

Clinical Policy: Olaparib (Lynparza)

Reference Number: CP.PHAR.360

Effective Date: 10.03.17

Last Review Date: 05.22

Line of Business: Commercial, HIM, 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:

- 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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 \geq 18 years;
4. For brand Lynparza requests, medical justification supports inability to use generic olaparib, if available (e.g., contraindications to excipients);
5. 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 \geq 3 lines of platinum-based chemotherapy (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
 - b. Completed \geq 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;
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/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

B. Breast Cancer (must meet all):

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. For brand Lynparza requests, medical justification supports inability to use generic olaparib, if available (e.g., contraindications to excipients);
5. 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;
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/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

C. Pancreatic Adenocarcinoma (must meet all):

1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. For brand Lynparza requests, medical justification supports inability to use generic olaparib, if available (e.g., contraindications to excipients);
5. 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);

6. Received > 16 weeks of platinum-based chemotherapy with no disease progression;
7. Member has not previously received a PARP inhibitor (e.g., Rubraca[®], Talzenna[®], Zejula[®]);
8. 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 – 12 months or duration of request, whichever is less

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 \geq 18 years;
7. For brand Lynparza requests, medical justification supports inability to use generic olaparib, if available (e.g., contraindications to excipients);
8. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
9. Failure of abiraterone (Zytiga[®]) or Xtandi[®] (enzalutamide), unless clinically significant adverse effects are experienced or both are contraindicated;
10. Member has not previously received a PARP inhibitor (e.g., Rubraca[®], Talzenna[®], Zejula[®]);
11. 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 – 12 months or duration of request, whichever is less

E. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit 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 brand Lynparza requests, medical justification supports inability to use generic olaparib, if available (e.g., contraindications to excipients);
4. 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;
5. For adjuvant therapy in breast cancer, total duration of therapy does not exceed 1 year;
6. 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/HIM – 12 months

Commercial – 12 months or duration of request, whichever is less

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 2

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 (Cytosan [®])	Various	Varies
docetaxel (Taxotere [®])	Various	Varies
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 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 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 1, 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 4, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Add new indication for treatment of gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer.	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 1 st -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 and RT4: added new FDA indication and NCCN Compendium supported use in pancreatic adenocarcinoma; 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; for all indications, added requirement for no prior PARP inhibitor use.	06.02.20	08.20
1Q 2021 annual review: added new template language regarding redirection to generic if available for oral oncology agents; references to HIM.PHAR.21 revised to HIM.PA.154; 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	10.04.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
that total treatment duration as adjuvant therapy in breast cancer does not exceed 1 year; references reviewed and updated.		
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
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.	05.13.22	

Important Reminders

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in 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.

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