



Olaparib (Lynparza)

FOR WHOM IS THIS DRUG APPROVED?

OVARIAN CANCER

- » As maintenance therapy for patients with recurrent ovarian epithelial, fallopian tube, and primary peritoneal cancer who have a complete or partial response (CR/PR) to platinum-based chemotherapy regardless of *BRCA* status.
- » As maintenance therapy for patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated advanced ovarian epithelial, fallopian tube, and primary peritoneal cancer who have a complete or partial response to frontline platinum-based chemotherapy.
- » In combination with bevacizumab (Avastin) maintenance treatment of patients with advanced ovarian cancer who have a CR/PR to first-line platinum-based chemotherapy with bevacizumab and whose cancer is associated with homologous recombination deficiency (HRD). Positive HRD status is defined by either a deleterious or suspected deleterious *BRCA* mutation and/or by genomic instability.

BREAST CANCER

- » Patients with germline *BRCA*-positive, HER2-negative metastatic breast cancer who have previously received chemotherapy. Patients with hormone receptor-positive disease must also have had prior endocrine therapy.
- » Patients with germline *BRCA*-mutated, HER2-negative, high-risk early breast cancer who have undergone chemotherapy before or after surgery. Patients with hormone receptor-positive disease must also have had prior endocrine therapy.

PANCREATIC CANCER

- » Patients with germline *BRCA*-mutated metastatic pancreatic adenocarcinoma whose disease has not progressed after at least 16 weeks of a first-line platinum-based chemotherapy regimen.

PROSTATE CANCER

- » Patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide (Xtandi) or abiraterone acetate (Zytiga).

WHAT EFFICACY DATA BACK IT UP?

Olaparib has been studied in several phase 2 and 3 trials across various malignancies.

In the phase 3 SOLO-1 trial (NCT01844986), patients with *BRCA* mutation–positive advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer achieved a 70% reduction in risk of disease progression or death in patients with frontline maintenance olaparib than with placebo. In the phase 3 SOLO-2 trial (NCT01874353), maintenance treatment with olaparib yielded a 70% reduction in the risk of progression or death compared with placebo for patients with platinum-sensitive, relapsed, *BRCA*-mutant ovarian cancer. The phase 3 PAOLA-1 trial (NCT02477644) revealed that the combination of olaparib and bevacizumab led to a 41% reduction in the risk of disease progression or death compared with bevacizumab alone in patients with HRD-positive advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who have CR/PR to platinum-based chemotherapy plus bevacizumab (HR, 0.59; 95% CI, 0.49-0.72; $P < .001$). After a median follow-up of 22.9 months, the median PFS was 22.1 vs 16.6 months, respectively. In the subgroup of patients with *BRCA* gene mutation–positive cancers, the PFS benefit was even more profound (HR, 0.31; 95% CI, 0.20-0.47).

In germline *BRCA*-positive, HER2-negative metastatic breast cancer, patients who received olaparib monotherapy experienced a 42% improvement in invasive disease-free survival in the phase 3 OlympiAD trial (NCT02000622) compared with standard therapy (HR, 0.58; 95% CI, 0.46-0.74; $P < .0001$). In March 2022, findings from the phase 3 OlympiA (NCT02032823) trial found that olaparib reduced the risk of death by 32% compared with placebo (HR, 0.68; 98.5% CI, 0.47-0.97; $P = .009$) in *BRCA*-mutated, HER2-negative, high-risk early breast cancer. Furthermore, the 3-year survival rate was 92.8% with the PARP inhibitor compared with 89.1% for placebo.

In the phase 3 POLO trial (NCT02184195), patients with germline *BRCA*-mutated metastatic pancreatic cancer achieved a median progression-free survival (PFS) of 7.4 months with olaparib compared with 3.8 months on placebo (HR, 0.53; 95% CI, 0.35-0.81; $P = .0035$). Moreover, after 2 years, 22.1% of patients in the olaparib group had no disease progression vs 9.6% in the placebo group.





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Findings from the phase 3 PROfound trial (NCT02987543) showed that olaparib induced a 66% reduction in the risk of disease progression or death compared with abiraterone acetate or enzalutamide (HR, 0.34; 95% CI, 0.25-0.47; $P < .0001$) in patients with *BRCA1/2*- or ATM-mutant mCRPC.⁸

HOW IT WORKS

PARP enzymes are involved in DNA repair and are specifically responsible. 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, leading to cell death.

HOW IT'S ADMINISTERED

Olaparib is an oral drug manufactured in 150-mg and 100-mg tablets. Olaparib is taken by mouth, twice daily. It can be taken without or without food. Olaparib should be taken as prescribed, and capsules should be swallowed whole. Do not crush, dissolve, or open capsules.

THE RECOMMENDED DOSE

The recommended dosing for metastatic breast cancer is 300 mg by mouth every 12 hours.

HOW TO MANAGE ASSOCIATED ADVERSE EVENTS

The most common types of adverse events (AEs) associated with olaparib are hematologic and gastrointestinal (GI). Anemia is the most common hematologic toxicity and occurs in up to 45% of patients. Neutropenia and thrombocytopenia are less common. A dose reduction should be considered for recurrent anemia (hemoglobin < 8 mg/dL) and/or to avoid multiple blood transfusions. Olaparib is considered moderately emetogenic, and 5-HT₃ receptor antagonists (eg, ondansetron) are recommended as prophylaxis. Consider reducing dose for persistent nausea requiring daily antiemetics and/or resulting in greater than 5% weight loss. Rare but serious AEs include secondary myelodysplastic syndrome/acute myeloid leukemia ($< 2\%$) and pneumonitis. If prolonged hematologic toxicity is observed (\geq grade 2 or > 4 weeks), further evaluation is warranted. Interrupt treatment and evaluate promptly for new or worsening respiratory symptoms (eg, cough, dyspnea,

wheezing) or radiographic abnormalities. Olaparib should be permanently discontinued if pneumonitis is confirmed.

The dose should be continued until disease progression unless there is toxicity, in which case it can be reduced to 200 mg every 12 hours or 100 mg every 12 hours. A dose adjustment is recommended for a creatinine clearance (CrCl) of 31 to 50 mL/min. The medication has not been studied in patients with CrCl below 30 mL/min or end-stage renal disease. No adjustment is needed for hepatic impairment.

WHAT TO INFORM PATIENTS ABOUT

Patients about to begin treatment with olaparib should be advised to avoid grapefruit juice and Seville oranges as both may increase the level of olaparib in the blood.

ADVICE FOR NURSES WHO ADMINISTER THIS AGENT

Prior to initiating olaparib, health care professionals should rule out pregnancy, kidney dysfunction, and lung and breathing problems. Safety and monitoring parameters include obtaining a pregnancy test at baseline in female patients, complete blood count with differential at baseline and monthly thereafter, and ongoing monitoring for signs and symptoms of thromboembolism.

HOW TO SAFELY HANDLE THIS AGENT

Olaparib should be stored in its original container and in a cool and dry environment to protect it from moisture.

IMPORTANT LABEL UPDATE

In August 2022, AstraZeneca voluntarily withdrew the indication for the treatment of adult patients with deleterious or suspected germline *BRCA*-mutant advanced ovarian cancer who have been treated with 3 or more lines of chemotherapy. New treatment of patients who meet these criteria should not be initiated and patients who are receiving olaparib in this setting should consult their physician to make an informed decision on their ongoing care.²

REFERENCES

1. Lynparza. Prescribing information. AstraZeneca Pharmaceuticals LP; 2022. Accessed August 15, 2022. bit.ly/3AVZyC
2. Important prescribing information: Lynparza. AstraZeneca. August 26, 2022. Accessed September 29, 2022. <https://bit.ly/3C4k4ud>

