PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Kisqali® (ribociclib tablets – Pfizer Labs); Kisqali® Femara® Co-Pack (ribociclib tablets; letrozole tablets, co-packaged for oral use – Pfizer Labs)

DATE REVIEWED: 04/15/2020

OVERVIEW

Kisqali, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated in combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.[1-3] Kisqali Femara Co-Pack has the same indication with the AI, letrozole being provided.[4] Kisqali (not Co-Pack) is also indicated in combination with fulvestrant for the treatment of postmenopausal women with HR+, HER2-negative advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy.

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 any of the CDK4/6 inhibitors in combination with an AI or fulvestrant as a first-line treatment option for recurrent or Stage IV HR+ and HER2-negative disease in postmenopausal women or premenopausal patient receiving ovarian ablation or suppression (category 1).[8] The compendium 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.[9] 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.[10] 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.

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.[7] The use of AI therapy with LHRH has been reported.[8-9] Only limited data are available with Kisqali use in men with breast cancer as first-line endocrine therapy in combination with anastrozole, exemestane, or letrozole or for combination use with fulvestrant. 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.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Kisqali and Kisqali Femara Co-Pack. 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

I. Coverage of Kisqali 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 or ii):
     - **i.** Kisqali will be used in combination with anastrozole, exemestane, or letrozole; OR
     - **ii.** Kisqali will be used in combination with fulvestrant ; AND
   - **D)** The patient has not had disease progression while on Kisqali, Ibrance (palbociclib capsules), or Verzenio (abemaciclib 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, 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)** Patient meets one of the following criteria (i or ii):
     - **i.** The patient meets both of the following criteria (a and b):
       - **a)** Kisqali will be used in combination with anastrozole, exemestane, or letrozole; AND
       - **b)** 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; OR
     - **ii.** Kisqali will be used in combination with fulvestrant; AND
   - **D)** Patient has not had disease progression while on Kisqali, Ibrance (palbociclib capsules), or Verzenio (abemaciclib tablets).

***** Refer to the Policy Statement.

Other Uses With Supportive Evidence

1. **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)** Patient meets ONE of the following criteria (i or ii):
     - **i.** Patient meets BOTH of the following criteria (a and b):
       - **a)** Patient is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin]); AND
       - **b)** Kisqali will be used in combination with anastrozole, exemestane, or letrozole; OR
     - **ii.** Kisqali will be used in combination with fulvestrant ; AND
   - **D)** Patient has not had disease progression while on Kisqali, Ibrance (palbociclib capsules), or Verzenio (abemaciclib tablets).

***** Refer to the Policy Statement.

II. Coverage of Kisqali Femara Co-Pack is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Breast Cancer in 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)** If the patient is premenopausal or perimenopausal, then 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)** The patient has not had disease progression while on Kisqali, Ibrance (palbociclib capsules), or Verzenio (abemaciclib tablets).

***** Refer to the Policy Statement.

Other Uses With Supportive Evidence

1. **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 is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin]); AND

D) The patient has not had disease progression while on Kisqali, Ibrance (palbociclib capsules), or Verzenio (abemaciclib tablets).

***** Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Kisqali or Kisqali Femara 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. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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. Kisqali® tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018.
2. Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med*. 2016;375(18):1738-1748.
3. Data on file. AMCP Formulary Dossier Version 4.0. Kisqali® (ribociclib). Novartis Pharmaceuticals Corporation; received March 20, 2017.
4. Kisqali® Femara® Co-Pack tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2019.
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.
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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.
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10. 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.