PRIOR AUTHORIZATION POLICY

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

DATE REVIEWED: 04/15/2020

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;[1-2]
2. In combination with fulvestrant for the treatment of women with HR+, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.[1,3] 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.[1,4]

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).[5-6] Most breast cancers in women (71%) are HR+, HER2-negative; these cancers tend to be slow-growing and less aggressive than other subtypes.[6] 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+.[7] About 12% of breast cancers are HR+ and HER2+, and tend to be higher grade and more aggressive than HR+ cancers.[6] 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 3.2020 – March 6, 2020) recommend CDK 4/6 inhibitor in combination with fulvestrant for first-line therapy (category 1, preferred regimen) in HR+/HER2-negative recurrent or Stage IV (metastatic) disease.[8] This combination can also be used as second/subsequent-line preferred therapy if CDK4/6 inhibitor was not used previously (category 1). CDK 4/6 inhibitors + aromatase inhibitor is also a preferred regimen in guidelines (category 1, preferred). Verzenio is also recommended as "useful in certain circumstances" as a single agent in HR+, HER2-negative breast cancer after progression on prior endocrine therapy and prior chemotherapy in the metastatic setting (category 2A). The above recommendations for CDK4/6 inhibitors is for use in postmenopausal women or premenopausal women receiving ovarian ablation or suppression. 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. 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.[5] The use of AI therapy with LHRH has been reported. Information is not available using Verzenio in men with breast cancer. However, available real-world data suggest comparable efficacy and safety profiles in men as in women; it is reasonable to recommend CDK4/6 inhibitors in combination with an aromatase inhibitor or fulvestrant, everolimus, and PIK3CA inhibitors to men based on extrapolation of data from studies comprised largely of female participants with advanced breast cancer.

The NCCN guidelines state in a footnote that if there is disease progression on CDK4/6 inhibitor therapy, there are limited data to support an additional line of therapy with another CDK4/6-containing regimen.[8] The limited data are based on a multicenter analysis which evaluated clinical outcomes in patients (n = 58) with HR+/HER2-negative metastatic breast cancer who received Verzenio after disease progression on Ibrance or Kisqali.[9] At data cutoff, 34% of patients (n = 20/58) had progressive disease, while 36% of patients (n = 21/58) had treatment duration exceeding 6 months. The median PFS was 5.8 months. There are no published data with additional line of therapy with Ibrance or Kisqali, if the patient has progressed on Verzenio.

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 fulvestrant ; 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. Note: Examples are anastrozole, exemestane, letrozole, tamoxifen, Fareston® [toremifene], exemestane plus everolimus, fulvestrant, everolimus plus fulvestrant 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.

   ***** 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 fulvestrant; 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 Note: Examples are anastrozole, exemestane, letrozole, tamoxifen, Fareston® [toremifene], exemestane plus everolimus, fulvestrant, everolimus plus fulvestrant 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 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 fulvestrant; 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 Note: Examples are anastrozole, exemestane, letrozole, tamoxifen, Fareston (toremifene), exemestane plus everolimus, fulvestrant, everolimus plus fulvestrant 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.

***** 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; March 2020.
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 3.2020 – March 6, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 13, 2020.
9. Wander SA, Zangardi M, Niemierko A, et al. A multicenter analysis of abemaciclib after progression on palbociclib in patients (pts) with hormone-receptor-positive (HR+)/HER2- metastatic breast cancer (MBC). *J Clin Oncol*. 2019;37:15_suppl, 1057-1057.