Clinical Policy: Olaparib (Lynparza)

Reference Number: ERX.SPA.222
Effective Date: 12.01.17
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Olaparib (Lynparza®) is a poly (ADP-ribose) polymerase (PARP) inhibitor.

FDA Approved Indication(s)
Lynparza is indicated for the:

- Maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza
- Use in combination with bevacizumab 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
- Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy
- Treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza
- Treatment of patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer 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 treatment. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza
- For the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza
- For the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza
- For the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER-2)- negative high risk metastatic breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lynparza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Ovarian Cancer (must meet all)**:**

1. Diagnosis of epithelial ovarian, fallopian tube, or primary peritoneal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a, b, c, or d):
   a. Both i and ii:
      i. Documentation of a deleterious or suspected deleterious germline BRCA mutation as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
      ii. Failure of ≥ 3 lines of platinum-based chemotherapy (*see Appendix B*) unless clinically significant adverse effects are experienced or all are contraindicated;
   b. Completed ≥ 2 platinum-based chemotherapy regimens and is in a complete or partial response;
   c. Both i and ii:
      i. Documentation of a deleterious or suspected deleterious germline or somatic BRCA-mutation as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
      ii. Completed a platinum-based chemotherapy regimen and is in a complete or partial response;
   d. Both i and ii:
      i. Disease is associated with HRD-positive status defined by one of the following (1 or 2):
         1) Documentation of a deleterious or suspected deleterious BRCA mutation as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
         2) Documentation of genomic instability;
      ii. Both of the following (1 and 2):
         1) Completed a bevacizumab- and platinum-based chemotherapy regimen as first-line therapy, and is in a complete or partial response (*see Appendix B*);
         2) Lynparza is prescribed in combination with bevacizumab;
5. Member has not previously received a PARP inhibitor (e.g., Rubraca®, Talzenna®, Zejula®);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 600 mg (4 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Breast Cancer (must meet all)**:**

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has all of the following characteristics (a, b, and c):
   a. HER2-negative;
   b. Deleterious germline BRCA 1/2 mutations as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
   c. High risk, metastatic or recurrent;
5. Member has not previously received a PARP inhibitor (e.g., Rubraca®, Talzenna®, Zejula®);
6. Request meets one of the following (a or b):*

a. Dose does not exceed 600 mg (4 tablets) per day;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

C. Pancreatic Adenocarcinoma (must meet all)**:**

1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Documentation of deleterious or suspected deleterious germline BRCA mutation as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
5. Received > 16 weeks of platinum-based chemotherapy with no disease progression;
6. Member has not previously received a PARP inhibitor (e.g., Rubraca®, Talzenna®, Zejula®);
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 600 mg (4 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

D. Prostate Cancer (must meet all):

1. Diagnosis of metastatic castration-resistant prostate cancer;
2. Documentation of disease progression despite bilateral orchiectomy or other androgen deprivation therapy (ADT) (*see Appendix D*);
3. Documentation of a deleterious or suspected deleterious germline or somatic HRR gene mutation as confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx);
4. Member does not have a *PPP2R2A* gene mutation;
5. Prescribed by or in consultation with an oncologist or urologist;
6. Age ≥ 18 years;
7. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
8. Failure of abiraterone (Zytiga®) or Xtandi® (enzalutamide), unless clinically significant adverse effects are experienced or both are contraindicated;
9. Member has not previously received a PARP inhibitor (e.g., Rubraca®, Talzenna®, Zejula®);
10. Request meets one of the following (a or b):*
    a. Dose does not exceed 600 mg (4 tablets) per day;
    b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

E. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Lynparza for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For HRD-positive ovarian cancer within the first 15 months of combination therapy with bevacizumab: Documentation of continued bevacizumab therapy, unless contraindications or clinically significant adverse effects to bevacizumab have developed;
4. For adjuvant therapy in breast cancer, total duration of therapy does not exceed 1 year;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 600 mg (4 tablets) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADP: adenosine diphosphate
ADT: androgen deprivation therapy
AML: acute myeloid leukemia
BRCA: breast cancer gene
FDA: Food and Drug Administration
gBRCAm: mutations in the germline BRCA genes
GnRH: gonadotropin-releasing hormone
HER: human epidermal growth factor receptor
HR: hormone receptor
HRD: homologous recombination deficiency
HRR: homologous recombination repair
LHRH: luteinizing hormone-releasing hormone
mCRPC: metastatic castration-resistant prostate cancer
MDS: myelodysplastic syndrome
NCCN: National Comprehensive Cancer Network
PARP: poly (ADP-ribose) polymerase

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ovarian Cancer		
Alimta® (pemetrexed)	Various	Varies
Alkeran® (melphalan)	Various	Varies
Avastin® (bevacizumab)	Various	Varies
carboplatin (Paraplatin®)	Various	Varies
cisplatin (Platinol-AQ®)	Various	Varies
cyclophosphamide (Cytoxan®)	Various	Varies
docetaxel (Taxotere®)	Various	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
doxorubicin (Doxil®, Adriamycin®)	Various	Varies
etoposide (Vepesid®)	Various	Varies
gemcitabine (Gemzar®)	Various	Varies
ifosfamide (Ifex®)	Various	Varies
irinotecan (Camptosar®)	Various	Varies
oxaliplatin (Eloxatin®)	Various	Varies
topotecan (Hycamtin®)	Various	Varies
Hexalen (altretamine)	Various	Varies
Pancreatic Adenocarcinoma		
FOLFIRINOX (leucovorin, fluorouracil, irinotecan, oxaliplatin)	Various	Varies
gemcitabine + cisplatin	Various	Varies
Prostate Cancer		
abiraterone (Zytiga®) + prednisone	Abiraterone 1,000 mg PO QD + prednisone 5 mg PO BID	Abiraterone 1,000 mg/day + prednisone 10 mg/day
Xtandi® (enzalutamide)	Xtandi 160 mg PO QD	160 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) have been confirmed in patients treated with Lynparza. The majority of the cases (17 of 22) were fatal. If MDS/AML is confirmed, discontinue Lynparza.
- The FDA approved Lynparza with a genetic test called BRACAnalysis CDx, a companion diagnostic that will detect the presence of mutations in the BRCA genes (gBRCAm) in blood samples from patients with ovarian cancer. Additional information is available at http://www.fda.gov/companiondiagnostics.
- Lynparza is not indicated for patients with mCRPC with a *PPP2R2A* mutation due to an unfavorable risk-benefit profile for this mutation.
- CRPC is prostate cancer that progresses clinically, radiographically, or biochemically despite castrate levels of serum testosterone (< 50 ng/dL). Per NCCN guidelines for the treatment of prostate cancer, ADT should be continued in the setting of CRPC while additional therapies are applied.
- Examples of ADT include:
  - Bilateral orchiectomy (surgical castration)
  - Luteinizing hormone-releasing hormone (LHRH) given with or without an anti-androgen:
    - LHRH (or GnRH) agonists: Zoladex® (goserelin), Vantas® (histrelin), leuprolide (Lupron Depot®, Eligard®), and Trelstar® (triptorelin)
    - Anti-androgens: bicalutamide (Casodex®), flutamide, nilutamide (Nilandron®), Xtandi (enzalutamide), Erleada® (apalutamide)
  - LHRH antagonist: Firmagon® (degarelix), Orgovyx® (relugolix)
- There is insufficient data regarding the use of consecutive PARP inhibitors. Most PARP inhibitor pivotal trials excluded prior PARP inhibitor use, the NCCN does not make any explicit recommendations (other than for ovarian cancer, where they state data is limited), and there are no randomized controlled trials evaluating such use.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast, ovarian, pancreatic, prostate cancers	300 mg PO BID	600 mg/day

VI. Product Availability

Tablets: 100 mg, 150 mg

VII. References

1. Lynparza Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP. March 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208558s019s020lbl.pdf. Accessed April 27, 2022.
2. Olaparib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 4, 2021.
3. National Comprehensive Cancer Network. Breast Cancer Version 8.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 4, 2021.
4. National Comprehensive Cancer Network. Ovarian Cancer Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed October 4, 2021..
5. National Comprehensive Cancer Network. Pancreatic Adenocarcinoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed October 4, 2021..
6. National Comprehensive Cancer Network. Prostate Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 15, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Add new indication for treatment of gBRCAm, HER2-negative metastatic breast cancer. Increased all approval durations to length of benefit.	02.20.18	05.18
4Q 2018 annual review: breast cancer: added NCCN off-label uses and summarized NCCN and FDA-approved uses for improved clarity; all indications: removed language “as detected by an FDA approved test”; references reviewed and updated.	07.05.18	11.18
1Q 2019 annual review: criteria added for new FDA indication for 1st-line maintenance treatment of gBRCAm or sBRCAm advanced ovarian cancer; removed capsule formulation from policy since it has been discontinued; references reviewed and updated.	01.22.19	02.19
RT4: updated FDA indication for maintenance treatment of ovarian cancer from “Select patients with gBRCAm advanced epithelial ovarian, fallopian tube or primary peritoneal cancer for therapy based on an FDA-approved companion diagnostic for Lynparza” to “Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza” per updated verbiage in PI; no change to criteria.	07.09.19	
1Q 2020 annual review: added off-label NCCN Compendium supported use in pancreatic adenocarcinoma; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	10.30.19	02.20
Criteria added for two newly FDA-approved indications: 1) HRD-positive ovarian cancers in combination with bevacizumab after bevacizumab primary therapy, and 2) HRR-mutated mCRPC; converted pancreatic adenocarcinoma from off-label to an FDA-approved use; for all indications, added requirement for no prior PARP inhibitor use.	06.02.20	08.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.15.20	02.21
1Q 2022 annual review: added that mutation analysis must be confirmed on a CLIA approved diagnostic test (e.g., Foundation One CDx or BRAC Analysis CDx); added in continued therapy section that total treatment duration as adjuvant therapy in breast cancer does not exceed 1 year; references reviewed and updated.	10.04.21	02.22
RT4: added newly FDA approved indication: For the adjuvant treatment of HER-2 negative, high risk metastatic breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy.	04.26.22	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.