

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### ***APPLICATION NUMBER:***

**216387Orig1Orig2s000**

***Trade Name:*** Calquence

***Generic or Proper Name:*** Acalabrutinib

***Sponsor:*** AstraZeneca UK Limited

***Approval Date:*** August 4<sup>th</sup>, 2022

***Indication:***

- Treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy

# CENTER FOR DRUG EVALUATION AND RESEARCH

## 216387Orig1Orig2s000

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**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**216387Orig1Orig2s000**

**APPROVAL LETTER**

NDA 216387/Original 1

**NDA APPROVAL**

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 new drug application (NDA) dated and received October 4, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Calquence (acalabrutinib) tablets.

NDA 216387 provides for the use of Calquence (acalabrutinib) tablets for the following indications which, for administrative purposes, we have designated as follows:

- NDA 216387/Original 1 – treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- NDA 216387/Original 2 – treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy

The subject of this action letter is NDA 216387/Original 1. A separate action letter will be issued for NDA 216387/Original 2.

### **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.

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

### **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 (Prescribing Information, text for the Patient Package Insert) 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 via publicly available labeling repositories.

### **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling submitted on August 3, 2022, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 216376**.” Approval of this submission by FDA is not required before the labeling is used.

### **DATING PERIOD**

Based on the stability data submitted to date, the expiry dating period for Calquence (acalabrutinib) tablets shall be 24 months from the date of manufacture when stored at 20-25°C.

### **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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable.

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

<sup>2</sup> 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>.

## **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>

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

## **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 via email at [denise.felluca@fda.hhs.gov](mailto:denise.felluca@fda.hhs.gov) or at 301-796-4574.

Sincerely,

*{See appended electronic signature page}*

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

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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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>.

<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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/s/  
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NICOLE J GORMLEY  
08/04/2022 04:48:24 PM



NDA 216387/Original 2

**ACCELERATED APPROVAL**

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

Dear Dr. Yu:

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- NDA 216387/Original 1 – treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- NDA 216387/Original 2 – treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy

The subject of this action letter is NDA 216387/Original 2. A separate action letter will be issued for NDA 216387/Original 1.

**APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.



## **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 (Prescribing Information, text for the Patient Package Insert). 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 via publicly available labeling repositories.

## **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling submitted on August 3, 2022, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 216387.**” Approval of this submission by FDA is not required before the labeling is used.

## **DATING PERIOD**

Based on the stability data submitted to date, the expiry dating period for Calquence (acalabrutinib) tablets shall be 24 months from the date of manufacture when stored at 20-25°C.

## **ACCELERATED APPROVAL REQUIREMENTS**

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trials with due diligence. If postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 314.530, withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated July 20, 2022. This requirement, along with required completion dates, is listed below.

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

<sup>2</sup> 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>.

- 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.

Trial Completion: 10/2023

Final Report Submission: 11/2024

Submit clinical protocols to your IND 118717 for this product. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each requirement in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of subjects entered into each study/trial.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated “**Subpart H Postmarketing Requirement(s).**”

### **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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable.

### **PROMOTIONAL MATERIALS**

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover

letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

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>

## **REPORTING REQUIREMENTS**

We remind you that you must comply with the 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 via email at [denise.felluca@fda.hhs.gov](mailto:denise.felluca@fda.hhs.gov) or at 301-796-4574.

Sincerely,

*{See appended electronic signature page}*

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

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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<sup>3</sup> <https://www.fda.gov/media/128163/download>.

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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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NICOLE J GORMLEY  
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