DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202317

NDA APPROVAL

Ceptaris Therapeutics, Inc.
Attention: Lisa Wittmer, M.S., Ph.D.
Vice President, Regulatory Affairs
101 Lindenwood Drive, Suite 400
Malvern, PA 19355

Dear Dr. Wittmer:

Please refer to your New Drug Application (NDA) dated February 27, 2013, received February 27, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Valchlor (mechlorethamine) gel 0.016%.

We acknowledge receipt of your amendments dated March 26, 2013, April 1, 2013, May 24, 2013, June 25, 27, 2013, July 1, 10, 23, 26, 29, 2013 and August 2, 6, 7, 12, 16, 19, 22, 23, 2013. The February 27, 2013, submission constituted a complete response to our May 4, 2012, action letter.

This new drug application provides for the use of Valchlor (mechlorethamine) gel 0.016% for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received at least one prior skin-directed therapy.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

- Update the issue date to 8/2013 in the medication guide
- Correct the web address in Section 15 to: http://www.osha.gov/SLTC/hazardousdrugs/index.html
- Highlights (Warnings and Precautions): Flammable gel: VALCHLOR is an alcohol-based gel. Avoid fire, flame, and smoking until the gel has dried (2.2, 5.6).
- Section 14, Paragraph 1, Sentence 1: The efficacy of VALCHLOR was assessed in a randomized, multicenter, observer-blind, active-controlled, non-inferiority clinical trial of 260 patients with Stage IA, IB, and IIA mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL) who had received at least one prior skin-directed therapy.
- Section 14, title of Table 2: Efficacy in Patients with Mycosis Fungoides-Type CTCL (MF-CTCL)

We note that your August 22, 2013, submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

We acknowledge your July 29, 2013, submission containing final printed carton and container labels.

ADVISORY COMMITTEE

Your application for Valchlor (mechlorethamine) gel 0.016% was not referred to an FDA advisory committee because this drug is not the first in its class.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a known serious risk of inadvertent exposure of anyone other than the patient to the serious multisystem risks of Valchlor (mechlorethamine) gel 0.016%.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

PMR 2081 - An assessment and analysis of spontaneous reports of inadvertent exposure of anyone other than the patient who has been exposed to Valchlor (mechlorethamine) gel 0.016%. Specialized follow-up should be obtained on these cases to collect additional information on the events. This enhanced pharmacovigilance should continue for a period of 2 years from the date of approval. The following components should be assessed and analyzed in a final report:

- Expedited reports of both serious and non-serious outcomes for all initial and follow-up adverse drug experiences resulting from secondary exposure to the skin, mucous membranes, and eyes of individuals other than the patients being treated submitted as Postmarketing 15-day "Alert Reports";
- A summary and line listing of all secondary exposure events from postmarketing sources, including consumer reports, solicited reports, and foreign reports submitted in each PADER/PBRER; and
- Documentation of attempts to contact all reporters of events, and obtain findings about the events, including but not limited to the circumstances leading to the exposure, ultimate highest severity of the exposure, and resolution status.

The timetable you submitted on August 6, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	10/2013
Study Completion:	10/2015
Final Report Submission:	12/2015

Submit the protocol(s) to your IND 067839, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Janet Higgins, Regulatory Project Manager, at (240) 402-0330.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, M.D.
Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
08/23/2013