Clinical Policy: Abemaciclib (Verzenio)
Reference Number: CP.PHAR.355
Effective Date: 12.01.17
Last Review Date: 11.20
Line of Business: Commercial, HIM, Medicaid

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 an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women 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 women 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 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. Verzenio is prescribed in one of the following ways (a, b, or c):
         a. In combination with fulvestrant;
         b. As a single agent after disease progression on an endocrine therapy and chemotherapy (e.g., docetaxel, gemcitabine);
c. In combination with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane), and:
   i. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
6. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Ibrance®, Kisqali®);
7. 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 – Length of Benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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. 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 – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is
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.PHAR.21 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endocrine Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anastrozole (Arimidex®)</td>
<td>1 mg PO QD</td>
<td>1 mg/day</td>
</tr>
<tr>
<td>exemestane (Aromasin®)</td>
<td>25 mg PO QD</td>
<td>25 mg/day</td>
</tr>
<tr>
<td>Fareston® (toremifene)</td>
<td>60 mg PO QD</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>Faslodex® (fulvestrant)</td>
<td>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</td>
<td>500 mg/day</td>
</tr>
<tr>
<td>letrozole (Femara®)</td>
<td>2.5 mg PO QD</td>
<td>2.5 mg/day</td>
</tr>
<tr>
<td>tamoxifen (Nolvadex®, Soltamox®)</td>
<td>20 to 40 mg PO QD</td>
<td>40 mg/day</td>
</tr>
<tr>
<td>megestrol acetate</td>
<td>40 mg PO QID</td>
<td>160 mg/day</td>
</tr>
<tr>
<td><strong>Chemotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>capecitabine (Xeloda®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>carboplatin (Paraplatin®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>cisplatin (Platinol-AQ®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>cyclophosphamide (Cytoxan®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>docetaxel (Taxotere®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>doxorubicin (Lipodox®, Doxil®, Adriamycin®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>epirubicin (Ellence®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>gemcitabine (Gemzar®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
</tbody>
</table>
### CLINICAL POLICY

**Abemaciclib**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halaven® (eribulin)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>Ixempra® (ixabepilone)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>Paclitaxel (Abraxane®, Taxol®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine®)</td>
<td>Various</td>
<td>Varies</td>
</tr>
</tbody>
</table>

*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.

**V. Dosage and Administration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen*</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>In combination with fulvestrant or an aromatase inhibitor: 150 mg PO BID</td>
<td>Combination therapy: 300 mg/day</td>
</tr>
<tr>
<td></td>
<td>As monotherapy: 200 mg PO BID</td>
<td>Monotherapy: 400 mg/day</td>
</tr>
</tbody>
</table>

*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**

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>10.24.17</td>
<td>11.17</td>
</tr>
<tr>
<td>New indication added for initial endocrine therapy in combination with aromatase inhibitor for breast cancer; added specialist requirement.</td>
<td>03.20.18</td>
<td>05.18</td>
</tr>
<tr>
<td>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.</td>
<td>07.06.18</td>
<td>02.19</td>
</tr>
<tr>
<td>4Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>08.19.19</td>
<td>11.19</td>
</tr>
<tr>
<td>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.</td>
<td>07.14.20</td>
<td>11.20</td>
</tr>
</tbody>
</table>

**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.

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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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