# palbociclib (Ibrance®)

EOCCO POLICY

## Policy Type: PA/SP  Pharmacy Coverage Policy: EOCCO050

### Description

Palbociclib (Ibrance) is an orally administered CDK4/6 kinase inhibitor that reduces cellular proliferation of estrogen receptor-positive breast cancer.

### Length of Authorization

- Initial: Six months
- Renewal: 12 months

### Quantity limits

| Product Name | Dosage Form | Indication | Quantity Limit |
|---|---|---|---|
| palbociclib (Ibrance) | 75 mg capsules/tablets* | Breast cancer, advanced or metastatic, Her2-negative, hormone receptor-positive, in combination with fulvestrant following endocrine therapy<br><br>Breast cancer, advanced or metastatic, HER2-negative, hormone receptor-positive in men or postmenopausal women as initiation therapy in combination with an aromatase inhibitor | 21 capsules or tablets/28 days |
| | 100 mg capsules/tablets* | | 21 capsules or tablets/28 days |
| | 125 mg capsules/tablets* | | 21 capsules or tablets/28 days |

*Please note: Beginning April 1st, 2020 the capsule formulation will no longer be available as the tablet formulation will be taking its place.

### Initial Evaluation

I. Palbociclib (Ibrance) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. The medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. The medication will not be used in combination with other CDK4/6 inhibitors (e.g., ribociclib [Kisqali], abemaciclib [Verzenio]); **AND**
   D. The member has not previously progressed on or after treatment with another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio]); **AND**
   E. A diagnosis of **breast cancer** when the following are met:

1. The member has a diagnosis of hormone receptor-positive (HR+) and HER2-negative (HER2-) disease; **AND**
2. Disease is advanced (stage III) or metastatic (stage IV); **AND**
3. The medication is being prescribed for one of the following settings;
    i. Initial endocrine based therapy for a man or postmenopausal woman (natural or pharmacotherapy-induced); **AND**
        a. Palbociclib (Ibrance) will be administered in combination with an aromatase inhibitor (e.g., letrozole [Femara], anastrozole [Armidex], exemestane [Aromasin]); **AND**
        b. If the member is male, a GnRH analog (e.g., goserelin [Zoladex], leuprolide [Lupron]); will be administered along with an aromatase inhibitor concurrently; **OR**
    ii. Following progression after endocrine therapy in a man or woman (regardless of menopausal status); **AND**
        a. Palbociclib (Ibrance) will be administered in combination with fulvestrant (Faslodex)

II. Palbociclib (Ibrance) is considered investigational when used for all other conditions, including but not limited to:
    A. In combination with, or following progression on or after, another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio])
    B. Pancreatic neuroendocrine tumors (pNET)
    C. Ovarian cancer
    D. Central nervous system cancers (e.g., glioma, astrocytoma, head and neck, etc.)
    E. Colorectal cancer
    F. Urothelial cancer
    G. Leukemias and lymphomas
    H. Non-small-cell lung cancer
    I. Liposarcoma

## Renewal Evaluation

I. Member is 18 years of age or older; **AND**
II. The medication is prescribed by, or in consultation with, an oncologist; **AND**
III. Palbociclib (Ibrance) is not used in combination with other CDK4/6 inhibitors (e.g., ribociclib [Kisqali], abemaciclib [Verzenio]); **AND**
IV. Documentation is provided indicating disease response with palbociclib (Ibrance) as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
V. Absence of unacceptable toxicity from the medication

**Supporting Evidence**

I. Clinical trials for the approval of palbociclib (Ibrance) evaluated adults with breast cancer of the following characteristics: HR+, HER2-, advanced (stage III) or metastatic (stage IV). Two settings were evaluated; Initial endocrine based therapy in combination with an aromatase inhibitor and in combination with fulvestrant after progression on initial endocrine therapy. Initial FDA-approvals were indicated for women only.

II. Palbociclib (Ibrance) was further FDA-approved for breast cancer in men in 2019. The approval was based on data from electronic health records and post marketing reports of real-world use in male patients. The sources of data included the following: IQVIA Insurance database, Flatiron Health Breast Cancer database, Pfizer global safety database. Guidelines recommend that men on an aromatase inhibitor and palbociclib (Ibrance) be administered a GnRH analog concurrently. Available evidence suggests that those treated with aromatase inhibitor monotherapy has been associated with inferior outcomes; likely due to inadequate estradiol suppression.

III. There is lack of scientific evidence from randomized controlled trials supporting the safety and/or efficacy for increased dosing or frequency. The dosing recommendation is one capsule once daily, with various doses for tolerability and dose adjustments for safety considerations, in 21 out of 28-day cycles. Increasing the dose beyond 125 mg per day, or dosing more than 21 out of every 28 days has not been evaluated.

IV. Postmenopausal status may be reached in women via ovarian suppression through GnRH therapy (pharmacotherapy-induced) for several weeks prior to palbociclib (Ibrance) administration, bilateral oophorectomy (surgically-induced), ovarian irradiation, or natural menopause. Either is considered acceptable status for aforementioned criteria.

V. There is lack of scientific evaluation for safety and efficacy of palbociclib (Ibrance) used concurrently, or following progression on or after, with another CDK 4/6 inhibitor. As of April 2019, NCCN guidelines stated “If there is disease progression while on a CDK4/6 inhibitor), there is no data to support an additional line of therapy with another CDK4/6 inhibitor-containing regimen. Of note, those that are unable to tolerate other CDK4/6 inhibitors and are switching to palbociclib (Ibrance) prior to progression would be acceptable candidates for therapy.

VI. Known serious toxicities of palbociclib (Ibrance) include, but are not limited to, the following: neutropenia, embryo-fetal toxicity, thromboembolism, and hepatotoxicity. Common adverse events include, but are not limited to, the following: diarrhea, nausea, fatigue, abdominal pain, anemia, leukopenia, anorexia, vomiting, headache, dysgeusia, alopecia, thrombocytopenia, stomatitis, constipation, increase in liver enzymes, cough, pruritus, dizziness, increase creatinine levels, arthralgia, peripheral edema, respiratory infections, rash.

## Investigational or Not Medically Necessary Uses

I. Palbociclib (Ibrance) has not been FDA-approved, or sufficiently studied for safety and efficacy, for the conditions or settings listed below:
   A. In combination with, or following progression on, another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio])
   B. Pancreatic neuroendocrine tumors (pNET)
   C. Ovarian cancer
   D. Central nervous system cancers (e.g., glioma, astrocytoma, head and neck, etc.)
   E. Colorectal cancer
   F. Urothelial cancer
   G. Leukemias and lymphomas
   H. Non-small-cell lung cancer
   I. Liposarcoma. Palbociclib (Ibrance) was evaluated in a phase II, nonrandomized, open-label, without comparator clinical trial that assessed the surrogate endpoint of progression-free survival. The quality of this evidence is considered very low, and clinical value of this medication in liposarcoma, specifically dedifferentiated liposarcomas (WD/DDLS), is unknown at this time.

## References

1. Palbociclib [Prescribing Information]. New York, NY: Pfizer Inc. April, 2019.
2. UpToDate. Ma C.X., Sparano J.A.. Treatment approach to metastatic hormone receptor-positive, HER2-negative breast cancer: endocrine therapy and targeted agents. March, 2019. Available at: https://www.uptodate.com/contents/treatment-approach-to-metastatic-hormone-receptor-positive-her2-negative-breast-cancer-endocrine-therapy-and-targeted-agents?search=metastatic%20hormone%20receptor%20positive%20breast%20cancer&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed May, 2019.
3. UpToDate. Gradishar W.J., Ruddy K.J. Breast cancer in men. February, 2019. Available at: https://www.uptodate.com/contents/breast-cancer-in-men?search=male breast cancer&source=search_result&selectedTitle=1~39&usage_type=default&display_rank=1. Accessed May, 2019.
4. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer V1.2019. March 14, 2019. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
5. Iwata H, Im SA, Masuda N, et al. PALOMA-3: Phase III Trial of Fulvestrant With or Without Palbociclib in Premenopausal and Postmenopausal Women With Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer That Progressed on Prior Endocrine Therapy-Safety and Efficacy in Asian Patients. *J Glob Oncol*. 2017;3(4):289-303.
6. Kim ES, Scott LJ. Palbociclib: A Review in HR-Positive, HER2-Negative, Advanced or Metastatic Breast Cancer. *Target Oncol*. 2017;12(3):373-383.
7. Finn R.S., Martin M., Rugo H.S., et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med*. 2016;375(20): 1925-1936.
8. Pfizer Press Release. U.S. FDA Approves Ibrance (palbociclib) for the Treatment of Men with HR+, HER2-, Metastatic Breast Cancer. April 4, 2019. Available at: https://www.pfizer.com/news/press-release/press-release-detail/u_s_fda_approves_ibrance_palbociclib_for_the_treatment_of_men_with_hr_her2_metastatic_breast_cancer. Access May, 2019.

## Policy Implementation/Update:

| | |
|---|---|
| Date Created | February 2015 |
| Date Effective | March, 2016 |
| Last Updated | March 2020 |
| Last Reviewed | 02/2016, 05/2019 |

| Action and Summary of Changes | Date |
|---|---|
| Updated QL box to inform about transition to tablets | 03/2020 |
| Criteria update with new indication and FDA-approval of breast cancer in men. Criteria updated to avoid combination use or use after progression on another CDK4/6 inhibitor. Age criteria added. Approval durations increased. | 05/2019 |
| Criteria updated based on NCCN guidelines and PALOMA3 trial to allow treatment after disease progression on prior endocrine therapy. | 01/2016 |