CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212436Orig1s000

CLINICAL REVIEW(S)

Date	October 31, 2019
From	Laleh Amiri-Kordestani Associate Director of DOP1
Subject	Designated Signatory Authority Review
NDA/BLA # and Supplement#	NDA 212436; Associated with NDA 207103
Applicant	Pfizer, Inc
Date of Submission	January 31, 2019
PDUFA Goal Date	November 31, 2019
Proprietary Name	IBRANCE®
Established or Proper Name	Palbociclib
Dosage Form(s)	Tablets: 125 mg, 100 mg, and 75 mg.
Proposed Indication(s)/Population(s)	IBRANCE is indicated for the treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine based therapy in postmenopausal women; or • fulvestrant in women with disease progression following endocrine therapy.
Dosing Regimen(s)	125 mg once daily taken orally with or without food for 21 days followed by 7 days off treatment.
Indication(s)/Population(s)	IBRANCE is indicated for the treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine based therapy in postmenopausal women; or • fulvestrant in women with disease progression following endocrine therapy.
Recommendation on Regulatory Action	*Approval*

Background

Palbociclib (IBRANCE®) is an inhibitor of cyclin-dependent kinases (CDK) 4 and 6. IBRANCE (Palbociclib) was originally approved in 2015 with a capsule formulation under NDA 207103. IBRANCE capsule is indicated for the treatment of hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. The recommended starting dose of IBRANCE capsule is 125 mg once daily taken with food for 21 days followed by 7 days off treatment. The capsule should be administered with food to reduce variability in drug absorption and to mitigate drug-drug-interactions with gastric acid reducing agents.

In the current submission, the applicant seeks the full approval of newly developed IBRANCE tablet formulation for oral use in the currently marketed indications of the capsule formulation. Ibrance tablets are formulated as immediate release film-coated tablet supplied in 75 mg, 100 mg, and 125 mg strength, same strength as the currently approved capsules. The tablets are packaged in (b) (4) blisters (b) (4) The proposed dosing regimen of the commercial tablets is same with the commercial capsule formulation: 125 mg once daily taken orally with or without food for 21 days followed by 7 days off treatment. The Applicant submits pharmacokinetic (PK) evidence from clinical studies in healthy volunteers to support the approval of the proposed tablet formulation. No changes were made to the efficacy or safety sections of the USPI. The application references the original safety and efficacy data from NDA 207103.

Conclusions on the Substantial Evidence of Effectiveness

This recommendation for the regular approval of palbociclib tablet formulation, according to 21 Code of Federal Regulations (CFR) 314.126(a)(b), is mainly based on pharmacokinetic (PK) evidence from clinical studies in healthy volunteers. The Office of Clinical Pharmacology concluded that the proposed tablet formulation allows for administration of palbociclib with or without food and concomitant administration of proton pump inhibitors (PPIs) under any food intake condition. The applicant provided adequate pharmacokinetic evidence from clinical studies in healthy volunteers to support the proposed tablet formulation. (See Dr Pengfei Song, CDTL review).

All review disciplines were in agreement with approval of palbociclib tablet formulation and did not identify any outstanding issues that precluded approval.

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/s/

LALEH AMIRI KORDESTANI
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Division of Oncology Products 1
CLINICAL LABELING REVIEW

Date	*Electronic Stamp Date*
Application Type	PAS
Application Number	NDA 212436
Name of Drug	IBRANCE® (palbociclib) Tablets
Sponsor	Pfizer, Inc.
Submission Date	January 31, 2019
Regulatory Project Manager	Kim Robertson
Clinical Reviewer	Preeti Narayan
Clinical Team Leader	Harpreet Singh
Cross-Disipline Team Leader	Pengfei Song
Associate Division Director	Laleh Amiri-Kordestani

Background and Summary Description:

IBRANCE® is a kinase inhibitor indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

- an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men; or
- fulvestrant in patients with disease progression following endocrine therapy.

This NDA seeks full approval for IBRANCE® (palbociclib) proposed tablet formulation for oral use in the currently marketed indications. The tablet formulation allows administration of palbociclib with or without food and concomitant administration of proton pump inhibitors (PPIs) under any food intake condition.
The current commercial capsule formulation of palbociclib is labeled to be administered with food to reduce variability in drug absorption and to mitigate drug-drug-interactions (DDIs) with gastric acid reducing agents (local antacids, H2-receptor antagonists [H2RAs], and PPIs). The IBRANCE USPI was revised to reflect the new dose administration recommendations and update the relevant pharmacokinetic (PK) data. Bioequivalence data was submitted to support the application.

No changes were made to the efficacy or safety sections of the USPI. The application references the original safety and efficacy data from NDA 207103. The tablet formulation has been only tested as single-dose administrations in healthy volunteers in 4 studies. There were no deaths, SAEs, or new unexpected TEAEs fom these studies.

Final Recommendation: Clinical has reviewed and agrees with the labeling edits (b) (4)

(b) (4)

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