KISQALI / KISQALI FEMARA CO-PACK (ribociclib) / (ribociclib & letrozole)

RATIONALE FOR INCLUSION IN PA PROGRAM

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: (1)

1. in combination with an aromatase inhibitor for the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer at high risk of recurrence.
2. for the treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer in combination with:
    a. an aromatase inhibitor as initial endocrine-based therapy; or
    b. fulvestrant as initial endocrine-based therapy or with disease progression following endocrine therapy.

FDA-approved indications: Kisqali Femara Co-Pack, a co-packaged product containing ribociclib, a kinase inhibitor, and letrozole, an aromatase inhibitor, is indicated: (2)

1. for the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer at high risk of recurrence.
2. as initial endocrine-based therapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer therapy.

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).

Summary

Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib/letrozole) are indicated for the treatment of patients with HR-positive, HER2-negative stage II, III, or advanced or metastatic breast cancer. Liver function tests, electrocardiograms, complete blood count, 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; September 2024.
2. Kisqali Femara Co-Pack [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2024.
3. NCCN Drugs & Biologics Compendium® Ribociclib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.