CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Olaparib (Lynparza®)

Version: 1.0

EFFECTIVE DATE: 2/1/2025

NantHealth® | Eviti®

Please note the following:

Olaparib (Lynparza®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Olaparib (Lynparza): Discussion

Olaparib inhibits polyadenosine diphosphate ribose polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. These enzymes play a role in normal cellular functions such as DNA transcription, cell cycle regulation, and DNA repair. Olaparib has been shown to inhibit the growth of certain tumor cell lines in vitro and reduce tumor growth in mouse xenograft models of human cancer, both as a standalone treatment and following platinum-based chemotherapy. Increased cytotoxicity and anti-tumor activity were observed with olaparib treatment in cell lines and mouse tumor models with breast cancer gene (BRCA) deficiencies.[1]

PARP inhibitors work by two potential mechanisms that allow the persistence of spontaneously occurring single strand breaks due to a loss of enzymatic function and prevent the release of PARP from DNA (termed PARP trapping). Both mechanisms lead to persistent single strand breaks, collapsed replication forks, and resultant double-strand breaks. Repair of double strand breaks can occur by either homologous recombination or non-homologous end-joining (NHEJ).

In cells with BRCA 1 and 2 mutations or other homologous recombination (HR) deficiencies, PARP inhibition leads to a process called 'synthetic lethality.' This occurs when two DNA repair mechanisms are effectively shut down, forcing the cell to rely on NHEJ, which ultimately results in cell death. This makes PARP inhibitors unique, as they target and exploit a specific defect in cancer cells.[2,3]

The most common adverse reactions associated with olaparib include myelodysplastic syndrome/acute myeloid leukemia, pneumonitis, embryo-fetal toxicity, anemia, nausea, fatigue, asthenia, vomiting, diarrhea, dyspepsia, headache, decreased appetite, nasopharyngitis, pharyngitis, upper respiratory infection (URI), cough, arthralgia, musculoskeletal pain, myalgia, back pain, dermatitis, rash, and abdominal pain or discomfort.

Olaparib is approved by the Food and Drug Administration (FDA) for the following cancer types: breast, ovarian, pancreatic, and prostate.[1]

The National Comprehensive Cancer Network (NCCN) endorses olaparib for the following cancer types: breast, ovarian, pancreatic, prostate, and uterine.[4,5,6,7,8]

Olaparib: Definitions

- **BRCA1 and BRCA 2 Mutations** - Genetic alterations in the BRCA1 and BRCA2 genes are responsible for producing proteins that help repair damaged DNA. When these genes are mutated, their ability to repair DNA is compromised, leading to an increased risk of developing certain cancers.[2]
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Homologous Recombination (HR)** - A DNA repair process crucial for the accurate repair of DNA damage.[2]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

Olaparib: Policy

Note: Coverage of olaparib will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Olaparib will be considered for coverage when the following criteria are met:

Breast Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Adjuvant treatment of patients with deleterious or suspected deleterious BRCA gene mutations (gBRCAm) human epidermal growth factor receptor 2 (HER2)-negative high risk early breast cancer, who have been treated with neoadjuvant or adjuvant chemotherapy; OR
4. Deleterious or suspected deleterious gBRCAm, HER2-negative metastatic disease who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy[1]; OR

Invasive Breast Cancer

For **NCCN** required criteria coverage:

5. Adjuvant therapy following adjuvant chemotherapy in human epidermal growth factor receptor 2 (HER2)-negative germline BRCA 1/2 mutated disease for one of the following:
   a) Hormone receptor-negative and pT1a (≤0.5cm) and pN1mi
   b) Hormone receptor-negative and pT1b (0.6-1.0cm) or pT1c-pT3 (>1cm) and pN0 or pN1mi
   c) Hormone receptor-negative and pN+ (≥1 ipsilateral metastases >2mm)
   d) Hormone receptor-positive and pN2/pN3 (≥4 ipsilateral metastases >2mm); OR
6. Adjuvant therapy for one year in patients who have received preoperative chemotherapy and have residual disease that is germline BRCA 1/2 mutated ypT1-4, N0 or ypN≥1 and human epidermal growth factor receptor 2 (HER2)-negative; OR
7. First-line therapy (may be considered for a later line) as a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2-negative, BRCA 1/2-germline mutated disease that is hormone receptor-positive with visceral crisis or endocrine therapy refractory; OR
8. Single agent therapy for recurrent unresectable (local or regional) or stage IV (M1) triple-negative breast cancer (TNBC) BRCA 1/2-germline mutated disease for one of the following:
   a) First-line therapy if PD-L1 CPS <10
   b) Second-line therapy; OR
9. Single agent therapy for recurrent unresectable (local or regional) or stage IV (M1) disease with germline PALB2 mutations; OR
10. Fourth-line therapy and beyond as a single agent for recurrent, unresectable (local or regional) or stage IV (M1) HER2-positive, BRCA 1/2-germline mutated disease for one of the following:
    a) Hormone receptor-negative
    b) Hormone receptor-positive; OR
11. Emerging biomarkers and novel therapies for patients with stage IV (M1) disease including activity in somatic BRCA1/2 mutations as a single agent for one of the following:
    a) Third-line therapy and beyond in human epidermal growth factor receptor 2 (HER2)-negative disease
    b) Fourth-line therapy and beyond in HER2-positive disease; OR

Inflammatory Breast Cancer

For **NCCN** required criteria coverage:

12. Adjuvant therapy for one year in patients who have received preoperative chemotherapy and have residual disease that is germline BRCA 1/2 mutated and human epidermal growth factor receptor 2 (HER2)-negative; OR
13. Adjuvant therapy following adjuvant chemotherapy in HER2-negative germline BRCA 1/2 mutated disease for one of the following:
    a) Hormone receptor negative and pT1a (≤0.5cm) and pN1mi
    b) Hormone receptor-negative and pT1b (0.6-1.0cm) or pT1c-pT3 (>1 cm) and pN0 or pN1mi
    c) Hormone receptor-negative and pN+ (≥1 ipsilateral metastases >2mm)
    d) Hormone receptor-positive and pN2/pN3 (≥4 ipsilateral metastases >2mm); OR

14. Adjuvant therapy for one year in patients who have received preoperative chemotherapy and have residual disease that is germline BRCA 1/2 mutated and human epidermal growth factor receptor 2 (HER2)-negative; OR
15. Single agent therapy for recurrent unresectable (local or regional) or stage IV (M1) disease with germline PALB2 mutations; OR
16. First-line therapy (may be considered for a later line) as a single agent for patients with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-negative, BRCA 1/2-germline mutated disease that is hormone receptor-positive with visceral crisis or endocrine therapy refractory; OR
17. Single agent therapy for patients with no response to preoperative systemic treatment, or recurrent unresectable (local or regional) or stage IV (M1) triple-negative breast cancer (TNBC) BRCA 1/2-germline mutated disease for one of the following:
    a) First-line therapy if PD-L1 CPS <10
    b) Second-line therapy; OR
18. Fourth-line therapy and beyond as a single agent for patients with no response to preoperative systemic treatment, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive, BRCA 1/2-germline mutated disease for one of the following:
    a) Hormone receptor-negative
    b) Hormone receptor-positive; OR
19. Emerging biomarkers and novel therapies for patients with stage IV (M1) disease include activity in somatic BRCA1/2 mutations as a single agent for one of the following:
    a) Third-line therapy and beyond in HER2-negative disease
    b) Fourth-line therapy and beyond in HER2-positive disease.[4]

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Maintenance treatment for deleterious or suspected deleterious germline or somatic BRCA-mutated advanced disease who are in complete or partial response to first-line platinum-based chemotherapy; OR
4. In combination with bevacizumab for the maintenance treatment of patients with advanced disease, 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 one of the following:
    a) Deleterious or suspected deleterious BRCA mutation
    b) Genomic instability; OR
5. Maintenance treatment of patients with deleterious or suspected deleterious germline or somatic BRCA-mutated recurrent disease who are in complete or partial response to platinum-based chemotherapy[1]; OR

Carcinosarcoma (Malignant Mixed Müllerian Tumors)

For **NCCN** required criteria coverage:

6. Maintenance therapy for stage II-IV carcinosarcoma with a germline or somatic BRCA1/2 mutation if in complete response (CR) or partial response (PR) after primary therapy for one of the following:
   a) Single agent
   b) In combination with bevacizumab following primary therapy including bevacizumab; OR
7. Single agent therapy for persistent disease or recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy; OR
8. Single agent maintenance therapy, if not previously used, or if the disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.

   Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor[5]; OR

Clear Cell Carcinoma of the Ovary

For **NCCN** required criteria coverage:

9. Maintenance therapy for stage II-IV clear cell carcinoma with a germline or somatic BRCA1/2 mutation if in complete response (CR) or partial response (PR) after primary therapy for one of the following:
   a) Single agent
   b) In combination with bevacizumab following primary therapy including bevacizumab; OR
10. Single agent for persistent disease or recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy; OR
11. Single agent maintenance therapy, if not previously used, or if disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.

    Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor; OR

Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

For **NCCN** required criteria coverage:

12. Maintenance therapy for stage II-IV high-grade serous or grade 2/3 endometrioid carcinoma if in complete response (CR) or partial response (PR) after primary therapy for one of the following:
    a) Single agent in patients with a germline or somatic BRCA1/2 mutation
    b) In combination with bevacizumab following primary therapy including bevacizumab if BRCA1/2 wild-type, or unknown, and HR deficient

c) In combination with bevacizumab following primary therapy including bevacizumab in patients with a germline or somatic BRCA1/2 mutation; OR

13. Single agent for persistent disease or recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy; OR
14. Single agent maintenance therapy if not previously used, or if the disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.

    Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor; OR

Grade 1 Endometrioid Carcinoma

For **NCCN** required criteria coverage:

15. Single agent for persistent disease or recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy; OR
16. Single agent maintenance therapy, if not previously used, or if the disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.

    Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor; OR

Low-Grade Serous Carcinoma

For **NCCN** required criteria coverage:

17. Single agent for platinum-sensitive or platinum-resistant recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy; OR
18. Single agent maintenance therapy, if not previously used, or if the disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.

    Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor; OR

Mucinous Neoplasms of the Ovary

For **NCCN** required criteria coverage:

19. Single agent maintenance therapy, if not previously used, or if disease has not progressed during prior PARP-inhibitor treatment for those with a deleterious or suspected deleterious germline or somatic BRCA 1/2 mutation and platinum-sensitive recurrent disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response

    Note: Discontinue bevacizumab before initiating maintenance therapy with a PARP inhibitor; OR

20. Single agent for persistent disease or recurrence in patients with deleterious germline BRCA mutation who have been treated with two or more lines of chemotherapy.[5]

Pancreatic Adenocarcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Maintenance therapy for patients with deleterious or suspected deleterious gBRCAm metastatic adenocarcinoma, whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen[1]; OR

For **NCCN** required criteria coverage:

4. Maintenance therapy for metastatic disease (if previous first-line platinum-based chemotherapy was given) and if the patient has a good performance status (ECOG PS 0-1), with good biliary drainage and adequate nutritional intake) or an intermediate performance status (ECOG 2), and no disease progression (after at least 4-6 months of chemotherapy, assuming acceptable tolerance), as a single agent for germline BRCA1/2 mutations.[6]

Prostate Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Treatment for deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed after prior treatment with enzalutamide or abiraterone; OR
4. Treatment in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC)[1]; OR

For **NCCN** required criteria coverage:

5. In combination with abiraterone or fine-particle abiraterone with concurrent steroids (prednisone or methylprednisolone) for treatment of castration-resistant distant metastatic

(M1) disease for those who have a pathogenic BRCA 1/2 mutation (germline and/or somatic) for one of the following:
   a) Received no prior docetaxel and no prior novel hormone therapy
   b) Progression on prior docetaxel and no prior novel hormone therapy; OR
6. Single agent for castration-resistant distant metastatic (M1) disease for patients who have been treated previously with androgen receptor-directed therapy and have a pathogenic mutation (germline and/or somatic) in a homologous recombination repair gene (HRRm) which include BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D or RAD54L, and if one of the following:
   a) Progression on prior novel hormone therapy and no prior docetaxel was given (preferred if BRCA mutation; useful in certain circumstances for HRRm other than BRCA1/2)
   b) Progression on prior docetaxel and a novel hormone therapy.

   Note: Continue androgen deprivation therapy (ADT) to maintain castrate levels of serum testosterone (<50 ng/dL).[7]

Uterine Neoplasms - Uterine Sarcoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy for advanced, recurrent/metastatic, or inoperable disease as a single agent, may be considered for BRCA2-altered leiomyosarcoma (LMS) for one of the following:
   a) Known or suspected extrauterine disease, diagnosed by biopsy or myomectomy
   b) Disease that is not suitable for primary surgery (disease is not amenable to resection or the patient is not suitable for surgery based on comorbidities)
   c) Additional therapy following total hysterectomy ± bilateral salpingo-oophorectomy (TH ± BSO) for stage II-III LMS
   d) Additional therapy following TH ± BSO for stage IV LMS
   e) Preoperatively or postoperatively for recurrent disease with resectable isolated metastases
   f) Recurrent disease with unresectable isolated metastases or disseminated disease
   g) Radiologically isolated vaginal/pelvic recurrence if no prior radiation therapy (RT), given in combination with RT
   h) Radiologically isolated vaginal/pelvic recurrence if prior RT was or was not given.[8]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Olaparib: References

1. Olaparib (Lynparza) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208558s028lbl.pdf. Accessed February 4, 2025.
2. Montemorano et al. Role of Olaparib as Maintenance Treatment for Ovarian Cancer: The Evidence to Date. https://pmc.ncbi.nlm.nih.gov/articles/PMC6938196/. Accessed February 4, 2025.
3. Bochum et al. Olaparib. https://pubmed.ncbi.nlm.nih.gov/30069770/. Accessed February 4, 2025.
4. National Comprehensive Cancer Network. Breast Cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed February 4, 2025.
5. National Comprehensive Cancer Network. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed February 4, 2025.
6. National Comprehensive Cancer Network. Pancreatic Adenocarcinoma. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed February 4, 2025.
7. National Comprehensive Cancer Network. Prostate Cancer. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed February 4, 2025.
8. National Comprehensive Cancer Network. Uterine Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 4, 2025.

Olaparib: Coding (CPT®, ICD 10, and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C25.9	Pancreatic adenocarcinoma
C48.2	Primary peritoneal cancer
C50.9	Breast cancer/invasive/inflammatory
C54.1	Grade 1 endometrioid carcinoma
C54.9	Carcinosarcoma (malignant mixed Müllerian tumors)

C55.9	Uterine neoplasms - uterine sarcoma
C56.9	Ovarian cancer/clear cell carcinoma/mucinous neoplasms of the ovary/low-grade serous carcinoma
C57.0	Fallopian tube cancer
C61	Prostate cancer
J8999	Olaparib

Olaparib: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	2/1/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	2/25/2025
6	Revision Changes:	