Clinical Policy Title:	palbociclib
Policy Number:	RxA.163
Drug(s) Applied:	Ibrance®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of Business

Background

Palbociclib (Ibrance®) is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6). It 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 in men; or
- Fulvestrant in patients with disease progression following endocrine therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
palbociclib (Ibrance®)	Breast cancer	125 mg PO once daily for 21 consecutive days followed by 7 days off treatment	125 mg/day

Dosage Forms

- Capsules: 75 mg, 100 mg, 125 mg
- Tablet: 75 mg, 100 mg, 125 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Age ≥ 18 years;
4. Disease has all of the following characteristics (a, b, and c):
   a. HR-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. HER2-negative;
   c. Advanced (locally recurrent) or metastatic;

5. Ibrance® is prescribed in combination with one of the following (a or b):
   a. An aromatase inhibitor (e.g., letrozole, anastrozole, exemestane), and:
      i. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
   b. Fulvestrant after disease progression on an endocrine therapy;
6. Disease has not progressed on prior CDK4/6 inhibitor therapy;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 125 mg (1 tablet or 1 capsule) per day on Days 1 to 21 of a 28-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Soft Tissue Sarcoma (off-label) (must meet all)**:**

1. Diagnosis of retroperitoneal well-differentiated/dedifferentiated liposarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, metastatic, or progressive;
5. Disease has not progressed on prior CDK4/6 inhibitor therapy;
6. Ibrance® will be used as a single agent;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*Prescriber must submit supporting evidence*). *

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Ibrance® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If breast cancer, dose is ≥ 75 mg per day;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 125 mg (1 tablet or 1 capsule) per day on Days 1 to 21 of a 28-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

CDK: cyclin-dependent kinase
ER: estrogen receptor
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
NCCN: National Comprehensive Cancer Network
PR: progesterone receptor

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Endocrine Therapy		
anastrozole (Arimidex®)	1 mg PO once daily	1 mg/day
exemestane (Aromasin®)	25 mg PO once daily	25 mg/day
Fareston® (toremifene)	60 mg PO once daily	60 mg/day
Faslodex® (fulvestrant)	500 mg IM into the buttocks slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter	500 mg/day
letrozole (Femara®)	2.5 mg PO once daily	2.5 mg/day
tamoxifen (Soltamox®)	20 to 40 mg PO once daily	40 mg/day
megestrol acetate	40 mg PO four times daily	160 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic .

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- For disease progression while on a CDK4/6 inhibitor, there is no data to support retreatment with another CDK4/6 inhibitor-containing regimen.
- Fluoxymesterone and ethinyl estradiol for breast cancer are other endocrine therapies, but they are no longer commercially available.

References

1. Ibrance® Prescribing Information. New York, NY; Pfizer Labs; September 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/207103Orig1s012lbl.pdf. Accessed March 31, 2021.
2. Ibrance® Prescribing Information. New York, NY; Pfizer Labs; November 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212436lbl.pdf. Accessed March 31, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 31, 2021.
4. National Comprehensive Cancer Network. Breast Cancer Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 31, 2021.
5. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 1.2021. Available at: https://www.nccn.org/patients/guidelines/content/PDF/sarcoma-patient.pdf . Accessed March 31, 2021.
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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was updated. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial and Continued Therapy Approval criteria: Commercial approval duration was updated. 6. Added “Disease has not progressed on prior CDK4/6 inhibitor therapy” to initial approval criteria for both indications; 7. APPENDIX B was updated: tamoxifen brand Nolvadex was removed as it was discontinued. 8. References were updated.	08/03/2020	09/14/2020
Policy was reviewed:	03/31/2021	06/10/2021

1. Dosing frequency abbreviations were expanded. 2. Clinical policy section standard verbiage was updated to include “The provision of prescriber samples…”. 3. Appendix B for therapeutic alternatives standard verbiage updated. 4. References were updated.		