Indication
KISQALI® is a kinase inhibitor indicated in combination with:
• an aromatase inhibitor for the treatment of pre/peri 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; or
• fulvestrant 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.

The KISQALI® (ribociclib) FEMARA® (letrozole) Co-Pack is indicated as initial endocrine-based therapy for the treatment of pre/peri or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

IMPORTANT SAFETY INFORMATION
QT interval prolongation. KISQALI® (ribociclib) and the KISQALI® (ribociclib) FEMARA® (letrozole) Co-Pack have been shown to prolong the QT interval in a concentration-dependent manner. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation. Across clinical trials in patients with advanced or metastatic breast cancer treated with KISQALI in combination with an aromatase inhibitor or fulvestrant (“KISQALI treatment groups”), 14 of 1054 patients (1%) had >500 ms postbaseline QTf value, and 59 of 1054 (6%) had a >60 ms increase from baseline in QTf intervals. These ECG changes were reversible with dose interruption and most occurred within the first 4 weeks of treatment. No cases of torsades de pointes were reported. In MONALEESA-2, on the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of ventricular tachycardia or sudden death were reported in MONALEESA-7 or MONALEESA-3.

Please click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

*Based on a search of phase III clinical trials of 200 or more women.
Prescribe the KISQALI FEMARA Co-Pack with 1 prescription

- Write the prescription as illustrated below and specify the KISQALI dose: 600 mg, 400 mg, or 200 mg
- For your premenopausal patients, write a separate prescription for the LHRH agonist of your choice
- KISQALI is also available to be prescribed with the endocrine therapy of your choice

1 free treatment cycle for a rapid start

Your patients are eligible to receive a 1-treatment-cycle supply of KISQALI FEMARA, the KISQALI FEMARA Co-Pack, and/or generic letrozole at no cost.

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI or the KISQALI FEMARA Co-Pack only in patients with QTc values <450 ms. Repeat ECG at approximately Day 14 of the first cycle, at the beginning of the second cycle, and as clinically indicated. Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting therapy with KISQALI or the KISQALI FEMARA Co-Pack therapy.

Avoid the use of KISQALI or the KISQALI FEMARA Co-Pack in patients who already have or who are at significant risk of developing QT prolongation, including patients with:

- Long QT syndrome
- Uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina, and bradyarrhythmias
- Electrolyte abnormalities
- Avoid using KISQALI or the KISQALI FEMARA Co-Pack with drugs known to prolong the QT interval and/or strong CYP3A inhibitors, as this may lead to prolongation of the QTc interval.

Increased QT prolongation with concomitant use of tamsulosin. KISQALI is not indicated for concomitant use with tamsulosin. In MONALEESA-7: the observed mean QTcF increase from baseline was 10 ms higher in the tamsulosin + placebo subgroup compared with the NSAI + placebo subgroup. In the placebo arm, an increase of +60 ms from baseline occurred in 4 of 490 patients (1%) receiving tamsulosin, and in no patients receiving an NSAI.

Hepatobiliary toxicity. Across clinical trials in patients with advanced or metastatic breast cancer, increases in transaminases were observed. Across all trials, grade 3 or 4 increases in alanine aminotransferase (ALT) (10% vs 2%) and aspartate aminotransferase (AST) (7% vs 2%) were reported in the KISQALI and placebo arms, respectively.

Neutropenia. Across clinical trials in patients with advanced or metastatic breast cancer, neutropenia was the most frequently reported adverse reaction (AR) (74%), and a grade 3-4 decrease in neutrophil count (based on laboratory findings) was reported in 58% of patients in the KISQALI treatment groups. Among the patients who had grade 3 or 4 neutropenia, the median time to resolution of grade 3 or 4 neutropenia (range 3 days to grade 4 normalization or grade 3 was 12 days in the KISQALI treatment groups.

Neutropenia was reported in 7% of patients in the KISQALI treatment groups. Treatment discontinuation due to neutropenia was 0.8%.

Perform blood count (CBC) before initiating therapy with KISQALI or the KISQALI FEMARA Co-Pack. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation. Recommendations for patients who have elevated AST/ALT grade ≥3 at baseline have not been established.

In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times the upper limit of normal (ULN), with normal alkaline phosphatase, in the absence of cholestasis occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI. No cases occurred in MONALEESA-7.

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Embryofetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of KISQALI to pregnant rats and rabbits during organogenesis caused embryofetal toxicities at maternal exposures that were 0.6- and 1.5- times the human clinical exposure, respectively, based on area under the curve. Letrozole caused embryofetal toxicities in rats and rabbits at maternal exposures that were below the maximum recommended human dose (MRHD) on a milligrams per square meter basis. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI or the KISQALI FEMARA Co-Pack and for at least 3 weeks after the last dose.

Adverse reactions. Across clinical trials of patients with advanced or metastatic breast cancer, the most common ARs reported in the KISQALI treatment groups (pooled incidence ≥20%) were neutropenia (74% vs 59%), nausea (55% vs 27%), infections (25% vs 30%), fatigue (39% vs 20%), diarrhea (28% vs 26%), leukopenia (30% vs 3%), vomiting (27% vs 16%), alopecia (34% vs 24%), headache (24% vs 22%), constipation (24% vs 16%), rash (20% vs 9%), and cough (22% vs 5%). The most common grade 3/4 ARs reported at a pooled frequency ≥5% were neutropenia (59% vs 2%), leukopenia (15% vs 2%), abnormal LFTs (5% vs 2%), abnormal AST (5% vs 1%), anemia (4% vs 2%), and lymphopenia (5% vs 1%).

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI-containing arm vs placebo arm (all grades, pooled incidence ≥20%) and <5% higher than placebo arm) were leukocyte count decrease (94% vs 49%), procalcitonin decrease (93% vs 25%), hemoglobin decrease (66% vs 38%), lymphocyte count decrease (63% vs 26%), AST increase (47% vs 38%), ALT increase (44% vs 36%), creatinine increase (38% vs 31%), and platelet count decrease (39% vs 9%). The most common grade 3/4 laboratory abnormalities (incidence ≥5%) were neutrophil count decrease (59% vs 2%), leukocyte count decrease (32% vs 16%), lymphocyte count decrease (15% vs 4%), ALT increase (10% vs 2%), and AST increase (7% vs 2%).
KISQALI® (ribociclib) and the KISQALI® (ribociclib) FEMARA® (letrozole) Co-Pack have been shown to prolong the QT interval in a concentration-dependent manner. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation. Across clinical trials in patients with advanced or metastatic breast cancer treated with KISQALI in combination with an aromatase inhibitor or fulvestrant (“KISQALI treatment groups”), 14 of 1054 patients (1%) had a postbaseline QTcF value, and 59 of 1054 (6%) had a 60 ms increase from baseline in QTcF intervals. These ECG changes were reversible with dose interruption and most occurred within the first 4 weeks of treatment. No cases of torsades de pointes were reported. In MONALEESA-2, on the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-7 or MONALEESA-3.

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- Fulvestrant 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.

**Prescribe the KISQALI FEMARA Co-Pack with 1 prescription**

- For premenopausal patients, write a separate prescription for each drug. Please see accompanying full Prescribing Information for KISQALI and full Prescribing Information for FEMARA.

**KISQALI FEMARA Co-Pack**

- One free treatment cycle of the KISQALI FEMARA Co-Pack is available for patients with a valid prescription for the KISQALI. One free treatment cycle of FEMARA is available for patients with a valid prescription for FEMARA (including generic letrozole), including for patients who have not been prescribed KISQALI or another Novartis product.

**Access to the KISQALI FEMARA Co-Pack**

- Your patients are eligible to receive a 1-treatment-cycle supply of KISQALI, FEMARA, the KISQALI FEMARA Co-Pack, and/or generic letrozole at no cost.†

**Prescription Writing**

- For convenient prescription writing, the KISQALI FEMARA Co-Pack is indicated as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)+/HER2- breast cancer studies; recruiting; not yet recruiting; ID: XXXXXXXXX

**Package Contains**

- A 28-day supply of both KISQALI® (ribociclib) and FEMARA® (letrozole) in a Co-Pack.

**Important Safety Information**

- These ECG changes were reversible with dose interruption and most occurred within the first 4 weeks of treatment. No cases of torsades de pointes were reported. In MONALEESA-2, on the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-7 or MONALEESA-3.

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- For premenopausal patients, write a separate prescription for each drug. Please see accompanying full Prescribing Information for KISQALI and full Prescribing Information for FEMARA.

**KISQALI FEMARA Co-Pack**

- One free treatment cycle for a rapid start

- Write the prescription as illustrated below and specify the KISQALI dose: 600 mg, 400 mg, or 200 mg

- Prescription for the LHRH agonist of your choice

- For your premenopausal patients, write a separate prescription for KISQALI, FEMARA, the KISQALI FEMARA Co-Pack, and/or generic letrozole, including patients who have not been prescribed KISQALI or another Novartis product.

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