

Policy Coverage and Prior Authorization Considerations for LYNPARZA® (olaparib) + Bevacizumab in the First-Line Maintenance Setting for Women With HRD-Positive Advanced Ovarian Cancer

LYNPARZA in combination with bevacizumab was approved on May 8, 2020, for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either a deleterious or suspected deleterious *BRCA* mutation and/or genomic instability. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.^{1,2}

The approval was based on PAOLA-1, the first and only phase 3, randomized, double-blind trial designed to demonstrate the efficacy and safety of a PARP inhibitor when added to an established maintenance therapy, bevacizumab, in patients with advanced ovarian cancer following first-line platinum-based chemotherapy.²⁻⁴

- 1 LYNPARZA's latest FDA approval in advanced ovarian cancer includes patients eligible for first-line maintenance treatment with HRD-positive disease**
- 2 Eligible patients must have demonstrated a complete or partial response with first-line, platinum-based chemotherapy**
- 3 LYNPARZA is the only PARP inhibitor approved with an established maintenance therapy, bevacizumab**

Tumor testing for HRD informs treatment eligibility for LYNPARZA + bevacizumab for patients with advanced ovarian cancer²



HRD is caused by impaired DNA repair mechanisms, such as *BRCA* mutations⁵



All women with a *BRCA* mutation are HRD-positive, but *BRCA* mutations are not the only cause of HRD⁵



Approximately 50% of women with ovarian cancer have HRD-positive disease⁶

LYNPARZA in combination with bevacizumab is approved with the companion diagnostic Myriad myChoice CDx® test.⁷



HRD testing should be performed on tumor tissue at diagnosis⁸



HRD-positive disease is indicated by either a deleterious or suspected deleterious *BRCA* mutation and/or genomic instability⁹

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in <1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The duration of therapy in patients who developed secondary MDS/AML varied from <6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy, and some also had a history of more than one primary malignancy or of bone marrow dysplasia.

Please see additional Important Safety Information throughout and accompanying complete Prescribing Information, including Patient Information (Medication Guide).

BRCA=BRCA1/2; *CAN*=cancer susceptibility gene; *DNA*=deoxyribonucleic acid; *FDA*=US Food and Drug Administration; *PARP*=poly (ADP-ribose) polymerase.

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olaparib
tablets 150 mg

Policy Coverage and Prior Authorization Criteria to Consider **for LYNPARZA**



Please consider the following information when updating prior authorization forms and policy coverage criteria for LYNPARZA²:



Patient has confirmed advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer



Patient has confirmed HRD-positive disease defined by either a deleterious or suspected deleterious *BRCA* mutation and/or genomic instability



Patient demonstrated a complete or partial response with first-line, platinum-based chemotherapy and is eligible for LYNPARZA + bevacizumab first-line maintenance therapy

Policy Coverage and Prior Authorization Criteria to Consider **for HRD Testing**



Please consider the following information as it pertains to your policy coverage criteria for HRD testing:



Patient has confirmed advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer

The Myriad myChoice CDx test
is the approved companion diagnostic for LYNPARZA for the detection of HRD-positive disease.⁷ Other tests that identify HRD can also be used to determine a patient's HRD status and inform treatment decisions.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) (cont'd): Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (\leq Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood count weekly until recovery.

If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. Discontinue LYNPARZA if MDS/AML is confirmed.

Please see additional Important Safety Information throughout and accompanying complete Prescribing Information, including Patient Information (Medication Guide).

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Pneumonitis: Occurred in <1% of patients exposed to LYNPARZA, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

ADVERSE REACTIONS—First-Line Maintenance Advanced Ovarian Cancer in Combination with Bevacizumab

Most common adverse reactions (Grades 1-4) in $\geq 10\%$ of patients treated with LYNPARZA/bevacizumab compared to a $\geq 5\%$ frequency for placebo/bevacizumab in the **first-line maintenance setting** for PAOLA-1 were: nausea (53%), fatigue (including asthenia) (53%), anemia (41%), lymphopenia (24%), vomiting (22%) and leukopenia (18%). In addition, the most common adverse reactions ($\geq 10\%$) for patients receiving LYNPARZA/bevacizumab irrespective of the frequency compared with the placebo/bevacizumab arm were: diarrhea (18%), neutropenia (18%), urinary tract infection (15%) and headache (14%).

In addition, venous thromboembolic events occurred more commonly in patients receiving LYNPARZA/bevacizumab (5%) than in those receiving placebo/bevacizumab (1.9%).

Most common laboratory abnormalities (Grades 1-4) in $\geq 25\%$ of patients for LYNPARZA in combination with bevacizumab in the **first-line maintenance setting** for PAOLA-1 were: decrease in hemoglobin (79%), decrease in lymphocytes (63%), increase in serum creatinine (61%), decrease in leukocytes (59%), decrease in absolute neutrophil count (35%) and decrease in platelets (35%).

DRUG INTERACTIONS

Anticancer Agents: Clinical studies of LYNPARZA in combination with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

CYP3A Inhibitors: Avoid concomitant use of strong or moderate CYP3A inhibitors. If a strong or moderate CYP3A inhibitor must be co-administered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

CYP3A Inducers: Avoid concomitant use of strong or moderate CYP3A inducers when using LYNPARZA. If a moderate inducer cannot be avoided, there is a potential for decreased efficacy of LYNPARZA.

USE IN SPECIFIC POPULATIONS

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of LYNPARZA have not been established in pediatric patients.

Hepatic Impairment: No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). There are no data in patients with severe hepatic impairment (Child-Pugh classification C).

Renal Impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51-80 mL/min estimated by Cockcroft-Gault). In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the dose of LYNPARZA to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤ 30 mL/min).

Please see accompanying complete Prescribing Information, including Patient Information (Medication Guide).

References: 1. LYNPARZA® (olaparib) approved by FDA as first-line maintenance treatment with bevacizumab for HRD-positive advanced ovarian cancer [press release]. Kenilworth, NJ: Merck & Co., Inc.; May 8, 2020. <https://www.mrknewsroom.com/news-release/oncology/lynparza-olaparib-approved-fda-first-line-maintenance-treatment-bevacizumab-hr>. Accessed May 11, 2020. 2. LYNPARZA [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. 3. Ray-Coquard I, Pautier P, Pignata S, et al; PAOLA-1 Investigators. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med*. 2019;381(25):2416-2428. 4. ClinicalTrials.gov website. <https://clinicaltrials.gov>. Accessed April 29, 2020. 5. Gee ME, Faraahi Z, McCormick A, Edmondson RJ. DNA damage repair in ovarian cancer: unlocking the heterogeneity. *J Ovarian Res*. 2018;11(1):50. 6. Sun H, Cao D, Ma X, et al. Identification of a prognostic signature associated with DNA repair genes in ovarian cancer. *Front Genet*. 2019;10:839. 7. Myriad receives FDA approval of myChoice CDx® as companion diagnostic for Lynparza™ (olaparib) in patients with advanced ovarian cancer [press release]. Salt Lake City, UT: Myriad Genetics Inc; May 11, 2020. <https://myriad.com/investors/news-release/news-release-detail/?newsItemid=21171>. Accessed May 11, 2020. 8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V.1.2020. © National Comprehensive Cancer Network, Inc; 2020. All rights reserved. Accessed April 3, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. 9. myChoice CDx® Technical Information. bit.ly/myChoiceCDxSpecs. Accessed February 21, 2020.

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