

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Ibrance® (palbociclib capsules – Pfizer Labs)

**TAC APPROVAL DATE:** 04/03/2019

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### OVERVIEW

Ibrance, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated for the treatment of hormone receptor positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:

1. An aromatase inhibitor (AI) as initial endocrine-based therapy in postmenopausal women; or ;<sup>1-3</sup>
2. Faslodex® (fulvestrant intramuscular injection) for the treatment of women with disease progression following endocrine therapy.<sup>1,4-5</sup>

### Disease Overview

Based on molecular profiling, breast cancer is classified as HR+ (estrogen receptor positive [ER+] and/or progesterone receptor positive [PgR+]), HER2+, or triple negative (ER-negative, PgR-negative, and HER2-negative).<sup>6-7</sup> Most breast cancers in women (71%) are HR+, HER2-negative; these cancers tend to be slow-growing and less aggressive than other subtypes.<sup>7</sup> HR+, HER2-negative tumors are associated with the most favorable prognosis compared with other subtypes, particularly in the short-term, in part because expression of hormone receptors is predictive of a favorable response to hormonal therapy. In men, about 85% of breast cancers are ER+ and 70% are PgR+.<sup>8</sup> About 12% of breast cancers are HR+ and HER2+, and tend to be higher grade and more aggressive than HR+ cancers.<sup>7</sup> About 5% of breast cancers are HER2+ and do not express hormone receptors. These cancers tend to be more aggressive than other breast cancers and have a poorer short-term prognosis compared with ER+ breast cancers. About 12% of breast cancers in women are triple negative and have a poorer short-term prognosis than other subtypes.

### Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 1.2019 – March 14, 2019) recommend CDK 4/6 inhibitors in combination with an AI as a treatment option for recurrent or Stage IV HR+, HER2-negative disease in postmenopausal women (category 1, preferred regimen).<sup>9</sup> It is also recommended in pre/perimenopausal women treated with ovarian suppression/ablation. Also, CDK 4/6 inhibitor plus Faslodex is recommended for HR+, HER2-negative recurrent or metastatic breast cancer as first-line therapy (category 1); this is noted in a footnote. Ibrance is FDA-approved for combination use with Faslodex upon progression on or after prior adjuvant or metastatic endocrine therapy in postmenopausal women or for premenopausal women receiving ovarian suppression with a LHRH. For either use, the guidelines recommend that men with breast cancer be treated similarly to postmenopausal women, except that the use of an AI is ineffective without concomitant suppression of testicular steroidogenesis. If there is disease progression while on CDK 4/6 inhibitor therapy, there are no data to support an additional line of therapy with another CDK 4/6-containing regimen. The NCCN compendium notes that Ibrance + AI and Ibrance + Faslodex are preferred regimens in HR+, HER2-negative disease in postmenopausal women (no visceral crisis) or premenopausal women treated with ovarian ablation/suppression.<sup>14</sup> There is no reference to first-line or subsequent therapy in the recommendations.

The NCCN guidelines on soft tissue sarcoma (version 2.2019 – February 4, 2019) recommend Ibrance as single-agent therapy for the treatment of WD-DDLS for retroperitoneal sarcomas (category 2A).<sup>8</sup>

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## **POLICY STATEMENT**

Prior authorization is recommended for prescription benefit coverage of Ibrance. All approvals are provided for 3 years in duration unless otherwise noted below. In the clinical criteria, as appropriate, an asterisk (\*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual's gender identity or gender expression; men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Ibrance is recommended in those who meet the following criteria:

### **FDA-Approved Indications**

- 1. Breast Cancer in Postmenopausal Women\***. Approve for 3 years if the patient meets the following criteria (A, B, C, and D):
  - A)** Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}] disease; AND
  - B)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - C)** The patient meets ONE of the following criteria (i or ii):
    - i.** Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
    - ii.** Ibrance will be used in combination with Faslodex (fulvestrant intramuscular injection); AND
  - D)** The patient has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

\* Refer to the Policy Statement.

- 2. Breast Cancer in Pre/Perimenopausal Women\***. Approve for 3 years if the patient meets the following criteria (A, B, C, D, and E):
  - A)** Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}] disease; AND
  - B)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - C)** The patient is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin)), or has had surgical bilateral oophorectomy or ovarian irradiation; AND
  - D)** Patient meets ONE of the following conditions (i or ii):
    - i.** Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
    - ii.** Ibrance will be used in combination with Faslodex (fulvestrant intramuscular injection); AND
  - E)** Patient has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

\* Refer to the Policy Statement.

### **Other Uses With Supportive Evidence**

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- 3. Breast Cancer in Men\***. Approve for 3 years if the patient meets the following criteria (A, B, C, and D):
- A)** Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}] disease; AND
  - B)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - C)** Patient meets ONE of the following criteria (i or ii):
    - i.** Patient meets BOTH of the following criteria (a and b):
      - a)** Patient is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex [goserelin]); AND
      - b)** Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
    - ii.** Ibrance will be used in combination with Faslodex (fulvestrant intramuscular injection); AND
  - D)** Patient has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

\* Refer to the Policy Statement.

- 4. Liposarcoma.** Approve for 3 years if the patient has well-differentiated/dedifferentiated liposarcoma (WD-DDLS).

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ibrance has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below.

- 1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### REFERENCES

1. Ibrance® capsules [prescribing information]. New York, NY: Pfizer Labs; February 2018.
  2. Finn RS, Martin M, Rugo HS, et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med.* 2016;375(20):1925-1936.
  3. Finn RS, Crown JP, Lang I, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomized phase 2 study. *Lancet Oncol.* 2015;16:25-35.
  4. Turner NC, Ro J, Andre F, et al. Palbociclib in hormone-receptor-positive advanced breast cancer. *N Engl J Med.* 2015;373:209-219.
  5. Cristofanilli M, Turner NC, Bondarenko I, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. *Lancet Oncol.* 2016;17(4):425-439.
  6. National Cancer Institute: PDQ® Breast cancer treatment. National Cancer Institute. Date last modified February 4, 2018 Available at: <https://www.cancer.gov/types/breast/hp/breast-treatment-pdq>. Accessed on March 2, 2018.
  7. American Cancer Society. *Breast Cancer Facts & Figures 2017-2018*. Atlanta: American Cancer Society, Inc. 2017. Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf>. Accessed on March 2, 2018.
  8. National Cancer Institute: PDQ® Male breast cancer treatment. Bethesda, MD: National Cancer Institute. Date last modified February 8, 2018. <https://www.cancer.gov/types/breast/hp/male-breast-treatment-pdq>. Accessed on March 2, 2018.
  9. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (Version 1.2019 – March 14, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on April 1, 2019.
  10. Rugo HS, Rumble RB, Macrae E, et al. Endocrine therapy for hormone receptor-positive metastatic breast cancer: American Society of Clinical Oncology guideline. *J Clin Oncol.* 2016;34(25):3069-3103.
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11. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 2.2019 – February 4, 2019) © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on April 4, 2019.
12. The NCCN Drugs & Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on April 1, 2019. Search terms: palbociclib.

#### **OTHER REFERENCES UTILIZED**

- Harbeck N, Iyer S, Turner N, et al. Quality of life with palbociclib plus fulvestrant in previously treated hormone receptor-positive, HER2-negative metastatic breast cancer: patient-reported outcomes from the PALOMA-3 trial. *Ann Oncol.* 2016;27(6):1047-1054.
  - Bell T, Crown JP, Lang I, et al. Impact of palbociclib plus letrozole on pain severity and pain interference with daily activities in patients with estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer as first-line treatment. *Curr Med Res Opin.* 2016;32(5):959-965.
  - Verma S, Bartlett CH, Schnell P, et al. Palbociclib in combination with fulvestrant in women with hormone receptor-positive/HER2-negative advanced metastatic breast cancer: detailed safety analysis from a multicenter, randomized, placebo-controlled, phase III study (PALOMA-3). *Oncologist.* 2016;21:1165-1175.
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**HISTORY**

<b>Type of Revision</b>	<b>Summary of Changes*</b>	<b>TAC Approval Date</b>
Annual revision	Breast Cancer criteria were revised to change from estrogen receptor positive to hormone receptor positive. Criteria for Breast Cancer in Women were revised to move the criteria previously in Other Uses with Supportive Evidence to FDA-Approved Indications. Criteria for Breast Cancer in Men were moved to Other Uses With Supportive Evidence. Criteria were added for Liposarcoma.	03/02/2016
Selected revision	In the Policy Statement, added legal language to define woman and man in the Breast Cancer indications. This is noted with "*" next to "woman", "women", and "men" in the indications/criteria. A note was added below the approval criteria to refer to the Policy Statement.	10/05/2016
Annual revision	Added definition to hormone receptor positive (i.e., estrogen receptor positive or progesterone receptor positive). In criteria for postmenopausal, premenopausal, and perimenopausal patients using Ibrance in combination with Faslodex, added that the patient has not previously taken Kisqali in combination with letrozole, anastrozole, or exemestane.	03/29/2017
DEU revision 08/10/2017	Updated indication for endocrine-based therapy due to revised prescribing information, and updated guidelines summary.	--
Annual revision	Breast Cancer in Women: <ul style="list-style-type: none"> <li>• The word "initial" was added to first-line endocrine therapy.</li> <li>• LHRH agonist was replaced with GnRH agonist.</li> <li>• Prior endocrine therapy that was previously a list of examples, was revised to be a list of at least one of the listed endocrine therapies. Afinitor plus Faslodex or tamoxifen and exemestane plus Afinitor were added to the list and "high-dose" was removed from ethinyl estradiol. Ibrance, Kisqali and Verzenio are endocrine therapies not included in this list.</li> <li>• Added a criterion that applies to all of the indications in women that the patient has not had disease progression while on Ibrance, Kisqali, or Verzenio.</li> </ul> Breast Cancer in Men: <ul style="list-style-type: none"> <li>• LHRH agonist was replaced with GnRH agonist.</li> <li>• The word "initial" was added to first-line endocrine therapy. Tamoxifen was added to the list of first-line (initial) endocrine therapies.</li> <li>• Added a criterion that the patient has not had disease progression while on Ibrance, Kisqali, or Verzenio.</li> </ul>	03/07/2018
Selected revision	Separated out criteria for Postmenopausal and Pre/Perimenopausal women for clarity. Under Breast Cancer in Men criteria, deleted tamoxifen from list of endocrine therapy agents that can be used as combination therapy with Ibrance. Added Ibrance plus Faslodex combination therapy as option for men if progressed on at least one endocrine therapy.	09/12/2018
Annual revision	Deleted criteria in all approval conditions which require patient to try a prior endocrine therapy before approving for Ibrance + Faslodex. Likewise, deleted criteria that required Ibrance + aromatase inhibitors use (e.g., letrozole) only as initial therapy. NCCN guidelines support first-line or subsequent therapy use.	04/03/2019

TAC – Therapeutic Assessment Committee; LHRH – Luteinizing hormone-releasing hormone; DEU – Drug Evaluation Unit; GnRH – gonadotropin-releasing hormone; FDA – Food and Drug Administration; \* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.