

Clinical Policy: Palbociclib (Ibrance)

Reference Number: CP.PHAR.125

Effective Date: 10.01.15

Last Review Date: 11.22

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Palbociclib (Ibrance[®]) is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK 4/6).

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 in men; or
- Fulvestrant in patients with disease progression following endocrine therapy.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] 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. Age \geq 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, 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) as part of initial endocrine-based therapy, and:
 - i. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
 - b. Fulvestrant;
6. If member is a premenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);

7. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Verzenio[®], Kisqali[®]);
8. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
9. For brand Ibrance requests, member must use generic palbociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
10. Request meets one of the following (a or b):*
 - a. Dose does not exceed (i and ii):
 - i. 125 mg per day on Days 1 to 21 of a 28-day cycle;
 - ii. 1 capsule or tablet 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:

Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

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 \geq 18 years;
4. Disease is unresectable;
5. Prescribed as a single agent;
6. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
7. For brand Ibrance requests, member must use generic palbociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. 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:

Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
4. If breast cancer, dose is ≥ 75 mg per day;
5. For brand Ibrance requests, member must use generic palbociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed (i and ii):
 - i. 125 mg per day on Days 1 to 21 of a 28-day cycle;
 - ii. 1 capsule or tablet 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:

Medicaid/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Use as adjuvant therapy in early-stage (stage 0-III) breast cancer.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDK: cyclin-dependent kinase	iDFS: invasive disease-free survival
ER: estrogen receptor	LHRH: luteinizing hormone-releasing hormone
ET: endocrine therapy	NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration	PR: progesterone receptor
HER2: human epidermal growth factor receptor 2	
HR: hormone receptor	

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

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.
- Although the FDA labeled indication limits combination use with fulvestrant to second line for breast cancer, the NCCN recommends this combination as both first and second line (category 1).
- Beginning in April 2020, Pfizer announced they would be switching Ibrance from capsules to tablets. The tablets allow increased flexibility with administration, dose tracking (weekly blister packs), and address dietary concerns (do not contain lactose or gelatin). These formulations are bioequivalent.
- In the Phase 3 PALbociclib CoLlaborative Adjuvant Study (PALLAS) open-label trial, 5,760 patients with stage II-III HR+/HER2-negative early breast cancer were randomized to receive either 2 years of Ibrance with adjuvant endocrine therapy (ET), or ET alone. The primary objective was to compare invasive disease-free survival (iDFS) between arms. At the second interim data analysis, after a median follow-up of 23.7 months (351 events), iDFS was similar between the two arms, with 3-year iDFS of 88.2% for Ibrance plus ET, and 88.5% for ET alone (HR 0.93, 95% CI 0.76-1.15), crossing a pre-specified futility boundary.
- Ovarian ablation may be accomplished by surgical oophorectomy or by ovarian irradiation. Ovarian suppression utilizes luteinizing hormone-releasing hormone (LHRH) agonists that result in suppression of luteinizing hormone and release of follicle-stimulating hormone from pituitary and reduction in ovarian estrogen production. LHRH agonists include goserelin and leuprolide.

V. Dosage and Administration

Indication	Dosing Regimen*	Maximum Dose
Breast cancer	125 mg PO QD for 21 consecutive days followed by 7 days off treatment	125 mg/day

*If a dose reduction to < 75 mg/day is required, therapy should be discontinued.

VI. Product Availability

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

VII. References

1. Ibrance Capsules Prescribing Information. New York, NY; Pfizer Labs; September 2019. Available at: www.ibrance.com/. Accessed July 29, 2022.
2. Ibrance Tablets Prescribing Information. New York, NY; Pfizer Labs; November 2019. Available at: www.ibrance.com/. Accessed July 29, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 29, 2022.
4. National Comprehensive Cancer Network. Breast Cancer Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 29, 2022.
5. 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.
6. Mayer EL, Gnani MI, DeMichele A, et al. PALLAS: A randomized phase III trial of adjuvant palbociclib with endocrine therapy versus endocrine therapy alone for HR+/HER2-early breast cancer. Presented at: European Society of Medical Oncology (ESMO) Virtual Congress 2020; September 19-21, 2020. LBA12.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; added commercial line of business; summarized NCCN and FDA-approved uses for improved clarity; added age; added specialist involvement in care for soft tissue sarcomas; references reviewed and updated.	07.05.18	11.18
No significant changes: added updated FDA indication for use in men; no change to criteria required.	04.10.19	
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.09.19	11.19
Added HIM line of business; added that member has not previously failed another CDK 4/6 inhibitor therapy for breast cancer.	02.18.20	05.20
Added tablet formulation.	08.18.20	
4Q 2020 annual review: for breast cancer, modified to allow first-line use with fulvestrant per NCCN category 1 recommendation; for retroperitoneal liposarcoma, modified to allow only unresectable disease (removed metastatic and progressive options)	10.01.20	11.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
per NCCN category 2A recommendation; added coverage exclusion for use as adjuvant therapy for early stage (stage II-III) breast cancer, based on PALLAS trial results; references reviewed and updated.		
Breast cancer: clarified that combination use with an aromatase inhibitor should be for initial endocrine based therapy per FDA/NCCN and added that premenopausal women should be treated with ovarian ablation/suppression per NCCN; all indications: added requirement for no concurrent use with another CDK 4/6 inhibitor therapy.	06.24.21	08.21
4Q 2021 annual review: no significant changes; added generic redirection language; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.11.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
4Q 2022 annual review: no significant changes; revised generic redirection language to “must use” per updated template; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.29.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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