

## Olaparib: Drug information

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

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

**Brand Names: US** Lynparza

**Brand Names: Canada** Lynparza

**Pharmacologic Category** Antineoplastic Agent, PARP Inhibitor

**Dosing: Adult** **Note:** Olaparib is available as 100 mg and 150 mg tablets and as 50 mg capsules. Do not substitute the 50 mg capsules for the 100 mg or 150 mg tablets on a mg-per-mg basis due to differences in dosing and bioavailability.

**Ovarian cancer, advanced (BRCA-mutated):** Oral:

*Capsules:* 400 mg twice daily (12 hours apart) until disease progression or unacceptable toxicity (Domchek 2016)

*Tablets:* 300 mg twice daily (12 hours apart) until disease progression or unacceptable toxicity

**Ovarian cancer, recurrent (maintenance):** Oral: *Tablets:* 300 mg twice daily (12 hours apart) until disease progression or unacceptable toxicity

**Breast cancer, metastatic, HER2-negative, BRCA-mutated (off-label use):** Oral: *Tablets:* 300 mg twice daily until disease progression or unacceptable toxicity (Robson 2017)

**Missed doses:** If a dose is missed, administer the next dose at its scheduled time.

**Dosage adjustment for concomitant therapy with CYP3A inhibitors:** Avoid concomitant use with moderate or strong CYP3A inhibitors (consider alternative agents with less CYP3A inhibition). If coadministration with a **moderate** CYP3A inhibitor cannot be avoided, reduce dose to 200 mg twice daily (capsules) or 150 mg twice daily (tablets). If coadministration with a **strong** CYP3A inhibitor cannot be avoided, reduce dose to 150 mg twice daily (capsules) or 100 mg twice daily (tablets).

**Dosing: Geriatric** Refer to adult dosing.

### Dosing: Renal Impairment

CrCl 51 to 80 mL/minute: No dosage adjustment necessary; monitor closely for toxicity, as an increase in

mean AUC has been observed in patients with mild impairment.

CrCl 31 to 50 mL/minute:

*Capsules:* Reduce dose to 300 mg twice daily.

*Tablets:* Reduce dose to 200 mg twice daily.

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

ESRD: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

## Dosing: Hepatic Impairment

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

Moderate-to-severe impairment (Child-Pugh classes B and C): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

## Dosing: Adjustment for Toxicity

Consider therapy interruption or dose reduction if adverse reactions occur.

*Capsules:* The recommended dose reduction is to 200 mg twice daily; if further reduction is required, reduce dose to 100 mg twice daily.

*Tablets:* The recommended dose reduction is to 250 mg twice daily; if further reduction is required, reduce dose to 200 mg twice daily.

Pneumonitis: Discontinue

Secondary AML/MDS: Discontinue

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

Capsule, Oral:

Lynparza: 50 mg

Tablet, Oral:

Lynparza: 100 mg, 150 mg

**Generic Equivalent Available (US)** No

**Prescribing and Access Restrictions** Olaparib is available only through the designated specialty pharmacy Biologics, Inc. For further information on patient assistance, product availability, and prescribing instructions, please refer to the following website:

<http://myaccess360.com/hcp/reimbursement/Oncology.aspx?product=lynparza> or call 1-844-275-2360.

**Medication Guide and/or Vaccine Information Statement (VIS)** An FDA-approved

patient medication guide, which is available with the product information and as follows, must be dispensed with this medication:

Lynparza capsules:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/206162s008lbl.pdf#page=16](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206162s008lbl.pdf#page=16)

Lynparza tablets:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/208558s000lbl.pdf#page=23](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208558s000lbl.pdf#page=23)

## Administration

Administer with or without food. Swallow capsules whole; do not chew, dissolve, or open capsule. Do not administer if capsules appear deformed or show evidence of leakage. Swallow tablets whole; do not chew, crush, dissolve, or divide tablet.

Based on a pharmacokinetic study, the rate of absorption was slower and the peak exposure was decreased when administered with a high-fat meal; however, the extent of absorption was not affected; nausea and vomiting were reported more frequently when olaparib was administered in a fasted state (Plummer 2015).

Olaparib is available as 100 mg and 150 mg tablets and as 50 mg capsules. Due to differences in dosing and bioavailability, do **not** substitute the 50 mg capsules for the 100 mg or 150 mg tablets on a mg-per-mg basis.

## Hazardous Drugs Handling Considerations

This medication is not on the NIOSH (2016) list; however, it may meet 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. Assess risk to determine appropriate containment strategy (USP-NF 2017).

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

**Ovarian cancer, advanced (BRCA-mutated):** Capsules, tablets: Treatment of deleterious or suspected deleterious germline BRCA-mutated (as detected by an approved test) advanced ovarian cancer in patients who have been treated with 3 or more prior lines of chemotherapy

**Ovarian cancer, recurrent (maintenance):** Tablets: Maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in patients who are in a complete or partial response to platinum-based chemotherapy.

## Use: Off-Label

## Medication Safety Issues

### Sound-alike/look-alike issues

Olaparib may be confused with niraparib, osimertinib, rucaparib

Lynparza may be confused with Lenvima

### 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 (10% to <20%), edema

Central nervous system: Fatigue (including weakness; 66% to 68%), headache (10% to 26%), dizziness (10% to <20%)

Dermatologic: Skin rash (10% to 25%)

Endocrine & metabolic: Hypomagnesemia

Gastrointestinal: Nausea (64% to 76%), abdominal pain (43%), vomiting (32% to 43%), diarrhea (28% to 33%), dysgeusia (10% to 27%), decreased appetite (22% to 25%), dyspepsia (≤25%), stomatitis (≤20%), constipation (10% to <20%)

Genitourinary: Urinary tract infection (10% to <20%)

Hematologic & oncologic: Decreased white blood cell count (69%; grades 3/4: 5%), decreased absolute lymphocyte count (52% to 67%; grades 3/4: 10% to 17%), anemia (23% to 44%; grades 3/4: 4% to 20%), decreased neutrophils (25% to 51%; grades 3/4: 7% to 8%), decreased platelet count (26% to 42%; grades 3/4: 2% to 6%)

Infection: Influenza (≤36%)

Neuromuscular & skeletal: Musculoskeletal pain (21% to 32%), arthralgia (≤30%), myalgia (≤30%), back pain (10% to 25%)

Renal: Increased serum creatinine (≤44%)

Respiratory: Upper respiratory tract infection (26% to 43%), nasopharyngitis (≤36%), rhinitis (≤36%), sinusitis (≤36%), cough (10% to 21%), dyspnea (10% to <20%)

1% to ≤10%:

Cardiovascular: Hypertension, venous thrombosis (including pulmonary embolism)

Central nervous system: Anxiety, depression, insomnia, peripheral neuropathy

Dermatologic: Pruritus, xeroderma (including eczema)

Endocrine & metabolic: Hot flash, hyperglycemia

Genitourinary: Dysuria, urinary incontinence, vulvovaginal disease

Hematologic & oncologic: Myelodysplastic syndrome (acute myeloid leukemia;  $\leq 2\%$ )

Miscellaneous: Fever

<1%, postmarketing, and/or case reports: Dermatitis, hypersensitivity, pneumonitis, skin rash

## Contraindications

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

*Canadian labeling:* Hypersensitivity to olaparib or any component of the formulation.

## Warnings/Precautions

### **Concerns related to adverse effects:**

- Bone marrow suppression: Anemia, neutropenia, thrombocytopenia and lymphopenia have been reported. Monitor complete blood counts at baseline and monthly thereafter; do not initiate olaparib until any hematologic toxicity caused by previous chemotherapy has resolved to  $\leq$  grade 1. If prolonged hematologic toxicity occurs during therapy, interrupt treatment and monitor blood counts weekly until recovered; if counts do not recover to  $\leq$  grade 1 after 4 weeks, further evaluation (including bone marrow and cytogenetic analyses) is necessary.
- GI toxicity: Nausea and vomiting (usually mild to moderate) may commonly occur.
- Hypersensitivity: Hypersensitivity reactions, including rash and dermatitis, have been reported.
- Pulmonary toxicity: Pneumonitis (including some fatalities) has occurred rarely. Interrupt treatment for new or worsening respiratory symptoms such as cough, dyspnea, fever, wheezing, or radiologic abnormalities; evaluate promptly. Discontinue treatment if pneumonitis is confirmed.
- Secondary malignancy: Myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) have been reported (rarely) in clinical trials and long-term follow up, mostly in patients with documented BRCA mutation. Most MDS/AML cases were fatal. Additional cases of MDS/AML have been reported in patients treated with olaparib in combination studies. The duration of olaparib therapy prior to development of the secondary cancers ranged from less than 6 months to greater than 2 years; all patients had received prior chemotherapy with platinum agents and/or other DNA-damaging medications, including radiation; some of these patients had a prior history of cancer or bone marrow dysplasia. If prolonged hematologic toxicity occurs and blood counts do not recover to  $\leq$  grade 1 after 4 weeks, further evaluation (including bone marrow and cytogenetic analyses) is necessary. If MDS/AML is confirmed, discontinue therapy.

### **Disease-related concerns:**

- Renal impairment: Monitor closely for toxicity in patients with mild or moderate renal impairment.

Dosage adjustment is recommended for moderate 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.

**Dosage form specific issues:**

- Dosage form selection: Olaparib is available as 100 mg and 150 mg tablets and as 50 mg capsules. Do not substitute the 50 mg capsules for the 100 mg or 150 mg tablets on a mg-per-mg basis due to differences in dosing and bioavailability.

**Metabolism/Transport Effects** Substrate of CYP3A4 (major), P-glycoprotein/ABCB1; **Note:**

Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

## Drug Interactions

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

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

Bitter Orange: May increase the serum concentration of Olaparib. *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*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors).  
*Risk X: Avoid combination*

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

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

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*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Olaparib. Management: Avoid use of strong CYP3A4 inhibitors in patients being treated with olaparib. If such concurrent use cannot be avoided, the dose of olaparib should be reduced to 150 mg twice daily. *Risk X: Avoid combination*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers).  
*Risk C: Monitor therapy*

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

### *Avoid combination*

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

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

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

Idelalisib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk X: Avoid combination*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Pitolisant: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers).  
Management: Combined use of pitolisant with a CYP3A4 substrate that has a narrow therapeutic index should be avoided. Other CYP3A4 substrates should be monitored more closely when used with pitolisant. *Risk D: Consider therapy modification*

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

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors).  
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*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

**Food Interactions** Coadministration with grapefruit or Seville oranges may increase olaparib plasma concentrations. Management: Avoid concomitant administration with grapefruit, grapefruit juice, Seville oranges, or Seville orange juice.

**Pregnancy Implications** Adverse events were observed in animal reproduction studies at doses less than human exposure. Based on animal reproduction studies and the mechanism of action, olaparib may be expected to cause adverse events to the fetus. Women of reproductive potential should use highly effective contraception during therapy and for at least 6 months after the last olaparib dose. In women of reproductive potential, pregnancy testing is recommended prior to treatment initiation.

**Breast-Feeding Considerations** It is not known if olaparib is present in breast milk. Due to the

potential for serious adverse reactions in the breastfed infant, the manufacturer recommends that lactating women should not breastfeed during treatment and for 1 month after the last olaparib dose.

**Dietary Considerations** Avoid grapefruit, grapefruit juice, Seville oranges, or Seville orange juice.

**Monitoring Parameters** Complete blood count at baseline and monthly thereafter, or as clinically indicated (weekly until recovery for prolonged hematologic toxicity), renal function, pregnancy test (prior to treatment initiation in women of reproductive potential); monitor for signs/symptoms of AML/MDS and pneumonitis. Monitor adherence.

**Mechanism of Action** Olaparib is a poly (ADP-ribose) polymerase (PARP) enzyme inhibitor, including PARP1, PARP2, and PARP3. PARP enzymes are involved in DNA transcription, cell cycle regulation, and DNA repair. Olaparib is a potent oral PARP inhibitor which induces synthetic lethality in BRCA1/2 deficient tumor cells through the formation of double-stranded DNA breaks which cannot be accurately repaired, which leads to disruption of cellular homeostasis and cell death (Ledermann 2012).

## Pharmacodynamics/Kinetics

Absorption: Rapid; delayed with a high-fat meal (extent of absorption not significantly altered)

Distribution: Capsule:  $167 \pm 196$  L; Tablet:  $158 \pm 136$  L

Protein binding: ~82%

Metabolism: Primarily hepatic via CYP3A4; the majority of metabolism is through oxidation with some metabolites undergoing subsequent glucuronide or sulfate conjugation

Bioavailability: Tablet formulation has higher bioavailability than the capsule formulation.

Half-life elimination, terminal: Capsule:  $11.9 \pm 4.8$  hours; Tablet:  $14.9 \pm 8.2$  hours

Time to peak: Capsule: 1 to 3 hours; Tablet: 1.5 hours

Excretion: Urine (44%, mostly metabolites); feces (42%, mostly metabolites)

## Pricing: US

### Capsules (Lynparza Oral)

50 mg (112): \$3774.96

### Tablets (Lynparza Oral)

100 mg (60): \$8089.20

150 mg (60): \$8089.20

**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.

**Brand Names: International** Linparza (UA); Lyhnparza (FI); Lynparza (AT, CR, CZ, DE, DK, DO, EE, ES, FR, GB, GT, HK, HN, HR, HU, IE, IL, IS, KR, LT, LU, LV, MY, NI, NL, NO, PA, PL, PT, RO, SE, SI,



SK, SV); Lynparza Hard (SG)

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