QT prolongation and ECG testing with KISQALI

PERCEPTIONS & FACTS

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

Indications

KISQALI is indicated for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer (mBC) in combination with:

- an aromatase inhibitor as initial endocrine-based therapy; or
- fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy

IMPORTANT SAFETY INFORMATION

Interstitial lung disease/pneumonitis. Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with KISQALI and other CDK4/6 inhibitors.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, MONALEESA-7), 1.6% of patients had ILD/pneumonitis of any grade, 0.4% had grade 3/4, and 0.1% had a fatal outcome. Additional cases of ILD/pneumonitis have occurred in the postmarketing setting, some resulting in death.

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Learn about the low incidence of QT prolongation with KISQALI—and the easy way to help your patients manage it

Patient portrayal.

- While serious, understanding the facts may help inform your treatment decision
- Cardiotoxicity is one of many important factors in making a treatment decision[1]
- QT prolongation is the only cardiotoxicity reported for KISQALI[1]

Make sure you have all the facts to give your patients the best possible care

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Interstitial lung disease/pneumonitis (continued). Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis, which may include hypoxia, cough, and dyspnea. In patients who have new or worsening respiratory symptoms suspected to be due to ILD or pneumonitis, interrupt KISQALI immediately and evaluate the patient. Permanently discontinue KISQALI in patients with severe ILD/pneumonitis or any recurrent symptomatic ILD/pneumonitis.

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PERCEPTION #1

QT prolongation is a common problem with KISQALI

Reveal the fact

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Severe cutaneous adverse reactions. Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with KISQALI.

If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Early consultation with a dermatologist is recommended to ensure greater diagnostic accuracy and appropriate management.

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Perception Fact

Perception: QT prolongation is a common problem with KISQALI

FACT: KISQALI has been shown to prolong the QT interval, but incidence was low[1]

IN A POOLED ANALYSIS ACROSS 3 PHASE III TRIALS OF 1054 PRE- AND POSTMENOPAUSAL PATIENTS TREATED WITH KISQALI + AN AI OR FULVESTRANT[1]:

1.4% (15/1054) had a >500 ms postbaseline QTcF value[1]

5.8% (61/1054) experienced a >60 ms increase from baseline in QTcF interval[1]

The average incidence of QTcF >480 ms across all 3 trials was 5.4% for patients taking KISQALI[2-4]

- There were no **reported cases** of torsades de pointes[1]
- KISQALI has been shown to prolong the QT interval in a concentration-dependent manner[1]
- In MONALEESA-2, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation[1]
- Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Severe cutaneous adverse reactions (continued). If SJS, TEN, or DiHS/DRESS is confirmed, permanently discontinue KISQALI. Do not reintroduce KISQALI in patients who have experienced SCARs or other life-threatening cutaneous reactions during KISQALI treatment.

QT interval prolongation. KISQALI has been shown to prolong the QT interval in a concentration-dependent manner.

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PERCEPTION #2

Severe QT prolongation with KISQALI is very common

Reveal the fact

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Avoid KISQALI in patients who are at significant risk of developing torsades de pointes (TdP), including those with:

- congenital long QT syndrome;
- uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism;
- electrolyte abnormalities;
- taking drugs known to prolong QT interval and/or strong CYP3A inhibitors as this may lead to prolongation of the QTcF interval.

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Perception: Severe QT prolongation with KISQALI is very common

FACT: Among patients who experienced QT prolongation, the incidence of severe cases was low

Incidence of severe QT prolongation in patients receiving KISQALI[2-4]

	>500 ms postbaseline QTcF value	>60 ms increase from baseline in QTcF intervals
MONALEESA-2: KISQALI + AI in 1L postmenopausal patients	<1% (2/334)	3% (10/334)
MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients	2% (8/483)	6% (31/483)
MONALEESA-7: KISQALI + AI in 1L premenopausal patients	NOT REPORTED	7% (18/245)

In MONALEESA-2, in the KISQALI + AI treatment arm, there was 1 (0.3%) case of sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-3 or MONALEESA-7.[1]

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, and MONALEESA-7) who received 600 mg KISQALI plus NSAI or fulvestrant, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >60 ms QTcF increase from baseline. QTcF prolongation was reversible with dose interruption. The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI. There were no reported cases of torsades de pointes. In MONALEESA-2, in 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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PERCEPTION #3

QT prolongation with KISQALI is irreversible

Reveal the fact

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Perform electrocardiogram (ECG) in all patients prior to starting KISQALI. Initiate treatment with KISQALI only in patients with QTcF values <450 ms. Repeat ECG at approximately Day 14 of the first cycle and as clinically indicated.

Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of KISQALI, at the beginning of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI.

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Perception: QT prolongation with KISQALI is irreversible

FACT: ECG changes in patients were manageable and reversible with dose interruption and reduction

Dose modification and management for QT prolongation[1]

QTcF prolongation >480 ms and ≤500 ms	Interrupt treatment until recovery to <481 ms; resume at next lower dose level • If QTcF ≥481 ms reoccurs, interrupt dose until recovery; resume at next lower dose level
QTcF prolongation >500 ms	Interrupt treatment until recovery to <481 ms; resume at next lower dose level • If QTcF >500 ms reoccurs, discontinue KISQALI • Permanently discontinue KISQALI if QTcF interval prolongation is either >500 ms or >60 ms change from baseline AND associated with torsades de pointes, polymorphic ventricular tachycardia, syncope, or signs/symptoms of serious arrhythmia

In case of QTcF prolongation at any given time during treatment, more frequent ECG monitoring is recommended.[1]

The majority of QTcF prolongation occurred within the first four weeks of KISQALI treatment.

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Increased QT prolongation with concomitant use of tamoxifen. KISQALI is not indicated for concomitant use with tamoxifen. Avoid use of tamoxifen with KISQALI. In MONALEESA-7, the observed mean QTcF increase from baseline was >10 ms higher in the tamoxifen + placebo subgroup compared with the nonsteroidal aromatase inhibitor (NSAI) + placebo subgroup. In the placebo arm, an increase of >60 ms from baseline occurred in 6/90 (7%) of patients receiving tamoxifen, and in no patients receiving an NSAI. An increase of >60 ms from baseline in the QTcF interval was observed in 14/87 (16%) of patients in the KISQALI and tamoxifen combination and in 18/245 (7%) of patients receiving KISQALI plus an NSAI.

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PERCEPTION #4

ECG testing must continue for the duration of therapy and is an added complication

Reveal the fact

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity. In patients with advanced or mBC, drug-induced liver injury and increases in transaminases occurred with KISQALI.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) treated with KISQALI, grade 3 or 4 increases in ALT and AST occurred in 11% and 8%, respectively. Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 92 days for the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. The median time to resolution to grade ≤2 was 21 days in the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST >3x the ULN and total bilirubin >2x the ULN, with normal alkaline phosphatase, in the absence of cholestasis (Hy's Law) occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI.

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Perception: ECG testing must continue for the duration of therapy and is an added complication

FACT: Testing is straightforward, with 2 ECGs required, both completed within the first 2 weeks of treatment*

ECG changes in patients were manageable and reversible with dose interruption and reduction[1]

Assessment	Baseline	Cycle 1 Day 14
ECG	✓	✓

Monitoring requirements based on a 28-day treatment cycle.
*Additional monitoring may be required as clinically indicated.

KISQALI should only be initiated in patients with QTcF <450 ms. In case of QTcF prolongation during therapy, more frequent assessments are recommended.[1]

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity (continued). Perform liver function tests (LFTs) before initiating KISQALI. Monitor LFTs 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.

Neutropenia. KISQALI causes concentration-dependent neutropenia. In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) who received KISQALI plus NSAI or fulvestrant, 75% had neutropenia, 62% had grade 3/4 decrease in neutrophil count (based on laboratory findings), and 1.7% had febrile neutropenia. The median time to grade ≥2 neutropenia was 17 days. The median time to resolution of grade ≥3 neutropenia to grade <3 was 12 days. Treatment discontinuation due to neutropenia was required in 1% of patients.

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Optimizing patients' cardiovascular health when considering KISQALI

Considerations prior to initiating therapy

Patients may have multifactorial baseline cardiac issues or cardiovascular risk factors that can be managed. If baseline cardiovascular conditions can be managed and patients are not on medications that prolong the QT interval, treatment with KISQALI may be considered where appropriate.[1]

- Avoid KISQALI in patients who are at significant risk of developing Torsades de Pointes (TdP), including those:
  - with congenital long QT syndrome
  - with uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism
  - with electrolyte abnormalities
  - taking drugs known to prolong QT interval and/or strong CYP3A inhibitors as this may lead to prolongation of the QTcF interval
- Perform ECG in all patients prior to starting KISQALI
- KISQALI should only be initiated in patients with QTcF <450 ms
- Monitor serum electrolytes prior to the initiation of treatment, at the beginning of the first 6 cycles, and as clinically indicated. Correct any electrolyte abnormalities prior to treatment

Select drugs that prolong the QT interval

- Avoid using KISQALI with drugs known to prolong the QT interval and/or strong CYP3A inhibitors, as this may lead to prolongation of the QTcF interval[1]
  - Antiarrhythmic medicines (including, but not limited to, amiodarone, disopyramide, procainamide, quinidine, and sotalol)
  - chloroquine
  - clarithromycin
  - methadone
  - ondansetron
  - pimozide
  - halofantrine
  - haloperidol
  - moxifloxacin
  - bepridil
  - grapefruit or grapefruit juice

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia (continued). Perform complete blood count (CBC) before initiating therapy with KISQALI. 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 neutropenia, KISQALI may require dose interruption, reduction, or discontinuation.

Embryo-fetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose.

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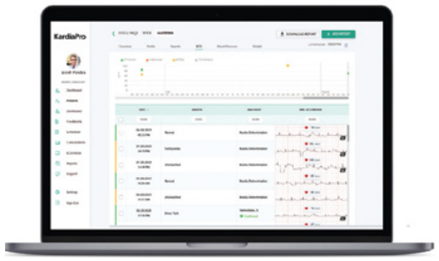
ECG testing made accessible

The KISQALI ECG Device Monitoring Program can provide you with an AliveCor® KardiaMobile 6L ECG device so your patients can receive their ECG testing in seconds in your office or at home.

If you are unable to perform ECGs in-office, contact Novartis Oncology about the ECG Device Monitoring Program.

For in-office readings, use the **KardiaStation Professional app** to record an ECG with the KardiaMobile 6L



Use the **KardiaPro web-based portal** to access QTcF results from in-office and at-home readings

The KardiaStation Professional app is available for download on Android™ and iOS devices.

Limitations apply. KISQALI ECG Device Monitoring Program is only permitted to be used for monitoring or evaluating a patient for the current or potential administration of ribociclib. The equipment or services are not permitted to be used for any purpose outside of the scope of the program. You must not bill any entity or person for any equipment or services relating to the provision or interpretation of the ECG. In the event that you fail to abide by the rules of the KISQALI ECG Device Monitoring Program, your participation in the program may be terminated or modified at any time without prior notice, and you may be subject to additional remedies. Additional terms and conditions apply.

Sunshine Act costs may apply.

Learn more about ECG assessment scheduling to get your patient started on KISQALI ▸

In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen.[1]

IMPORTANT SAFETY INFORMATION (continued)

Adverse reactions. Most common (incidence ≥20%) adverse reactions include infections, nausea, fatigue, diarrhea, vomiting, headache, constipation, alopecia, cough, rash, and back pain.

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, AST increased, gamma-glutamyl transferase increased, ALT increased, creatinine increased, platelets decreased, and glucose serum decreased.**

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Important Safety Information

Indications

KISQALI is indicated for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer (mBC) in combination with:

- an aromatase inhibitor as initial endocrine-based therapy; or
- fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy

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Interstitial lung disease/pneumonitis. Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with KISQALI and other CDK4/6 inhibitors.

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Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis, which may include hypoxia, cough, and dyspnea. In patients who have new or worsening respiratory symptoms suspected to be due to ILD or pneumonitis, interrupt KISQALI immediately and evaluate the patient. Permanently discontinue KISQALI in patients with severe ILD/pneumonitis or any recurrent symptomatic ILD/pneumonitis.

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If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Early consultation with a dermatologist is recommended to ensure greater diagnostic accuracy and appropriate management.

If SJS, TEN, or DiHS/DRESS is confirmed, permanently discontinue KISQALI. Do not reintroduce KISQALI in patients who have experienced SCARs or other life-threatening cutaneous reactions during KISQALI treatment.

QT interval prolongation. KISQALI has been shown to prolong the QT interval in a concentration-dependent manner.

Avoid KISQALI in patients who are at significant risk of developing torsades de pointes (TdP), including those with:

- congenital long QT syndrome;
- uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism;
- electrolyte abnormalities;
- taking drugs known to prolong QT interval and/or strong CYP3A inhibitors as this may lead to prolongation of the QTcF interval.

Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, and MONALEESA-7) who received 600 mg KISQALI plus NSAI or fulvestrant, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >60 ms QTcF increase from baseline. QTcF prolongation was reversible with dose interruption. The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI. There were no reported cases of torsades de pointes. In MONALEESA-2, in 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.

Perform electrocardiogram (ECG) in all patients prior to starting KISQALI. Initiate treatment with KISQALI only in patients with QTcF values <450 ms. Repeat ECG at approximately Day 14 of the first cycle and as clinically indicated.

Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of KISQALI, at the beginning of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI.

Increased QT prolongation with concomitant use of tamoxifen. KISQALI is not indicated for concomitant use with tamoxifen. Avoid use of tamoxifen with KISQALI. In MONALEESA-7, the observed mean QTcF increase from baseline was >10 ms higher in the tamoxifen + placebo subgroup compared with the nonsteroidal aromatase inhibitor (NSAI) + placebo subgroup. In the placebo arm, an increase of >60 ms from baseline occurred in 6/90 (7%) of patients receiving tamoxifen, and in no patients receiving an NSAI. An increase of >60 ms from baseline in the QTcF interval was observed in 14/87 (16%) of patients in the KISQALI and tamoxifen combination and in 18/245 (7%) of patients receiving KISQALI plus an NSAI.

Hepatotoxicity. In patients with advanced or mBC, drug-induced liver injury and increases in transaminases occurred with KISQALI.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) treated with KISQALI, grade 3 or 4 increases in ALT and AST occurred in 11% and 8%, respectively. Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 92 days for the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. The median time to resolution to grade ≤2 was 21 days in the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST >3x the ULN and total bilirubin >2x the ULN, with normal alkaline phosphatase, in the absence of cholestasis (Hy's Law) occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI.

Perform liver function tests (LFTs) before initiating KISQALI. Monitor LFTs 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.

Neutropenia. KISQALI causes concentration-dependent neutropenia. In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) who received KISQALI plus NSAI or fulvestrant, 75% had neutropenia, 62% had grade 3/4 decrease in neutrophil count (based on laboratory findings), and 1.7% had febrile neutropenia. The median time to grade ≥2 neutropenia was 17 days. The median time to resolution of grade ≥3 neutropenia to grade <3 was 12 days. Treatment discontinuation due to neutropenia was required in 1% of patients.

Perform complete blood count (CBC) before initiating therapy with KISQALI. 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 neutropenia, KISQALI may require dose interruption, reduction, or discontinuation.

Embryo-fetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose.

Adverse reactions. Most common (incidence ≥20%) adverse reactions include infections, nausea, fatigue, diarrhea, vomiting, headache, constipation, alopecia, cough, rash, and back pain.

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, AST increased, gamma-glutamyl transferase increased, ALT increased, creatinine increased, platelets decreased, and glucose serum decreased.**

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Abbreviations and references

Abbreviations: 1L=first line; 2L=second line; AI=aromatase inhibitor; CYP3A=cytochrome P450, family 3, subfamily A; ECG=electrocardiogram; QTcF=QT interval corrected by Fridericia's formula.

References: 1. Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. *Ann Oncol.* 2018;29(7):1541-1547. doi:10.1093/annonc/mdy155 **3.** Slamon DJ, Neven P, Chia S, et al. Phase III randomized study of ribociclib and fulvestrant in hormone receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer: MONALEESA-3. *J Clin Oncol.* 2018;36(24):2465-2472. doi:10.1200/JCO.2018.78.9909 **4**. Tripathy D, Im S-A, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomised phase 3 trial. *Lancet Oncol.* 2018;19(7):904-915. doi:10.1016/S1470-2045(18)30292-4

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