Clinical Policy Title:	olaparib
Policy Number:	RxA.401
Drug(s) Applied:	Lynparza®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Olaparib (Lynparza®) is a poly (ADP-ribose) polymerase (PARP) inhibitor.
Lynparza® is indicated for:

- Ovarian cancer
  - 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®.
  - 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 fist-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either:
    - a deleterious or suspected BRCA mutation, and/or
    - genomic instability.
  - Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza®.
  - Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in 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®.
- Breast cancer
  - Treatment of patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have previously 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®.
- Pancreatic cancer
  - Treatment of adult patients with deleterious or suspected deleterious g*BRCA*m 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®.
- Prostate cancer

- 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®.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
olaparib (Lynparza®)	Ovarian cancer	300 mg orally twice daily	600 mg/day
	Breast cancer	300 mg orally twice daily	600 mg/day
	Pancreatic cancer	300 mg orally twice daily	600 mg/day
	Prostate cancer	300 mg orally twice daily	600 mg/day

Dosage Forms

- Tablets: 100 mg, 150 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 deleterious or suspected deleterious germline BRCA mutation;
      ii. Failure of ≥ 3 lines of platinum-based chemotherapy (see Appendix B), unless contraindicated or clinically significant adverse effects are experienced;
   b. Completed ≥ 2 platinum-based chemotherapy regimens and is in a complete or partial response;
   c. Both i and ii:
      i. Documentation of deleterious or suspected deleterious germline or somatic BRCA-mutation;
      ii. Completed a platinum-based chemotherapy regimen and is in a complete or partial response;
   d. All i, ii, and iii:
      i. Cancer is associated with homologous recombination deficiency (HRD)-positive status defined by deleterious or suspected deleterious germline BRCA mutation and/or genomic instability
      ii. In complete or partial response to first-line platinum-based chemotherapy
      iii. Prescribed in combination with bevacizumab
5. Request meets one of the following (a or b):
   a. Dose does not exceed 600 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use

(prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

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. Mutations in the BRCA genes;
   c. Metastatic or recurrent;
5. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy.
6. Request meets one of the following (a or b):
   a. Dose does not exceed 600 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Pancreatic Cancer (must meet all):
1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has mutations in the BRCA genes;
5. Received > 16 weeks of platinum-based chemotherapy with no disease progression;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 600 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Prostate Cancer (must meet all):
1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has mutations in the HRR genes;
5. Received prior treatment with enzalutamide or abiraterone with disease progression;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 600 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance 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. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 600 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ADP: adenosine diphosphate
AML: acute myeloid leukemia
BRCA: breast cancer gene
FDA: Food and Drug Administration
gBRCAm: mutations in the germline BRCA genes
HER: human Epidermal growth factor receptor 2
HR: hormone receptor
HRR: homologous recombination repair
MDS: myelodysplastic yndrome
MCRPC: etastatic castration-resistant prostate cancer
NCCN: National Comprehensive Cancer
PARP: poly (ADP-ribose) polymerase

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ovarian Cancer		
Alimta® (pemetrexed)	Various	Varies
melphalan (Alkeran®, Evomela®)	Various	Varies
bevacizumab (Avastin® Mvasi™, Zirabev®)	Various	Varies
carboplatin (Paraplatin®)	Various	Varies
cisplatin	Various	Varies
cyclophosphamide	Various	Varies
docetaxel	Various	Varies
doxorubicin (Doxil®, Adriamycin®)	Various	Varies
etoposide	Various	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
gemcitabine	Various	Varies
ifosfamide (Ifex®)	Various	Varies
irinotecan (Camptosar®, Onivyde®)	Various	Varies
oxaliplatin	Various	Varies
topotecan (Hycamtin®)	Various	Varies

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- NCCN recommended uses (2A):
  - Ovarian cancer: preferred single-agent therapy in patients with BRCA mutated genes for persistent disease or recurrence following three or more lines of therapy.
  - Ovarian cancer: maintenance therapy for patients with platinum-sensitive disease who have completed two or more lines of platinum-based therapy and are in a complete or partial response.
  - Breast cancer: single agent for recurrent or stage IV (M1) HER2-negative, BRCA 1/2-germline mutated disease that is:
    - Hormone receptor-negative
    - Hormone receptor-positive with visceral crisis and endocrine therapy refractory.
  - Pancreatic Cancer: first Line maintenance therapy for metastatic BRCA 1/2-germline mutated disease.
  - Prostate Cancer: single agent for HRR Gene-mutated Metastatic Castration-Resistant disease.
- Myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) have been confirmed in approximately 1.5% of patients treated with Lynparza®. The majority of the cases were fatal. If MDS/AML is confirmed, discontinue Lynparza®.
- The FDA approved Lynparza® with a genetic test called BRAC analysis 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.

References

1. Lynparza® Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP. March 2021. Available at: https://www.lynparza.com/. Accessed June 1, 2021.
2. Olaparib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 1, 2021.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 4.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 1, 2021.
4. National Comprehensive Cancer Network Guidelines. Ovarian Cancer Version 1.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed June 1, 2021.
5. National Comprehensive Cancer Network Guidelines. Pancreatic Adenocarcinoma Version 2.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed June 1, 2021.
6. National Comprehensive Cancer Network Guidelines. Prostate Cancer Version 2.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed June 1, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated 2. Drug(s) Applied was updated 3. Line of Business Policy Applies to was updated 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Commercial approval duration and Medicaid/HIM approval duration updated. 6. Added new indication for treatment of g*BRCA*m metastatic pancreatic adenocarcinoma and germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) 7. Updated APPENDIX B: Therapeutic Alternatives to remove Platinol-AQ, Cytoxan, Vepesid, Gemzar, Eloxatin and Hexalen® (altretamine) due to discontinuation and to include Evomela, Mvasi, Zirabev, Onivyde as new brands 8. Updated APPENDIX D: General Information to include information of Pancreatic Cancer and Prostate Cancer treatment 9. Updated Initial Approval Criteria for Ovarian Cancer to include first line maintenance treatment of HRD-positive advanced ovarian cancer in combination with bevacizumab 10. References were updated	6/19/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample "The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Initial Approval Criteria I.B.5 was updated to include “Patients with hormone receptor (HR)-positive breast cancer…” 3. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Initial Approval Criteria and Continued Therapy Approval Criteria was updated to remove HIM approval duration.	06/01/2021	09/14/2021

5. Appendix B: Therapeutic Alternatives verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance…". 6. Appendix B was updated to remove inactive brand name ”Taxotere” from drug name. 7. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 8. Appendix C was updated to include “Contraindications…” and “Boxed Warning…” 9. Appendix D was updated to include" approximately 1.5% of patients…” 10. References were reviewed and updated.		