CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210259Orig1s000

PRODUCT QUALITY REVIEW(S)

Recommendation: APPROVAL

NDA 210259
Review #1

Drug Name/Dosage Form	Acalabrutinib Capsules
Strength	100 mg
Route of Administration	Oral
Rx/OTC Dispensed	R_x
Applicant	Acerta Pharma B.V.
US agent, if applicable	Yasameen Qazen

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Original Submission	13-Jun-17	All
Amendment (SD 4)	13-Jul-17	Process
Amendment (SD 0014)	25-Aug-17	Facilities
Amendment (SD 0015)	25-Aug-17	Process, DS
Amendment (SD 0017)	30-Aug-17	DS, DP
Amendment (SD 0018)	08-Sept-17	DS

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Drug Master File/Drug Substance	Linsey Saunders and Paresma Patel	Anamitro Banerjee
Drug Product	Rajiv Agarwal	Anamitro Banerjee
Process	Quamrul Majumder	Rakhi Shah
Microbiology	n/a	n/a
Facility	Ruth Moore	Zhihao Peter Qiu
Biopharmaceutics	Yang Zhao	Okponanabofa Eradiri
Regulatory Business Process Manager	Rabiya Laiq	n/a
Application Technical Lead	Sherita McLamore	n/a
Laboratory (OTR)	n/a	n/a
Environmental	Rajiv Agarwal	Anamitro Banerjee

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Review Completed	Comments
(b) (4)	Type IV		(b) (4)	N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA
	Type III			N/A	No Review	Adequate information provided in the NDA

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	118717	

2. CONSULTS

N/A

Executive Summary

I. Recommendations and Conclusion on Approvability

OPQ recommends **APPROVAL** of NDA 210259 for Calquence (acalabrutinib) capsules, 100 mg. As part of this action, OPQ grants a (b)(4)-month re-test period for the drug substance when stored at or below (b)(4)°C, and a 24-month drug product expiration period when stored at stored at controlled room temperature (25°C/60% RH). There are no outstanding issues and no post-approval quality agreements to be conveyed to the applicant.

II. Summary of Quality Assessments

A. Product Overview

NDA 210259 was submitted for Calquence (acalabrutinib) capsules, 100 mg in accordance with section 505(b)(1) of the Food, Drug and Cosmetic Act. Acalabrutinib is an orally bioavailable, Bruton tyrosine kinase inhibitor (BTK) indicated for patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. Acalabrutinib is an NME which was originally investigated under IND 118717 and received orphan designation in September 2015.

Acalabrutinib is a small chiral molecule that is manufactured as a single enantiomer (S) in a linear manner. Acalabrutinib is a BCS class 2 compound that exhibits BCS class 1 characteristics under *in vivo* conditions. The drug product, Calquence (acalabrutinib) capsules, 100 mg, is presented as a (b)(4) hard gelatin capsule, with a blue cap and yellow body, printed with 'ACA 100mg' in black ink and containing 100 mg of acalabrutinib, microcrystalline cellulose, pregelatinized startch, sodium starch glycolate and magnesium stearate.

The dosing regimen for Calquence (acalabrutinib) capsules is 100 mg orally twice daily.

Based on the information provided in this application (original submission and in responses to information requests), OPQ considers all review issues adequately addressed and potential risks to patient safety, product efficacy, and product quality mitigated appropriately. Accordingly, OPQ recommends APPROVAL of NDA 210259 and grants a (b)(4)-month re-test period for the drug substance and a 24 month expiration period for the drug product when stored at ICH controlled room temperature in the commercial packaging.

Proposed Indication(s) including Intended Patient Population	Indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
Duration of Treatment	Duration of treatment is until disease progression or unacceptable toxicity

Maximum Daily Dose	200 mg
Alternative Methods of Administration	None

B. Quality Assessment Overview

Drug Substance

(b) (4)

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