Drug Monograph

A - Drug Name

palbociclib

COMMON TRADE NAME(S): Ibrance™

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B - Mechanism of Action and Pharmacokinetics

Palbociclib is a selective, reversible small molecule inhibitor of cyclin-dependent kinases (CDK) 4 and 6. The drug inhibits cyclin D-CDK 4/6 complex activity, blocking cell cycle progression from G1 to S phase. Palbociclib in combination with an anti-estrogen agent inhibits cell proliferation and induction of cell senescence in estrogen receptor (ER) positive breast cancer models.

Absorption	Bioavailability	46% (mean)
	Peak plasma levels	4 to 12 hours
	Time to reach steady state	8 days
	Effects with food	When administered with food, AUC and C_{max} increased up to 22% and 26%, respectively; food had no significant impact on exposure variability. Palbociclib tablets may be taken with or without food.
Distribution	PPB	85%
Metabolism	Palbociclib undergoes hepatic metabolism via oxidation and sulfonation, primarily by CYP3A and sulfotransferase (SULT2A1) enzymes; acylation and glucuronidation are minor metabolic pathways.	

	Inactive metabolites	Yes
Elimination	Half-life	29 hours (mean plasma)
	Feces	74% (2% unchanged)
	Urine	18% (7% unchanged)

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C - Indications and Status

Health Canada Approvals:

- Breast cancer

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

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D - Adverse Effects

Emetogenic Potential: Minimal – No routine prophylaxis; PRN recommended

The following adverse effects occurred in patients with breast cancer treated with palbociclib plus fulvestrant in a Phase III study, where the incidence was at least 2% greater than the placebo plus fulvestrant arm. The table also includes severe or life-threatening adverse effects from other sources or post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Venous thromboembolism (2%)	E
Dermatological	Alopecia (15%)	E
	Erythema multiforme (<1%)	E
	Rash, pruritus (14%)	E
Gastrointestinal	Anorexia (13%)	E
	Constipation (17%)	E

	Diarrhea (19%)	E
	Mucositis (25%)	E
	Nausea, vomiting (29%)	E
General	Edema - limbs (8%)	E
	Fatigue (38%)	E
Hematological	Myelosuppression ± infection, bleeding (79%) (62% severe)	E
Nervous System	Dizziness (11%)	E
	Dysgeusia (6%)	E
	Headache (21%)	E
	Insomnia (11%)	E
Renal	Creatinine increased (6%)	E
Respiratory	Cough, dyspnea (13%)	E
	Pneumonitis (1%)	E

* "*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 palbociclib include myelosuppression ± infection, bleeding, fatigue, nausea, vomiting, mucositis, headache, diarrhea, constipation, alopecia, rash, pruritus and anorexia.

Neutropenia was the most frequently reported adverse effect with a median onset of 15 days. Febrile neutropenia, including one fatal case, has been reported in 2% of patients across clinical trials.

Infections were reported more frequently. Patients should be warned of the increased risk of infection and promptly report any occurrences of fever to their health care team.

Severe or life-threatening **interstitial lung disease/pneumonitis** has been reported in combination with endocrine therapy in clinical trials and post-marketing (including fatal cases).

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E - Dosing

Refer to protocol by which 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.

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

Adults:

Oral: 125 mg Daily on Days 1 to 21, every 28 days

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

Dosage with Toxicity:

Dose Level	Palbociclib Dose (mg/day) (21 days on, 7 days off)
0	125
-1	100
-2	75
-3	If further dose reduction required, discontinue.

Toxicity	Grade	Palbociclib Dose
Hematologic	3	Day 1: Hold and repeat CBC within 1 week. When recovered to Grade ≤ 2, re-start next cycle at same dose. Day 15 of 1st 2 cycles: Continue current dose to complete the cycle. Repeat CBC day 22. If Grade 4 on Day 22, see Grade 4 recommendation below. Consider dose reduction if > 1 week recovery or recurrent Grade 3 neutropenia in subsequent cycles.
	3 with fever ≥ 38.5^{o}C and/or infection	Hold until recovery to Grade ≤ 2. Restart at the next lower dose.
	4	Hold until recovery to Grade ≤ 2. Restart at the next lower dose.
Symptoms of interstitial lung disease (ILD)/pneumonitis (treatment–related)	Any	Hold dose and investigate; discontinue if severe ILD confirmed.
Other non-hematologic	3 or 4 (if persisting despite medical treatment)	Hold until recovery to Grade ≤ 1 or Grade ≤ 2 (if not considered a safety risk). Restart at the next lower dose.

Dosage with Hepatic Impairment:

Mean fraction of unbound palbociclib in plasma increased with worsening hepatic function.

Hepatic Impairment	Starting Dose
Mild - Moderate (Child-Pugh class A and B)	No dosage adjustment needed.
Severe (Child-Pugh class C)	75 mg once daily (days 1 to 21; q28 days). Monitor for toxicity.

Dosage with Renal Impairment:

No adjustment is required for CrCl ≥ 15 mL/min. There is no data available in patients requiring hemodialysis.

Dosage in the elderly:

No overall differences in efficacy were observed between patients aged 65 and older compared to younger patients. When combined with letrozole, patients ≥ 65 were more likely to experience anemia.

Dosage based on gender:

Gender and body weight had no significant effect on drug exposure.

Dosage based on ethnicity:

No dose modification is required based on pharmacokinetic, safety and efficacy data across Asian and non-Asian populations.

Children:

The safety and efficacy of palbociclib has not been studied in children under 18 years.

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F - Administration Guidelines

- Palbociclib may be given with or without food.
- Tablets should be swallowed whole and not chewed, crushed, opened, or split prior to administration.
- If a patient vomits or misses a dose, an extra dose should not be taken to make up for the vomited or missed dose. The next dose should be taken at the usual time.
- Grapefruit, pomegranate, starfruit, Seville oranges, their juices or products should be avoided during palbociclib treatment.
- Tablets should be stored at 15 to 30^{o}C in original packaging to protect from moisture.

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G - Special Precautions

Contraindications:

- Patients who are hypersensitive to palbociclib or any ingredient in the formulation or component in the container.

Other Warnings/Precautions:

- As dizziness has been reported, patients should exercise caution when driving or operating machinery.

Other Drug Properties:

- Carcinogenicity: Unknown
  An increased incidence of microglial cell tumors was observed male rats; the relevance to humans is unknown.

Pregnancy and Lactation:

- Genotoxicity: Probable
- Mutagenicity: No
- Fetotoxicity: Documented in animals
- Pregnancy:
  Palbociclib is not recommended for use in pregnancy.
  - Adequate contraception should be used by patients who can become pregnant and their partners during treatment, and for at least **3 weeks** after the last dose.
  - Adequate contraception should be used by patients who produce sperm and their partners during treatment, and for at least **14 weeks** after the last dose.
- Excretion into breast milk: Unknown
- Breastfeeding:
  Breastfeeding is not recommended.
- Fertility effects: Probable
  Animal data suggest that palbociclib may affect male fertility. Sperm preservation should be considered prior to starting treatment.

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H - Interactions

Palbociclib is a substrate and weak inhibitor of CYP3A and a moderate substrate of P-gp. Drug interactions are possible with strong CYP3A inducers and inhibitors. Palbociclib is not an inhibitor of CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19 and 2D6 and not an inducer of CYP1A2, 2B6, 2C8 and 3A4 in vitro.

The drug has a low potential to inhibit drug transporters P-gp, BCRP, OAT1, OAT3, OCT2, OATP1B1 and OATP1B3. Palbociclib is not a substrate of OATP1B1 and OATP1B3 (in vitro studies).

There are no drug interactions with letrozole or goserelin.

AGENT	EFFECT	MECHANISM	MANAGEMENT
CYP3A inhibitors (e.g. ketoconazole, clarithromycin, ritonavir, fruit or juice from grapefruit, Seville oranges or starfruit)	↑ palbociclib concentration and/or toxicity (e.g. itraconazole ↑ palbociclib exposure by 87%)	↓ metabolism of palbociclib	Avoid strong CYP3A inhibitors.
Strong and moderate CYP3A inducers (e.g. phenytoin, rifampin, dexamethasone, carbamazepine, phenobarbital, St. John's Wort, etc)	↓ palbociclib concentration and/or efficacy (e.g. rifampin ↓ palbociclib exposure by 85%)	↑ metabolism of palbociclib	Avoid strong CYP3A inducers. If use of moderate inducer cannot be avoided, no dose adjustment to palbociclib is needed.
Sensitive CYP3A substrates with narrow therapeutic indices (e.g. midazolam, cyclosporine, everolimus, pimozide, fentanyl, quinidine, sirolimus, tacrolimus, ergotamine, dihydroergotamine)	↑ substrate concentration and/or toxicity (e.g. palbociclib ↑ midazolam exposure by 61%)	Palbociclib is a weak inhibitor of CYP3A.	Consider reducing the dose of sensitive CYP3A substrates with narrow therapeutic indices
Statins which are substrates of CYP3A4 and/or	↑ risk of rhabdomyolysis	Palbociclib may ↑ statin concentration	Close monitoring is recommended.

BCRP (e.g. atorvastatin, lovastatin, rosuvastatin and simvastatin)

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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 and before each cycle, on day 15 of the first 2 cycles, one week after Grade 3 neutropenia, and as clinically indicated. If neutropenia Grade 2 or less in the first 6 cycles, may monitor every 3rd cycle thereafter
Liver function tests	Baseline and as clinically indicated
Renal function tests	Baseline and as clinically indicated
Clinical toxicity assessment for infection, bleeding, thromboembolism, pneumonitis, rash, headache, mucositis, fatigue and GI effects	At each visit

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

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J - Supplementary Public Funding

Exceptional Access Program (EAP Website)

- palbociclib - 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

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K - References

Finn RS, Crown JP, Lang I, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol. 2015 Jan;16(1):25-35.

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.

Product Monograph: Ibrance (palbociclib). Pfizer Canada Inc. July 4, 2025.

September 2025 Updated Pharmacokinetics, Adverse Effects, Administration Guidelines, Warnings/Precautions, Pregnancy/Lactation and Interactions sections

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L - Disclaimer

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

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