RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Kisqali 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 treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, as initial endocrine-based therapy
2. in combination with fulvestrant (Faslodex) for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on 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. as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer

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 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 is a kinase inhibitor that inhibits tumor growth in patients with advanced or metastatic HR-positive, HER2-negative breast cancer when used in combination with an aromatase inhibitor as initial endocrine-based therapy for pre/perimenopausal or used in combination with fulvestrant (Faslodex) as initial endocrine-based therapy or following disease progression on endocrine therapy in postmenopausal women. 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