



Our STN: BL 125703/91

**SUPPLEMENT APPROVAL**

October 1, 2021

Kite Pharma, Inc.  
Attention: Polina Kinchev  
2400 Broadway  
Santa Monica, CA 90404

Dear Ms. Kinchev:

We have approved your request submitted March 31, 2021, received April 1, 2021, to supplement your Biologics License Application (BLA) under section 351(a) of the Public Health Service Act for brexucabtagene autoleucel to add a new indication for adult patients with relapsed or refractory (r/r) B-cell precursor acute lymphoblastic leukemia (ALL).

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT02601313, NCT02614066, NCT02625480, NCT03624036, and NCT04162756.

## **LABELING**

We hereby approve the draft content of labeling Package Insert submitted under amendment 0150, October 1, 2021 and the draft carton and container labels submitted under amendment 0, dated March 31, 2021.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via 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 Package Insert submitted on October 1, 2021 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* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

## **CARTON AND CONTAINER LABELS**

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on March 31, 2021, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications>.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125703 at the time of use and include implementation information on Form FDA 356h.

## **ADVERTISING AND PROMOTIONAL LABELING**

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration  
Center for Biologics Evaluation and Research  
Document Control Center  
10903 New Hampshire Ave.  
WO71–G112  
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

## **PEDIATRIC REQUIREMENTS**

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 indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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

## **POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)**

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct post-marketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to identify a serious risk of secondary malignancies associated with use of brexucabtagene autoleucl.

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

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following study:

1. A postmarketing, prospective, multicenter, observational study to assess the long-term safety of brexucabtagene autoleucl and the risk of all secondary malignancies occurring after treatment with brexucabtagene autoleucl. The study will include at least 500 adult patients with r/r B-cell precursor ALL, who will be followed for 15 years after the product administration.

We acknowledge the timetable you submitted on August 5, 2021, which states that you will conduct this study, according to the following schedule:

Final Protocol Submission: October 15, 2021

Study Completion Date: August 31, 2041

Final Report Submission: August 31, 2042

Please submit the protocol to your IND 16675, with a cross-reference letter to BLA STN BL 125703/0 explaining that this protocol was submitted to the IND. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit final study reports to the BLA. If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement to BLA STN BL 125703/0. For administrative purposes, all submissions related to this postmarketing study required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**

- **Supplement contains Required Postmarketing Final Report under Section 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. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of the approval of BLA STN BL 125703/0 until all requirements and commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at <http://www.fda.gov/Drugs/Guidance/ComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm>.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 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 periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

## **RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS**

The “YESCARTA and TECARTUS REMS” was originally approved on July 24, 2020, and consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

The most recent REMS modification under STNs BL 125703/108 and BL 125643/344 approved on October 1, 2021, includes changes to the REMS training material, REMS Knowledge Assessment, and REMS Website to align with labeling changes related to your new indication for adult patients with r/r B-cell precursor ALL.

The timetable for submission of assessments of the REMS remains the same as that approved on July 24, 2020.

There are no changes to the REMS assessment plan described in our July 24, 2020, letter.

We will include information contained in the above-referenced supplement in your BLA files.

Sincerely,

Tejashri Purohit-Sheth, MD  
Director  
Division of Clinical Evaluation  
and Pharmacology/Toxicology  
Office of Tissues and Advanced Therapies  
Center for Biologics Evaluation and Research