Clinical Policy: Niraparib (Zejula)

Reference Number: CP.PHAR.408
Effective Date: 06.01.17
Last Review Date: 02.23
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
- 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

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 meets one of the following (a or b):
   a. Both i and ii:
      i. Newly diagnosed stage II-IV disease;
      ii. Completed first-line platinum-based chemotherapy regimen and is in a complete or partial response;
   b. Both i and ii *(see Appendix F)*:
      i. Documentation of deleterious or suspected deleterious germline BRCA-mutation;
      ii. Completed platinum-based chemotherapy and is in a complete or partial response;

6. Zejula is prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. In combination with bevacizumab for platinum-sensitive persistent disease or recurrence for one of the following (i or ii):
      i. Radiographic and/or clinical relapse in members with previous complete remission and relapse after ≥ 6 months after completing prior chemotherapy;
      ii. Immediate treatment for serially rising CA-125 in members that previously received chemotherapy;
7. Member has not previously received a PARP inhibitor (e.g., Lynparza®, Rubraca®, Talzenna®);
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 300 mg per day;
      ii. 3 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

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.

II. Continued Therapy

A. Ovarian Cancer (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. 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. 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 both of the following (i and ii):
      i. 300 mg per day;
      ii. 3 capsules 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
gemcitabine (Gemzar®)	Various	Varies
ifosfamide (Ifex®)	Various	Varies
irinotecan (Camptosar®)	Various	Varies
oxaliplatin (Eloxatin®)	Various	Varies
topotecan (Hycamtin®)	Various	Varies
Hexalen® (altretamine)	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.

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	300 mg PO QD	300 mg/day

VI. Product Availability

Capsule: 100 mg

VII. References

1. Zejula Prescribing Information. Durham, NC.: GlaxoSmithKline.; December 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208447s025lbl.pdf. Accessed January 3, 2023.
2. Niraparib. In: National Comprehensive Cancer Networks Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 3, 2023.
3. National Comprehensive Cancer Network. Ovarian Cancer Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed January 3, 2023.
4. 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 October 17, 2022.
5. 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 January 3, 2023.
6. 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 January 3, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created. Adopted from CP.CPA.200 Niraparib (Zejula)	11.20.18	02.19
1Q 2020 annual review: criteria added for expanded FDA-indication in advanced ovarian, fallopian tube, or primary peritoneal cancer after treated with three or more prior chemotherapy regimens and whose cancer is associated with HRD positive status; references reviewed and updated.	11.26.19	02.20
Criteria added for expanded FDA-indication as maintenance treatment in advanced ovarian, fallopian tube, or primary peritoneal cancer in patients who are in a complete or partial response to first-line platinum-based chemotherapy; added that Zejula must be used as a single agent or in combination with bevacizumab per NCCN recommendations; added requirement for no prior PARP inhibitor use.	06.02.20	08.20

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
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

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.