



NDA 210259/S-011  
NDA 216387/S-005

## **SUPPLEMENT APPROVAL FULFILLMENT OF POSTMARKETING REQUIREMENTS**

AstraZeneca UK Limited  
c/o AstraZeneca Pharmaceuticals LP  
Attention: Vanessa Yu, PhD  
Regulatory Affairs Director  
One MedImmune Way  
Gaithersburg, MD 20878

Dear Dr. Yu:

Please refer to your supplemental new drug applications (sNDAs) dated and received August 2, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Calquence (acalabrutinib) capsules, NDA 210259/S-011, and tablets, NDA 216387/S-005.

These Prior Approval supplemental new drug applications provide for a new indication for Calquence in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are ineligible for autologous hematopoietic stem cell transplantation (HSCT).

These sNDAs also provide for conversion to traditional approval for the following indication: Calquence for the treatment of adult patients with MCL who have received at least one prior therapy.

### **APPROVAL & LABELING**

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

### **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

### **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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert), with the addition of any labeling changes in pending “Changes Being Effectuated” (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*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, 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 these supplemental applications, 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).

### **SUBPART H FULFILLED**

We approved NDAs 210259 and 216387/Original 2 under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of these supplements (NDAs 210259/S-011 and 216387/S-005) fulfill your commitments made under 21 CFR 314.510.

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

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidance periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

## **FULFILLMENT OF POSTMARKETING REQUIREMENTS**

We have received your submission dated August 2, 2024, containing the final report for the following postmarketing requirement listed in the October 31, 2017, approval letter for NDA 210259.

- 3291-1 Submit the complete final report and datasets demonstrating clinical efficacy and safety from a randomized, double-blind, placebo-controlled, clinical trial of Calquence in combination with standard immunochemotherapy versus immunochemotherapy alone in patients with mantle cell lymphoma.

We have received your submission dated August 2, 2024, containing the final report for the following postmarketing requirement listed in the August 3, 2022, approval letter for NDA 216387/Original 2.

- 4311-1 Complete a randomized, double-blind, placebo-controlled clinical trial of acalabrutinib in combination with standard immunochemotherapy versus immunochemotherapy alone in patients with mantle cell lymphoma to obtain data on clinical efficacy and safety.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

This completes all of your postmarketing requirements acknowledged in our October 31, 2017, letter for NDA 210259 and in our August 3, 2022, letter for NDA 216387/Original 2. You are not required to report on the status of closed (released or fulfilled) PMRs/PMCs in your annual report required under 21 CFR 314.81(b)(2)(vii) of the FDCA.

## **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*.<sup>3</sup>

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

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](http://FDA.gov).<sup>4</sup> Information and Instructions for completing the form can be found at [FDA.gov](http://FDA.gov).<sup>5</sup>

### **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, please contact Denise Felluca, Regulatory Project Manager, at [denise.felluca@fda.hhs.gov](mailto:denise.felluca@fda.hhs.gov) or at 301-796-4574.

Sincerely,

*{See appended electronic signature page}*

Nicholas Richardson, DO, MPH  
Deputy Director  
Division of Hematologic Malignancies II  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### **ENCLOSURE:**

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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**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.**  
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/s/  
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