Drug Monograph

A - Drug Name

ribociclib

COMMON TRADE NAME(S): Kisqali™

back to top

B - Mechanism of Action and Pharmacokinetics

Ribociclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6. The cyclin D-CDK4/6 complex regulates cell cycle progression through phosphorylation of the retinoblastoma protein (pRb). Inhibition of pRb phosphorylation arrests the cell cycle in the G1 phase, suppressing DNA synthesis and inhibiting cancer cell growth.

Absorption	Effects with food	No clinically significant effect on Cmax and AUC when administered with a high-fat, high-calorie meal
	Peak plasma levels	1 to 4 hours
	Time to reach steady state	8 days
	Bioavailability	66% (after a single dose)
Distribution	PPB	70%
	Distribution Sites	Equally distributed between red blood cells and plasma
	Cross blood brain barrier?	Relatively low brain penetration observed in animals with intact blood brain barriers.

Metabolism	• Ribociclib undergoes extensive hepatic metabolism mainly via CYP3A4. • No major metabolite was considered to have clinically relevant contribution to efficacy and safety.	
	Active metabolites	No
	Inactive metabolites	Yes
Elimination	Ribociclib is eliminated mainly via the feces, with a small contribution from the renal route.	
	Half-life	32 hours
	Feces	69% (total dose); 17% unchanged
	Urine	23% (total dose); 12% unchanged

back to top

C - Indications and Status

Health Canada Approvals:

- Breast cancer

Refer to the product monograph for a full list and details of approved indications.

back to top

D - Adverse Effects

Emetogenic Potential: Minimal – No routine prophylaxis; PRN recommended

The adverse effects reported below were based on a phase III study of postmenopausal women with breast cancer, receiving ribociclib plus letrozole or placebo plus letrozole, where the incidence was ≥ 2% more than placebo. Severe or life-threatening adverse effects from other sources and post-marketing are also included.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	QT interval prolonged (5%) (1% severe)	E
	Venous thromboembolism (4%) (may be severe)	E
Dermatological	Alopecia (35%)	E
	Rash, pruritus (24%) (may be severe)	I E
	Toxic epidermal necrolysis (rare)	E
Gastrointestinal	Abdominal pain (21%)	E
	Anorexia, weight loss (22%)	E
	Constipation (30%)	E
	Diarrhea (41%) (2% severe)	E
	Dry mouth (14%)	E
	Dyspepsia (11%)	I E
	Mucositis (16%)	E
	Nausea, vomiting (55%) (3% severe)	I
General	Edema - limbs (19%)	E
	Fatigue (43%)	E
Hematological	Myelosuppression ± infection, bleeding (77%) (64% severe)	E
Hepatobiliary	↑ LFTs (23%) (12% severe; <1% hepatotoxicity)	D
Metabolic / Endocrine	Abnormal electrolyte(s) (5%) (↓ Ca, ↓ K, ↓ PO4; 4% severe)	E
Musculoskeletal	Musculoskeletal pain (27%)	E
Nervous System	Dysgeusia (10%)	E
	Headache (29%)	E
	Insomnia (17%)	E
	Syncope (2%)	E
Ophthalmic	Dry eye (6%)	E
	Watering eyes (12%)	E
Renal	Creatinine increased (11%) (< 1% severe)	E
Respiratory	Dyspnea (16%)	E
	Pneumonitis (rare) (may be severe)	E D

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for ribociclib include myelosuppression ± infection, bleeding, nausea, vomiting, fatigue, diarrhea, alopecia, constipation, headache, musculoskeletal pain, rash, pruritus, and ↑ LFTs.

Neutropenia was the most frequently reported side effect in patients treated with ribociclib plus any combination. The median time to onset for Grade ≥ 2 neutropenia was 17 days, while the median time to resolution to Grade < 3 was 12 days.

Drug induced liver injury [ALT or AST > 3 x upper limit of normal (ULN) and total bilirubin > 2 x ULN, without cholestasis] or **Hy's Law** has been reported with ribociclib combination therapy. In patients treated with ribociclib plus letrozole or fulvestrant, recovery to normal levels occurred within 154 days or within 121 to 532 days, respectively, after ribociclib discontinuation.

Median time to onset of **QTcF** > 480 msec was 15 days regardless of combination and these changes were reversible upon withholding the dose or modification. QTc prolongation is expected to be maximal between days 8 to 21 of the 28-day cycle during steady state treatment.

back to top

E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Hypokalemia, hypomagnesemia and hypocalcemia should be corrected prior to starting or continuing ribociclib.

Ribociclib should be started only in patients with QTcF < 450 msec.

Pre/perimenopausal women, and men, treated with ribociclib and an aromatase inhibitor or fulvestrant should also be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to local clinical practice.

Adults:

Advanced or Metastatic Breast Cancer:

Oral: 600 mg/day on Days 1 to 21, followed by 7 days off treatment, in 28-day cycles

In combination with an aromatase inhibitor (e.g., letrozole) or fulvestrant. Refer to regimen monographs for dosing details.

Early Breast Cancer:

Refer to the product monograph for details.

Dosage with Toxicity:

Advanced or Metastatic Breast Cancer:

Dose Level	Ribociclib Dose (mg/day) (21 days on, 7 days off)
0	600
-1	400
-2	200
-3	Discontinue

Toxicity	Severity		Ribociclib Dose
Neutropenia	Grade 3 (ANC 0.5 to <1 x 10^9/L)		Hold dose until ANC ≥ 1 x 10^9/L, then restart at the same dose level. If recurs, hold dose until ANC ≥ 1 x 10^9/L, then restart with 1 dose level ↓.
	Grade 4 (ANC <0.5 x 10^9/L) or febrile neutropenia		Hold dose until ANC ≥ 1 x 10^9/L, then restart with 1 dose level ↓.
QTcF	> 480 msec		Hold dose until QTcF resolves to ≤ 480 msec, then restart with 1 dose level ↓. If recurs, hold dose until QTcF resolves to ≤ 480 msec, then restart with 1 dose level ↓.
	> 500 msec		Hold dose until QTcF resolves to ≤ 480 msec, then restart with 1 dose level ↓.
Torsade de Pointes, or polymorphic ventricular tachycardia, unexplained syncope or Signs/symptoms of serious arrhythmia	Any		Discontinue.
Bilirubin ≤ 2 x ULN	and	AST and/or ALT >3 to 5 x ULN (Grade 2)	If Baseline Grade 2: continue at current dose. If Baseline Grade 0-1: hold dose until ≤ baseline, then restart at the same dose. If recurs, hold dose until ≤ baseline, then restart with 1 dose level ↓.
	and	AST and/or ALT >5 to 20 x ULN (Grade 3)	Hold dose until ≤ baseline, then restart with 1 dose level ↓. If recurs, discontinue.

	and	AST and/or ALT >20 x ULN (Grade 4)	Discontinue.
Bilirubin > 2 x ULN, in the absence of cholestasis	and	AST and/or ALT >3 x ULN (Grade ≥ 2) irrespective of baseline	Discontinue.
Interstitial lung disease (ILD)/pneumonitis	Grade 2 (symptomatic)		Hold dose until recovery to Grade ≤ 1, then restart with 1 dose level ↓.
	Grade 3 or 4		Discontinue.
Severe cutaneous reactions (e.g. progressive widespread skin rash often with blisters or mucosal lesions)	Any		Discontinue.
Other related toxicity	Grade 3		Hold dose until Grade ≤ 1, then restart at same dose. If recurs, hold dose until Grade ≤ 1, then restart with 1 dose level ↓.
	Grade 4		Discontinue.

Dosage with Hepatic Impairment:

Ribociclib has not been studied in patients with moderate or severe hepatic impairment (ALT or AST ≥ 5 x ULN or total serum bilirubin ≥ ULN [except documented Gilbert's syndrome]).

Advanced or Metastatic Breast Cancer:

Hepatic Impairment	Ribociclib Starting Dose
Mild (Child-Pugh class A)	No dose adjustment recommended
Moderate (Child-Pugh class B)	400 mg once daily; initiate treatment only if benefit outweighs risk
Severe (Child-Pugh class C)	400 mg once daily; initiate treatment only if benefit outweighs risk

Dosage with Renal Impairment:

Advanced or Metastatic Breast Cancer:

Creatinine Clearance†	Ribociclib Starting Dose
≥ 30	No dose adjustment recommended.
15 to < 30	200 mg daily*; initiate treatment only if benefit outweighs risk.
< 15	No data available.

†Reported as eGFR (mL/min/1.73m^2)

*No data in breast cancer patients; data from healthy or non-cancer patients with severe renal impairment.

Dosage in the elderly:

No adjustment of the starting dose is required. No overall difference in safety was observed between patients over 65 years of age and younger patients.

Dosage based on gender:

No clinically relevant effects of gender on ribociclib pharmacokinetics parameters.

Dosage based on ethnicity:

No clinically relevant effects of race on ribociclib pharmacokinetics parameters.

Children:

The safety and efficacy of ribociclib in pediatric patients have not been established.

back to top

F - Administration Guidelines

- Administer ribociclib with or without food, approximately at the same time each day, preferably in the morning.
- Tablets should be swallowed whole and not chewed, crushed or split prior to swallowing. Tablets that are broken, cracked, or otherwise not intact should not be ingested.
- If the patient vomits after taking ribociclib, do not give an extra dose; give the next dose at the usual time.
- If a dose is missed, it should be skipped and the next dose given at the usual time, the next day. Patients should not take extra doses to make up for a missed dose.
- Grapefruit, starfruit, Seville oranges, their juices or products should be avoided during ribociclib treatment.
- **Confirm the storage information that is listed on the product packaging.** There is a new ribociclib supply that requires storage in a refrigerator between 2-8°C. Once dispensed, patients should store ribociclib between 20-25°C for up to 2 months. Keep in the original package to protect from moisture.

back to top

G - Special Precautions

Contraindications:

- Patients with hypersensitivity to this drug or to any ingredient in the formulation.
- Patients with untreated congenital long QT syndrome, a QTcF interval of ≥ 450 msec at baseline, and those who are at significant risk of developing QTc prolongation (for example, uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina and bradyarrhythmia).

Other Warnings/Precautions:

- Ribociclib is associated with concentration-dependent QTc prolongation, with expected maximal QTc prolongation during steady state treatment between days 8 and 21 of the 28-day cycle.
- Exercise caution in patients who are suspected to be at an increased risk of Torsades de Pointes during treatment with a QT-prolonging drug.
- Avoid use in patients with uncorrected hypokalemia, hypomagnesemia, or hypocalcemia and other risk factors.
- Use in caution in patients at risk of thromboembolic events.
- Patients should exercise caution when driving or operating machinery due to syncope.

Other Drug Properties:

- Carcinogenicity: Unknown
- Phototoxicity: Unlikely

Pregnancy and Lactation:

- Genotoxicity: No
- Embryotoxicity: Documented in animals
- Fetotoxicity: Documented in animals
- Teratogenicity: Documented in animals
- Pregnancy:
  Ribociclib is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **21 days** after the last dose.
- Excretion into breast milk: Documented in animals
- Breastfeeding:
  Breastfeeding is not recommended during treatment and for at least **21 days** after the last dose.
- Fertility effects: Probable
  Documented in animal studies in male animals

back to top

H - Interactions

- Ribociclib is primarily metabolized by CYP3A is a time-dependent inhibitor of CYP3A. Therefore, medicinal products which can influence CYP3A enzyme activity may alter the pharmacokinetics of ribociclib and ribociclib can affect the pharmacokinetics of co-administered CYP3A substrates. Ribociclib has weak inhibitory effects on CYP1A2 substrates though no induction of CYP1A2, CYP2B6, CYP2C9 or CYP3A4 was observed *in vitro*.
- Ribociclib may inhibit BCRP, OCT2, Multidrug and Toxic Compound Extrusion Protein-1 (MATE1) and human Bile Salt Export Pump (BSEP). Monitor patients closely when co-administering ribociclib and substrates of these transporters.
- There is no clinically relevant interaction with letrozole, exemestane, anastrozole or fulvestrant.
- There is no expected interaction with goserelin.

AGENT	EFFECT	MECHANISM	MANAGEMENT
CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, ritonavir, fruit or juice from grapefruit, Seville oranges or starfruit)	↑ ribociclib exposure (e.g. ritonavir ↑ ribociclib exposure by 3.2-fold)	↓ metabolism of ribociclib	Avoid strong CYP3A4 inhibitors. If unavoidable, ↓ ribociclib dose by 200mg (i.e. from 600mg to 400mg). After discontinuation of strong CYP3A4 inhibitor, resume ribociclib dose used prior to initiating the CYP3A4 inhibitor (after a washout period of at least 5 half-lives). Monitor closely.
CYP3A4 inducers (e.g. phenytoin, rifampin, dexamethasone, carbamazepine, phenobarbital, St. John's Wort, etc)	↓ ribociclib exposure (e.g. rifampin ↓ ribociclib exposure by 89%)	↑ metabolism of ribociclib	Avoid strong CYP3A4 inducers.
CYP3A4 substrates with narrow therapeutic index (e.g. alfentanil, cyclosporine, dihydroergotamine, ergotamine,	↑ CYP3A4 Substrate exposure (e.g. ribociclib ↑ midazolam exposure by 280%)	↓ metabolism of CYP3A4 Substrate	Avoid CYP3A4 substrates with a narrow therapeutic index. If unavoidable, consider reducing dose of substrate.

everolimus, fentanyl, midazolam, pimozide, quinidine, sirolimus and tacrolimus)			
Drugs that may prolong QT (e.g. amiodarone, procainamide, sotalol, venlafaxine, amitriptyline, sunitinib, methadone, chloroquine, clarithromycin, haloperidol, fluconazole, moxifloxacin, domperidone, ondansetron, etc)	↑ risk of QT prolongation	Additive	Avoid concomitant use. If must co-administer, monitor as clinically indicated.
Drugs that disrupt electrolyte levels (e.g. loop/thiazide diuretics, laxatives, amphotericin B, high dose corticosteroids)	serum electrolyte imbalance	↓ electrolyte levels	Avoid to the extent possible.
Drugs that reduce heart rate (e.g. beta blockers, calcium channel blockers, digoxin)	↑ risk of arrhythmia		Avoid to the extent possible.
Tamoxifen	↑ risk of QT prolongation	↑ tamoxifen exposure by 2-fold with co-administration	Combined use is not recommended.
Statins	↑ risk of rhabdomyolysis	CDK inhibitors may ↑ statin exposure (Health Canada, 2025)	Consider close monitoring

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline, every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles and as clinically indicated
Liver function tests	Baseline, every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles and as clinically indicated (more frequent monitoring required in patients with ≥ Grade 2 LFTs)
Electrolytes, including potassium, magnesium, calcium, and phosphorous	Baseline, at regular intervals during steady-state treatment in later cycles and as clinically indicated (for example, patients with QTc prolongation)
ECG	Baseline, repeat on day 14 of cycle 1, and then as clinically indicated (more frequent monitoring in patients at risk)
Renal function tests	Baseline and as clinically indicated
Clinical toxicity assessment of infection, bleeding, thromboembolism (close monitoring in patients at risk), pneumonitis, gastrointestinal and skin effects, and fatigue	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Supplementary Public Funding

Exceptional Access Program (EAP Website)

- ribociclib - For the treatment of patients with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER 2)-negative, unresectable locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant according to clinical criteria

back to top

K - References

Hortobagyi, G. N. et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. New Engl. J. Med. 375, 1738–1748 (2016).

Product monograph: Kasqali (ribociclib). Novartis Pharmaceuticals. June 12, 2025.

Summary Safety Review - Cyclin-dependent Kinase Inhibitors (abemaciclib, palbociclib and ribociclib) and HMG-CoA Reductase Inhibitors (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin) (Statins) - Assessing the Potential Risk of Rhabdomyolysis Due to Drug Interaction. Health Canada. Accessed April 25, 2025.

September 2025 Updated Pharmacokinetics, Adverse Effects, Dosing, Administration Guidelines, Pregnancy/Lactation, Interactions, and Monitoring sections

back to top

L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top