



## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Verzenio™ (abemaciclib tablets – Eli Lilly and Company)

**TAC APPROVAL DATE:** 04/03/2019

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### OVERVIEW

Verzenio, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated for the following uses:

1. In combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer;<sup>1-2</sup>
2. In combination with Faslodex® (fulvestrant intramuscular injection) for the treatment of women with HR+, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.<sup>1,3</sup> Pre/perimenopausal women treated with Verzenio plus Faslodex should be treated with a gonadotropin-releasing hormone (GnRH) agonist according to current clinical practice standards.
3. As monotherapy for the treatment of adult patients with HR+, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.<sup>1,4</sup>

### Disease Overview

Based on molecular profiling, breast cancer is classified as HR+ (estrogen receptor positive [ER+] and/or progesterone receptor positive [PgR+]), HER2+, or triple negative (ER-negative, PgR-negative, and HER2-negative).<sup>5-6</sup> Most breast cancers in women (71%) are HR+, HER2-negative; these cancers tend to be slow-growing and less aggressive than other subtypes.<sup>6</sup> HR+, HER2-negative tumors are associated with the most favorable prognosis compared with other subtypes, particularly in the short-term, in part because expression of hormone receptors is predictive of a favorable response to hormonal therapy. In men, about 85% of breast cancers are ER+ and 70% are PgR+.<sup>7</sup> About 12% of breast cancers are HR+ and HER2+, and tend to be higher grade and more aggressive than HR+ cancers.<sup>6</sup> About 5% of breast cancers are HER2+ and do not express hormone receptors. These cancers tend to be more aggressive than other breast cancers and have a poorer short-term prognosis compared with ER+ breast cancers. About 12% of breast cancers in women are triple negative and have a poorer short-term prognosis than other subtypes.

### Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 1.2019 – March 14, 2019) recommend CDK 4/6 inhibitor in combination with Faslodex for first-line therapy (Category 1, preferred regimen).<sup>8</sup> According to Verzenio FDA approval, it can also be used after progression on prior endocrine therapy for treatment of recurrent or Stage IV, HR+, HER2-negative breast cancer in postmenopausal women. CDK 4/6 inhibitors + aromatase inhibitor is also a preferred regimen in guidelines (Category 1, preferred). Verzenio is also recommended as a single agent in postmenopausal women with HR+, HER2-negative breast cancer after progression on prior endocrine therapy and prior chemotherapy in the metastatic setting (category 2A). The guidelines recommend that men with breast cancer be treated similarly to postmenopausal women, except that the use of an AI is ineffective without concomitant suppression of testicular steroidogenesis.

The NCCN guidelines state that men with breast cancer should be treated similarly to postmenopausal women, except that use of an AI is ineffective without concomitant suppression of testicular steroidogenesis.<sup>8</sup> In men with breast cancer, tamoxifen is generally used rather than an AI, because the data supporting use of an AI in men are limited.<sup>5</sup> The use of AI therapy with LHRH has been reported. Information is not available using Verzenio in men with breast cancer.

## **POLICY STATEMENT**

Prior authorization is recommended for prescription benefit coverage of Verzenio. All approvals are provided for 3 years in duration unless otherwise noted below. In the clinical criteria, as appropriate, an asterisk (\*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual's gender identity or gender expression; men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Verzenio is recommended in those who meet the following criteria:

### **FDA-Approved Indications**

- 1. Breast Cancer in Postmenopausal Women\*.** Approve for 3 years if the patient meets the following criteria (A, B, C, and D):
  - A)** Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}] disease; AND
  - B)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - C)** The patient meets ONE of the following criteria (i, ii, or iii):
    - i.** Verzenio will be used in combination with anastrozole, exemestane, or letrozole; OR
    - ii.** Verzenio will be used in combination with Faslodex (fulvestrant intramuscular injection); OR
    - iii.** The patient meets the following conditions (a, b, and c):
      - a)** Verzenio will be used as monotherapy; AND
      - b)** The patient's breast cancer has progressed on at least one prior endocrine therapy (e.g., anastrozole, exemestane, letrozole, tamoxifen, Fareston<sup>®</sup> [toremifene], exemestane plus Afinitor<sup>®</sup> [everolimus], Faslodex [fulvestrant intramuscular injection], Afinitor plus Faslodex or tamoxifen, megestrol acetate, fluoxymesterone, ethinyl estradiol); AND
      - c)** The patient has tried chemotherapy for metastatic breast cancer; AND
  - D)** The patient has not had disease progression while on Verzenio, Ibrance (palbociclib capsules), or Kisqali (ribociclib tablets).

\* Refer to the Policy Statement.

- 2. Breast Cancer in Pre/Perimenopausal Women.\*** Approve for 3 years if the patient meets the following criteria (A, B, C, D, and E):
  - A)** Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}] disease; AND
  - B)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND

- C) The patient is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex [goserelin]), or has had surgical bilateral oophorectomy or ovarian irradiation; AND
- D) Patient meets ONE of the following conditions (i, ii, or iii):
  - i. Verzenio will be used in combination with anastrozole, exemestane, or letrozole; OR
  - ii. Verzenio will be used in combination with Faslodex (fulvestrant intramuscular injection); OR
  - iii. Patient meets the following conditions (a, b, and c):
    - a) Verzenio will be used as monotherapy; AND
    - b) The patient’s breast cancer has progressed on at least one prior endocrine therapy (e.g., anastrozole, exemestane, letrozole, tamoxifen, Fareston® [toremifene], exemestane plus Afinitor® [everolimus], Faslodex [fulvestrant intramuscular injection], Afinitor plus Faslodex or tamoxifen, megestrol acetate, fluoxymesterone, ethinyl estradiol); AND
    - c) The patient has tried chemotherapy for metastatic breast cancer; AND
- E) Patient has not had disease progression while on Ibrance (palbociclib capsules), Kisqali (ribociclib tablets), or Verzenio.

\* Refer to the Policy Statement.

### Other Uses With Supportive Evidence

- 3. **Breast Cancer in Men\***. Approve for 3 years if the patient meets the following criteria (A, B, C, and D):
  - A) Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive {ER+} and/or progesterone receptor positive {PR+}]disease; AND
  - B) Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - C) The patient meets ONE of the following criteria (i, ii, or iii):
    - i. The patient meets BOTH of the following conditions (a and b):
      - a) The patient is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex [goserelin]); AND
      - b) Verzenio will be used in combination with anastrozole, exemestane, or letrozole; OR
    - ii. Verzenio will be used in combination with Faslodex (fulvestrant intramuscular injection); OR
    - iii. The patient meets the following conditions (a, b, and c):
      - a) Verzenio will be used as monotherapy; AND
      - b) The patient’s breast cancer has progressed on at least one prior endocrine therapy (e.g., anastrozole, exemestane, letrozole, tamoxifen, Fareston (toremifene), exemestane plus Afinitor (everolimus), Faslodex (fulvestrant intramuscular injection), Afinitor plus Faslodex or tamoxifen, megestrol acetate, fluoxymesterone, ethinyl estradiol); AND
      - c) The patient has tried chemotherapy for metastatic breast cancer; AND
  - D) The patient has not had disease progression while on Verzenio, Ibrance (palbociclib capsules), or Kisqali (ribociclib tablets).

\* Refer to the Policy Statement.

### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Verzenio has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

1. Verzenio™ tablets [prescribing information]. Indianapolis, IN: Eli Lilly and Company; February 2018.
2. Goetz MP, Toi M, Campone M, et al. MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol*. 2017;35(32):3638-3646.
3. Sledge GW Jr, Toi M, Neven P, et al. MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2-advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol*. 2017;35(25):2875-2884.
4. Dickler MN, Tolaney SM, Rugo HS, et al. MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR(+)/HER2(-) metastatic breast cancer. *Clin Cancer Res*. 2017;23(17):5218-5224.
5. National Cancer Institute: PDQ® Breast cancer treatment. National Cancer Institute. Date last modified February 4, 2018. Available at: <https://www.cancer.gov/types/breast/hp/breast-treatment-pdq>. Accessed on March 2, 2018.
6. American Cancer Society. *Breast Cancer Facts & Figures 2017-2018*. Atlanta: American Cancer Society, Inc. 2017. Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf>. Accessed on March 2, 2018.
7. National Cancer Institute: PDQ® Male breast cancer treatment. National Cancer Institute. Date last modified February 8, 2018. Available at: <https://www.cancer.gov/types/breast/hp/male-breast-treatment-pdq>. Accessed on March 2, 2018.
8. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (Version 1.2019 – March 14, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on April 1, 2019.

**HISTORY**

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	New policy.	10/04/2017
Annual revision	<p>Breast Cancer in Women:</p> <ul style="list-style-type: none"> <li>• Criteria were added for first-line (initial) endocrine therapy. See policy for details. This use was recently FDA approved.</li> <li>• Prior endocrine therapy that was previously a list of examples, was revised to be a list of at least one of the listed endocrine therapies. Afinitor plus Faslodex or tamoxifen were added to the list and “high-dose” was removed from ethinyl estradiol. Ibrance, Kisqali and Verzenio are endocrine therapies not included in this list.</li> <li>• Added a criterion that applies to all of the indications in women that the patient has not had disease progression while on Ibrance, Kisqali, or Verzenio.</li> <li>• The monotherapy use was revised to add that the patient’s breast cancer has relapsed or progressed during prior endocrine therapy with a list of those agent listed. The monotherapy use applies to post- pre- and peri-menopausal patients.</li> </ul> <p>Breast Cancer in Men:</p> <ul style="list-style-type: none"> <li>• This is a new Other Uses with Supportive Evidence indication. Criteria include first-line (initial) endocrine therapy and use as monotherapy. See policy for details.</li> </ul>	03/07/2018
Selected revision	Separated out criteria for Postmenopausal and Pre/Perimenopausal women for clarity. Under Breast Cancer in Men criteria, deleted tamoxifen from list of endocrine therapy agents that can be used as combination therapy with Verzenio. Added Verzenio plus Faslodex combination therapy as option for men if progressed on at least one endocrine therapy.	09/12/2018
Annual revision	Deleted requirement in all conditions that Verzenio + aromatase inhibitor use should be in first-line setting. For use of Verzenio + Faslodex, deleted requirement to try a prior endocrine therapy since guidelines recommend first-line use. In the monotherapy criteria, re-worded to state patient has progressed on at least one prior endocrine therapy and changed the list of endocrine therapies to examples.	04/03/2019

TAC – Therapeutic Assessment Committee; LHRH – Luteinizing hormone-releasing hormone; GnRH – gonadotropin-releasing hormone;\* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; TAC – Therapeutic Assessment Committee.