Clinical Policy: Rucaparib (Rubraca)

Reference Number: CP.PHAR.350
Effective Date: 09.01.17
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

Rucaparib (Rubraca®) is a poly (ADP-ribose) polymerase (PARP) inhibitor.

FDA Approved Indication(s)

Rubraca is indicated:

Ovarian cancer

- For the 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.

Prostate cancer

- For the treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (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 for Rubraca.

  This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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 Rubraca 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. For brand Rubraca requests, member must use generic rucaparib, if available, unless contraindicated or clinically significant adverse events are experienced;
5. Prescribed as a single agent;
6. Member meets one of the following (a or b):*
   a. Both i and ii *(see Appendix F)*:
      i. Documentation of deleterious or suspected deleterious *BRCA* mutation;

ii. Completed platinum-based chemotherapy and is in a complete or partial response;

b. Both i and ii:
   i. Newly diagnosed stage II-IV disease (e.g., grade 2-3 endometroid carcinoma);
   ii. Completed first-line platinum-based chemotherapy regimen and is in a complete or partial response;

**Prior authorization may be required*

7. Member has not previously received a PARP inhibitor (e.g., Lynparza®, Talzenna®, Zejula®) (*see Appendix D*);
8. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i or ii):
      i. 1,200 mg per day;
      ii. 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. Prostate Cancer (must meet all)**:**

1. Diagnosis of metastatic CRPC as evidenced by disease progression despite androgen deprivation therapy (ADT) (*see Appendix D*);
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. Documented deleterious germline and/or somatic BRCA mutation;
5. For Rubraca requests, member must use generic rucaparib, if available, unless contraindicated or clinically significant adverse events are experienced;
6. Prescribed concurrently with systemic ADT (*see Appendix D*) or member has had a bilateral orchiectomy;
7. Failure of both of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a and b):
   a. A taxane-based regimen (e.g., docetaxel);*
      **Prior authorization may be required for taxanes*
   b. An androgen receptor-directed therapy (e.g., abiraterone, enzalutamide);
      **Prior authorization may be required for androgen receptor-directed therapies*
8. Member has not previously received a PARP inhibitor (e.g., Lynparza, Talzenna, Zejula) (*see Appendix D*);
9. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i or ii):
      i. 1,200 mg per day;
      ii. 4 capsules 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. Off-label NCCN Compendium Recommended Indications (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Pancreatic adenocarcinoma;
   b. Uterine neoplasms;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Rubraca requests, member must use generic rucaparib, if available, unless contraindicated or clinically significant adverse events are experienced;
5. Mutations in the *BRCA* genes;
6. Prescribed as a single agent subsequent therapy (*see Appendix B*);
7. Member has not previously received a PARP inhibitor (e.g., Lynparza, Talzenna, Zejula) (*see Appendix D*);
8. Dose is within FDA maximum limit for any FDA-approved indication or 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. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 Rubraca for a covered indication and has received this medication for at least 30 days;

2. For ovarian cancer: If request is for use in an adult member with a deleterious *BRCA* mutation who has been treated with two or more chemotherapies, provider attestation of acknowledgement for withdrawal for this indication due to risk of detrimental effect on overall survival (OS) in patients who used Rubraca *(see Appendix E)*;
3. For ovarian cancer: If request is for maintenance use in an adult member with non-deleterious *BRCA* mutation who is in a complete or partial response to platinum-based chemotherapy, provider attestation of acknowledgement for possible OS detriment with Rubraca use in this population *(see Appendix F)*;
4. Member is responding positively to therapy;
5. For Rubraca requests, member must use generic rucaparib, if available, unless contraindicated or clinically significant adverse events are experienced;
6. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed any of the following (i or ii):
      i. 1,200 mg per day;
      ii. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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

ADT: androgen deprivation therapy
BRCA: breast cancer susceptibility gene
CRPC: castration resistant prostate cancer
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
LHRH: luteinizing hormone-releasing hormone
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: examples of chemotherapy agents		
Alimta® (pemetrexed)	Varies	Varies
Alkeran® (melphalan)		
Avastin® (bevacizumab)		
carboplatin (Paraplatin®)		
cisplatin (Platinol-AQ®)		
cyclophosphamide (Cytoxan®)		
docetaxel (Taxotere®)		
doxorubicin (Doxil®, Adriamycin®)		
etoposide (Vepesid®)		
gemcitabine (Gemzar®)		
ifosfamide (Ifex®)		
irinotecan (Camptosar®)		
oxaliplatin (Eloxatin®)		
topotecan (Hycamtin®)		
Hexalen® (altretamine)		
paclitaxel		
Prostate Cancer		
docetaxel	75 mg/m^2 IV for 6 cycles	Varies
abiraterone (Zytiga®, Yonsa®)	Zytiga: 1,000 mg PO BID in combination with prednisone Yonsa: 500 mg PO QD in combination with methylprednisolone	1,000 mg QD; 1,000 mg BID if taking a strong CYP3A4 inducer Yonsa: 500 mg QD; 500 mg BID if taking a strong CYP3A4 inducer
enzalutamide (Xtandi®)	160 mg PO QD	160 mg/day; 240 mg/day if taking a strong CYP3A4 inducer

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pancreatic Adenocarcinoma		
FOLFIRINOX (leucovorin, fluorouracil, irinotecan, oxaliplatin)	Various	Varies
gemcitabine + cisplatin	Various	Varies
Uterine Sarcoma		
Doxorubicin	Various	Varies
Docetaxel/gemcitabine	Various	Varies
Doxorubicin/trabectedin	Various	Varies
Doxorubicin/ifosfamide	Various	Varies
Doxorubicin/dacarbazine	Various	Varies

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
- CRPC is prostate cancer that progresses clinically, radiographically, or biochemically despite castrate levels of serum testosterone (< 50 ng/dL). Per the NCCN, androgen deprivation therapy (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; also known as GnRH) given with or without an anti-androgen:
    - LHRH 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 are 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 in this regard (other than for ovarian cancer, where it states data is limited), and there are no randomized controlled trials evaluating such use.

Appendix E: Withdrawal of Third-Line BRCA-Mutated Ovarian Cancer Indication
- Clovis Oncology, manufacturer of Rubraca, voluntarily withdrew Rubraca for the treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies. The withdrawal became effective as of June 10, 2022.

- The decision was made in consultation with the FDA and based on ARIEL4 results showing a detrimental effect in terms of OS that was observed for rucaparib compared to the chemotherapy-containing control arm.
- As OS detriment, for patients randomized to Rubraca, was observed at the final analysis of OS (70% of deaths reported). In the intention-to-treat population, median OS was 19.5 months in the Rubraca group compared to 25.4 months in the chemotherapy group, resulting in a HR of 1.31 (95% CI: 1.00, 1.73; p= 0.0507).
- Physicians should not initiate new treatment with rucaparib for adult patients with deleterious *BRCA* mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.

Appendix F: Restricted Ovarian Cancer Second-Line Setting Indication to BRCA-Mutated Population

- The restriction to the *BRCA*-mutated population was based on the ARIEL3 final OS data that was submitted to the FDA by Clovis Oncology. Results showed patients without BRCA mutations with or without homologous recombination deficiency positive status had an increased risk of death with Rubraca (28% and 15%, respectively). The FDA requested that Clovis Oncology voluntarily revise the label to limit the indication of Rubraca in this second-line maintenance treatment to *BRCA*-mutated patients only.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Ovarian cancer	600 mg PO BID.	1,200 mg/day
Metastatic CRPC	600 mg PO BID. Patients receiving Rubraca should also receive a GnRH analog concurrently or should have had bilateral orchiectomy	1,200 mg/day

VI. Product Availability

Tablets: 200 mg, 250 mg, 300 mg

VII. References

1. Rubraca Prescribing Information. Boulder, CO: Clovis Oncology, Inc.; September 2023. Available at: https://www.rubracahcp.com/wp-content/uploads/RubracaUSPI.pdf. Accessed November 18, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 18, 2024.
3. National Comprehensive Cancer Network. Ovarian Cancer Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed November 18, 2024.
4. National Comprehensive Cancer Network. Prostate Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 19, 2024.
5. Dear Health Care Provider June 2022 Letter (Rucaparib). Clovis Oncology. Available at: https://www.rubracahcp.com/wp-content/themes/rubracahcp/temp-landing-assets/pdf/DearHealthcareProviderJun2022.pdf. Accessed November 19, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: mCRPC label update to require FDA-approved diagnostic test - no change to mCRPC indication. 1Q 2021 annual review: oral oncology generic redirection language added; for ovarian cancer, single-agent therapy clarification added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.14.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	10.04.21	02.22
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: treatment of BRCA-mutated ovarian cancer after 2 or more therapies changed to off-label usage due to FDA withdrawal but still supported by NCCN; revised oral oncology generic redirection language.	06.23.22	
Template changes applied to other diagnoses/indications and continued therapy section.	09.21.22	
1Q 2023 annual review: RT4: updated ovarian cancer indication limiting to BRCA-mutated population; revised initial criteria to reflect new FDA language and NCCN 5.2023 recommendations; added prescriber attestation requirements for use in ovarian cancer indications that have been withdrawn in continued therapy section; updated Appendix D; added Appendix E and F; references reviewed and updated.	01.17.23	02.23
1Q 2024 annual review: for prostate cancer, updated failure of "abiraterone (Zytiga®), unless member has previously failed Yonsa® (abiraterone) or Xtandi® (enzalutamide)" criteria to "an androgen receptor-directed therapy (e.g. abiraterone, enzalutamide)" to align with FDA indication and NCCN compendium; updated Appendix D with removal of outdated NCCN Ovarian Cancer guideline information; references reviewed and updated.	10.25.23	02.24
1Q 2025 annual review: for ovarian cancer, updated criteria for "newly diagnosed stage II-IV disease (e.g., grade 2-3 endometroid carcinoma)" as supported by NCCN; added off-label criteria for pancreatic adenocarcinoma and uterine neoplasms as supported by NCCN compendium and guidelines; references reviewed and updated.	11.18.24	02.25

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. 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.

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.