Clinical Policy: Abemaciclib (Verzenio)

Reference Number: CP.PHAR.355
Effective Date: 12.01.17
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

Abemaciclib (Verzenio®) is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6).

FDA Approved Indication(s)

Verzenio is indicated:

- In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20% as determined by an FDA approved test.
- In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- In combination with fulvestrant for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- As monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

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 Verzenio 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 both of the following characteristics (a and b):
   a. HR-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. HER2-negative;

5. Verzenio is prescribed in one of the following ways (a or b):
   a. For advanced, recurrent or metastatic disease, one of the following (i, ii, or iii):
      i. In combination with fulvestrant;
      ii. As a single agent after disease progression on an endocrine therapy and chemotherapy (e.g., docetaxel, gemcitabine) in the metastatic setting;
      iii. In combination with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) as part of initial endocrine based therapy, and:
         1. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
   b. For node-positive, early breast cancer with a high risk of recurrence, both of the following (i and ii):
      i. As adjuvant treatment;
      ii. In combination with endocrine therapy (tamoxifen or an aromatase inhibitor);
6. If prescribed as part of combination therapy and 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., Ibrance®, Kisqali®);
8. Verzenio is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Ibrance, Kisqali);
9. For brand name Verzenio requests, member must use generic abemaciclib, 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 one of the following (i or ii):
       i. For combination therapy: 300 mg per day (two 150 mg tablets per day);
       ii. For monotherapy: 400 mg per day (two 200 mg 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:
Medicaid/HIM – 6 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.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Verzenio for breast cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Dose is ≥ 100 mg per day;
4. Verzenio is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Ibrance, Kisqali);
5. For brand name Verzenio requests, member must use generic abemaciclib, 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 one of the following (i or ii):
      i. For combination therapy: 300 mg per day (two 150 mg tablets per day);
      ii. For monotherapy: 400 mg per day (two 200 mg tablets per day);
   b. New dose is supported by practice guideline 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 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

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

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
exemestane (Aromasin®)	25 mg PO QD	25 mg/day
Fareston® (toremifene)	60 mg PO QD	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 QD	2.5 mg/day
tamoxifen (Nolvadex®, Soltamox®)	20 to 40 mg PO QD	40 mg/day
megestrol acetate	40 mg PO QID	160 mg/day
Chemotherapy		
capecitabine (Xeloda®)	Various	Varies
carboplatin (Paraplatin®)	Various	Varies
cisplatin (Platinol-AQ®)	Various	Varies
cyclophosphamide (Cytoxan®)	Various	Varies
docetaxel (Taxotere®)	Various	Varies
doxorubicin (Lipodox®, Doxil®, Adriamycin®)	Various	Varies
epirubicin (Ellence®)	Various	Varies
gemcitabine (Gemzar®)	Various	Varies
Halaven® (eribulin)	Various	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ixempra® (ixabepilone)	Various	Varies
paclitaxel (Abraxane®, Taxol®)	Various	Varies
vinorelbine (Navelbine®)	Various	Varies

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

- NCCN recommendations in breast cancer:
  - The NCCN recommends that men with breast cancer be treated similarly to postmenopausal women, except that the use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.
  - The NCCN supports use of Verzenio in premenopausal women when used concomitantly with an aromatase inhibitor or fulvestrant. Along with this combination therapy, patients should also be treated with ovarian ablation/suppression. Ovarian ablation can be achieved with surgical oophorectomy or ovarian irradiation. Ovarian suppression can be achieved with luteinizing hormone-releasing hormone agonists (e.g., goserelin, leuprolide).
  - Although the FDA labeled indication limits combination use with fulvestrant to second line, the NCCN recommends this combination as both first and second line (category 1).
- 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.
- While studies have demonstrated the prognostic value of Ki-67 as a biomarker and its usefulness in predicting response and clinical outcome, the data require larger analytical and clinical validation. Therefore, the NCCN Breast Cancer Panel does not recommend assessment of Ki-67 (NCCN Guideline version 04.2022).

V. Dosage and Administration

Indication	Dosing Regimen*	Maximum Dose
Breast cancer	In combination with fulvestrant or an aromatase inhibitor: 150 mg PO BID As monotherapy: 200 mg PO BID	Combination therapy: 300 mg/day Monotherapy: 400 mg/day

**If a dose reduction to < 100 mg/day is required, therapy should be discontinued.*

VI. Product Availability

Tablets: 50 mg, 100 mg, 150 mg, 200 mg

VII. References

1. Verzenio Prescribing Information. Indianapolis, IN: Eli Lilly and Company; October 2021. Available at: http://www.verzenio.com. Accessed June 21, 2022.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically.
3. National Comprehensive Cancer Network. Breast Cancer Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 21, 2022.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 21, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.24.17	11.17
New indication added for initial endocrine therapy in combination with aromatase inhibitor for breast cancer; added specialist requirement.	03.20.18	05.18
4Q 2018 annual review: added requirement for an agent that suppresses testicular steroidogenesis if male and using aromatase inhibitors per NCCN; references reviewed and updated.	07.06.18	02.19
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.19.19	11.19
4Q 2020 annual review: added HIM line of business; modified to allow first-line use with fulvestrant per NCCN category 1 recommendation; added that member has not previously failed another CDK 4/6 inhibitor therapy; references reviewed and updated.	07.14.20	11.20
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 if request is for combination treatment per NCCN; added requirement for no concurrent use with another CDK 4/6 inhibitor therapy.	06.30.21	08.21
4Q 2021 annual review: added clarification that Verzenio prescribed as a single agent after disease progression should be used after progression on a therapy that is used in the metastatic setting per NCCN Compendium; RT4: added new indication for the adjuvant treatment of breast cancer; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; added legacy Wellcare initial auth durations (WCG.CP.PHAR.355 to retire); oral oncology generic redirection language added; references reviewed and updated.	11.10.21	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; WCG-specific policy was retired and that approval duration was consolidated to 6 months	06.21.22	11.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
for the initial authorization; references reviewed and updated. Template changes applied to other diagnoses/indications.		

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.

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.