BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

KISQALI® (ribociclib)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Kisqali (ribociclib) 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. 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. **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

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Kisqali (ribociclib) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

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 with response defined as:
   a. No evidence of disease progression
   b. 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 such as:
   a. Interstitial Lung Disease/Pneumonitis
   b. 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
   c. Liver toxicity
   d. Neutropenia

6. There are no significant interacting drugs

Renewal duration: 12 months

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- 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.

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)

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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

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.

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.