

Ribociclib: Drug information

Copyright 1978-2017 Lexicomp, Inc. All rights reserved.

(For additional information [see "Ribociclib: Patient drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

Brand Names: US Kisqali 200 Dose; Kisqali 400 Dose; Kisqali 600 Dose

Pharmacologic Category Antineoplastic Agent, Cyclin-Dependent Kinase Inhibitor

Dosing: Adult

Breast cancer, advanced or metastatic: Females (HR-positive, HER-2 negative): Oral: 600 mg once daily for 21 days, followed by a 7-day rest period to complete a 28-day treatment cycle (in combination with continuous letrozole); continue until disease progression or unacceptable toxicity (Hortobagyi 2016). May also be administered in combination with other aromatase inhibitors.

Missed doses: If a dose is missed or vomited, do not administer an additional dose that day. Resume ribociclib dosing with the next usual dose.

Dosage adjustment for concomitant strong CYP3A inhibitors: Avoid concomitant use with strong CYP3A inhibitors and consider alternatives with less potential for CYP3A inhibition. If coadministration with a strong CYP3A inhibitor cannot be avoided, reduce ribociclib dose to 400 mg once daily. If the strong inhibitor is discontinued, increase ribociclib dose (after at least 5 inhibitor half-lives have elapsed) to the dose used prior to initiating the strong CYP3A inhibitor.

Dosing: Geriatric Refer to adult dosing.

Dosing: Renal Impairment

CrCl 30 to <90 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling; however, based on a pharmacokinetic analysis, exposure was not affected.

CrCl <30 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

Hepatic impairment at baseline:

Mild impairment (Child-Pugh class A): No dosage adjustment necessary.

Moderate or severe impairment (Child-Pugh class B or C): Reduce initial dose to 400 mg/day.

Hepatobiliary toxicity *during* treatment (see Dosing - Adjustment for Toxicity for dose adjustment

levels):

Elevations from baseline **without** total bilirubin increase >2 times the upper limit of normal (ULN):

Grade 1 (ALT and/or AST elevated >1 to 3 times ULN): No dosage adjustment necessary.

Grade 2 (ALT and/or AST elevated >3 to 5 times ULN): If baseline was below grade 2, interrupt treatment until recovery to baseline or lower and then resume ribociclib at the same dose level. For recurrent grade 2 elevations, interrupt treatment until recovery and then resume ribociclib at the next lower dose level. If baseline was at grade 2, no dosage adjustment necessary.

Grade 3 (ALT and/or AST elevated >5 to 20 times ULN): Interrupt treatment until recovery to baseline or lower and then resume ribociclib at the next lower dose level. For recurrent grade 3 elevations, discontinue ribociclib.

Grade 4 (ALT and/or AST elevated >20 times ULN): Discontinue ribociclib.

Combined ALT and/or AST elevations >3 times ULN **with** total bilirubin increase >2 times ULN (in the absence of cholestasis), regardless of baseline grade: Discontinue ribociclib.

Dosing: Adjustment for Toxicity

Recommended ribociclib dosage adjustment levels:

Starting dose: 600 mg/day.

First dose reduction: Reduce to 400 mg/day.

Second dose reduction: Reduce to 200 mg/day.

If further dose reduction below 200 mg/day is needed, discontinue ribociclib.

Note: For dosage adjustment of concomitant aromatase inhibitor therapy refer to monograph and/or prescribing information.

Hematologic toxicity:

Grade 1 or 2 neutropenia (ANC 1,000/mm³ to below the lower limit of normal): No dosage adjustment necessary.

Grade 3 neutropenia (ANC 500 to <1,000/mm³): Interrupt treatment until recovery to grade 2 or lower and then resume ribociclib at the same dose. For recurrent grade 3 neutropenia, interrupt treatment until recovery and then resume ribociclib at the next lower dose level.

Grade 3 neutropenia with neutropenic fever (a single episode of fever >38.3°C or fever above 38°C for more than 1 hour and/or concurrent infection): Interrupt treatment until recovery to grade 2 or lower and then resume ribociclib at the next lower dose level.

Grade 4 neutropenia (ANC <500/mm³): Interrupt treatment until recovery to grade 2 or lower and then resume ribociclib at the next lower dose level.

Nonhematologic toxicity:

Cardiovascular: QT prolongation:

QTcF >480 msec: Interrupt treatment; when QTcF resolves to <481 msec, may resume ribociclib at the same dose level. If QTcF \geq 481 msec recurs, interrupt treatment until QTcF resolves to <481 msec and resume ribociclib at the next lower dose level.

QTcF >500 msec: Interrupt treatment for QTcF >500 msec on at least 2 separate ECGs (within the same visit); if QTcF resolves to <481 msec, may resume ribociclib at the next lower dose level. If QTcF interval prolongation is **either** >500 msec **or** >60 msec increase from baseline **AND** associated with torsades de pointes, polymorphic ventricular tachycardia, unexplained syncope, or signs/symptoms of serious arrhythmia, permanently discontinue ribociclib.

Other nonhematologic toxicities (based on Common Toxicity Criteria for Adverse Events Version 4):

Grade 1 or 2: No dosage adjustment necessary. Initiate appropriate medical management and monitoring as indicated.

Grade 3: Interrupt treatment until recovery to grade 1 or lower and then resume ribociclib at the same dose level. If grade 3 toxicity recurs, interrupt treatment until recovery to grade 1 or lower and then resume ribociclib at the next lower dose level.

Grade 4: Discontinue ribociclib.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral:

Kisqali 200 Dose: 200 mg (21s) [contains soybean lecithin]

Kisqali 400 Dose: 200 mg (42s) [contains soybean lecithin]

Kisqali 600 Dose: 200 mg (63s) [contains soybean lecithin]

Generic Equivalent Available (US) No

Administration Oral: May be administered with or without food. Administer at approximately the same time each day (and at the same time as letrozole [or other aromatase inhibitor]), preferably in the morning. Swallow tablets whole; do not crush, chew, or split tablets (do not ingest broken or cracked tablets).

Hazardous Drugs Handling Considerations

Hazardous agent (meets NIOSH 2016 criteria). This medication is not on the NIOSH (2016) list; however, it meets the criteria for a hazardous drug. Drugs are classified as hazardous based on their properties; the properties of a hazardous drug include one or more of the following characteristics: carcinogenic, teratogenic (or other developmental toxicity), reproductive toxicity, organotoxic at low doses, genotoxic, and/or new agents with structural or toxicity profiles similar to existing hazardous agents.

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules (NIOSH 2016).

Use Breast cancer, advanced or metastatic: Treatment of hormone receptor (HR)-positive, human

epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer (in combination with an aromatase inhibitor) in postmenopausal women as initial endocrine-based therapy.

Medication Safety Issues

Sound-alike/look-alike issues:

Ribociclib may be confused with palbociclib, ribavirin, riboflavin

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its lists of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Cardiovascular: Peripheral edema (12%)

Central nervous system: Fatigue (37%), headache (22%), insomnia (12%)

Dermatologic: Alopecia (33%), skin rash (17%), pruritus (14%)

Endocrine & metabolic: Decreased serum potassium (11%)

Gastrointestinal: Nausea (52%), diarrhea (35%), vomiting (29%), constipation (25%), decreased appetite (19%), stomatitis (12%), abdominal pain (11%)

Genitourinary: Urinary tract infection (11%)

Hematologic & oncologic: Neutropenia (75%; grade 3: 50%; grade 4: 10%), leukopenia (33%; grade 3: 20%; grade 4: 1%), decreased platelet count (29%; grade 3: 1%), anemia (18%; grade 4: <1%), abnormal phosphorus levels (decreased; 13%; grade 3: 5%; grade 4: 1%), lymphocytopenia (11%; grade 3: 6%; grade 4: 1%)

Hepatic: Increased serum ALT (\leq 46%), increased serum AST (\leq 44%), increased serum bilirubin (\leq 18%)

Neuromuscular & skeletal: Back pain (20%)

Renal: Increased serum creatinine (20%)

Respiratory: Dyspnea (12%)

Miscellaneous: Fever (13%)

1% to 10%:

Cardiovascular: Prolonged Q-T interval on ECG (3%), syncope (3%)

Hematologic & oncologic: Febrile neutropenia (2%)

Hepatic: Decreased serum bilirubin ($\leq 1\%$)

Contraindications There are no contraindications listed in the manufacturer's labeling.

Warnings/Precautions

Concerns related to adverse effects:

- Bone marrow suppression: Neutropenia commonly occurs, including grades 3 and 4 neutropenia. The median time to onset for grade 2 or higher neutropenia was 16 days. The median recovery for grade 3 or higher neutropenia was 15 days (resolution to normal levels or to less than grade 3 toxicity). Neutropenic fever has been observed. Monitor blood counts (baseline, every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles and as clinically necessary). Neutropenia may require treatment interruption, dose reduction and/or discontinuation (depending on the severity). Anemia, thrombocytopenia, and lymphopenia have also been observed.
- Hepatobiliary toxicity: ALT and/or AST elevations have been observed, including grade 3 or 4 events. The median time to onset for grade 3 or higher transaminase elevations was 57 days; the median time for grade 3 or higher elevations to resolve to grade 2 or lower was 24 days. Concurrent elevation of ALT or AST >3 times ULN and total bilirubin >2 times ULN (with normal alkaline phosphatase and in the absence of cholestasis) occurred (rare); all cases resolved following ribociclib discontinuation. Monitor liver function tests (baseline, every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles and as clinically necessary). Depending on the severity, hepatobiliary toxicity may require treatment interruption, dose reduction and/or discontinuation.
- QT prolongation: Ribociclib is associated with concentration-dependent QT prolongation, with an estimated mean increase in the QT interval exceeding 20 msec at the mean steady-state C_{max} of a 600 mg once daily dose. QTcF interval prolongation >500 msec has been observed, as well as QTcF prolongations >60 msec from baseline. QT interval changes occurred within the initial 4 weeks of ribociclib therapy and were reversible with treatment interruption. Torsades de pointes has not been reported, although syncope occurred in a small percentage of patients. One sudden death was reported in a patient with grade 3 hypokalemia and grade 2 QT prolongation who was receiving ribociclib in combination with letrozole. Evaluate ECG prior to treatment initiation. Initiate treatment only in patients with QTcF <450 msec. Repeat ECG on day 14 of cycle 1, at the beginning of cycle 2, and as clinically indicated. Monitor serum electrolytes (including potassium, magnesium, calcium, and phosphorous) prior to treatment, at the beginning of the first 6 cycles, and as clinically indicated. Correct electrolyte abnormality prior to treatment. QT prolongation may require treatment interruption, dose reduction and/or discontinuation. Avoid ribociclib use in patients who have or are at risk for developing QTc prolongation, including patients with long QT syndrome, uncontrolled or significant cardiac disease (eg, recent MI, HF, unstable angina, bradyarrhythmias), or electrolyte abnormalities. Also avoid using ribociclib with medications known to prolong the QTc interval and/or strong CYP3A inhibitors (may prolong the QTcF interval).

Disease-related concerns:

- Hepatic impairment: Reduced initial doses are recommended for moderate to severe impairment.

Concurrent drug therapy issues:

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency

adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Metabolism/Transport Effects Substrate of CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Inhibits** CYP3A4 (moderate)

Drug Interactions

(For additional information: [Launch drug interactions program](#)) Lexicomp®

AmLODIPine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of AmLODIPine. *Risk C: Monitor therapy*

Apixaban: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Apixaban. *Risk C: Monitor therapy*

Aprepitant: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Aprepitant. *Risk X: Avoid combination*

Asunaprevir: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Asunaprevir. *Risk X: Avoid combination*

Avanafil: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Avanafil. Management: The maximum avanafil adult dose is 50 mg per 24-hour period when used together with a moderate CYP3A4 inhibitor. Patients receiving such a combination should also be monitored more closely for evidence of adverse effects. *Risk D: Consider therapy modification*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bilastine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Blonanserin: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Blonanserin. *Risk C: Monitor therapy*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Bosentan: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Bosentan. Management: Concomitant use of both a CYP2C9 inhibitor and a CYP3A inhibitor or a single agent that inhibits both enzymes with bosentan is likely to cause a large increase in serum concentrations of bosentan and is not recommended. See monograph for details. *Risk C: Monitor therapy*

Bosutinib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Bosutinib. *Risk X: Avoid combination*

Brexpiprazole: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Brexpiprazole. Management: The brexpiprazole dose should be reduced to 25% of usual if used together with both a moderate CYP3A4 inhibitor and a strong or moderate CYP2D6 inhibitor, or if a moderate CYP3A4 inhibitor is used in a CYP2D6 poor metabolizer. *Risk C: Monitor therapy*

Bromocriptine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Bromocriptine. Management: The bromocriptine dose should not exceed 1.6 mg daily with use of a moderate CYP3A4 inhibitor. The Cycloset brand specifically recommends this dose limitation, but other bromocriptine products do not make such specific recommendations. *Risk D: Consider therapy modification*

Budesonide (Systemic): CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Budesonide (Systemic). *Risk X: Avoid combination*

Budesonide (Topical): CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Budesonide (Topical). Management: Per US prescribing information, avoid this combination. Canadian product labeling does not recommend strict avoidance. If combined, monitor for excessive glucocorticoid effects as budesonide exposure may be increased. *Risk D: Consider therapy modification*

Buprenorphine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Cannabis: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Cannabis. More specifically, tetrahydrocannabinol and cannabidiol serum concentrations may be increased. *Risk C: Monitor therapy*

Cilostazol: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Cilostazol. Management: Consider reducing the cilostazol dose to 50 mg twice daily in adult patients who are also receiving moderate inhibitors of CYP3A4. *Risk D: Consider therapy modification*

Cobimetinib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Cobimetinib. Management: Avoid the concomitant use of cobimetinib and moderate CYP3A4 inhibitors. If concurrent short term (14 days or less) use cannot be avoided, reduce the cobimetinib dose to 20 mg daily. *Risk X: Avoid combination*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Colchicine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Colchicine. Management: Reduce colchicine dose as directed when using with a moderate CYP3A4 inhibitor, and increase monitoring for colchicine-related toxicity. Use extra caution in patients with impaired renal and/or hepatic function. *Risk D: Consider therapy modification*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Ribociclib. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Ribociclib. Management: Avoid use of ribociclib with strong CYP3A4 inhibitors when possible; if combined use cannot be avoided, reduce ribociclib dose to 400 mg once daily. *Risk D: Consider therapy modification*

CYP3A4 Substrates: CYP3A4 Inhibitors (Moderate) may decrease the metabolism of CYP3A4

Substrates. **Exceptions:** Alitretinoin (Systemic); Praziquantel; Vinorelbine. *Risk C: Monitor therapy*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dapoxetine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Dapoxetine. Management: The dose of dapoxetine should be limited to 30 mg/day when used together with a moderate inhibitor of CYP3A4. *Risk D: Consider therapy modification*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Deflazacort: CYP3A4 Inhibitors (Moderate) may increase serum concentrations of the active metabolite(s) of Deflazacort. Management: Administer one third of the recommended deflazacort dose when used together with a strong or moderate CYP3A4 inhibitor. *Risk D: Consider therapy modification*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyron: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Domperidone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Domperidone. *Risk X: Avoid combination*

DOXOrubicin (Conventional): CYP3A4 Inhibitors (Moderate) may increase the serum concentration of DOXOrubicin (Conventional). Management: Seek alternatives to moderate CYP3A4 inhibitors in patients treated with doxorubicin whenever possible. One U.S. manufacturer (Pfizer Inc.) recommends that these combinations be avoided. *Risk D: Consider therapy modification*

Dronabinol: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Dronabinol. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Eletriptan: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Eletriptan. Management: The use of eletriptan within 72 hours of a moderate CYP3A4 inhibitor should be avoided. *Risk D: Consider therapy modification*

Eplerenone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Eplerenone. Management: When used concomitantly with moderate inhibitors of CYP3A4, eplerenone dosing recommendations vary by indication and international labeling. See full drug interaction monograph for details. *Risk D: Consider therapy modification*

Everolimus: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Everolimus. Management: Everolimus dose reductions are required for patients being treated for subependymal giant cell astrocytoma or renal cell carcinoma. See prescribing information for specific dose adjustment and monitoring recommendations. *Risk D: Consider therapy modification*

FentaNYL: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of FentaNYL. Management: Monitor patients closely for several days following initiation of this combination, and adjust fentanyl dose as necessary. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Flibanserin: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Flibanserin. *Risk X: Avoid combination*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Grapefruit Juice: May increase the serum concentration of Ribociclib. *Risk X: Avoid combination*

GuanFACINE: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of GuanFACINE. Management: Reduce the guanfacine dose by 50% when initiating this combination. *Risk D: Consider therapy modification*

Highest Risk QTc-Prolonging Agents: May enhance the QTc-prolonging effect of other Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

HYDROcodone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of HYDROcodone. *Risk C: Monitor therapy*

Hydroxychloroquine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

HydrOXYzine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of HydrOXYzine. Management: This combination is specifically contraindicated in some non-U.S. labeling. *Risk D: Consider therapy modification*

Ibrutinib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ibrutinib. Management: If a moderate CYP3A inhibitor must be used, consider reducing the dose of ibrutinib to 140mg daily and monitor closely for signs of toxicity. *Risk X: Avoid combination*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Ifosfamide: CYP3A4 Inhibitors (Moderate) may decrease serum concentrations of the active metabolite(s) of Ifosfamide. *Risk C: Monitor therapy*

Imatinib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Imatinib. *Risk C: Monitor therapy*

Indapamide: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk D: Consider therapy modification*

Ivabradine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ivabradine. *Risk X: Avoid combination*

Ivabradine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

Ivacaftor: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ivacaftor. Management: Ivacaftor dose reductions are required; consult full monograph content for specific age- and weight-based recommendations. No dose adjustment is needed when using ivacaftor/lumacaftor with a moderate CYP3A4 inhibitor. *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lomitapide: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Lomitapide. *Risk X: Avoid combination*

Lurasidone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Lurasidone. Management: Lurasidone US labeling recommends reducing lurasidone dose by half with a moderate CYP3A4 inhibitor. Some non-US labeling recommends initiating lurasidone at 20 mg/day and limiting dose to 40 mg/day; avoid concurrent use of grapefruit products. *Risk D: Consider therapy modification*

Manidipine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Manidipine. *Risk C: Monitor therapy*

MiFEPRIStone: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

Mirodenafil: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Mirodenafil. *Risk C: Monitor therapy*

Moderate Risk QTc-Prolonging Agents: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

Naldemedine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Naldemedine. *Risk C: Monitor therapy*

Naloxegol: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Naloxegol. *Risk X: Avoid combination*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

NiMODipine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of NiMODipine. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Olaparib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Olaparib.
Management: Avoid use of moderate CYP3A4 inhibitors in patients being treated with olaparib. If such concurrent use cannot be avoided, the dose of olaparib should be reduced to 200 mg twice daily. *Risk X: Avoid combination*

OxyCODONE: CYP3A4 Inhibitors (Moderate) may enhance the adverse/toxic effect of OxyCODONE. CYP3A4 Inhibitors (Moderate) may increase the serum concentration of OxyCODONE. Serum concentrations of the active metabolite Oxymorphone may also be increased. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Pimozide: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Pimozide. *Risk X: Avoid combination*

Pomegranate: May increase the serum concentration of Ribociclib. *Risk X: Avoid combination*

Probucol: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

Promazine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying): May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

Ranolazine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ranolazine.
Management: Limit the ranolazine adult dose to a maximum of 500 mg twice daily in patients concurrently receiving moderate CYP3A4 inhibitors (e.g., diltiazem, verapamil, erythromycin, etc.). *Risk D: Consider therapy modification*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Rupatadine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Rupatadine. *Risk C: Monitor therapy*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

SAXagliptin: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of SAXagliptin. *Risk C: Monitor therapy*

Sildenafil: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Sildenafil. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Simeprevir. *Risk X: Avoid combination*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor*

therapy

Sonidegib: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Sonidegib.

Management: Avoid concomitant use of sonidegib and moderate CYP3A4 inhibitors when possible. When concomitant use cannot be avoided, limit CYP3A4 inhibitor use to less than 14 days and monitor for sonidegib toxicity (particularly musculoskeletal adverse reactions). *Risk D: Consider therapy modification*

St John's Wort: May decrease the serum concentration of Ribociclib. *Risk X: Avoid combination*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Suvorexant: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Suvorexant. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Teneligliptin: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tetrahydrocannabinol: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Tetrahydrocannabinol. *Risk C: Monitor therapy*

Ticagrelor: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ticagrelor. *Risk C: Monitor therapy*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Tolvaptan: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Tolvaptan. *Risk X: Avoid combination*

Trabectedin: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Trabectedin. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Udenafil: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Udenafil. *Risk C: Monitor therapy*

Ulipristal: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Ulipristal. Management: This is specific for when ulipristal is being used for signs/symptoms of uterine fibroids (Canadian indication). When ulipristal is used as an emergency contraceptive, patients receiving this

combination should be monitored for ulipristal toxicity. *Risk X: Avoid combination*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Venetoclax: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Venetoclax. Management: Reduce the venetoclax dose by at least 50% in patients requiring these combinations. *Risk D: Consider therapy modification*

Vilazodone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Vilazodone. *Risk C: Monitor therapy*

Vindesine: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Vindesine. *Risk C: Monitor therapy*

Vinflunine: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk X: Avoid combination*

Xipamide: May enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Zopiclone: CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Zopiclone. Management: The starting adult dose of zopiclone should not exceed 3.75 mg if combined with a moderate CYP3A4 inhibitor. Monitor patients for signs and symptoms of zopiclone toxicity if these agents are combined. *Risk D: Consider therapy modification*

Food Interactions

Food: A high-fat, high-calorie meal does not affect the rate or extent of ribociclib absorption.

Pomegranates, pomegranate juice, and grapefruits may inhibit the metabolism of ribociclib and increase its systemic exposure. Management: Avoid pomegranate, pomegranate juice, and grapefruits during therapy.

Pregnancy Implications Adverse events were observed in animal reproduction studies. Based on the mechanism of action, ribociclib may be expected to cause fetal harm if used during pregnancy. Women of reproductive potential should have a pregnancy test prior to treatment and use effective contraception during treatment and for at least 3 weeks after the last dose. Although not approved for use in men, animal data suggests that ribociclib may affect male fertility.

Breast-Feeding Considerations It is not known if ribociclib is present in breast milk. Due to the potential for adverse events in the breastfed infant, the manufacturer does not recommend breastfeeding during therapy or for at least 3 weeks after the last dose.

Dietary Considerations Avoid pomegranate, pomegranate juice, and grapefruits.

Monitoring Parameters May be administered with or without food. Take at approximately the same time each day (and at the same time as letrozole), preferably in the morning. Swallow tablets whole, do not crush, chew, or split tablets (do not ingest broken or cracked tablets).

Mechanism of Action Ribociclib is a small molecule cyclin-dependent kinase (CDK) inhibitor which is selective for CDK 4 and 6; it blocks retinoblastoma protein phosphorylation and prevents progression through the cell cycle, resulting in arrest at the G1 phase (Hortobagyi 2016). The combination of ribociclib and an aromatase inhibitor causes increased inhibition of tumor growth compared with each agent alone.

Pharmacodynamics/Kinetics

Distribution: V_{ss}/F : 1,090 L

Protein binding: ~70%

Metabolism: Extensively hepatic, predominantly via CYP3A4; undergoes oxidation to circulating metabolites M13, M4, and M1, although clinical activity is primarily due to the parent drug.

Half-life elimination; Terminal: ~30 to 55 hours

Time to peak: 1 to 4 hours

Excretion: Feces (69%; 17% as parent drug, 14% as metabolite M1, ≤3% as other metabolites); Urine (23%; 12% as parent drug, 4% as M1, ≤3% as other metabolites)

Pricing: US

Tablets (Kisqali 200 Dose Oral)

200 mg (21): \$5256.00

Tablets (Kisqali 400 Dose Oral)

200 mg (42): \$10512.00

Tablets (Kisqali 600 Dose Oral)

200 mg (63): \$13140.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

Use of UpToDate is subject to the [Subscription and License Agreement](#).

REFERENCES

1. Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. *N Engl J Med*. 2016;375(18):1738-1748. [PubMed 27717303]

2. *Kasqali (ribociclib) [prescribing information]*. East Hanover, NJ: Novartis Pharmaceuticals; March 2017.
3. US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed March 15, 2017.
4. US Department of Health and Human Services (NIH/NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_40_conversion. Last accessed March 2017.

Topic 112288 Version 11.0