CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208855Orig1s000

PRODUCT QUALITY REVIEW(S)

Recommendation: Approval

NDA 208855
Review #1

Drug Name/Dosage Form	Verzenio (abemacicilib) tablets
Strength	50 mg, 100 mg, 150 mg, 200 mg
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Eli Lilly and Company
US agent, if applicable	N/A

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Original NDA 0001	08/15/2017	Drug Product

Quality Review Team

DISCIPLINE	REVIEWER	BRANCH/DIVISION
Drug Substance	N/A	
Drug Product	Xiao Hong Chen	CDER/OPQ/ONDP/DNDP1
Process	N/A	

Facility	N/A	
Biopharmaceutics	N/A	
Regulatory Business Process Manager	Kristine Leahy	CDER/OPQ/OPRO/DRBPMI
Application Technical Lead (ATL)	Xiao Hong Chen	CDER/OPQ/ONDP/DNDP1
ORA	N/A	
Environmental Analysis (EA)	Xiao Hong Chen	CDER/OPQ/ONDP/DNDP1

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs: N/A

DMF #	Type	Holder	Item Referenced	Status	Date Review Completed	Comments

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

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	208716	CMC information is reference to NDA 208716

2. CONSULTS

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH	N/A			
Clinical	N/A			

Executive Summary

I. Recommendations and Conclusion on Approvability

CMC information for this NDA was provided by referencing the applicant's own NDA 208716. No new CMC information was submitted in the NDA except information regarding environmental analysis. The applicant requested categorical exclusion per 21 CFR25.31 (b).

This NDA is recommended **Approval** from the CMC perspective.

II. Summary of Quality Assessments

A. Product Overview

Proposed Indication(s) including Intended Patient Population	VERZENIO™ is a kinase inhibitor indicated: • in combination with fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy. • as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.
Duration of Treatment	Until disease progression or unacceptable toxicity

Maximum Daily Dose	Recommended dose: When used in combination with fulvestrant, the recommended dose of VERZENIO is 150 mg taken orally twice daily. When used as monotherapy, the recommended dose of VERZENIO is 200 mg taken orally twice daily.
Alternative Methods of Administration	None.

B. Quality Assessment Overview

The applicant references NDA 208716 for CMC information. No new CMC information was submitted in the NDA except information regarding environmental analysis. The applicant requested categorical exclusion per 21 CFR25.31 (b).

Eli Lilly and Company claims a Categorical Exclusion from the requirement for an environmental assessment to support a NDA 208855 abemaciclib.

The annual peak sales volume of abemaciclib in the United States will be less than (b) (4) Assuming a daily discharge of water to sewage treatment facilities in the United States is about 1.26 x 1011 liters (Environmental Protection Agency, *2012 Clean Watershed Needs Survey,* Technical Data), a maximum expected introduction concentration of abemaciclib will be less than (b) (4):

Expected Introduction Concentration = (b) (4)

It was noted that if the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion (1 µg/L), a categorical exclusion is deemed appropriate by 21 CFR 25.31 (b).

Based on the maximum expected introduction concentration, Eli Lilly and Company claims a categorical exclusion from the need to conduct an environmental assessment for abemaciclib for this application. Additionally, there are no extraordinary circumstances for this proposed action, i.e. there is no known impact upon endangered species, abemaciclib does not have estrogenic, androgenic or thyroid activity, and there is no data that suggest there is potential for serious harm to the environment at the expected level of exposure. A review of the available environmental data has been conducted to ensure that the action will not have any appreciable environmental impact.

Evaluation: Acceptable. Abemaciclib has been approved under Eli Lilly's NDA 208716 for the same indication. A categorical exclusion per 21 CFR25.31 (b) was requested for NDA 208716, and was reviewed by Dr. Olen Stephens and was found to be acceptable. The indication for the current NDA is the same as those for NDA 208716 and does not appear to lead to significant increase in patient population in the US. In the current NDA, the applicant provided justification and data based on the indications proposed in this NDA rather than comparing to those in the approved NDA (208716). The provided data and justification appear to support the applicant's categorical exclusion per 21 CFR25.31 (b), and is deemed acceptable.

C. Special Product Quality Labeling Recommendations (NDA only)
N/A.

D. Final Risk Assessment (see Attachment)

Application Technical Lead Name and Date:
Xiao Hong Chen, Ph.D.

3-Nov-2017

Xiao Chen

Digitally signed by Xiao Chen
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