PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/22/2023; selected revision 06/07/2023

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 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 *gBRCA* 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 2.2023 – February 7, 2023) 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 and second-line therapy for patients with programmed cell death ligand 1 combined positive score (PD-L1 CPS) < 10 (category 1). There is a footnote which states PARP inhibitors can be considered for a later line for those with *BRCA*1/2 mutation (category 2A); however, available evidence suggests it is more effective if used earlier. Lynparza is also recommended as a single-agent for recurrent, unresectable, or stage IV HER2-positive disease with a *BRCA*1/2 mutation (category 2A). It is noted that although Lynparza is FDA-approved for HER2-negative disease, the NCCN panel supports use in any breast cancer subtype with a *BRCA1* or *BRCA2* mutation. The guidelines also state that addition of 1 year of adjuvant Lynparza is an 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 2A). The guidelines state that adjuvant Lynparza therapy can be given with endocrine therapy.

- **Ovarian Cancer**: NCCN guidelines (version 1.2023 – December 22, 2022) 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 ("Preferred"; category 1); Lynparza can be used in this setting without a BRCA mutation (category 2A). The guidelines recommend Lynparza as single-agent targeted therapy for treatment of patients with deleterious germline *BRCA* mutated advanced (persistent disease or recurrence) ovarian cancer following two or more lines of chemotherapy (category 3).
- **Pancreatic Cancer:** NCCN guidelines (version 2.2022 – December 6, 2022) 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 1.2023 – September 16, 2022) recommend Lynparza as "Useful in Certain Circumstances" for mCRPC with germline or somatic HRR mutation for patients who have received prior novel hormone therapy (i.e. abiraterone, Xtandi® [enzalutamide capsule or tablet], Nubeqa® [darolutamide tablet], or Erleada® [apalutamide tablet]) [category 1; category 2B if the patient has visceral metastases and has tried docetaxel].[5] 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 1.2023 – December 22, 2022) 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 the following criteria (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 the following criteria (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 the following criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following criteria (i or ii):
   i. Patient meets both of the following criteria for first-line maintenance therapy (a and b):
      a) Patient has a germline or somatic *BRCA* mutation-positive disease as confirmed by an approved test; AND
      b) Patient is in complete or partial response to first-line platinum-based chemotherapy regimen; OR
      Note: Examples are carboplatin with paclitaxel, carboplatin with doxorubicin, docetaxel with carboplatin.
   ii. Patient is in complete or partial response after at least two platinum-based chemotherapy regimens.
   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 the following criteria (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 the following criteria (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 the following criteria (A, B, C, D, and E):

A) Patient is ≥ 18 years of age; AND

B) Patient has metastatic castration resistant prostate cancer; AND

C) Patient meets one of the following criteria (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), Orgovyx (relugolix tablets).

ii. Patient has had a bilateral orchiectomy; AND

D) Patient meets the following criteria (i or ii):

i. Patient meets the following criteria (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 the following criteria (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. **Ovarian Cancer – Treatment.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   Note: This also includes fallopian tube, or primary peritoneal cancer.
   A) Patient is ≥ 18 years of age; AND
   B) Patient has a germline *BRCA*-mutation as confirmed by an approved test; AND
   C) Patient has progressed on two or more prior lines of chemotherapy.

8. **Uterine Leiomyosarcoma**. Approve for 1 year if the patient meets the following criteria (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 1.2023 – December 22, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – February 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.
4. The NCCN Pancreatic Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2022 – December 6, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.
5. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 1.2023 – September 16, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 20, 2023.
6. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2023 – December 22, 2023). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 20, 2023.
7. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023. Search term: olaparib.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Breast Cancer – Recurrent or Metastatic Disease:** The words 'recurrent or metastatic disease" were added to the condition of approval. The word "recurrent" was added to the criteria, "Patient has metastatic germline BReast Cancer (*BRCA)* mutation positive breast cancer. The following criteria were removed:	02/02/2022

	patient has hormone receptor positive (HR+) (i.e. estrogen receptor [ER]+ and/or progesterone reception [PR]+) disease and patient has been treated with prior endocrine therapy or patient is considered inappropriate for endocrine therapy; patient has triple negative disease (i.e., ER-negative, PR-negative, and human epidermal growth factor receptor 2 [HER2]-negative); and patient has been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. The following criteria was added: patient has HER2-negative breast cancer. **Ovarian – Treatment:** Criteria for patients currently receiving Lynparza was removed. The word "initial therapy" was also removed. A note was added that this indication also includes fallopian tube, or primary peritoneal cancer. Criteria was changed from progression on three or more lines to chemotherapy to two or more prior lines of chemotherapy. **Prostate Cancer**: The words "castration resistant" were removed from the condition of approval and added to the criteria. The requirement, "Patient has been previously treated with abiraterone or Xtandi (enzalutamide capsules)" was reworded to, "at least one androgen receptor-directed therapy" and abiraterone or Xtandi (enzalutamide capsules) were moved to the Note which lists out the androgen receptor directed therapy. The following drugs: Nubeqa (darulutamide tablets) or Erleada (apalutamide tablets) were also added to the list of medications in the Note. **Breast Cancer – Adjuvant Therapy:** This condition of approval was added to the Other Uses with Supportive Evidence section based on National Comprehensive Cancer Network (NCCN) guideline updates. **Uterine Leiomyosarcoma:** This condition of approval was added to the Other Uses with Supportive Evidence section based on NCCN guideline updates.	
Update	**03/14/2022: Breast Cancer – Adjuvant Therapy:** Condition of approval and criteria were moved from Other Uses with Supportive Evidence to FDA-approved indications due to FDA approval for this indication.	N/A
Selected Revision	**Breast Cancer – Recurrent or Metastatic Disease:** The duration of approval was changed from 3 years to 1 year. **Ovarian Cancer – Treatment:** The duration of approval was changed from 3 years to 1 year. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer – Maintenance, Monotherapy:** The duration of approval was changed from 3 years to 1 year. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer – Maintenance, Combination Therapy:** The duration of approval was changed from 3 years to 1 year. **Pancreatic Cancer – Maintenance Therapy:** The duration of approval was changed from 3 years to 1 year. **Prostate Cancer:** The duration of approval was changed from 3 years to 1 year. **Uterine Leiomyosarcoma:** The duration of approval was changed from 3 years to 1 year.	06/22/2022
Update	**09/07/2022:** The following indication was removed from the overview section due to removal of indication from FDA labeling: Ovarian cancer, treatment of adults with deleterious or suspected deleterious germlime BReast CAncer (g*BRCA)*-mutated advanced disease who have been treated with three or more prior lines of chemotherapy.	N/A

	Ovarian Cancer – Treatment: The indication and criteria were removed from the FDA approved use section and moved into Other Uses with Supportive Evidence.	
Selected Revision	**Breast Cancer – Adjuvant Therapy:** The criteria for hormone receptor positive and hormone receptor negative patients were removed. The criterion that patient has tried neoadjuvant or adjuvant therapy was added.	11/16/2022
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 *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

BRCA – BReast CAncer; HER2 – Human epidermal growth factor receptor 2; GnRH – Gonadotropin-releasing hormone; HR+ – hormone receptor positive; ER+ – estrogen receptor positive; PR+ – progesterone-receptor positive; NCCN – National Comprehensive Cancer Network.