olaparib (Lynparza®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO048

Description

Olaparib (Lynparza) is an orally administered poly (ADP-ribose) polymerase (PARP) enzymes inhibitor including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
olaparib (Lynparza)	100 mg tablets	Breast cancer, metastatic, HER2-negative, germline BRCA-mutated (gBRCAm); Ovarian cancer, advanced gBRCAm; Ovarian cancer, first-line maintenance therapy for gBRCAm or somatic BRCA-mutated (sBRCAm) or homologous recombination deficient-positive (HRD); Ovarian cancer, recurrent (maintenance therapy); Pancreatic cancer, first-line therapy for gBRCA-mutated, metastatic adenocarcinoma; Prostate cancer, metastatic castration-resistant, homologous recombination repair (HRR) gene-mutated	120 tablets/30 days
	150 mg tablets		

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888-788-9821
PHARMACY
888-474-8539
BEHAVIORAL HEALTH
800-493-0040

Initial Evaluation

I. Olaparib (Lynparza) may be considered medically necessary when the following criteria below are met:
   A. Prescribed by, or in consultation with, a specialist in oncology; **AND**
   B. Not used in combination with other anti-cancer agents, unless otherwise outlined in the criteria below; **AND**
   C. The patient has not progressed on or after prior PARP inhibitor therapy (e.g., niraparib [Zejula], rucaparib [Rubraca]); **AND**
   D. A diagnosis of:
      1. **Ovarian cancer, Recurrent Maintenance**; **AND**
         i. Diagnosis of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer; **AND**
         ii. Has completed at least TWO prior platinum-based (e.g., cisplatin, carboplatin, oxaliplatin) chemotherapy regimens; **AND**
         iii. The tumor is considered to be platinum-sensitive (i.e., the patient is responsive to their most recent platinum-based regimen, as defined by complete or partial response for more than 6 months); **AND**
         iv. Provider attests, with supporting documentation, that member's recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer has not progressed since the most recent platinum-based (e.g., cisplatin, carboplatin, oxaliplatin) chemotherapy regimen; **OR**
      2. **Ovarian cancer, First-line Maintenance; AND**
         i. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) of gBRCAm OR sBRCAm; **AND**
         ii. Has not received bevacizumab in prior treatment; **OR**
            a. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) gHRDm (homologous recombination deficient-positive mutation); **AND**
            b. Member has had a positive response to prior bevacizumab treatment and bevacizumab will be continued; **AND**
         iii. Diagnosis of advanced (stage ≥III) epithelial ovarian, fallopian tube, or primary peritoneal cancer; **AND**
         iv. Has completed at least ONE prior platinum-based chemotherapy regimen (e.g., cisplatin, carboplatin, oxaliplatin); **AND**
         v. The tumor is considered to be platinum-sensitive (i.e., the patient is responsive to their most recent platinum-based regimen, as defined by a complete or partial response for more than 6 months); **AND**

vi. Provider attest with supporting documentation that member's epithelial ovarian, fallopian tube, or primary peritoneal cancer has not progressed since the most recent platinum-based (e.g., cisplatin, carboplatin, oxaliplatin) chemotherapy regimen; **OR**

3. **Ovarian cancer, Advanced; AND**
   i. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) gBRCAm OR sBRCAm; **AND**
   ii. Diagnosis of advanced (stage ≥III) epithelial ovarian, fallopian, or primary peritoneal cancer; **AND**
   iii. Has progression of disease following THREE or more prior lines of chemotherapy; **OR**
4. **Breast cancer; AND**
   i. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) gBRCAm; **AND**
   ii. Diagnosis of HER2-negative, metastatic breast cancer; **AND**
   iii. Has received prior treatment with both an anthracycline (e.g., doxorubicin) AND a taxane (e.g., paclitaxel) in the neoadjuvant, adjuvant, or metastatic setting; **AND**
   iv. Has NOT received more than TWO prior chemotherapy regimens in the metastatic setting; **AND**
   v. Has progression of disease on at least ONE prior endocrine therapy in the adjuvant or metastatic setting; **OR**
      a. Endocrine therapy has been deemed inappropriate by the treating healthcare provider; **OR**
5. **Pancreatic cancer, First-line Maintenance; AND**
   i. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) gBRCAm; **AND**
   ii. Diagnosis of metastatic pancreatic adenocarcinoma; **AND**
   iii. The member has received at least 16 weeks of continuous treatment with a platinum-based chemotherapy regimen (e.g., cisplatin, carboplatin, oxaliplatin) that was administered as first-line therapy; **AND**
   iv. Provider attests that the disease has not progressed while on first-line platinum-based chemotherapy regimen (e.g., cisplatin, carboplatin, oxaliplatin); **OR**
6. **Prostate cancer, Metastatic castration-resistant; AND**
   i. Documentation of deleterious (pathogenic) or suspected deleterious (likely pathogenic) alteration in at least **one** of the following HRR genes: ATM, BRCA1, BRCA2; **AND**
   ii. Has progressed on prior enzalutamide or abiraterone treatment; **AND**

iii. Member has had a prior bilateral orchiectomy; **OR**
   a. Used in combination with luteinizing-hormone-releasing hormone analog therapy (e.g. leuprolide (Eligard, Lupron), histrelin (Vantas))

II. Olaparib (Lynparza) is considered investigational when used for all other conditions, including but not limited to:
   A. Breast cancer without metastasis, and/or HER2-negative breast cancer, and/or breast cancer without gBRCAm
   B. Pancreatic cancer without metastasis, and without gBRCAm
   C. Metastatic, gBRCAm pancreatic cancer that has progressed on first line platinum-based chemotherapy
   D. Metastatic, castration-resistant prostate cancer with a tumor mutation NOT listed above (including BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, or RAD54L)
   E. Use after disease progression on or after prior PARP inhibitor therapy
   F. Use in combination with other anti-cancer agents

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Clinical documentation of response to treatment (e.g. stabilization of disease or decrease in tumor size/spread)

Supporting Evidence

I. In the pivotal trials for maintenance treatment of recurrent ovarian cancer and first-line maintenance therapy for ovarian cancer with gBRCAm or sBRCAm, eligible patients had completed at least ONE course of platinum-based chemotherapy.
II. In the pivotal trials for first-line maintenance therapy for ovarian cancer with gBRCAm or sBRCAm **non-eligible** patients included: patients with early stage disease (FIGO State I, IIA, IIB, or IIC) and patients with prior bevacizumab treatment.
III. Subjects were randomized to treatment allocation within eight weeks after completion of the last dose of platinum-based chemotherapy. The intent is that treatment is started within a

reasonable timeframe consistent with a maintenance treatment plan (i.e., as close to 8 weeks as possible), but recognize that scheduling or other factors may impact the ability of a patient to start exactly within these first eight weeks. There can be some flexibility within reason but use clinical judgement and patient specific factors when assessing this criterion to ensure this is falling within the maintenance treatment timeframe vs subsequent therapy.

IV. In the pivotal trial for breast cancer with metastatic, HER2-negative and gBRCAm, eligible patients had received neoadjuvant, adjuvant, or treatment for metastatic disease with an anthracycline (unless it was contraindicated) and a taxane.

- Approximately 70% of patients had received treatment in the metastatic setting; however, patients had received no more than two previous chemotherapy regimens for metastatic disease. More than two therapies in other settings (e.g., neoadjuvant, adjuvant) did not apply to this criterion.
- Eligible patients in this trial could have hormone-receptor positive metastatic breast cancer (i.e., estrogen-receptor positive, progesterone-receptor positive, or both) or triple negative metastatic breast cancer. Patients with hormone-receptor positive disease had received at least one endocrine therapy (adjuvant therapy or therapy for metastatic disease) and had disease progression during therapy, unless they had disease for which endocrine therapy was considered to be inappropriate.

V. The pivotal trial (POLO), is a phase 3 trial that studied metastatic, gBRCAm pancreatic cancer; eligible patients had received a minimum of 16 weeks of first-line platinum based chemotherapy (cisplatin, carboplatin, or oxaliplatin) and had not progressed while on the first-line platinum based chemotherapy. The patients were randomized in a 3:2 ratio to receive maintenance olaparib (Lynparza) or placebo with the primary end point progression-free survival. The median progression-free survival was statistically significant, 7.4 months in the olaparib (Lynparza) arm compared to 3.8 months in the placebo arm (HR 0.53 [95% CI, 0.35-0.81], p=0.0035). The interim analysis of overall survival showed no difference between the olaparib and placebo groups (median, 18.9 months vs. 18.1 months; hazard ratio for death, 0.91; 95% CI, 0.56 to 1.46; P=0.68). Additionally, quality of life was based on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, there was no significant between-group differences in health-related quality of life, as indicated by the overall change from baseline in the global quality-of-life score (on a 100-point scale, with higher scores indicating better quality of life (between-group difference, −2.47 points; 95% CI, −7.27 to 2.33)).

- As it currently stands, treatment with olaparib (Lynparza) in the setting of metastatic gBRCam pancratic cancer showed no difference in overall survival (OS) and quality of life (QoL) when compared to placebo. Therefore, limited exception should be granted to those who do not meet the criteria for metastatic, gBRCAm pancreatic cancer as stated in this policy.
- The preferred systemic regimens for metastatic, gBRCAm pancreatic cancer include:
    i. FOLFIRINOX or modified FOLFIRINOX ± subsequent chemoradiation

ii. Gemcitabine + albumin-bound paclitaxel ± subsequent chemoradiation

VI. PAOLA-1, the phase 3 trial that studied olaparib (Lynparza) as dual therapy with bevacizumab for maintenance therapy for advanced ovarian cancer, was a double-blind, randomized, placebo-controlled trial with the primary endpoint of progression free survival (PFS). The primary endpoint results of the predefined subgroups of HRD-positive, HRD-negative, or unknown found only a statistically significant difference in PFS in the HRD-positive subjects (HR: 0.33, 95% CI: 0.25, 0.45) and not the HRD-negative or unknown patients (HR: 0.92, 95% CI: 0.72, 1.17). Subjects enrolled in the trial had Stage III or IV disease and had a successful response to prior taxane-based chemotherapy.

VII. PROfound, the phase 3 trial that studied olaparib (Lynparza) in metastatic castration-resistant prostate cancer, enrolled men with homologous recombination repair (HRR) gene mutations in at least one of 15 prespecified HRR genes. Eligible patients had either a history of bilateral orchiectomy or were using luteinizing-hormone-releasing hormone analog therapy and had progressed on enzalutamide or abiraterone acetate or both, and were randomized (2:1) to receive either olaparib (Lynparza) or investigator's choice of enzalutamide or abiraterone acetate. Subjects were assigned cohorts based on HRR mutation (Cohort A: ATM, BRCA1, BRCA2; Cohort B: BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, or RAD54L). The primary endpoint was progression free survival (PFS) in Cohort A, and was significant between the treatment groups (HR: 0.34, 95% CI: 0.25, 0.47; p<0.001). Additionally, overall survival (OS) in Cohort A was significantly different between treatment groups (HR: 0.69, 95% CI: 0.50, 0.97; p=0.0175). PFS and OS were studied in Cohort B as exploratory endpoints and the results were not statistically significant and did not suggest improved outcomes with olaparib (Lynparza) over abiraterone or enzalutamide in those patients.

Investigational or Not Medically Necessary Uses

I. Breast cancer without metastasis, and/or HER2-negative breast cancer, and/or breast cancer without gBRCAm
   A. The safety and efficacy of olaparib in the breast cancer setting has only been established in patients with metastatic, HER2-negative, and gBRCA mutation.

II. Pancreatic cancer without metastasis, and without gBRCAm
   A. The safety and efficacy of olaparib in the pancreatic cancer setting has only been established in patients with metastatic disease with gBRCAm who has not progressed on the first-line platinum based chemotherapy.

III. Metastatic, gBRCAm pancreatic cancer that has progressed on first line platinum based chemotherapy

A. The safety and efficacy of olaparib in the pancreatic cancer setting has only been established in patients with metastatic disease with gBRCAm who has not progressed on the first-line platinum based chemotherapy.

IV. Use after disease progression on, or after, prior PARP inhibitor therapy
   A. There is no evidence to support the use of a subsequent PARP inhibitor following progression of disease on another PARP inhibitor.

V. Metastatic castration-resistant prostate cancer with other tumor mutations (including BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, or RAD54L)
   A. The phase 3 trial PROfound studied olaparib (Lynparza) versus enzalutamide or abiraterone in Cohort A (ATM, BRCA1, BRCA2) and Cohort B (BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, or RAD54L). While statistically significant differences in progression free survival (PFS) and overall survival (OS) were found in treatment with olaparib (Lynparza) in Cohort A and pooled Cohort A+B, the same was not found in Cohort B alone. Exploratory endpoints found PFS in Cohort B (HR: 0.88; 95% CI: 0.58, 1.36) and OS in Cohort B (HR: 0.73; 95% CI: 0.45, 1.23) not to be statistically significant and does not indicate improved patient outcomes with use of olaparib (Lynparza) over enzalutamide or abiraterone in these patients.

References

1. Lynparza [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals. December 2019.
2. Kaufman, B, Shapira-Frommer, R, Schmutzler, RK, et al. Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation. *J Clin Oncol.* 2015 Jan: 33(3):244-50. PMID 25366685.
3. Robson, M, Im, S, Senkus, E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*. 2017 Aug: 377(6):523-533. PMID: 28578601.
4. Ledermann, J, Harter, P, Gourley, M, et al. Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. *N Engl J Med.* 2012 Apr: 366(15):1382-92. PMID 22452356.
5. Pukade-Lauraine, E, Ledermann J, Selle, F, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation 9SOLO2/ENGOT-Ov21): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2017 Sep 18(9):1274-1284. PMID: 28754483.
6. NCCN Clinical Practice Guidelines in Oncology™. Ovarian Cancer v.5.2017. [cited 2/23/2018]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf
7. NCCN Clinical Practice Guidelines in Oncology™. Breast Cancer v.4.2017. [cited 2/23/2018]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
8. NCCN Clinical Practice Guidelines in Oncology™. Pancreatic Adenocarcinoma v.1.2020. [cited 01/29/2020]; Available from: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic_blocks.pdf
9. Golan T, Hammel P, Reni M, et al. Maintenance Olaparib for Germline *BRCA*-Mutated Metastatic Pancreatic Cancer. *N Engl J Med.* 2019 July: 381:317-327. DOI: 10.1056/NEJMoa1903387
10. de Bono J, Mateo J, et al. Olaparib for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2020 May 28;382(22):2091-2102. doi: 10.1056/NEJMoa1911440.
11. Ray-Coquard I, Pautier P, et al. Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer. N Engl J Med. 2019 Dec 19;381(25):2416-2428. doi: 10.1056/NEJMoa1911361

Policy Implementation/Update:

Action and Summary of Changes	Date
Included new FDA expanded indications as first-line maintenance therapy in advanced HRD-positive ovarian cancer in combination with bevacizumab and metastatic castration-resistant prostate cancer with certain HRR mutations. Supporting evidence has been included in the policy.	10/2020
Included new FDA expanded indication as first-line maintenance therapy in pancreatic adenocarcinoma with metastasis, gBRCAm, and patients whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. The criteria for approval in the pancreatic adenocarcinoma setting is to label, and the supporting evidence has been included in this policy. Advanced ovarian cancer without gBRCAm has been removed from the investigational and experimental section since olaparib (Lynparza) is approved in ovarian cancer without gBRCAm or sBRCAm. Pancreatic cancer without gBRCAm, and pancreatic cancer that has progressed on platinum based chemotherapy have been added to the investigational and experimental section with supporting evidence. To improve clarity, for all the indications in this policy, the mutation documentation and the specific diagnoses have been separated out into individual criterion. Removal of toxicity question upon renewal as this is managed by the provider.	02/2020
Removal of DDID to reflect the most updated template version, removed the 8 weeks criterion around most recent platinum-based therapy in the setting of maintenance therapy in ovarian cancer; in place of the 8 weeks criterion, provider attestation and documentation is required instead.	12/2019
Criteria transitioned to policy format with the following additional updates: Included new FDA expanded indication as first-line maintenance therapy in ovarian cancer with gBRCAm or sBRCAm after complete or partial response to platinum-based chemotherapy. Additionally, a question was added to the renewal portion of this policy to assess for toxicity. Capsule formulation is no longer available; therefore, it has been removed from policy. Lastly, NCCN recognizes the term “deleterious” as pathogenic in the setting of gBRCAm OR sBRCAm; therefore, the policy has been updated to include the term “pathogenic” and “likely pathogenic” in parentheses next to the terms “deleterious” and “suspected deleterious” respectively.	03/2019
Criteria update: Added coverage criteria for ovarian cancer maintenance and metastatic breast cancer	02/2018