BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

KISQALI® (ribociclib)
Generic Equivalent (if available)

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/or 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 prior authorization 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.

Medical Necessity Requirements for KISQALI (ribociclib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an oncologist or in consultation with an oncologist

Indication
- Hormone receptor-positive, human epidermal growth factor receptor 2-negative stage II or III early breast cancer at high risk of recurrence, in combination with an aromatase inhibitor

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- Hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced or metastatic breast cancer in combination with EITHER:
  - An aromatase inhibitor as initial endocrine-based therapy
  - Fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy
- Other direct oncologic treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Electrocardiogram showing QTcF is less than 450 milliseconds
- Negative pregnancy test for women of reproductive potential
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety
- No concomitant use of strong CYP3A inducers (e.g., phenytoin, rifampin, carbamazepine, St. John's wort)
- No concomitant use of drugs known to prolong QT interval (e.g., amiodarone, disopyramide, procainamide, quinidine, sotalol, clarithromycin, haloperidol, methadone, moxifloxacin, bepridil, pimozide, ondansetron)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (QTcF, pregnancy test, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an oncologist

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Clinical Response
- Positive clinical response defined as no evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No significant drug-drug interactions or contraindications
- Dose of ribociclib is at least 200 mg
- No development of any of the following:
  - Recurrent symptomatic or severe interstitial lung disease/pneumonitis
  - Severe cutaneous adverse reactions
  - QTcF prolongation greater than 500 milliseconds or greater than 60 milliseconds over baseline with associated arrhythmia symptoms
  - Hepatobiliary toxicity
  - Neutropenia
  - Any other life-threatening toxicity
- No concomitant use of strong CYP3A inducers or drugs known to prolong QT interval

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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

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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:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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)

Luteinizing hormone-releasing hormone agonist:

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A substance that keeps the testicles and ovaries from having sex hormones by blocking other hormones that are needed to make them. In men, luteinizing hormone-releasing hormone agonists cause the testicles to stop making testosterone. In women, they cause the ovaries to stop making estrogen and progesterone. Some luteinizing hormone-releasing hormone agonists are used to treat prostate cancer. Also called GnRH agonist, GnRHa, gonadotropin-releasing hormone agonist or analog, and LHRH agonist.

Gonadotropin-Releasing Hormone Analog or Luteinizing hormone-releasing hormone (LHRH) agonist:

Zoladex (goserelin)
Eligard, Lupron (leuprolide)
Trelstar (triptorelin)

Antiandrogens:

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

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Kisqali (ribociclib) product information, revised by Novartis Pharmaceutical Corporation 09-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

Ma CX, Sparano JA. Treatment for hormone-receptor positive, HER2-negative advanced breast cancer. In: UpToDate, Burnstein HJ, Vora SR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through March 2025.Topic last updated March 20, 2025. Accessed April 17, 2025.

Gradishar WJ, Ruddy KJ. Breast cancer in men. In: UpToDate, Chagpar AB, Isaacs C, Vora SR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through March 2025. Topic last updated Marc 03, 2025. Accessed April 17, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer Version 4.2025 – Updated April 17, 2025. Available at https://www.nccn.org. Accessed April 17, 2025.

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.