Palbociclib: Drug information

(For additional information see "Palbociclib: Patient drug information")

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

Brand Names: US

Ibrance

Brand Names: Canada

Ibrance

Pharmacologic Category

Antineoplastic Agent, Cyclin-Dependent Kinase Inhibitor

Dosing: Adult

Note: Refer to aromatase inhibitor or fulvestrant monographs for respective dosing in combination with palbociclib.

Breast cancer, advanced, initial endocrine-based therapy: Females (HER-2 negative): Oral: 125 mg once daily for 21 days, followed by 7 days off, repeat every 28 days (in combination with continuous aromatase inhibitor therapy); continue until disease progression or unacceptable toxicity (Finn 2015).

Breast cancer, advanced (with disease progression following endocrine therapy): Females (HER-2 negative): Oral: 125 mg once daily for 21 days, followed by 7 days off, repeat every 28 days (in combination with fulvestrant [and an LHRH agonist (eg, goserelin) if pre- or perimenopausal]); continue until disease progression or unacceptable toxicity (Turner 2015).

Missed/vomited doses: If a dose is vomited or missed, an additional dose should not be taken that day. Resume dosing with the next scheduled daily dose.

Dosage adjustment for concomitant therapy:

Strong CYP3A inhibitors: Avoid concomitant use with strong CYP3A inhibitors (eg, azole antifungals, clarithromycin, nefazodone, protease inhibitors, telithromycin, verapamil, grapefruit or grapefruit juice) and consider alternatives with no or minimal CYP3A inhibition. If coadministration with a strong CYP3A inhibitor cannot be avoided, reduce palbociclib dose to 75 mg once daily. If the strong inhibitor is discontinued, increase palbociclib dose (after 3 to 5 inhibitor half-lives have elapsed) to the dose used prior to initiating the strong CYP3A inhibitor.

CYP3A inducers: Avoid concomitant use with strong CYP3A inducers.

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, since palbociclib exposure is not increased, dosage adjustments are not likely necessary.

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

Dosing: Hepatic Impairment

Mild impairment (total bilirubin ≤ULN and AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling, however, since palbociclib exposure is not increased, dosage adjustments are not likely necessary.

Moderate to severe impairment (total bilirubin >1.5 times ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Adjustment for Toxicity May require treatment interruption/delay, dose reduction, or discontinuation for some adverse reactions. The recommended first dose reduction is to 100 mg daily; if a second reduction is required, reduce dose to 75 mg daily. If dose reduction below 75 mg daily is required, discontinue treatment.

Hematologic toxicity (except lymphopenia unless associated with clinical events [eg, opportunistic infection]), according to Common Toxicity Criteria for Adverse Events Version 4:

Grade 1 or 2: No dosage adjustment required.

Grade 3:

Day 1 of cycle: Withhold palbociclib therapy and repeat CBC with differential within 1 week. When improved to ≤ grade 2, initiate the next cycle at the same dose.

Day 15 of first 2 cycles: If at grade 3, continue palbociclib therapy at current dose to complete the cycle. Repeat CBC with differential on day 22. If at grade 4 on day 22, withhold palbociclib treatment until resolved to ≤ grade 2. After resolution, resume at next lower dose. Consider dose reduction in future cycles if recovery from grade 3 neutropenia is prolonged (>1 week) or for recurrent grade 3 neutropenia on day 1 of subsequent cycles.

Grade 3 (ANC 500/mm^3 to <1,000/mm^3) plus fever ≥38.5°C and/or infection at any time: Withhold palbociclib treatment until resolved to ≤ grade 2. Resume at next lower dose upon restarting.

Grade 4 at any time: Withhold palbociclib treatment until resolved to ≤ grade 2. After resolution, resume at next lower dose.

Nonhematologic toxicity (according to Common Toxicity Criteria for Adverse Events Version 4):

Grade 1 or 2: No dosage adjustment required.

Grade 3 or higher (if persistent despite optimal medical management): Withhold palbociclib until symptoms resolve to ≤ grade 1 or ≤ grade 2 (if toxicity is not a safety risk); after resolution, resume at the next lower dose.

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

Capsule, Oral:

Ibrance: 75 mg, 100 mg, 125 mg

Generic Equivalent Available (US) No

Prescribing and Access Restrictions Palbociclib is available through specialty pharmacies. For more information, refer to http://www.ibrance.com/getting-ibrance

Administration Oral: Administer with food. Take at approximately the same time each day. Swallow whole, do not crush, chew, or open capsules prior to swallowing (do not ingest if capsules are broken, cracked, or not fully intact).

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 (initial endocrine-based therapy): 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

Breast cancer, advanced (with disease progression following endocrine therapy): Treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (in combination with fulvestrant) in women with disease progression following endocrine therapy

Medication Safety Issues

Sound-alike/look-alike issues:

Palbociclib may be confused with PAZOPanib

Ibrance may be confused with ibrutinib

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 Percentages reported as part of combination therapy.

>10%:

Central nervous system: Fatigue (41%), headache (26%), peripheral neuropathy (13%)

Dermatologic: Alopecia (18% to 22%), skin rash (17%)

Gastrointestinal: Nausea (25% to 34%), stomatitis (25% to 28%), diarrhea (21% to 24%), constipation (20%), vomiting (15% to 19%), decreased appetite (16%)

Hematologic & oncologic: Neutropenia (75% to 83%; grade 3: 48% to 55%; grade 4: 6% to 11%), decreased absolute lymphocyte count (81%; grade 3: 17%; grade 4: 1%), anemia (30% to 78%; grade 3: 3% to 5%; grade 4: ≤1%), leukopenia (43% to 53%; grade 3: 19% to 30%; grade 4: ≤1%), thrombocytopenia (17% to 23%; grade 3: 2%; grade 4: ≤1%)

Infection: Infection (47% to 55%)

Neuromuscular & skeletal: Weakness (8% to 13%)

Respiratory: Upper respiratory tract infection (31%), epistaxis (7% to 11%)

Miscellaneous: Fever (13%)

1% to 10%:

Cardiovascular: Pulmonary embolism (1% to 5%)

Dermatologic: Xeroderma (6%)

Gastrointestinal: Dysgeusia (7%)

Hematologic & oncologic: Febrile neutropenia (1%; grade 3: 1%)

Ophthalmic: Blurred vision (6%), increased lacrimation (6%), dry eye syndrome (4%)

Contraindications

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

Canadian labeling: Hypersensitivity to palbociclib or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: Neutropenia was commonly observed in clinical studies, including grades 3 and 4 neutropenia. The median time to the first neutropenia episode (any grade) was 15 days; the median duration of grade 3 or higher neutropenia was 7 days. Leukopenia, anemia, lymphocytopenia, thrombocytopenia, neutropenic fever, and neutropenic sepsis have also been reported. Monitor blood counts prior to initiating therapy and at the beginning of each cycle (as well as on day 15 of the first 2 cycles), and as clinically necessary; if neutropenia is limited to grades 1 or 2 in the first 6 cycles, monitor every 3 months (prior to the beginning of a cycle) and as clinically

indicated for subsequent cycles. Treatment interruption, delay, or dose reduction is recommended for grade 3 or 4 neutropenia.

• Gastrointestinal toxicity: Nausea, vomiting, diarrhea, and stomatitis (generally grade 1 or 2) were reported from clinical studies.

• Infection: Infections (including grades 3 and 4) were reported more frequently in patients receiving palbociclib and an antiestrogen compared with those receiving an antiestrogen only. Monitor for signs/symptoms of infection and manage appropriately.

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 (weak)

Drug Interactions

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

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

ARIPiprazole: CYP3A4 Inhibitors (Weak) may increase the serum concentration of ARIPiprazole. Management: Monitor for increased aripiprazole pharmacologic effects. Aripiprazole dose adjustments may or may not be required based on concomitant therapy and/or indication. Consult full interaction monograph for specific recommendations. *Risk C: Monitor therapy*

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*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

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

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

CYP3A4 Inducers (Moderate): May decrease the serum concentration of Palbociclib. Management: The US label does not provide specific recommendations concerning use with moderate CYP3A4 inducers, but the Canadian label recommends avoiding use of moderate CYP3A4 inducers. *Risk D: Consider therapy modification*

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

CYP3A4 Substrates: Palbociclib may increase the serum concentration of CYP3A4 Substrates. *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*

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

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*

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

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

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

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *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 (Weak) may increase the serum concentration of Flibanserin. *Risk C: Monitor therapy*

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 Palbociclib. *Risk X: Avoid combination*

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

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

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 (Weak) may increase the serum concentration of Lomitapide. Management: Patients on lomitapide 5 mg/day may continue that dose. Patients taking lomitapide 10 mg/day or more should decrease the lomitapide dose by half. The lomitapide dose may then be titrated up to a max adult dose of 30 mg/day. *Risk D: Consider therapy modification*

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 (Weak) 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*

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

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

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

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

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

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

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

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

St John's Wort: May decrease the serum concentration of Palbociclib. *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*

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

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *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*

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

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*

Food Interactions Coadministration with grapefruit may increase palbociclib plasma concentrations. Management: Avoid concomitant administration with grapefruit.

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

Breast-Feeding Considerations It is not known if palbociclib is present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended by the manufacturer during treatment and for at least 3 weeks after the last dose.

Dietary Considerations Avoid grapefruit.

Monitoring Parameters CBC with differential (prior to treatment initiation, every 2 weeks for first 2 cycles, then prior to each cycle, and as clinically indicated; if neutropenia is limited to grades 1 or 2 in the first 6 cycles, monitor every 3 months [prior to the beginning of a cycle] and as clinically indicated for subsequent cycles); pregnancy test prior to treatment initiation (in women of reproductive potential); monitor for signs/symptoms of infection.

Mechanism of Action Palbociclib is a reversible small molecule cyclin-dependent kinase (CDK) inhibitor which is selective for CDK 4 and 6. CDKs have a role in regulating progression through the cell cycle at the G1/S phase by blocking retinoblastoma (Rb) hyperphosphorylation (Finn 2015). Palbociclib reduces proliferation of breast cancer cell lines by preventing progression from the G1 to the S cell cycle phase. The combination of palbociclib with an antiestrogen provides for increased inhibition of Rb phosphorylation, downstream signaling, and tumor growth compared with each agent alone.

Pharmacodynamics/Kinetics

Absorption: Increased with high-fat, high-calorie food

Distribution: V_d (mean): 2,583 L

Protein binding: ~85%

Metabolism: Extensively hepatic; Major pathways: Oxidation and sulfonation, primarily by CYP3A and sulfotransferase (SULT) enzyme SULT2A1; Minor pathways: Acylation and glucuronidation

Bioavailability: Mean absolute bioavailability: 46%

Half-life elimination: 29 ± 5 hours

Time to peak: 6 to 12 hours

Excretion: Feces (~74%, primarily as metabolites); Urine (~18%; primarily as metabolites)

Pricing: US

Capsules (Ibrance Oral)

75 mg (21): $13155.66

100 mg (21): $13155.66

125 mg (21): $13155.66

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.

International Brand Names

Ibrance (AT, DK, HK, IS, LT, MY, PT, SG, SK)

REFERENCES

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