CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July – August

BRAND NAME
Ibrance®

GENERIC NAME
Palbociclib

MANUFACTURER
Pfizer Inc.

DATE OF APPROVAL
March 31, 2017

PRODUCT LAUNCH DATE
Already Launched

REVIEW TYPE

☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☒ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
Previous Indication:
Ibrance is indicated for:

- Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
  - Letrozole as initial endocrine-based therapy in postmenopausal women, or
  - Fulvestrant in women with disease progression following endocrine therapy.

CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July – August

Revised Indication:
"Letrozole as initial endocrine-based therapy in postmenopausal women" was revised to, "An aromatase inhibitor as initial endocrine-based therapy in postmenopausal women."

OFF-LABEL USES

- In combination with letrozole as initial endocrine-based therapy in men who will receive concomitant treatment for suppression of testicular steroidogenesis;
- In combination with fulvestrant in men with disease progression following endocrine therapy.

CLINICAL EFFICACY[1,2]

The conversion of the accelerated approval to full approval of Ibrance plus letrozole as first-line therapy for postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer was supported by the PALOMA-2 trial, an international, phase 3, randomized, double-blind, parallel-group, multicenter study. Additionally, the full approval broadened the use of Ibrance for this breast cancer subtype for use in combination with any aromatase inhibitor. Previously, Ibrance was approved for this indication for use only with letrozole.

Randomization was stratified by disease site (visceral versus non-visceral), disease-free interval (de novo metastatic versus ≤12 months from the end of adjuvant treatment to disease recurrence versus >12 months from the end of adjuvant treatment to disease recurrence), and nature of prior (neo) adjuvant anticancer therapies (prior hormonal therapies versus no prior hormonal therapy). A total of 666 postmenopausal women with ER-positive, HER2-negative breast cancer, who had not had prior treatment for advanced disease, were randomized 2:1 to Ibrance plus letrozole or placebo plus letrozole. Ibrance was given orally at a dose of 125 mg daily for 21 consecutive days followed by 7 days off treatment; all the patients received 2.5 mg of letrozole orally per day (continuous treatment). Patients received study treatment until objective disease progression, symptomatic deterioration, unacceptable toxicity, death, or withdrawal of consent, whichever occurred first.

The primary endpoint was investigator-assessed progression-free survival (PFS), defined as the time from randomization to radiologically confirmed disease progression, according to RECIST, version 1.1, or death during the study. The median PFS was 24.8 months (95% confidence interval [CI], 22.1 to not estimable) in the palbociclib–letrozole group, as compared with 14.5 months (95% CI, 12.9 to 17.1) in the placebo–letrozole group (hazard ratio for disease progression or death, 0.58; 95% CI, 0.46 to 0.72; P<0.001).

Secondary end points included overall survival, objective response (defined as a confirmed complete response or partial response), the duration of response, the clinical benefit response (defined as a confirmed complete response, a partial response, or stable disease for ≥24 weeks), patient-reported outcomes, pharmacokinetic effects, safety, and tissue biomarker assessments.

CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July – August

The main reason for permanent discontinuation of the study treatment was disease progression, which occurred in 172 patients (38.7%) in the palbociclib–letrozole group and in 125 patients (56.3%) in the placebo–letrozole group. Overall permanent discontinuation of study treatment as a result of adverse events occurred in 43 patients (9.7%) in the palbociclib–letrozole group (palbociclib or both palbociclib and letrozole) and in 13 patients (5.9%) in the placebo–letrozole group (placebo or both placebo and letrozole). Permanent discontinuation of palbociclib or matching placebo as a result of adverse events occurred in 33 patients (7.4%) in the palbociclib–letrozole group and in 10 patients (4.5%) in the placebo–letrozole group.

CONTRAINDICATIONS
None

BLACK BOX WARNINGS
None

DRUG INTERACTIONS
- CYP3A Inhibitors: Avoid concurrent use of Ibrance with strong CYP3A inhibitors. If the strong inhibitor cannot be avoided, reduce the Ibrance dose.
- CYP3A Inducers: Avoid concurrent use of Ibrance with strong CYP3A inducers.
- CYP3A Substrates: The dose of sensitive CYP3A4 substrates with narrow therapeutic indices may need to be reduced when given concurrently with Ibrance.

ADVERSE REACTIONS
Most common adverse reactions (incidence ≥10%) were neutropenia, infections, leukopenia, fatigue, nausea, stomatitis, anemia, alopecia, diarrhea, thrombocytopenia, rash, vomiting, decreased appetite, asthenia, and pyrexia.

DOSAGE AND ADMINISTRATION
Ibrance capsules are taken orally with food in combination with an aromatase inhibitor or fulvestrant.

The recommended dose of Ibrance is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days.

Administer the recommended dose of an aromatase inhibitor when given with Ibrance. Please refer to the Full Prescribing Information for the aromatase inhibitor being used.

When given with Ibrance, the recommended dose of fulvestrant is 500 mg administered on Days 1, 15, 29, and once monthly thereafter.

PRODUCT AVAILABILITY
Capsules: 75 mg, 100 mg, 125 mg

CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
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THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Kisqali® (ribociclib)	600 mg orally once daily for 21 consecutive days followed by 7 days off treatment (resulting in a complete cycle of 28 days), in combination with an aromatase inhibitor taken once daily throughout the 28-day cycle	Maximum dose: 600 mg/day

Boldface indicates generic availability

Utilization Management Recommendation
• There is not significant potential for inappropriate use. • Requiring utilization management to prevent off-label usage would be clinically appropriate.   o Recommended utilization management tool: prior authorization.
Product Comparison
• Not applicable

REFERENCES

[1] Ibrance Prescribing Information. New York, NY; Pfizer Labs; March 2017. Available at: www.ibrance.com/. Accessed April 19, 2017.
[2] Palbociclib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed April 19, 2017.