Pharmacy Policy Bulletin: J-0902 PARP Inhibitors – Commercial and Healthcare Reform	
Number: J-0902	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0902-018	**Original Date:** 06/04/2003
Effective Date: 06/24/2024	**Review Date:** 06/05/2024

Drugs Product(s):	• Akeega (niraparib and abiraterone acetate) • Lynparza (olaparib) • Rubraca (rucaparib) • Talzenna (talazoparib) • Zejula (niraparib)
FDA-Approved Indication(s):	• Akeega (niraparib and abiraterone acetate) ○ With prednisone for the treatment of adult patients with deleterious or suspected deleterious *BRCA*-mutated (*BRCA*m) metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved test for Akeega. • Lynparza (olaparib) **Ovarian Cancer** ○ Maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Patients with g*BRCA*m advanced epithelial ovarian, fallopian tube or primary peritoneal cancer are indicated to be selected for therapy based on an FDA-approved companion diagnostic for Lynparza. ○ Maintenance treatment in combination with bevacizumab for 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. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

	○ Maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy (e.g., carboplatin, oxaliplatin, etc.). Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. **Breast Cancer** ○ Adjuvant treatment of adult patients with deleterious or suspected deleterious g*BRCA*m, human epidermal growth factor 2 (*HER2*)-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. ○ Treatment of adult patients with deleterious or suspected deleterious g*BRCA*m, *HER2*-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients are indicated to be selected for therapy based on an FDA-approved companion diagnostic for Lynparza. ▪ Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. **Pancreatic Cancer** ○ Maintenance 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 mCRPC who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. ○ Treatment of adult patients in combination with abiraterone and prednisone or prednisolone for deleterious or suspected deleterious *BRCA*m mCRPC. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. • Rubraca (rucaparib) ○ Maintenance treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated 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 a deleterious *BRCA* mutation (germline and/or somatic)-associated mCRPC who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic test for Rubraca. • Talzenna (talazoparib) **Breast Cancer** ○ As a single agent, for the treatment of adult patients with deleterious or suspected deleterious g*BRCA*m *HER2*-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna. **Prostate Cancer** ○ Treatment of adult patients with HRR gene-mutated mCRPC in combination with enzalutamide. • Zejula (niraparib)

	○ Maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy. ○ Maintenance treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Zejula.

Background:	• Akeega contains niraparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor. Niraparib inhibits PARP enzymes that play a role in DNA repair leading to DNA damage, apoptosis, cell death and therefore decreasing tumor growth. Abiraterone inhibits CYP17, an enzyme required for androgen biosynthesis, which is expressed in testicular, adrenal, and prostatic tumor cells. • Zejula is an inhibitor of PARP enzymes, PARP-1 and PARP-2, which play a role in DNA repair. ○ In September 2022, GlaxoSmithKline withdrew from the US market the Zejula indication for advanced ovarian, fallopian tube, or primary peritoneal cancer after 3 or more prior chemotherapy regimens. This indication was previously granted FDA approval in 2019. ○ FDA-approved companion diagnostic tests for ovarian cancer include Myriad BRACAnalysis CDx. For additional information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools. • Lynparza inhibits PARP enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair. In vitro and in mouse xenograft models of human cancer, olaparib inhibits the growth of tumor cell lines with BRCA deficiencies, both as monotherapy and following platinum-based chemotherapy. Olaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complex, disrupting cellular homeostasis and resulting in cell death. ○ In August 2022, AstraZeneca withdrew from the US market the fourth-line and later g*BRCA*m advanced ovarian cancer indication for Lynparza. This indication was previously granted accelerated approval in 2014. In 2021, data from the SOLO-3 trial demonstrated no statistically significant difference in overall survival between olaparib and non-platinum chemotherapy groups. • Rubraca is an inhibitor of PARP enzymes, including PARP-1, PARP-2 and PARP-3, which play a role in DNA repair. In vitro studies have shown that rucaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. ○ In June 2022, Clovis withdrew from the US market the third-line ovarian cancer indication for Rubraca. This indication was previously granted accelerated approval in 2016. In 2022, data from the ARIEL4 trial demonstrated an increased risk of death in patients with BRCA-mutated ovarian cancer treated with Rubraca after 2 or more chemotherapies. • Talzenna is an inhibitor of PARP1 and PARP2, which play a role in DNA repair. Talzenna-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, decreased cell proliferation, and apoptosis. Talzenna anti-tumor activity was

	observed in human patient-derived xenograft breast cancer tumor models that expressed mutated or wild-type *BRCA* 1 and 2. ○ The efficacy of Talzenna was evaluated in a randomized, open-label, multi-center clinical study of 431 adult patients with g*BRCA*m *HER2*-negative locally advanced or metastatic breast cancer to receive Talzenna 1 mg or physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) until disease progression or unacceptable toxicity. ▪ All patients were required to have a known deleterious or suspected deleterious g*BRCA* mutation and must have received no more than three prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease. ▪ The primary endpoint was progression-free survival (PFS). ▪ The estimated median PFS was 8.6 months in the Talzenna arm versus 5.6 months in the chemotherapy arm (HR 0.54; 95% CI: 0.41, 0.71; p < 0.0001). ○ HRR gene mutations include *ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2,* or *RAD51C.* • Prescribing Considerations: ○ Kinase inhibitors should be prescribed under the supervision of a hematologist/oncologist. ○ Patients receiving PARP inhibitors for mCRPC should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Approval Criteria

I. Initial Authorization

A. Akeega

1. Prostate Cancer (ICD-10 C61)

When a benefit, coverage of Akeega may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of mCRPC.
c. Disease harbors a deleterious or suspected deleterious *BRCA* mutation per an FDA-approved companion diagnostic for Akeega.
d. The member is using Akeega in combination with prednisone.
e. The member meets one (1) of the following **(i. or ii.)**:
i. The member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog.
ii. The member has had a bilateral orchiectomy.

B. Lynparza

1. Advanced Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ICD-10 C56, C57, C48)

When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of advanced epithelial ovarian, fallopian tube or primary peritoneal cancer.
c. The member is in complete or partial response to first-line platinum-based chemotherapy (e.g., carboplatin, oxaliplatin) and meets one (1) of the following criteria **(i. or ii.)**:
i. The member has a diagnosis of deleterious or suspected deleterious *BRCA* mutated disease.

ii. The member meets both of the following criteria **((A) and B))**:
A) Disease is associated with homologous recombination deficiency (HRD) positive status as defined by at least one (1) of the following **(1) or 2))**:
1) A deleterious or suspected deleterious *BRCA* mutation
2) Genomic instability
B) The member is using Lynparza in combination with bevacizumab.

d. If the request is for a diagnosis of ovarian cancer, the member has had an FDA-approved companion diagnostic for Lynparza.

2. Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ICD-10 C56, C57, C48)

When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(a., through d.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer.
c. Disease harbors a deleterious or suspected deleterious germline or somatic *BRCA* mutation as detected by an FDA-approved companion diagnostic test for Lynparza.
d. The member is in complete or partial response to platinum-based chemotherapy (e.g., carboplatin, oxaliplatin).

3. Breast Cancer (ICD-10 C50)

When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of breast cancer.
c. Disease is classified as deleterious or suspected deleterious g*BRCA*m, HER2-negative.
d. The member meets one (1) of the following criteria **(i. or ii.):**
i. The member meets all of the following criteria **(A) and B)):**
A) Disease is classified as high-risk, early breast cancer.
B) The member has been treated with neoadjuvant or adjuvant chemotherapy.
ii. The member meets all of the following criteria **(A) and B)):**
A) The member has been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting.
B) If hormone receptor (HR)-positive, the member has been previously treated with or considered inappropriate for treatment with endocrine therapy.
e. The member has had an FDA-approved companion diagnostic test for Lynparza.

4. Pancreatic Cancer (ICD-10 C25)

When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is at least 18 years old.
b. The member has a diagnosis of metastatic pancreatic adenocarcinoma.
c. Disease harbors a deleterious or suspected deleterious g*BRCA* mutation.
d. Disease did not progress on at least 16 weeks of a first-line platinum-based chemotherapy regimen (e.g., FOLFIRINOX).
e. The member has had an FDA-approved companion diagnostic test for Lynparza.

5. Prostate Cancer (ICD-10 C61)

a. Homologous Recombination Repair (HRR) gene-mutated mCRPC

When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(i. through vi.)**:

i. The member is 18 years of age or older.
ii. The member has a diagnosis of metastatic castration-resistant prostate cancer (mCRPC).

iii. Disease harbors a deleterious or suspected deleterious germline or somatic homologous recombination repair (*HRR*) gene mutation.
iv. The member has progressed following prior treatment with one (1) of the following **(A) or B))**:
A) Enzalutamide (Xtandi)
B) Abiraterone
v. The member meets one (1) of the following **(A) or B))**:
A) The member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog.
B) The member has had a bilateral orchiectomy.
vi. The member has had an FDA-approved companion diagnostic for Lynparza.

b. *BRCA*-mutated mCRPC
When a benefit, coverage of Lynparza may be approved when all of the following criteria are met **(i. through v.):**
i. The member is 18 years of age or older.
ii. The member has a diagnosis of metastatic castration-resistant prostate cancer (mCRPC).
iii. Disease harbors a deleterious or suspected deleterious *BRCA* mutation per an FDA-approved companion diagnostic for Lynparza.
iv. The member is using Lynparza in combination with all of the following **(A) and B)):**
A) abiraterone
B) prednisone or prednisolone
v. The member meets one (1) of the following **(A) or B))**:
A) The member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog.
B) The member has had a bilateral orchiectomy.

C. Rubraca
1. Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ICD-10 C56, C57, C48)
When a benefit, coverage of Rubraca may be approved when all of the following criteria are met **(a. through d.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer.
c. Disease harbors a deleterious *BRCA* mutation (germline or somatic).
d. The member is in complete or partial response to platinum-based chemotherapy (e.g., carboplatin, oxaliplatin).

2. Prostate Cancer (ICD-10 C61)
When a benefit, coverage of Rubraca may be approved when all of the following criteria are met **(a. through g.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of prostate cancer.
c. Disease harbors a deleterious *BRCA* mutation (germline and/or somatic) per an FDA-approved test.
d. The member has metastatic disease.
e. The member has castration-resistant disease.
f. The member has been treated with both of the following **(i. and ii.)**:
i. Androgen receptor-directed therapy
ii. Taxane-based chemotherapy
g. The member meets one (1) of the following **(i. or ii.)**:
i. The member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog.
ii. The member has had a bilateral orchiectomy.

D. Talzenna

1. Breast Cancer (ICD-10 C50)

When a benefit, coverage of Talzenna may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of breast cancer and meets all of the following criteria **(i., ii., and iii.)**:

i. Diagnosis includes deleterious or suspected deleterious *gBRCAm.*

ii. Disease is classified as HER2-negative.

iii. Disease is locally advanced or metastatic.

c. The member will be using Talzenna as a single agent.

d. The member has had an FDA-approved companion diagnostic test for Talzenna.

2. Prostate Cancer (C61, Z19.2)

When a benefit, coverage of Talzenna may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of metastatic castration-resistant prostate cancer (mCRPC).

c. Disease harbors an HRR gene mutation.

d. The member will be using Talzenna in combination with enzalutamide.

e. The member meets one (1) of the following **(i. or ii.)**:

i. The member is concurrently receiving a gonadotropin-releasing hormone (GnRH) analog.

ii. The member has had a bilateral orchiectomy.

E. Zejula

1. Advanced Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ICD-10 C56, C57, C48)

When a benefit, coverage of Zejula may be approved when all of the following criteria are met **(a., b., and c.):**

a. The member is 18 years of age or older.

b. The member has a diagnosis of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.

c. The member is in complete or partial response to first-line platinum-based therapy (e.g., carboplatin, oxaliplatin).

2. Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ICD-10 C56, C57, C48)

When a benefit, coverage of Zejula may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

c. Disease harbors a deleterious or suspected deleterious germline *BRCA* mutation.

d. The member is in a complete or partial response to platinum-based chemotherapy (e.g., carboplatin, oxaliplatin).

e. If the request is for a diagnosis of recurrent ovarian cancer, the member has had an FDA-approved companion diagnostic test for Zejula.

II. Reauthorization:

When a benefit, reauthorization of a PARP inhibitor may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following criteria **(1. or 2.)**:

1. Disease improvement
2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

Refer to J-0699 and J-0807 for previous versions.

References:

1. Akeega [package insert]. Horsham, PA: Janssen Biotech Inc; August 2023.
2. Talzenna [package insert]. New York, NY: Pfizer; June 2023.
3. Lynparza [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; September 2023.
4. Rubraca [package insert]. Boulder, CO: Clovis Oncology, Inc; December 2022.
5. Zejula [package insert]. Durham, NC: GlaxoSmithKline; April 2023.
6. U.S Food & Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). Available at: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. Accessed September 5, 2023.