CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208870Orig1s000

CLINICAL REVIEW(S)

August 17, 2017

Division Director's Memorandum

NDA: 208870

Applicant: Jubilant DraxImage Inc

Product:
Drax Exametazime (Kit for the Preparation of technetium Tc99m Exametazime for leukocyte labeling) for intravenous use

Indication:
Leukocyte (white blood cell) labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease.

Review team:

CDTL	Danae Christodoulou
CMC Reviewer	Dhanalakshmi Kasi
CMC Reviewer	Martin Haber
Microbiology Reviewer	Samata Tiwari
Biopharm Reviewer	Poonam Delvadia
Facilities	Michael Klapal
Clinical Reviewer	Phillip Davis
Pharm/Tox Reviewer	Olayinka Dina
Clinical Pharmacology Reviewer	Christy John
ADL	Michele Fedowitz
Radiation Dosimetry	Stanley Stern
DMEPA	Idalia Rychlik
DPMH (Pediatrics)	Ethan Hausman
DPMH (Maternal Health)	Carrie Ceresa
OPDP	Zarna Patel
Biostatistician	Satish Misra
OPRO RBPM	Thao Vu
OSE SRPM	Tri Bui Nguyen
DPMH RPM	Lori Gorski
DMIP RPM	Alberta Davis-Warren

Summary:
Reference is made to the July 15, 2016 505(b)(2) New Drug Application submitted by Jubilant Draximage for Drax Exametazime for use in leukocyte-labeled scintigraphy in the localization of intra-abdominal infection and inflammatory bowel disease.

Reference is also made to the FDA review disciplines and the reviewers listed above and to the NDA review package. The reviews are complete. All outstanding issues have been resolved.

I concur with the findings of the reviewers and with the unanimous recommendation that the application be approved.

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/s/

LIBERO L MARZELLA
08/17/2017

Medical Officer Memo for 505(b)(2) NDA Application

(No module 5 clinical data submitted)

NDA:	208870
Drug Name:	Tc99m Exametazime (b) (4)
Sponsor:	Jubilant DraxImage Inc.
Submission Date:	20 July 2016
PDUFA Goal Date:	8/20/2017
Reviewer:	Phillip B. Davis, MD
Team Leader:	Nushin Todd

Executive Summary

Please see clinical review filed 3/22/2017 for additional information.

This submission is a 505(b)(2) application for Tc-99m Exametazime (formerly described as Tc99m HMPAO) for use in WC labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease. The sponsor is relying on the reference listed drug Ceretec (NDA 19829) for efficacy and safety data, and will not be including the indication of "detection of altered regional cerebral perfusion in stroke" in this new drug label.

With this memo, the reviewer notes that no financial disclosure information is required because no clinical studies were conducted for this NDA submission.

By:
Phillip Davis, MD
Medical Officer

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/s/

PHILLIP B DAVIS
08/01/2017

Medical Officer Review of 505(b)(2) NDA Application

(No module 5 clinical data submitted)

NDA:	208870
Drug Name:	Tc99m Exametazime (b) (4)
Sponsor:	Jubilant DraxImage Inc.
Submission Date:	20 July 2016
PDUFA Goal Date:	5/19/2017
Reviewer:	Phillip B. Davis, MD
Team Leader:	Nushin Todd

Executive Summary

This submission is a 505(b)(2) application for Tc-99m Exametazime (formerly described as Tc99m HMPAO) for use in WC labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease. The sponsor is relying on the reference listed drug Ceretec (NDA 19829) for efficacy and safety data, and does not wish to include the additional indication of "detection of altered regional cerebral perfusion in stroke" in this new drug label.

The data submitted in support of the sponsor's drug being sufficiently similar to the reference listed drug includes published literature (with Ceretec named in multiple journal articles), in vitro data (equivalence study), and the FDA approved drug label for Ceretec; these data are largely CMC based.

The major tasks to accomplish for approval include CMC verification of the quantitative and qualitative sufficient similarity to the RLD and review and revision of the proposed new drug label to ensure its acceptability as related to the RLD approved drug label, submitted literature and current clinical practice given Ceretec was initially approved in 1988.

This clinical reviewer has served only in a supportive role in the application to the DMIP Deputy Director of Labeling and Clinical Team Leader given there is no clinical data to review and the outstanding issues from a clinical perspective are related to the wording of the proposed drug label. The reviewer has no concerns regarding the efficacy or safety of Tc99m Exametazime and believes the application is approvable once CMC issues are satisfied and the package insert language is finalized.

Review

RLD Drug Approved Indication

Technetium Tc99m exametazime scintigraphy may be useful as an adjunct in the detection of altered regional cerebral perfusion in stroke.

Tc99m exametazime is indicated for leukocyte labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease.

Sponsor's Proposed Indication (as edited by DMIP review team)

Draximage Exametazime is a radioactive diagnostic agent indicated for WBCs [leukocytes] labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease.

Label Revisions
A full review of the of the important label revisions performed in order to adhere to the PLR format is submitted separately by the Associate Director of Labeling, Michele Fedowitz.

Concluding Remarks

The medical officer has no significant concerns regarding the safety or efficacy of the Tc99m Exametazime and believes the application is approvable once the CMC issues are resolved and labeling revisions completed.

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/s/

PHILLIP B DAVIS
03/22/2017

CLINICAL FILING CHECKLIST FOR NDA/BLA or Supplement

NDA/BLA Number: 208870 **Applicant:** Jubiliant DraxImage Inc. **Stamp Date:** July 20th, 2016

Drug Name: Technetium Tc99m Exametazime **NDA/BLA Type:** 505b(2)

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

	Content Parameter	Yes	No	NA	Comment
FORMAT/ORGANIZATION/LEGIBILITY					
1.	Identify the general format that has been used for this application, e.g. electronic common technical document (eCTD).	X			
2.	Is the clinical section legible and organized in a manner to allow substantive review to begin?			X	No clinical data submitted for review.
3.	Is the clinical section indexed (using a table of contents) and paginated in a manner to allow substantive review to begin?			X	
4.	For an electronic submission, is it possible to navigate the application in order to allow a substantive review to begin (*e.g.*, are the bookmarks adequate)?	X			
5.	Are all documents submitted in English or are English translations provided when necessary?	X			
LABELING					
6.	Has the applicant submitted a draft prescribing information that appears to be consistent with the Physician Labeling Rule (PLR) regulations and guidances (see http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm	X			
SUMMARIES					
7.	Has the applicant submitted all the required discipline summaries (*i.e.*, Module 2 summaries)?	X			The sponsor relies on RLD Ceretec (NDA 19829) for clinical data.
8.	Has the applicant submitted the integrated summary of safety (ISS)?			X	
9.	Has the applicant submitted the integrated summary of efficacy (ISE)?			X	
10.	Has the applicant submitted a benefit-risk analysis for the product?			X	
11.	Indicate if the Application is a 505(b)(1) or a 505(b)(2).	X			505(b)(2)
505(b)(2) Applications					
12.	If appropriate, what is the relied upon listed drug(s)?	X			Ceretec (NDA 19829)
13.	Did the applicant provide a scientific bridge demonstrating the relationship between the proposed product and the listed drug(s)/published literature?		X		Waiver submitted based on fulfilling 21CFR320.22(b)(1)(i) and (ii)
14.	Describe the scientific bridge (e.g., BA/BE studies)			X	
DOSAGE					
15.	If needed, has the applicant made an appropriate attempt to determine the correct dosage regimen for this product (e.g., appropriately designed dose-ranging studies)? Study Number: Study Title:			X	Right of reference submitted for RLD Ceretec (NDA 19829)

File name: 5_Clinical Filing Checklist for NDA_BLA or Supplement 010908

CLINICAL FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	NA	Comment
	Sample Size: Treatment Arms: Location in submission:				
EFFICACY					
16.	Do there appear to be the requisite number of adequate and well-controlled studies in the application? Pivotal Study #1 Indication: Pivotal Study #2 Indication:			X	Right of reference submitted for RLD Ceretec (NDA 19829)
17.	Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?			X	
18.	Do the endpoints in the pivotal studies conform to previous Agency commitments/agreements? Indicate if there were not previous Agency agreements regarding primary/secondary endpoints.			X	
19.	Has the application submitted a rationale for assuming the applicability of foreign data to U.S. population/practice of medicine in the submission?			X	
SAFETY					
20.	Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously requested by the Division?			X	
21.	Has the applicant submitted adequate information to assess the arythmogenic potential of the product (*e.g.*, QT interval studies, if needed)?			X	
22.	Has the applicant presented a safety assessment based on all current worldwide knowledge regarding this product?			X	
23.	For chronically administered drugs, have an adequate number of patients (based on ICH guidelines for exposure[1]) been exposed at the dosage (or dosage range) believed to be efficacious?			X	
24.	For drugs not chronically administered (intermittent or short course), have the requisite number of patients been exposed as requested by the Division?			X	
25.	Has the applicant submitted the coding dictionary[2] used for			X	

[1] For chronically administered drugs, the ICH guidelines recommend 1500 patients overall, 300-600 patients for six months, and 100 patients for one year. These exposures MUST occur at the dose or dose range believed to be efficacious.

[2] The "coding dictionary" consists of a list of all investigator verbatim terms and the preferred terms to which they were mapped. It is most helpful if this comes in as a SAS transport file so that it can be sorted

CLINICAL FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	NA	Comment
	mapping investigator verbatim terms to preferred terms?				
26.	Has the applicant adequately evaluated the safety issues that are known to occur with the drugs in the class to which the new drug belongs?			X	
27.	Have narrative summaries been submitted for all deaths and adverse dropouts (and serious adverse events if requested by the Division)?			X	
OTHER STUDIES					
28.	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?	X			
29.	For Rx-to-OTC switch and direct-to-OTC applications, are the necessary consumer behavioral studies included (*e.g.*, label comprehension, self selection and/or actual use)?			X	
PEDIATRIC USE					
30.	Has the applicant submitted the pediatric assessment, or provided documentation for a waiver and/or deferral?	X			
PREGNANCY, LACTATION, AND FEMALES AND MALES OF REPRODUCTIVE POTENTIAL USE					
31.	For applications with labeling required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, has the applicant submitted a review of the available information regarding use in pregnant, lactating women, and females and males of reproductive potential (e.g., published literature, pharmacovigilance database, pregnancy registry) in Module 1 (see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307 htm)?			X	
ABUSE LIABILITY					
32.	If relevant, has the applicant submitted information to assess the abuse liability of the product?			X	
FOREIGN STUDIES					
33.	Has the applicant submitted a rationale for assuming the applicability of foreign data in the submission to the U.S. population?			X	
DATASETS					
34.	Has the applicant submitted datasets in a format to allow reasonable review of the patient data?			X	
35.	Has the applicant submitted datasets in the format agreed to previously by the Division?			X	
36.	Are all datasets for pivotal efficacy studies available and complete for all indications requested?			X	
37.	Are all datasets to support the critical safety analyses available and complete?			X	
38.	For the major derived or composite endpoints, are all of the raw data needed to derive these endpoints included?			X	
CASE REPORT FORMS					
39.	Has the applicant submitted all required Case Report Forms in a legible format (deaths, serious adverse events, and			X	No clinical studies conducted for

as needed; however, if it is submitted as a PDF document, it should be submitted in both directions (verbatim -> preferred and preferred -> verbatim).

CLINICAL FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	NA	Comment
	adverse dropouts)?				approval.
40.	Has the applicant submitted all additional Case Report Forms (beyond deaths, serious adverse events, and adverse drop-outs) as previously requested by the Division?			X	
FINANCIAL DISCLOSURE					
41.	Has the applicant submitted the required Financial Disclosure information?			X	
GOOD CLINICAL PRACTICE					
42.	Is there a statement of Good Clinical Practice; that all clinical studies were conducted under the supervision of an IRB and with adequate informed consent procedures?			X	

IS THE CLINICAL SECTION OF THE APPLICATION FILEABLE? Yes

If the Application is not fileable from the clinical 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.

Phillip B. Davis 9/12/16

Reviewing Medical Officer Date

Clinical Team Leader Date

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/s/

PHILLIP B DAVIS
09/30/2016