NDA 212306/S-018

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING REQUIREMENT

Karyopharm Therapeutics, Inc.
Attention: HeiJen Sun, PhD
Executive Director, Global Regulatory Affairs
85 Wells Ave.
Suite 210
Newton, MA 02459

Dear Dr. Sun:

Please refer to your supplemental new drug application (sNDA) dated and received April 6, 2026, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xpovio (selinexor) tablet.

This Prior Approval supplemental new drug application provides for removal of the following indication, approved under accelerated approval, from the Xpovio product labeling, US Prescribing Information and Medication Guide:

> Xpovio (selinexor) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

You requested withdrawal of approval of this indication and waived the expedited withdrawal procedures set forth in section 506(c)(3) of the Food, Drug, and Cosmetic Act, as amended by the Food and Drug Omnibus Reform Act of 2022. You would have to obtain FDA approval of an efficacy supplement for FDA approval in order to resume marketing the product for this indication.

APPROVAL & LABELING

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 enclosed agreed-upon labeling.

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

FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

RELEASE FROM POSTMARKETING REQUIREMENT

We have received your submission dated April 6, 2026, related to the following postmarketing requirements listed in our June 22, 2020, approval letter:

3866-1 Submit the final report and datasets from a randomized, double-blind, placebo-controlled phase 3 trial that verifies and describes the clinical benefit of selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma. Patients should be randomized to receive chemoimmunotherapy with or without selinexor. The primary endpoint should be progression-free survival, with secondary endpoints that include overall survival and objective response rate.

Final Protocol Submission:	08/2020
Trial Completion:	12/2025
Final Report Submission:	04/2026

3866-2 Provide the interim and final analyses of a randomized phase 2 clinical trial of selinexor to characterize the safety and efficacy of at least two different dosing regimens of selinexor monotherapy in patients with relapsed or refractory diffuse large B-cell lymphoma after at least two prior lines of systemic therapy. Include one regimen with a lower starting dose

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

and one regimen with a prespecified transition to a lower continuation dose, than the dosing regimen of 60 mg orally on Days 1 and 3 of each week. The primary efficacy endpoint should be overall response rate by independent review committee assessment. Include a prospective characterization of the presentation, management, and outcome of treatment-emergent hyponatremia in the final report, including the results of diagnostic evaluations and the supportive care provided. The results of this trial may inform product labeling. Submit datasets with the final report.

Final Protocol Submission:	10/2020
Trial Completion:	06/2023
Final Report Submission:	10/2023

We have reviewed your submission and have determined that you are released from the above requirements as they are no longer needed because of your voluntary withdrawal of the DLBCL indication.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

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, contact Theresa Carioti, Chief Project Management Staff, at Theresa.Carioti@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Nicole Gormley, MD
Director
Division of Hematologic Malignancies II
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

NICOLE J GORMLEY
04/30/2026 01:55:33 PM