PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Lynparza Prior Authorization Policy
- Lynparza® (olaparib tablets – AstraZeneca)

REVIEW DATE: 02/28/2024; selected revision 06/05/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Lynparza, a poly (ADP-ribose) polymerase (PARP) inhibitor, is indicated for the following uses:[1]

- **Breast cancer**, with deleterious or suspected deleterious germline BReast Cancer (g*BRCA*) mutated, human epidermal growth factor 2 (HER2)-negative metastatic disease, in adults who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor-positive (HR+) breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy.
- **Breast cancer**, for the adjuvant treatment of deleterious or suspected deleterious g*BRCA* mutated HER2-negative high-risk early breast cancer in adults who have been treated with neoadjuvant or adjuvant chemotherapy.
- **Ovarian cancer, maintenance** treatment of deleterious or suspected deleterious germline or somatic *BRCA* mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, in adults who are in a complete or partial response to platinum-based chemotherapy.
- **Ovarian cancer, maintenance** treatment of deleterious or suspected deleterious germline or somatic *BRCA*-mutated advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer in adults who are in complete or partial response to first-line platinum-based chemotherapy.

- **Ovarian cancer, maintenance treatment in combination** with bevacizumab for advanced epithelial ovarian, fallopian tube or primary peritoneal cancer in adults 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.
- **Pancreatic adenocarcinoma,** maintenance treatment of deleterious or suspected deleterious g*BRCA* mutated metastatic disease, in adults whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.
- **Prostate cancer**, for the treatment of deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration resistant prostate cancer (mCRPC) in adults who have progressed following prior treatment with Xtandi® (enzalutamide tablets) or abiraterone.
- **Prostate cancer,** for the treatment of deleterious or suspected deleterious *BRCA*-mutated (*BRCA*m) mCRPC, in combination with abiraterone and prednisone or prednisolone in adults.

Guidelines

Lynparza is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):[7]

- **Breast Cancer:** NCCN guidelines (version 1.2024 – January 25, 2024) list single-agent Lynparza as a "Preferred Regimen" for first-line therapy for patients with a germline *BRCA 1/2* mutation for recurrent, unresectable, or stage IV HR-positive, HER2-negative disease, with visceral crisis or that is endocrine therapy-refractory (category 1).[2] For triple negative breast cancer with germline *BRCA*1/2 mutation, Lynparza is listed as a "Preferred Regimen" as first-line for patients with programmed cell death ligand 1 combined positive score (PD-L1 CPS) < 10 (category 1) and as second-line therapy (category 1). Lynparza is also recommended as a single-agent for recurrent, unresectable, or stage IV disease with a germline *BRCA*1/2 mutation (category 1). It is noted that although Lynparza is FDA-approved for HER2-negative disease, the NCCN panel supports use in any breast cancer subtype associated with a germline mutation. The guidelines also state that addition of 1 year of adjuvant Lynparza is an "Preferred Regimen" option for select patients with germline *BRCA*1/2 mutation after completion of adjuvant chemotherapy for the following scenarios: triple negative disease if patient has ≥ primary tumor (pT2) or ≥ pathologic lymph nodes (pN1) disease after adjuvant chemotherapy or patient has residual disease after preoperative chemotherapy (category 1); HR+, HER2-negative tumors if 1) ≥ 4 positive lymph nodes after adjuvant chemotherapy (category 2A) or 2) residual disease after preoperative therapy and a clinical stage, pathologic stage, estrogen receptor status, and tumor grade (CPS+EG) score ≥ 3 (category 1). The guidelines state that adjuvant Lynparza therapy can be given with endocrine therapy.
- **Ovarian Cancer**: NCCN guidelines (version 2.2024 – May 13, 2024) recommend Lynparza for maintenance therapy after primary treatment in

patients who have had a complete or partial response in the following situations: single-agent Lynparza for *BRCA*1/2 mutations (category 1 if bevacizumab was not used during primary therapy and category 2A if bevacizumab was used during primary therapy); Lynparza + bevacizumab if bevacizumab was used as part of primary therapy (*BRCA*1/2 wild-type or unknown and homologous recombination deficient [category 1]; germline/somatic *BRCA*1/2 mutation [category 1]).[3] The guidelines recommend use of Zejula® (niraparib capsules), Rubraca® (rucaparib tablets), or Lynparza as single-agent maintenance therapy options in patients with platinum-sensitive persistent or recurrent disease who have completed two or more lines of platinum-based therapy and are in complete or partial response for BRCA mutation (category 1 if not previously used; category 2A for all others).

- **Pancreatic Cancer:** NCCN guidelines (version 1.2024 – December 13, 2023) recommend Lynparza as a "Preferred Regimen" maintenance therapy for metastatic disease after the patient has tried first-line platinum-based chemotherapy.[4] It is specifically recommended in patients who have germline *BRCA1/2* mutations and who have not had disease progression after at least 4 to 6 months of chemotherapy (category 2A).
- **Prostate Cancer:** NCCN guidelines (version 4.2023 – September 7, 2023) recommend Lynparza for mCRPC in the following scenarios as "Useful in Certain Circumstances": Lynparza + abiraterone for patients with *BRCA* mutation as first-line therapy (category 1) and for patients who have received prior docetaxel therapy and no prior novel hormone therapy (category 2A); single-agent Lynparza for patients with an HRR mutation who have received prior novel hormone therapy, (category 1; category 2B if the patient has visceral metastases and has tried docetaxel). Prior novel hormone therapy includes abiraterone, Xtandi® [enzalutamide capsule or tablet], Nubeqa® [darolutamide tablet], or Erleada® [apalutamide tablet]). A footnote notes that Lynparza is a treatment option for patients with mCRPC and a pathogenic mutation (germline and/or somatic) in a HRR gene (*BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *RAD51B*, *RAD51C*, *RAD51D*, or *RAD54L),* who have been previously treated with androgen receptor-directed therapy. However, efficacy appears to be driven by the cohort of patients with at least one alteration in *BRCA2*, *BRCA1*, or *ATM*, and in particular by patients with *BRCA2* or *BRCA1* mutations based on exploratory gene-by-gene analysis. There may be heterogeneity of response to Lynparza for non-*BRCA* mutations based on the specific gene mutation.
- **Uterine Neoplasms:** NCCN guidelines (version 1.2024 – September 20, 2023) state that Lynparza may be considered as a single-agent second-line therapy as "Useful in Certain Circumstances", for *BRCA2*-altered uterine leiomyosarcoma (category 2A).[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Lynparza. All approvals are provided for the duration noted below.

- **Lynparza® (olaparib tablets – AstraZeneca)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Breast Cancer – Adjuvant Therapy.** Approve for 1 year (total) if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has germline *BRCA* mutation-positive breast cancer; AND
   C) Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
   D) Patient has tried neoadjuvant or adjuvant therapy.

2. **Breast Cancer – Recurrent or Metastatic Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has recurrent or metastatic disease; AND
   C) Patient has germline *BRCA* mutation-positive breast cancer.

3. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer – Maintenance, Monotherapy.** Approve for 1 year if the patient meets ALL of the following (A, B and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has a germline or somatic *BRCA* mutation positive disease as confirmed by an approved test; AND
   C) Patient is in complete or partial response to at least one platinum-based chemotherapy regimen.
   Note: Examples of platinum-based chemotherapy are carboplatin with gemcitabine, carboplatin with paclitaxel, cisplatin with gemcitabine.

4. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer – Maintenance, Combination Therapy.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is used in combination with bevacizumab; AND
   C) Patient has homologous recombination deficiency (HRD)-positive disease as confirmed by an approved test; AND
   Note: HRD-positive disease includes patients with *BRCA* mutation-positive disease.
   D) Patient is in complete or partial response to first-line platinum-based chemotherapy regimen. Note: Examples of chemotherapy regimens are

carboplatin with paclitaxel, carboplatin with doxorubicin, docetaxel with carboplatin.

5. **Pancreatic Cancer – Maintenance Therapy.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has a germline *BRCA* mutation-positive metastatic disease; AND
   C) The disease has not progressed on at least 16 weeks of treatment with a first-line platinum-based chemotherapy regimen.

6. **Prostate Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has metastatic castration resistant prostate cancer; AND
   C) Patient meets ONE of the following (i or ii):
      i. The medication is used concurrently with a gonadotropin-releasing hormone (GnRH) analog; OR
      Note: Examples are leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Vantas (histrelin acetate subcutaneous implant), Firmagon (degarelix acetate subcutaneous injection), and Orgovyx (relugolix tablets).
      ii. Patient has had a bilateral orchiectomy; AND
   D) Patient meets ONE of the following (i or ii):
      i. Patient meets BOTH of the following (a and b):
         a) Patient has germline or somatic homologous recombination repair (HRR) gene-mutated disease, as confirmed by an approved test; AND
         Note: HRR gene mutations include *BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *RAD51B*, *RAD51C*, *RAD51D*, or *RAD54L.*
         b) Patient has been previously treated with at least one androgen receptor-directed therapy; OR
         Note: Androgen-receptor-directed therapy includes: abiraterone, Xtandi (enzalutamide capsules and tablets), Nubeqa (darolutamide tablets), or Erleada (apalutamide tablets).
      ii. Patient meets BOTH of the following (a and b):
         a) Patient has a *BRCA* mutation; AND
         b) The medication is used in combination with abiraterone plus one of prednisone or prednisolone.

Other Uses With Supportive Evidence:

7. **Uterine Leiomyosarcoma**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has *BRCA2*-altered disease; AND
   C) Patient has tried one systemic regimen.

Note: Examples of a systemic regimen include one or more of the following products: dacarbazine, docetaxel, doxorubicin, epirubicin, gemcitabine, ifosfamide Yondelis (trabectedin intravenous infusion).

CONDITIONS NOT COVERED

- **Lynparza® (olaparib tablets – AstraZeneca)**

is(are) considered experimental, investigational or unproven for ANY other use(s)

REFERENCES

1. Lynparza® tablets [prescribing information]. Wilmington, DE: AstraZeneca; October 2022.
2. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (version 2.2024 – May 13, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2024.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – January 25, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 26, 2024.
4. The NCCN Pancreatic Adenocarcinoma Clinical Practice Guidelines in Oncology (version 1.2024 – December 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 26, 2024.
5. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 4.2023 – September 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 26, 2024.
6. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – September 20, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 26, 2024.
7. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 21, 2024. Search term: olaparib.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Breast Cancer – Recurrent or Metastatic Disease:** The criterion that the patient has human epidermal growth factor receptor 2 (HER2)-negative disease was removed. **Prostate Cancer:** The criterion that the patient does not have a *PPP2R2A* mutation was removed.	02/22/2023
Selected Revision	**Prostate Cancer**: An option to approve in a patient with a BReast CAncer *(BRCA)* mutation; and in combination with abiraterone plus one of prednisone or prednisolone was added. Lynparza received a new FDA labeled indication for the treatment of deleterious or suspected deleterious *BRCA*-mutated (*BRCA*m) metastatic castration resistant prostate cancer, in combination with abiraterone and prednisone or prednisolone in adults.	06/07/2023
Update	**10/5/2023:** The overview section was updated due to change in FDA labeling. The following was added, "deleterious or suspected deleterious germline or somatic *BRCAm*" to the indication of "ovarian cancer, maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, in adults who	--

	are in a complete or partial response to platinum-based chemotherapy."	
Annual Revision	**Ovarian, Fallopian Tube, or Primary Peritoneal Cancer – Maintenance, Monotherapy:** Criteria for first-line maintenance therapy, which stated patient is in complete or partial response to first-line platinum-based therapy was removed. Criterion which stated that patient is in complete or partial response after at least two platinum-based chemotherapy regimens was removed. The following criterion was added: patient is in complete or partial response to at least one platinum-based chemotherapy regimen.	02/28/2024
Selected Revision	**Ovarian Cancer – Treatment:** Condition of approval and criteria were removed from "Other Uses With Supportive Evidence."	06/05/2024

HER2 – Human epidermal growth factor receptor 2; *BRCA* – BReast CAncer; *BRCAm* – *BRCA* mutated