Clinical Policy: Palbociclib (Ibrance)

Reference Number: CP.PHAR.125
Effective Date: 10.01.15
Last Review Date: 11.25
Line of Business: Commercial, 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).

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** **California Exchange Plans** should not be approved using these criteria; for **California Exchange Plans** refer to the HIM.PA.173 Palbociclib (Ibrance) criteria*

FDA Approved Indication(s)

Ibrance is indicated:

- For the treatment of adult patients with 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; or
  - Fulvestrant in patients with disease progression following endocrine therapy.
- In combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, *PIK3CA*-mutated, HR-positive, HER2-negative, locally advanced, or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant 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)**:**

** Refer to HIM.PA.173 for California Exchange Plans*

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 (including locally advanced), recurrent, or metastatic;
5. Ibrance is prescribed in combination with one of the following (a, b, or c):
   a. Both of the following (i and ii):

i. An aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) as part of initial endocrine-based therapy;
ii. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);

b. Fulvestrant;
c. Inavolisib and fulvestrant, and all of the following (i, ii, and iii):
i. Disease is positive for PIK3CA mutation;
ii. Disease progression or recurrence on or after adjuvant endocrine therapy (*see Appendix B*);
iii. If male, prescribed in combination with an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);

6. If member is a premenopausal or perimenopausal 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 both of the following on Days 1 to 21 of a 28-day cycle (i and ii):
i. 125 mg per day;
ii. 1 capsule or 1 tablet per day;
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 – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Soft Tissue Sarcoma* (off-label) (must meet all)**:**
** Refer to HIM.PA.173 for California Exchange Plans*

1. Diagnosis of well-differentiated/dedifferentiated liposarcoma;
2. Request is for capsule formulation;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Disease is unresectable;
6. Prescribed as a single agent;
7. Ibrance is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Kisqali);
8. For brand Ibrance requests, member must use generic palbociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. 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 – 12 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) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial 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 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 both of the following on Days 1 to 21 of a 28-day cycle (i and ii):
      i. 125 mg per day;
      ii. 1 capsule or 1 tablet per day;
   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 – 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) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial 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 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 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
ER: estrogen receptor
ET: endocrine therapy
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
iDFS: invasive disease-free survival
LHRH: luteinizing hormone-releasing hormone
NCCN: National Comprehensive Cancer Network
PR: progesterone receptor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Endocrine therapy		
anastrozole (Arimidex®)	**Breast cancer:** 1 mg PO QD	1 mg/day
letrozole (Femara®)	**Breast cancer:** 2.5 mg PO QD	2.5 mg/day
exemestane (Aromasin®)	**Breast cancer:** 25 mg PO QD	25 mg/day
fulvestrant (Faslodex®)	**Breast cancer:** 500 mg IM as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter	See regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
tamoxifen (Nolvadex®, Soltamox®)	**Breast cancer:** 20 to 40 mg PO QD	40 mg/day

Drug names 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
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 for a cycle of 28 days	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; April 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/207103s020lbl.pdf. Accessed July 10, 2025.
2. Ibrance Tablets Prescribing Information. New York, NY; Pfizer Labs; April 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/212436s008lbl.pdf. Accessed July 10, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 12, 2025.
4. National Comprehensive Cancer Network. Breast Cancer Version 4.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 12, 2025.
5. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed August 12, 2025.
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.
7. Mayer EL, Gnant 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
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
RT4: updated FDA approved indication for breast cancer when used in combination with an aromatase inhibitor to include pre- and peri-menopausal women.	01.17.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.03.23	11.23
Per August SDC, removed HIM line of business.	08.22.23	12.23
4Q 2024 annual review: no significant changes; updated FDA approved indication section to align with prescriber information; references reviewed and updated.	07.12.24	11.24
Added statement disclaimer that California Exchange Plans should not be approved using these criteria and should use HIM.PA.173.	04.09.25	
RT4: for breast cancer, added newly approved indication for endocrine-resistant, PIK3CA-mutated, HR-positive, HER2-negative, locally advanced, or metastatic breast cancer to criteria.	05.06.25	
4Q 2025 annual review: for soft tissue sarcoma, removed "retroperitoneal" and added criteria "request is for capsule formulation" per NCCN; for initial approval criteria, extended approval duration from 6 months to 12 months for Medicaid; references reviewed and updated.	07.10.25	11.25

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.