Clinical Policy: Niraparib (Zejula)

Reference Number: CP.PHAR.408
Effective Date: 06.01.17
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

Niraparib (Zejula®) is a poly(ADP-ribose) polymerase (PARP) inhibitor.

FDA Approved Indication(s)

Zejula is indicated for:

- 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 and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined as either a deleterious or suspected deleterious *BRCA* mutation, and/or genomic instability
- 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

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 Zejula 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 Zejula requests, member must use generic niraparib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member is in complete response or partial response, and one of the following (a or b):
   a. Stage II-IV disease (e.g., high-grade serous or grade 2-3 endometroid carcinoma) and (i):
      i. Completed first-line platinum-based chemotherapy regimen;

b. HRD-positive disease or recurrent germline-*BRCA*-mutated disease, and both of the following (i and ii*; see Appendix F)*:
   i. Documentation of deleterious or suspected deleterious *BRCA*-mutation and/or genomic instability as confirmed on a CLIA approved diagnostic test (*see Appendix D)*;
   ii. Completed platinum-based chemotherapy;

6. Member has platinum-sensitive persistent or recurrent disease, and both of the following (a and b):
   a. One of the following (i or ii):
      i. Member has serially rising CA-125 and previously received chemotherapy;
      ii. Member has radiographic and/or clinical relapse with previous complete remission and relapsed ≥ 6 months after completing prior chemotherapy;
   b. Zejula is prescribed in combination with bevacizumab;
7. Zejula is prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. In combination with bevacizumab;
8. Member has not previously received a PARP inhibitor (e.g., Lynparza®, Rubraca®, Talzenna®);
9. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i or ii):
      i. 300 mg per day;
      ii. 3 capsules or 1 tablet 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. Uterine Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of uterine sarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Zejula requests, member must use generic niraparib, if available, unless contraindicated or clinically significant adverse effects 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®, Rubraca®, Talzenna®);
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

C. 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 Zejula 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 advanced HRD positive ovarian cancer after > 3 lines of chemotherapy, provider attestation of acknowledgement for withdrawal of this indication due to risk of detrimental effect on overall survival (OS) in patients who used Zejula *(see Appendix E)*;
3. For ovarian cancer: If request is for use in an adult member with non-germline *BRCA* mutated platinum sensitive recurrent ovarian cancer in the second or later line maintenance setting, provider attestation of acknowledgement for possible OS detriment with Zejula use in this population *(see Appendix F)*;
4. Member is responding positively to therapy;
5. For brand Zejula requests, member must use generic niraparib, if available, unless contraindicated or clinically significant adverse effects 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. 300 mg per day;
      ii. 3 capsules or 1 tablet 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 2 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

FDA: Food and Drug Administration
HRD: homologous recombination deficiency
OS: overall survival
PARP: poly(ADP-ribose) polymerase
PFS: progression free survival

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
doxorubicin (Doxil®, Adriamycin®)	Various	Varies
etoposide (Vepesid®)	Various	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
gemcitabine (Gemzar®)	Various	Varies
ifosfamide (Ifex®)	Various	Varies
irinotecan (Camptosar®)	Various	Varies
oxaliplatin (Eloxatin®)	Various	Varies
topotecan (Hycamtin®)	Various	Varies
Hexalen® (altretamine)	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
- 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 (other than for ovarian cancer, where they state data is limited), and there are no randomized controlled trials evaluating such use.
- Clinical trials utilized Myriad BRACAnalysis CDx to detect the presence of deleterious or suspected deleterious germline *BRCA* mutations in blood samples from patients with ovarian, fallopian tube, and primary peritoneal cancer. Additional information on FDA-approved companion diagnostic tests is available at http://www.fda.gov/companiondiagnostics.

Appendix E: Withdrawal of Advanced HRD Ovarian Cancer After > 3 Lines of Chemotherapy Indication
- GlaxoSmithKline, manufacturer of Zejula, voluntarily withdrew Zejula's FDA-approved indication for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status. The withdrawal became effective as of September 14, 2022 and does not affect other indications for Zejula.
- The decision was made in consultation with the FDA and based on totality of information from PARP inhibitors in the late line treatment setting in ovarian cancer. A potential detrimental effect on OS was observed with other (non-GlaxoSmithKline) PARP inhibitors in two independent randomized, active-controlled clinical trials conducted in a *BRCA* mutant 3L + advanced ovarian cancer population.
- The approval of Zejula for this indication was based on the QUADRA study (NCT02354586), a single-arm study which evaluated the safety and efficacy of niraparib

for this indication. The results from the QUADRA study (single arm, uncontrolled nature) offered no comparative OS information, which made it difficult to "assess any potential effect on Zejula on time to event endpoints."
- Physicians should not initiative new treatment with Zejula in the treatment indication of adult patients with advanced ovarian cancer, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with HRD positive status.

Appendix F: Restricted Second or Later Line Setting Indication to Germline BRCA Mutated Population
- GlaxoSmithKline, manufacturer of Zejula, restricted the indication of Zejula for the 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 received in the second or later line setting to the germline *BRCA*-mutated patient population only in the United States.
- The decision was made at the request of the FDA following the final OS analysis of the NOVA (NCT01847274) study. The observed OS results from NOVA study are shown:
  - Germline *BRCA*-mutated cohort (N = 203): median OS was 43.6 months for patients with Zejula compared to 41.6 months for patients on placebo (HR = 0.93 [95% CI 0.63, 1.36])
  - Non-germline *BRCA*-mutated cohort (N = 350): median OS was 31.3 months for patients treated with Zejula compared to 41.6 months for patients on placebo (HR = 1.10 [95% CI 0.83, 1.46])
  - Non-germline *BRCA*-mutated, HRD positive subgroup: median OS was 37.3 months for patients treated with Zejula compared to 41.4 months for patients on placebo (HR = 1.32 [95% CI 0.84, 2.06])
- The current OS results indicate possible OS detriment to patients in the overall non-germline *BRCA*-mutated cohort and to patients in the non-germline *BRCA*-mutated/HRD positive subgroup who received Zejula maintenance in this setting compared to placebo.
- Physicians who are currently treating patients with Zejula for patients with non-germline *BRCA*-mutated platinum sensitive recurrent ovarian cancer in the second or later line maintenance setting are asked to discuss this information with those patients for an individual benefit-risk assessment so that they can make an informed decision regarding their ongoing care.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Ovarian, fallopian tube, or primary peritoneal cancer	*HRD-positive disease* • For patients weighing < 77 kg OR with a platelet count < 150,000/mcL: 200 mg PO QD • For patients weighing ≥ 77 kg AND a platelet count ≥ 150,000/mcL: 300 mg PO QD	300 mg/day

Indication	Dosing Regimen	Maximum Dose
	Germline BRCA-mutated disease: 300 mg PO QD	

VI. Product Availability

- Capsule: 100 mg
- Tablets: 100 mg, 200 mg, 300 mg

VII. References

1. Zejula capsules Prescribing Information. Durham, NC.: GlaxoSmithKline.; April 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208447s027lbl.pdf. Accessed November 18, 2024.
2. Zejula tablets Prescribing Information. Durham, NC.: GlaxoSmithKline.; June 2025. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Zejula_Tablets/pdf/ZEJULA-TABLETS-PI-PIL.PDF. Accessed July 2, 2025.
3. Niraparib. In: National Comprehensive Cancer Networks Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 18, 2024.
4. National Comprehensive Cancer Network. Ovarian Cancer Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed July 2, 2025.
5. National Comprehensive Cancer Network. Uterine Neoplasms Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed November 18, 2024.
6. Dear Health Care Provider September 2022 Letter (Niraparib). GlaxoSmithKline. Available at: https://www.zejulahcp.com/content/dam/cf-pharma/hcp-zejulahcp-v2/en_US/pdf/ZEJULA%20%28niraparib%29%20Dear%20HCP%20Letter%20September%202022.pdf. Accessed November 18, 2024.
7. ClinicalTrials.gov. A Maintenance Study with Niraparib Versus Placebo in Patients with Platinum Sensitive Ovarian Cancer (NOVA). Available at: https://clinicaltrials.gov/ct2/show/NCT01847274. Accessed November 18, 2024.
8. Dear Health Care Provider December 2022 Letter (Niraparib). GlaxoSmithKline. Available at: https://www.zejulahcp.com/content/dam/cf-pharma/hcp-zejulahcp-v2/en_US/pdf/Zejula-(niraparib)DearHCPLetterDec2022.pdf. Accessed November 18, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: added new template language regarding redirection to generic if available for oral oncology agents; references reviewed and updated.	10.15.20	02.21
Per March SDC, add HIM line of business to policy.	03.26.21	05.21
1Q 2022 annual review: no significant changes; added legacy WCG initial auth durations (WCG.CP.PHAR.408 to be retired); references reviewed and updated.	10.04.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
Template changes applied to other diagnoses/indications.	09.23.22	
1Q 2023 annual review: RT4: removed previously approved indication for use in advanced HRD positive ovarian cancer after > 3 lines of chemotherapy due to change in NCCN 5.2022 guideline which changed indication from category 2a to 3; added prescriber attestation requirement for use in advanced HRD positive ovarian cancer after > 3 lines of chemotherapy; added Appendix E; consolidated Legacy Wellcare initial approval duration from 12 months to 6 months consistent with standard Medicaid initial approval duration; references reviewed and updated; RT4: updated indication for 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 to restricted use to the germline *BRCA*-mutated patient population; added provider attestation requirement for non-germline *BRCA*-mutated platinum sensitive recurrent ovarian cancer in the second or later line maintenance setting in continued therapy section; added Appendix F.	01.03.23	02.23
RT4: added BRCA-mutation must be confirmed on a CLIA approved diagnostic test (e.g., BRAC Analysis CDx); added new tablet formulation; references reviewed and updated.	05.11.23	
1Q 2024 annual review: no significant changes; references reviewed and updated.	11.10.23	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 and removed "for platinum-sensitive persistent disease or recurrence" for use in combination with bevacizumab criteria as NCCN compendium supports combination with bevacizumab use in various settings; added off-label criteria for uterine neoplasms as supported by NCCN compendium and guideline; references reviewed and updated.	11.18.24	02.25
RT4: updated indication for maintenance treatment of adult patients with advanced ovarian cancer in the first-line setting with restriction to those with HRD-positive tumors only per updated PI; for ovarian cancer, added criteria for members with platinum-sensitive persistent or recurrent disease per NCCN and revised tablet quantity limit from 3 tablets to 1 tablet.	07.02.25	

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.