Clinical Policy: Palbociclib (Ibrance)

Reference Number: PA.CP.PHAR.125
Effective Date: 01/18
Last Review Date: 07/18 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for Palbociclib (Ibrance®).

FDA Approved Indication(s)
Ibrance is indicated for the treatment of 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.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Ibrance is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Disease meets all of the following characteristics (a, b and c):
   a. Hormone receptor (HR)-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. Human epidermal growth factor receptor 2 (HER2)-negative;
   c. Disease is recurrent, advanced or metastatic;
4. Ibrance will be used for one of following indications (a or b):
   a. FDA approved indication (i or ii):
      i. In combination with an aromatase inhibitor (e.g., letrozole, anastrozole, or exemestane) as initial endocrine-based therapy in postmenopausal women;
      ii. In combination with fulvestrant in women with disease progression following endocrine therapy;
   b. Off-label NCCN recommended use (i or ii):
      i. In combination with an aromatase inhibitor (e.g., letrozole, anastrozole, or exemestane) as initial endocrine-based therapy in men who will receive concomitant treatment for suppression of testicular steroidogenesis;
      ii. In combination with fulvestrant in men with disease progression following endocrine therapy.
5. Request meets one of the following (a or b):
   a. Dose does not exceed 125 mg/day (1 tablet/day for 21 days);

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Soft Tissue Sarcoma (off-label) (must meet all):
1. Diagnosis of retroperitoneal well-differentiated/dedifferentiated liposarcoma;
2. Will be used as a single agent;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

II. C. Other diagnoses/indications: Refer to PA. CP.PMN.53 **Continued Approval**

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Required dose reduction to < 75 mg/day.
3. Request meets one of the following (a or b):
   a. Dose does not exceed 125 mg/day (1 tablet/day for 21 days);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Soft Tissue Sarcoma (off-label) (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):

a. New dose does not exceed 125 mg/day (1 tablet/day for 21 days).
b. New does is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

C. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Palbociclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6. Cyclin D1 and CDK4/6 are downstream of signaling pathways which lead to cellular proliferation. *In vitro*, palbociclib reduced cellular proliferation of estrogen receptor (ER)-positive breast cancer cell lines by blocking progression of the cell from G1 into S phase of the cell cycle. Treatment of breast cancer cell lines with the combination of palbociclib and antiestrogens leads to decreased retinoblastoma protein (Rb) phosphorylation resulting in reduced E2F expression and signaling, and increased growth arrest compared to treatment with each drug alone. *In vitro* treatment of ER-positive breast cancer cell lines with the combination of palbociclib and antiestrogens leads to increased cell senescence, which was sustained for up to 6 days following drug removal. *In vivo* studies using a patient-derived ER-positive breast cancer xenograft model demonstrated that the combination of palbociclib and letrozole increased the inhibition of Rb phosphorylation, downstream signaling and tumor growth compared to each drug alone.

Formulations:

Ibrance capsules for oral administration: 125 mg, 100 mg, and 75 mg

Appendices

Appendix A: Abbreviation Key

CDK: cyclin-dependent kinase
ER/PR: estrogen receptor/progesterone receptor
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
PFS: progression-free survival
Rb: retinoblastoma protein
WD-DDLS: well-differentiated/dedifferentiated liposarcoma

Reviews, Revisions, and Approvals	Date	Approval Date
Added prescriber specialty requirement. Added max dosing criteria Added criteria for off-label use for soft tissue sarcoma. References reviewed and updated.	02/18	

III. References

1. Ibrance Prescribing Information. New York, NY; Pfizer Labs; March 2017. Available at: www.ibrance.com/. Accessed November 14, 2017.
2. Palbociclib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed November 14, 2017.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.

4. National Comprehensive Cancer Network. Breast Cancer Version 3.2017. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Accessed November 14, 2016.
5. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 1.2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed November 14, 2016.
6. Dickson MA, Tap WD, Keohan ML, et al. Phase II trial of the CDK4 inhibitor PD0332991 in patients with advanced CDK4-amplified well differentiated or dedifferentiated liposarcoma. J Clin Oncol 2013;31(16):2024-2028.