envolve Pharmacy Solutions

Clinical Policy: Abemaciclib (Verzenio)

Reference Number: ERX.SPA.231
Effective Date: 06.01.18
Last Review Date: 11.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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., Kisqali®, Ibrance®);
8. Verzenio is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Ibrance, Kisqali);
9. For Verzenio requests, member must use 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:
Commercial – Length of Benefit
Medicaid – 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 Verzenio requests, member must use 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:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 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
Ixempra® (ixabepilone)	Various	Varies
paclitaxel (Abraxane®, Taxol®)	Various	Varies
vinorelbine (Navelbine®)	Various	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:
  - 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 8.2021).

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 November 11, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically.
3. National Comprehensive Cancer Network. Breast Cancer Version 8.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 11, 2021.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 11, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	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	11.18
4Q 2019 annual review: no significant changes; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.19.19	11.19
4Q 2020 annual review: 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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; oral oncology generic redirection language added; references reviewed and updated.	11.11.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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