# Clinical Policy: Inavolisib (Itovebi)

Reference Number: CP.PHAR.702
Effective Date: 12.01.24
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Inavolisib (Itovebi™) is an inhibitor of phosphatidylinositol 3-kinase (PI3K).

## FDA Approved Indication(s)

Itovebi is indicated in combination with palbociclib and fulvestrant for the treatment of adults with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (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 Itovebi 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 ≥ 18 years;
4. Disease has all of the following characteristics (a, b, c, and d):
   a. HR-positive (i.e., estrogen or progesterone receptor [ER/PR]-positive);
   b. HER2-negative;
   c. Advanced (local or regional), recurrent, or metastatic;
   d. Positive for PIK3CA mutation;
5. Itovebi is prescribed in combination with palbociclib and fulvestrant;
6. Disease progression or recurrence on or after adjuvant endocrine therapy (*see Appendix B)*;
7. If member is a premenopausal or perimenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);
8. If member is male, prescribed in combination with an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
9. For Itovebi requests, member must use inavolisib, 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 (i and ii):
        i. 9 mg per day;
        ii. 2 tablets 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: 12 months**

**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.

## II. Continued Therapy

**A. Breast Cancer** (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Itovebi for breast cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Itovebi requests, member must use inavolisib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. 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 (i and ii):
        i. 9 mg per day;
        ii. 2 tablets 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: 12 months**

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

ER: estrogen receptor
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
LHRH: luteinizing hormone-releasing hormone
NCCN: National Comprehensive Cancer Network
PI3K: phosphatidylinositol 3-kinase
PIK3CA: phosphatidylinositol 3-kinase catalytic subunit alpha
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®) | 1 mg PO QD | 1 mg/day |
| letrozole (Femara®) | 2.5 mg PO QD | 2.5 mg/day |
| exemestane (Aromasin®) | 25 mg PO QD | 25 mg/day |
| fulvestrant (Faslodex®) | 500 mg IM as two 5 mL injections, one in each buttock, | See regimen |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| | on days 1, 15, 29 and once monthly thereafter | |
| tamoxifen (Nolvadex®, Soltamox®) | 20 to 40 mg PO QD | 40 mg/day |
| **NCCN-recommended adjuvant therapy for HR-positive, HER2-negative disease** | | |
| CDK4/6 inhibitors to be used in combination with an aromatase inhibitor:<br>Kisqali® (ribociclib)<br>Verzenio® (abemaciclib)<br>Ibrance® (palbociclib) | Varies | Varies |

*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*
None reported

*Appendix D: General Information*
- NCCN recommendations in breast cancer
  - Ovarian ablation may be achieved with surgical oophorectomy or 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.
  - The NCCN recommends that men with breast cancer be treated similarly to postmenopausal women; however, it is preferred that when an aromatase inhibitor is used, a LHRH analog should be given concurrently.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Breast cancer | 9 mg PO QD | 9 mg/day |

## VI. Product Availability
Tablets: 3 mg, 9 mg

## VII. References
1. Itovebi Prescribing Information. South San Francisco, CA: Genentech USA, Inc.; January 2025. Available at: www.itovebi.com. Accessed July 24, 2025.
2. National Comprehensive Cancer Network. Breast Cancer Version 4.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 24, 2025.
3. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2025. URL: www.clinicalkeys.com/pharmacology.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 10.15.24 | 11.24 |
| 4Q 2025 annual review: added option for regionally advanced disease or recurrent disease per NCCN; clarified ovarian ablation or ovarian suppression is required if members are premenopausal or perimenopausal; added requirement to be prescribed in combination with an agent that suppresses testicular steroidogenesis if members are male; extended initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated. | 07.24.25 | 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.