niraparib (Zejula®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO139

Description

Niraparib (Zejula) is an orally administered poly (ADP-ribose) polymerase (PARP) inhibitor indicated for maintenance therapy, of ovarian, fallopian tube, or primary peritoneal cancer.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
niraparib (Zejula)	100 mg capsules	Maintenance for: recurrent or advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer	90 capsules/30 days

Initial Evaluation

I. Niraparib (Zejula) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Niraparib (Zejula) will be used as monotherapy; **AND**
   D. Member has **not** progressed on prior PARP inhibitor (e.g. olaparib [Lynparza], rucaparib [Rubraca]) therapy; **AND**
   E. Provider is requesting niraparib (Zejula) for **Maintenance** therapy; **AND**
      1. Member is in complete or partial response to their last platinum-based chemotherapy regimen (i.e., platinum-sensitive) (e.g. cisplatin, oxaliplatin, carboplatin); **AND**
      2. Provider attests that member's epithelial ovarian, fallopian tube, or primary peritoneal cancer has not progressed since the most recent platinum-based chemotherapy regimen (e.g. cisplatin, oxaliplatin, carboplatin); **AND**
      3. A diagnosis of one of the following:
         i. **Advanced (stage III or IV) ovarian, fallopian tube, or primary peritoneal cancer**; **AND**
            a. Member has completed at least **one** prior platinum-based chemotherapy regimen (e.g. cisplatin, oxaliplatin, carboplatin); **AND**

b. The member has **not** received bevacizumab (Avastin) in prior treatment; **AND**
c. Niraparib (Zejula) will **not** be used in combination with bevacizumab (Avastin); **OR**

ii. **Recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer**; **AND**
a. Member has experienced disease progression on or after at least two or more prior platinum-based chemotherapy regimens (e.g., cisplatin, carboplatin, oxaliplatin)

II. Niraparib (Zejula) is considered investigational when used for all other conditions, including but not limited to:
A. Used in combination with other chemotherapy or targeted therapy regimen.
B. Breast Cancer
C. Prostate Cancer
D. Lung Cancer
E. Advance Solid Tumors
F. Melanoma
G. Pancreatic cancer
H. Gastroesophageal cancer
I. Treatment of advanced ovarian cancer after 3 of more lines of therapy

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication is prescribed by, or in consultation with, an oncologist; **AND**
IV. Member has exhibited a response to therapy such as stabilization of disease or decrease in tumor size or spread.

Supporting Evidence

I. The safety and efficacy of niraparib (Zejula) in the setting of maintenance therapy for recurrent ovarian cancer was studied in a double-blind, placebo-controlled trial in adult patients with platinum-sensitive recurrent epithelial, ovarian fallopian tube, or primary peritoneal cancer. The patients were randomized 2:1 niraparib (Zejula) 300 mg orally daily or matched placebo within eight weeks of the last platinum-based chemotherapy regimen. The trial demonstrated a statistically significant improvement in progression free survival (PFS) for patients randomized to niraparib (Zejula) as compared with placebo in the gBRCAmut cohort and the non-gBRCAmut cohort.
   A. gBRCAmut Cohort: PFS in the niraparib (Zejula) arm was 21 and 5.5 in the placebo arm with a HR of 0.26 and 95% CI (0.17, 0.41).
   B. Non-gBRCAmut Cohort: PFS in the niraparib (Zejula) arm was 9.3 and 3.9 in the placebo arm with a HR of 0.45 and 95% CI (0.34, 0.61).

II. Therapy in the maintenance setting was initiated within eight weeks after completion of the last dose of platinum-based chemotherapy. Therefore, the inclusion of this as criteria (see above) is that treatment is started within a reasonable timeframe consistent with a maintenance treatment plan (i.e. as close to eight weeks as possible) while still recognizing that scheduling or other factors may impact the ability of a patient to start exactly within these first eight weeks.

III. Efficacy and safety of niraparib (Zejula) in the first-line maintenance treatment was assessed in a phase three, double-blind, randomized (PRIMA) clinical trial in patients with newly diagnosed advanced (stage III or IV) ovarian cancer. Seven hundred and thrity-three patients, who were in complete or partial response to first-line platinum-based chemotherapy, were randomized 2:1 to niraparib (Zejula) or matched placebo. Patients with and without homologous recombination deficiency (HRD, e.g. gBRCA*m*) were included. At the end of treatment period, niraparib (Zejula) treatment arm showed a statistically significant improvement in median progression free survival (PFS) as compared to placebo arm.
   A. Homologous recombination deficiency (HRD; e.g. gBRCA*m*) cohort: median PFS was 21.9 months in niraparib (Zejula) arm and 10.4 months in placebo arm (hazard ratio 0.43; 95% CI, 0.31 to 0.59; P<0.001)
   B. Overall population (without HRD; gBRCA*m*) cohort: median PFS was 13.8 months in niraparib (Zejula) arm and 8.2 months in placebo arm (HR 0.62; 95% CI, 0.5 to 0.76; *p*<0.001).

   None of the treated patients had a history of taking bevacizumab (Avastin). Therefore, efficacy and safety of niraparib (Zejula) after first-line therapy with bevacizumab (Avastin), or in combination with, bevacizumab (Avastin) is not supported.

IV. During PRIMA trial, serious adverse events occurred in 98.8% (N=478) patients in the treatment arm with 70.5% being grade ≥ 3. These numbers were 91.8% (N=224) and 46%, respectively in

the placebo arm. Serious adverse events led to 79.5% dose interruption rates, 70.9% dose reduction rates, and 12% treatment discontinuation in the treatment group vs. 18%, 8.2%, and 2.5%, respectively, in the placebo group.

V. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy to support the use of a subsequent PARP inhibitor following progression of disease on another PARP inhibitor.

Investigational or Not Medically Necessary Uses

I. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy for the use of niraparib (Zejula) in the following settings listed below:
   A. Used in combination with other chemotherapy or targeted therapy regimen.
   B. Breast Cancer
   C. Prostate Cancer
   D. Lung Cancer
   E. Advance Solid Tumors
   F. Melanoma
   G. Pancreatic cancer
   H. Gastroesophageal cancer
   I. Treatment of advanced ovarian cancer after 3 of more lines of therapy
      i. Niraparib (Zejula) was studied in the QUADRA trial, evaluating niraparib (Zejula) for the treatment of advanced ovarian cancer after three or more chemotherapies. This was a single arm trial with investigator assessment of objective response rate (ORR) as the efficacy outcome measure. Given the setting of the QUADRA trial (single arm, uncontrolled nature), no comparative overall survival information can be obtained from the study, and it is difficult to assess any potential effect of niraparib (Zejula) on time to event endpoints.
      ii. In September 2022, the manufacturer of niraparib (Zejula) voluntarily withdrew the indication for treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens. This withdrawal was based on a totality of information from PARP inhibitors in the late line treatment setting in ovarian cancer. A potential detrimental effect on overall survival was observed with two different PARP inhibitors in two independent randomized, active-controlled clinical trials conducted in a BRCA mutant 3L+ advanced ovarian cancer population.

References

1. Zejula [Prescribing Information]. Research Triangle Park, NC: GlaxoSmithKline LLC. September 2022.
2. González-Martín A, Pothuri B, Vergote I, et al. Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. *N Engl J Med*. 2019;381(25):2391-2402
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines). Ovarian Cancer Including: Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer & Less Common Histopathologies. Version 1.2020 [Updated March 11, 2020 Available from: https://www.nccn.org/professionals/physician_gls/pdf/ovarian_blocks.pdf
4. ASCO guidelines for gynecological cancer: PARP inhibitors in the management of ovarian cancer, J. Clin. Oncol.; 2020, e-pub 8/2020; DOI: 10.1200/JCO.20.01924

Policy Implementation/Update:

Action and Summary of Changes	Date
Removal of ovarian cancer indication in the late line (3+) treatment setting following voluntarily withdrawal of the indication by the manufacturer.	09/2022
Addition of new indication and supporting evidence for first-line maintenance therapy in women with advanced ovarian cancer; Updated policy format to categorize recommendation for niraparib (Zejula) based treatment OR maintenance therapy; added split fill management	09/2020
Criteria transition into policy with the following updates made: addition of supporting evidence and investigation section, broke out the different indications (treatment versus maintenance therapy) due to the newly approved indication for late-line treatment in women with recurrent ovarian cancer, included mutation status for the treatment of recurrent ovarian cancer, included criterion around prior PARP inhibitor use, increase initial approval duration from three months to six months to be consistent with other payers, included age criterion per label, and removed the 8 weeks criterion around most recent platinum-based therapy in the setting of maintenance therapy in recurrent ovarian cancer; in place of the 8 weeks criterion, provider attestation and documentation is required instead.	11/2019
Criteria created	08/2017