACOLOGY/TOXICOLOGY SECTION OF THE APPLICATION FILEABLE? __Yes____

Filing Comments: Jubilant DraxImage Inc. JDI) submitted NDA208870 (PIND123604) for the development of Technetium Tc-99m Exametazime (b) (4) under 505(b)(2). Exametazime ((b) (4) Hexamethylpropylene amine oxime or (b) (4) HMPAO) has been used previously in the nuclear community under the reference listed drug (RLD) name, Ceretec (99mTc-Exametazime).

Ceretec was approved in 1988 under NDA 19-829 for brain imaging. In 1995, this NDA was approved for white blood cell imaging as an additional indication. According to JDI, the formulation of Tc-99m Exametazime (b) (4) is identical to the RLD and contains the same active and inactive ingredients at the same concentrations and in the same dosage form. According to the meeting package, the proposed product, Tc-99m Exametazime is a well-established radiopharmaceutical, is not a new chemical entity and is not being submitted for a new indication. The sponsor considers that the clinical and nonclinical findings of previously approved application for Ceretec and related amendments could be used in support of JDI's projected NDA 505(b)(2).

If the NDA/BLA is not fileable from the pharmacology/toxicology perspective, state the reasons and provide comments to be sent to the Applicant. **(N/A)**

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter. **(None)**

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

Olayinka A. Dina, D.V.M, Ph.D.	08/24/2016
Reviewing Pharmacologist	Date
Adebayo Laniyonu, Ph.D.	08/24/2016
Team Leader/Supervisor	Date

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/s/

OLAYINKA A DINA
08/24/2016

ADEBAYO A LANIYONU
08/24/2016