PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/18/2017**
SECTION: DRUGS	**LAST REVIEW DATE: 5/19/2022**
	LAST CRITERIA REVISION DATE: 5/19/2022
	ARCHIVE DATE:

KISQALI® (ribociclib)
KISQALI® FEMARA® CO-PACK (ribociclib; letrozole)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Kisqali (ribociclib) and Kisqali-Femara (ribociclib-letrozole) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. **For Kisqali (ribociclib) only**, a confirmed diagnosis of **ONE** of the following:
    a. Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with **one** of the following:
        i. An aromatase inhibitor as initial endocrine-based therapy
        ii. Fluvestrant as initial endocrine-based therapy or following disease progression on endocrine-based therapy in postmenopausal woman or man [Note: men should also use a drug for suppression of testicular steroidogenesis]

    b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. **For Kisqali-Femara (ribociclib-letrozole) only**, a confirmed diagnosis of **ONE** of the following
    a. Initial endocrine-based therapy for the treatment of individuals with Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer

    b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

5. **ALL** of the following baseline tests have been completed before initiation of treatment:
    a. Electrocardiogram (ECG) showing QTcF is less than 450 ms
    b. A negative pregnancy test in a woman of reproductive potential
    c. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1

6. **Additional criteria for Kisqali-Femara (ribociclib-letrozole) Co-pack only:**
    a. Individual is unable to use the separate components Kisqali (ribociclib) and Femara (letrozole), medical record documentation showing inability to use separate components is required

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Kisqali (ribociclib) and Kisqali-Femara (ribociclib-letrozole) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual's condition responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

  3. Individual has been adherent with the medication

  4. Dose of ribociclib is at least 200 mg

  5. Individual has not developed any significant adverse drug effects that may exclude continued use
     a. Significant adverse effect such as:
        i. Interstitial Lung Disease/Pneumonitis
        ii. QTcF prolongation (QTcF > 500 ms or > 60 ms over baseline) associated with torsades de pointes, polymorphic ventricular tachycardia, unexplained syncope, or signs/symptoms of serious arrhythmia
        iii. Liver toxicity
        iv. Neutropenia

  6. There are no significant interacting drugs

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Kisqali (ribociclib) is a kinase inhibitor 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. Aromatase inhibitors include anastrozole, exemestane, or letrozole. Kisqali Femara Co-pack contains ribociclib and letrozole.

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Kinases are involved in numerous cellular functions, including cell signaling, growth, and division. The majority of breast cancers are hormone receptor-positive. They are stimulated to grow by the circulating female hormones estrogen and/or progesterone. Treatment of hormone receptor-positive breast cancer often involves hormonal therapies that suppress or block the action of estrogen. Growth of hormone receptor positive breast cancer is also dependent on the cyclin-dependent kinases 4 and 6 (CDK4 and CDK6), which promote progression through the various phases of the cell cycle that result in cell division.

Ribociclib is an inhibitor of CDK 4 and CDK 6 enzyme that promotes the growth and spread of cancer cells. These kinases are activated upon binding to D-cyclins and play a crucial role in the signaling pathways which lead to cell cycle progression and cellular proliferation. The cyclin D-CDK4/6 complex regulates cell cycle progression through phosphorylation of the retinoblastoma protein (pRb). Ribociclib decreases pRb phosphorylation leading to arrest in the G1 phase of the cell cycle and reduces cell proliferation in breast cancer cell lines.

Definitions:

QT interval – Fridericia formula:

$$QTcF = QT/RR^{0.33}$$

CDK 4/6 inhibitors:
Verzenio (abemaciclib)
Ibrance (palbociclib)
Kisqali (ribociclib)

Aromatase Inhibitors:
Arimidex (anastrozole)
Femara (letrozole)
Aromasin (exemestane)

Antiestrogens:
Faslodex (fulvestrant)
Tamoxifen
Fareston (toremifene)

Gonadotropin-Releasing Hormone Analog – for men with breast cancer along with aromatase inhibitors:
Zoladex (goserelin)
Vantas (histrelin)
Eligard, Lupron (leuprolide)
Trelstar (triptorelin)
Progestin Combination

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Antiandrogens:

Zytiga, Yonsa (abiraterone)
Erleada (apalutamide)
Casodex (bicalutamide)
Xtandi (enzalutamide)
Flutamide
Nilandron (nilutamide)

Resources:

Kisqali (ribociclib) product information, revised by Novartis Pharmaceutical Corporation 01-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 12, 2022.

Kisqali-Femara CO-PACK (ribociclib-letrozole) product information, revised by Novartis Pharmaceutical Corporation 12-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 12, 2022.

Ma CX, Sparano JA. Treatment approach to metastatic hormone-receptor positive, HER2-negative breast cancer: Endocrine therapy and targeted agents. In: UpToDate, Burnstein HJ, Vora SR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated February 07, 2022. Accessed May 12, 2022.

Gradishar WJ, Ruddy KJ. Breast cancer in men. In: UpToDate, Chagpar AB, Hayes DF, Vora SR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated April 06, 2022. Accessed May 12, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer Version 3.2022 – Updated May 07, 2022. Available at https://www.nccn.org. Accessed May 12, 2022.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.