PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/24/2021

OVERVIEW

Kisqali, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated in hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative **advanced or metastatic breast cancer** in the following settings:[1-3]

- In combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with.
- Kisqali (not Co-Pack) in combination with fulvestrant for the treatment of postmenopausal women, as initial endocrine based therapy or following disease progression on endocrine therapy.
- Kisqali Femara Co-Pack has the same indication with the aromatase inhibitor, letrozole being provided.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 1.2021 – January 15, 2021) recommend any of the CDK4/6 inhibitors in combination with an AI or fulvestrant as a first-line preferred 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).[3,4] CDK4/6 inhibitor + fulvestrant is recommended for second- and subsequent-line therapy, if CDK4/6 inhibitor was not previously used (category 1). However, the guidelines also state in a footnote that if there is disease progression on CDK4/6 inhibitor therapy or PI3K inhibitor, there are limited data to support an additional line of therapy with another CDK4/6-containing regimen.[3,5] For men with breast cancer, the compendium recommends they be treated similarly to postmenopausal women, except that the use of an AI is ineffective without concomitant suppression of testicular steroidogenesis.[4]

Supportive Data

A multicenter analysis evaluated clinical outcomes in patients (n = 58) with HR+/HER2-negative metastatic breast cancer who received Verzenio (abemaciclib tablets) after disease progression on Ibrance (palbociclib tablets) or Kisqali.[5] 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 progression-free survival (PFS) was 5.8 months. Another case report of Verzenio use after 10 lines of therapy, including Ibrance therapy is available, along with literature review of ongoing studies with other CDK 4/6 inhibitors after prior use of another inhibitor.[6] Ibrance and Kisqali also have ongoing studies assessing for their respective efficacy after progression on another CDK4/6 inhibitor.[7,8] Preliminary results from the Kisqali trial (TRINITI-1), a Phase I/II, open-label trial of triplet therapy (Kisqali + everolimus + exemestane) after progression on prior CDK 4/6 inhibitor and up to three lines of therapy are available.[9] A total of 95 patients were evaluated; 41.1% of patients demonstrated clinical benefit, exceeding the predefined primary endpoint threshold (> 10%). The response rate was 8.4% and the median PFS was 5.7 months, and the 1-year PFS was 33%.

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, and C):
   - **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.** Kisqali will be used in combination with anastrozole, exemestane, or letrozole; OR
     - **ii.** Kisqali will be used in combination with fulvestrant.

   ***** 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 is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist or has had surgical bilateral oophorectomy or ovarian irradiation; AND
     Note: Examples of GnRH agonists are Lupron (leuprolide), Trelstar (triptorelin), Zoladex (goserelin).
   - **D)** 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**.**

   ***** 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)** 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) analog; AND
Note: Examples are Lupron (leuprolide), Trelstar (triptorelin), Zoladex (goserelin], Firmagon (degarelix), Orgovyx (relugolix).
b) Kisqali will be used in combination with anastrozole, exemestane, or letrozole; OR

ii. Kisqali will be used in combination with fulvestrant.

***** 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, and C):
   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 or has had surgical bilateral oophorectomy or ovarian irradiation.
   Note: Examples of GnRH agonists are Lupron (leuprolide), Trelstar (triptorelin), Zoladex (goserelin).

   ***** 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, and C):
   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 is receiving a gonadotropin-releasing hormone (GnRH) analog.
   Note: Examples are Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin), Firmagon (degarelix), Orgovyx (relugolix).

   ***** Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Kisqali or Kisqali Femara Co-Pack is not recommended in the following situations:

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 2020.
2. Kisqali® Femara® Co-Pack tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 1.2021 – January 15, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 21, 2021.
4. The NCCN Compendium. © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Search term: ribociclib. Accessed on February 21, 2021.
5. 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.
6. Wender IO, Haines K, Jahanzeb M. Response to abemaciclib after 10 lines of therapy including palbociclib in metastatic breast cancer: a case report with literature review. *Oncol Ther*. 2020;8:351-358.
7. Novartis Pharmaceuticals. Study of ribociclib with everolimus + exemestance in HR+ HER2- locally advanced/metastatic breast cancer post progression on CDK 4/6 inhibitor. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2021 Feb 21]. Available at: https://www.clinicaltrials.gov/ct2/show/NCT02732119?term=02732119&draw=2&rank=1. NLM Identifier: NCT02732119.
8. Dana-Farber Cancer Institute, Pfizer. Palbociclib after CDK and endocrine therapy (PACE). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2021 Feb 21]. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03147287?term=03147287&draw=2&rank=1. NLM Identifier: NCT03147287.
9. Bardia A, Hurvitz SA, DeMichele A, et al. Triplet therapy (continuous ribociclib, everolimus, exemestane) in HR+/HER2- advanced breast cancer postprogression on a CDK4/6 inhibitor (TRINITI-1): efficacy, safety, and biomarker results. Abstract 1016. *J Clin Oncol.* 2019;37(15):1016-1016.

History

Type of Revision	Summary of Changes	Review Date
Annual Revision	Deleted criteria in all indications requiring Kisqali + aromatase inhibitors to be used as "first-line (initial) endocrine therapy". Now the combination can be used in any setting. Kisqali + Faslodex use was added to premenopausal women based on guidelines. For Kisqali + Faslodex use in postmenopausal women and men indications, deleted criteria requiring prior endocrine therapy use or that it be used as first-line endocrine therapy. For Kisqali Femara Co-Pack since approval is in "women" (includes postmenopausal and premenopausal), deleted specific reference to postmenopausal patient. Instead re-phrased to state, "If patient is premenopausal or perimenopausal…" then patient is receiving ovarian suppression/ablation. For premenopausal patients, added criteria that Kisqali can be used in combination with tamoxifen based on guidelines.	04/03/2019
Annual Revision	Criteria for Kisqali use in combination with tamoxifen as first-line therapy has been deleted for pre/perimenopausal women since it is no longer supported in guidelines due to QTc prolongation.	04/15/2020
Early Annual Revision	**All Breast Cancer Indications:** For Kisqali and Kisqali Femara Co-Pack deleted criteria requiring no disease progression on Kisqali, Ibrance (palbociclib) or Verzenio (abemaciclib), based on guidelines and available data. **Breast Cancer in Pre/Perimenopausal Women:** Examples of gonadotropin-releasing hormone (GnRH) agonists are moved from criteria to Note. **Breast Cancer in Men:** For this indication in Kisqali and Kisqali Femara Co-pack, GnRH "agonist" is changed to "analog". Also, the list of examples of GnRH analog agents are moved from criteria to Note. Firmagon (degarelix) and Orgovyx (relugolix) were added to example list. **Breast Cancer in Women:** Examples of gonadotropin- releasing hormone (GnRH) agonists are moved from criteria to Note.	02/24/2021