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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 31, 2017
Subject:	Kisqali	**Page:**	1 of 5

Last Review Date: June 13, 2024

Kisqali

Description

Kisqali (ribociclib), Kisqali Femara Co-Pack (ribociclib & letrozole)

Background
Kisqali (ribociclib) is a kinase inhibitor that inhibits cyclin-dependent kinase (CDK) 4 and 6. These kinases are activated upon binding to D-cyclins and play a crucial role in 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). In vitro, ribociclib decreased pRb phosphorylation leading to arrest in the G1 phase of the cell cycle and reduced cell proliferation in breast cancer cell lines. Combination of ribociclib and antiestrogen (e.g., letrozole) resulted in increased tumor growth inhibition compared to each drug alone. Additionally, the combination of ribociclib and fulvestrant resulted in tumor growth inhibition in an estrogen receptor positive breast cancer xenograft model (1-2).

Regulatory Status
FDA-approved indications: Kisqali is a kinase inhibitor indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: (1)

1. an aromatase inhibitor as initial endocrine-based therapy; or
2. fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy in postmenopausal women or in men.

FDA-approved indications: Kisqali Femara Co-Pack, a co-packaged product containing ribociclib, a kinase inhibitor, and letrozole, an aromatase inhibitor, is indicated as initial endocrine-based therapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer (2).

Monitor electrocardiograms (ECGs) and electrolytes prior to initiation of treatment with Kisqali. Repeat ECGs at approximately Day 14 of the first cycle and at the beginning of the second cycle, and as clinically indicated. Monitor electrolytes at the beginning of each cycle for 6 cycles, and as clinically indicated. Avoid using Kisqali with drugs known to prolong QT interval and/or strong CYP3A inhibitors (1).

Increases in serum transaminase levels have been seen with the use of Kisqali. Perform liver function tests (LFTs) before initiating therapy with Kisqali. Monitor LFTs every 2 weeks for first 2 cycles, at the beginning of each subsequent 4 cycles, and as clinically indicated. Based on severity of transaminase elevation, Kisqali may require dose interruption, reduction, or discontinuation (1).

Neutropenia was highly reported with the use of Kisqali. Perform complete blood count (CBC) prior to initiating therapy with Kisqali. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles, and as clinically indicated (1).

The safety and effectiveness of Kisqali have not been established in pediatric patients (1).

Related policies
Ibrance, Verzenio

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kisqali may be considered **medically necessary** if the conditions indicated below are met.

Kisqali may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Advanced or metastatic breast cancer

Kisqali ONLY

Patient must have **ONE** of the following:

1. Used in combination with an aromatase inhibitor
   a. Used as initial endocrine-based therapy
2. Used in combination with fulvestrant (Faslodex)
   a. Female patient **only**: patient is postmenopausal

Kisqali Femara Co-Pack ONLY

Patient must have the following:

1. Used as initial endocrine-based therapy

AND ALL of the following for **BOTH Kisqali** and **Kisqali Femara Co-Pack**:

1. Hormone receptor (HR)-positive
2. Human epidermal growth factor receptor 2 (HER2)-negative
3. Prescriber agrees to treat with a luteinizing hormone-releasing hormone (LNRH) agonist if clinically indicated
4. Prescriber agrees to monitor liver function tests (LFTs), electrocardiograms (ECGs), and electrolytes prior to initiation of treatment and before each cycle as clinically indicated

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Advanced or metastatic breast cancer

Kisqali ONLY

Patient must have **ONE** of the following:

1. Used in combination with an aromatase inhibitor
2. Used in combination with fulvestrant (Faslodex)
   a. Female patient **only**: patient is postmenopausal

AND ALL of the following for **BOTH KISQALI** and **KISQALI FEMARA CO-PACK**:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to treat with a luteinizing hormone-releasing hormone

(LNRH) agonist if clinically indicated

3. Prescriber agrees to monitor liver function tests (LFTs), electrocardiograms (ECGs), and electrolytes before each cycle as clinically indicated

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib/letrozole) are indicated for the treatment of patients with HR-positive, HER2-negative advanced or metastatic breast cancer. Liver function tests, electrocardiograms, and electrolytes are important parameters to monitor in these patients due to potential side effects. The safety and effectiveness of Kisqali have not been established in pediatric patients (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Kisqali while maintaining optimal therapeutic outcomes.

References

1. Kisqali [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2023.
2. Kisqali Femara Co-Pack [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.
3. NCCN Drugs & Biologics Compendium® Ribociclib 2024. National Comprehensive Cancer Network, Inc. Accessed on April 30, 2024.

Policy History

Date	Action
March 2017	New addition to PA
July 2017	Annual editorial review Addition of the requirement of prescriber agrees to monitor liver function tests (LFTs), electrocardiograms (ECGs) and electrolytes before each cycle as clinically indicated Addition of Kisqali Femara Co-Pack
December 2017	Annual review
March 2018	Annual review
August 2018	Addition of requirement of female gender, use in combination with fulvestrant in postmenopausal, used in combination with aromatase inhibitors as initial endocrine therapy
September 2018	Annual editorial review
March 2019	Removed postmenopausal from Kisqali Femara Co-Pack requirements
June 2019	Annual review
December 2019	Annual review and reference update
June 2020	Annual review and reference update
June 2021	Annual review and reference update
January 2022	Per package insert update: removed requirement of female gender and revised Kisqali plus fulvestrant requirement so only female patients must be postmenopausal. Added requirement “Prescriber agrees to treat with a luteinizing hormone-releasing hormone (LNRH) agonist if clinically indicated”
March 2022	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.