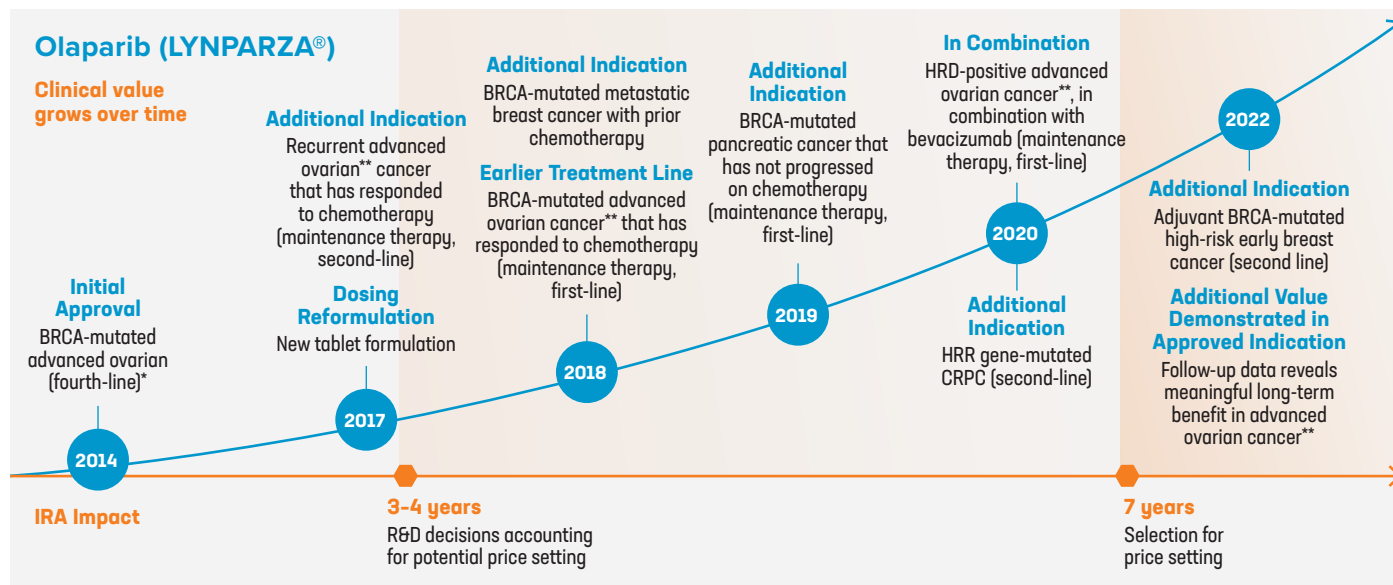


# Olaparib | LYNPARZA®

In 2014, olaparib became the first PARP inhibitor approved by the FDA.<sup>1</sup> PARP inhibitors are a type of targeted oral cancer treatment that help keep cancer cells from repairing damaged DNA, causing them to die.<sup>2</sup> Olaparib was initially granted accelerated approval for patients with advanced ovarian cancer who had already exhausted many treatment options and whose cancer tested positive for a BRCA mutation.<sup>1</sup> Continued development of this targeted cancer medicine has led to various additional indications in breast, ovarian, pancreatic, and prostate cancers and a dosing reformulation to improve patient convenience.<sup>3,4</sup> Olaparib has earned approval as maintenance therapy for some cancers, which is given to patients to help keep cancer from coming back after initial therapy.<sup>5</sup> Research has also revealed significant survival benefits that could not have been known until years after initial approval.



**Additional Indication (August 2017):** Approved as maintenance therapy for patients with recurrent advanced ovarian cancer\*\*, who have a response to chemotherapy, regardless of BRCA mutation status.<sup>3</sup> As recurrence rates in ovarian cancer patients are high, maintenance therapies are used to help prevent and extend the time until recurrence following surgery or positive response to chemotherapy.<sup>5,6</sup> In a clinical study, patients treated with olaparib were 27% more likely to be alive compared to patients taking no maintenance therapy.<sup>3</sup> A high proportion of patients diagnosed with ovarian cancer already have later stage disease.<sup>7</sup> As this type of cancer is a leading cause of cancer death in women, the availability of treatment options that can help extend survival in these patients is critically important.<sup>3</sup>

**Dosing Reformulation (August 2017):** Approved dosing reformulation switched the daily dosing regimen from many capsules twice per day to two tablets twice per day, improving patient convenience.<sup>3</sup>

**Additional Indication (January 2018):** Approved for patients with BRCA-mutated, HER2-negative metastatic breast cancer previously treated with chemotherapy. Olaparib was the first PARP inhibitor approved to treat this aggressive, difficult-to-treat cancer. In a clinical study, the therapy was shown to reduce risk of disease progression or death by 42% compared to standard of care chemotherapy.<sup>8</sup>

**Earlier Treatment Line (December 2018):** Approved as a first-line maintenance therapy for patients with BRCA-mutated advanced ovarian cancer\*\* who responded to chemotherapy.<sup>9</sup> The BRCA gene mutation is present in up to 15% of all ovarian cancer cases.<sup>10</sup> In a clinical trial, patients treated with olaparib were 70% more likely to live without their cancer getting worse compared to patients taking no maintenance therapy.<sup>9</sup>

**Additional Indication (December 2019):** Approved as a first-line maintenance therapy for patients with metastatic pancreatic cancer whose cancer tested positive for a BRCA mutation and whose disease has not progressed on chemotherapy. In a clinical study, olaparib nearly doubled the time patients lived without their cancer getting worse. Pancreatic cancer has the lowest survival rate among the most common cancers, making treatments that can extend survival critical for patients with this disease.<sup>11</sup>

**Use In Combination (May 2020):** Approved in combination with bevacizumab as a first-line maintenance treatment for patients with HRD-positive advanced ovarian cancer\*\* who have responded to chemotherapy. Approximately half of all patients with advanced ovarian cancer have a tumor that is HRD-positive. Clinical study results showed that treating patients with olaparib in combination with bevacizumab resulted in a median progression-free survival of 37.2 months compared to 17.7 months with bevacizumab alone.<sup>12</sup>

**Additional Indication (May 2020):** Approved to treat patients with a specific type of metastatic prostate cancer whose disease progressed after treatment with another medication. In a clinical study, patients treated with olaparib were 31% more likely to be alive compared to patients treated with another medication.<sup>13</sup>

**Earlier Disease Stage (March 2022):** Approved for the adjuvant treatment of patients with a specific high-risk early breast cancer (BRCA-mutated HER2-negative) after treatment with chemotherapy. In a clinical study, olaparib demonstrated a meaningful survival benefit, reducing the risk of death by 32% compared to placebo.<sup>14</sup>

**Additional Value Demonstrated in Approved Indication (September 2022):** Long-term follow up data showed improvement in survival for patients with BRCA-mutated advanced ovarian cancer who were treated with olaparib

as first-line maintenance therapy. A clinical study showed that a majority of patients taking olaparib were alive after seven years, which marked the longest follow-up for any PARP inhibitor in this setting. Given the high mortality rate associated with ovarian cancer this demonstration of long-term survival benefit marked a critically important advance for these patients.<sup>15</sup>

*"Indication voluntarily withdrawn: Although the early results from clinical studies supported the use of PARP inhibitors, including olaparib, as a treatment option for BRCA-mutated recurrent advanced ovarian cancer, longer-term overall survival data indicates that chemotherapy treatment may be more beneficial than PARP inhibitors for this indication. No other olaparib indications were affected, including indications for maintenance therapy in advanced ovarian cancer."<sup>16,17</sup>*

*\*\*Indication specifically includes epithelial ovarian, fallopian tube, or primary peritoneal cancer*

*BRCA: breast cancer gene, CRPC: castration resistant prostate cancer, HER2: human epidermal growth factor 2, HRD: homologous recombination deficiency, HRR: homologous recombination repair, PARP: poly ADP-ribose polymerase*

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- 1 AstraZeneca. "LYNPARZA™ approved by the US food and drug administration for the treatment of advanced ovarian cancer in patients with germline BRCA-mutations." <https://www.astrazeneca.com/media-centre/press-releases/2014/lynparza-approved-us-fda-brca-mutated-ovarian-cancer-treatment-19122014.%20html#>. Published December 19, 2014. Accessed June 13, 2023.
  - 2 National Cancer Institute, NCI Dictionary of Cancer Terms. "PARP inhibitor." <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/parp-inhibitor>. Accessed June 12, 2023.
  - 3 AstraZeneca. "Lynparza receives additional and broad approval in the US for ovarian cancer." <https://www.astrazeneca.com/media-centre/press-releases/2017/lynparza-receives-additional-and-broad-approval-in-the-us-for-ovarian-cancer-17082017.html>. Published August 17, 2017. Accessed June 13, 2023.
  - 4 Lynparza. [prescribing information]. AstraZeneca: Wilmington, DE, USA; 2023.
  - 5 National Cancer Institute, NCI Dictionary of Cancer Terms. "Maintenance Therapy." <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/maintenance-therapy>. Accessed June 13, 2023.
  - 6 Ovarian Cancer Research Alliance. "Recurrence." <https://ocrahope.org/patients/diagnosis-and-treatment/recurrence>. Accessed June 13, 2023.
  - 7 Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. *CA Cancer J Clin*. 2018;68(4):284-296.
  - 8 AstraZeneca. "Lynparza approved by US FDA in germline BRCA-mutated metastatic breast cancer." <https://www.astrazeneca.com/media-centre/press-releases/2018/lynparza-approved-by-us-fda-in-germline-brca-mutated-metastatic-breast-cancer-12012018.html>. Published January 12, 2018. Accessed June 13, 2023.
  - 9 AstraZeneca. "Lynparza approved by US FDA for 1st-line maintenance therapy in BRCA-mutated advanced ovarian cancer." <https://www.astrazeneca.com/media-centre/press-releases/2018/lynparza-approved-by-us-fda-for-1st-line-maintenance-therapy-in-brca-mutated-advanced-ovarian-cancer-19122018.html>. Published December 19, 2018. Accessed June 13, 2023.
  - 10 Ramus SJ, Gayther SA. The Contribution of BRCA1 and BRCA2 to Ovarian Cancer. *Mol Oncol*. 2009;3(2):138-50.
  - 11 AstraZeneca. "Lynparza approved in the US as a 1st-line maintenance treatment of germline BRCA-mutated metastatic pancreatic cancer." <https://www.astrazeneca.com/media-centre/press-releases/2019/lynparza-approved-in-the-us-as-a-1st-line-maintenance-treatment-of-germline-brca-mutated-metastatic-pancreatic-cancer-30122019.html>. Published December 30, 2019. Accessed June 13, 2023.
  - 12 AstraZeneca. "Lynparza approved in the US as 1st-line maintenance treatment with bevacizumab for HRD-positive advanced ovarian cancer." <https://www.astrazeneca.com/media-centre/press-releases/2020/lynparza-approved-in-the-us-as-1st-line-maintenance-treatment-with-bevacizumab-for-hrd-positive-advanced-ovarian-cancer.html>. Published May 11, 2020. Accessed June 13, 2023.
  - 13 AstraZeneca. "Lynparza approved in the US for HRR gene-mutated metastatic castration-resistant prostate cancer." <https://www.astrazeneca.com/media-centre/press-releases/2020/lynparza-approved-in-the-us-for-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer.html>. Published May 20, 2020. Accessed June 13, 2023.
  - 14 AstraZeneca. "Lynparza approved in the US as adjuvant treatment for patients with germline BRCA-mutated HER2-negative high-risk early breast cancer." <https://www.astrazeneca.com/media-centre/press-releases/2022/lynparza-approved-in-the-us-as-adjuvant-treatment-for-patients-with-germline-brca-mutated-her2-negative-high-risk-early-breast-cancer.html>. Published March 11, 2022. Accessed June 13, 2023.
  - 15 Merck. "LYNPARZA® (olaparib) in Combination With Bevacizumab, and as Monotherapy, Demonstrates Clinically Meaningful Long-Term Survival in Certain Patients With First-Line Advanced Ovarian Cancer in Exploratory Analyses of Two Phase 3 Trials." <https://www.merck.com/news/lynparza-olaparib-in-combination-with-bevacizumab-and-as-monotherapy-demonstrates-clinically-meaningful-long-term-survival-in-certain-patients-with-first-line-advanced-ovarian-cancer-in-expl/>. Published September 9, 2022. Accessed June 13, 2023. *Interim overall survival analysis. Final overall survival analysis ongoing.*
  - 16 AstraZeneca. "Important Prescribing Information." <https://www.lynparzahcp.com/content/dam/physician-services/us/590-lynparza-hcp-branded/hcp-global/pdf/solo3-dhcp-final-signed.pdf>. Published August 26, 2022. Accessed June 13, 2023.
  - 17 Facing Our Risk of Cancer Empowered. "Update: PARP inhibitors withdrawn as third-line or later treatment for recurrent ovarian cancer." <https://www.facingourrisk.org/XRAY/PARP-inhibitors-withdrawn-for-recurrent-ovarian-cancer>. Published October 4, 2022. Accessed June 13, 2023.