**Description**

Olaparib (Lynparza) is an orally administered targeted therapy [poly (ADP-ribose) polymerase (PARP) inhibitor] that is used in the treatment of advanced ovarian cancer when a germline BRCA mutation (gBRCAm) is present. Olaparib is indicated for recurrent disease that has not responded to at least three prior lines of chemotherapy treatment.
Policy/Criteria

I. Most contracts require prior authorization approval of olaparib prior to coverage. Olaparib may be considered medically necessary when criteria A, B, C and D below are met:
   A. A diagnosis of recurrent or metastatic ovarian cancer.
   AND
   B. Documentation of a deleterious germline BRCA mutation is provided.
   AND
   C. At least three prior chemotherapy regimens have been ineffective or not tolerated.
   AND
   D. Patient has not had prior PARP inhibitor therapy [such as rucaparib (Rubraca)] and documented disease progression.
   AND
   E. Olaparib will be used as monotherapy.

II. Administration, Quantity Limitations, and Authorization Period
   A. OmedaRx considers olaparib to be a self-administered medication.
   B. When prior authorization is approved, olaparib may be authorized in quantities up to 480 of 50 mg capsules per month (not to exceed 800 mg per day).
   C. Authorization may be reviewed at least every six months to confirm that current medical necessity criteria are met and that the medication is effective.

III. Olaparib is considered investigational when:
   A. Used in concomitantly with any other chemotherapy or targeted therapy (e.g. bevacizumab).
   B. Used for all other conditions, including but not limited to:
      1. Breast cancer
      2. Ewing’s Sarcoma
      3. Gastric cancer
      4. Head and neck cancer
      5. Non-small cell lung cancer (NSCLC)
      6. Pancreatic cancer
      7. Prostate cancer
Position Statement

- Olaparib is an orally administered poly (ADP-ribose) polymerase (PARP) inhibitor used as monotherapy in the treatment of advanced BRCA-mutated ovarian cancer.
- Olaparib received FDA accelerated approval based on its ability to shrink tumors. This evidence is of low quality as it is from a non-comparative study evaluating objective response rate in 137 patients.
- Objective response rate has not been shown to accurately predict beneficial clinical outcomes in the advanced ovarian cancer treatment setting. There is currently no data demonstrating improved clinical outcomes with olaparib.
- Current labeling positions olaparib as an option for heavily pretreated advanced ovarian cancer when three prior lines of chemotherapy have been used.
- Determination of BRCA mutation status is useful in identifying ovarian cancer patients with deleterious (harmful) or suspected deleterious BRCA mutations eligible for treatment with olaparib. BRCA mutations are associated with increased chemosensitivity; therefore it is assumed that a higher proportion of BRCA mutated ovarian cancer will be responsive to therapy in the fourth-line and beyond.
- Clinical trials of olaparib did not include women who received prior therapy with PARP inhibitor. Therefore, it is unknown if olaparib would be effective in women with disease progression on a PARP inhibitor.
- The National Comprehensive Cancer Network (NCCN) ovarian cancer guideline lists a number of options for recurrent disease, many of which are generically available. Choice of treatment in the recurrent setting is dependent on whether the disease is platinum-resistant or platinum-sensitive.
- Olaparib has the potential to cause myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) and pneumonitis. A majority of reported MDS/AML cases have been fatal.
- Olaparib is dosed at 400 mg orally twice daily. A total of sixteen capsules are given in two divided doses.
- There is interest in using olaparib in a variety of other cancers; however, the potential for providing clinical benefit in these conditions is still under investigation.
- The safety and efficacy of olaparib when used in combination with other anti-cancer therapies has not been evaluated. Olaparib is currently FDA-approved as monotherapy.

Clinical Efficacy

The evidence for efficacy for olaparib is of low quality as it is based on a single non-comparative trail evaluating objective response rate in patients with BRCA-mutated advanced ovarian cancer. Olaparib received conditional approval via the FDA’s accelerated approval pathway based on this unvalidated surrogate endpoint. Full approval is contingent on verification of clinical benefit in confirmatory trials. \[1,2\]

- Evidence is based on an open-label, non-comparative study in 137 patients with confirmed BRCA-mutated advanced ovarian cancer. \[3\]
* The study included 137 adult subjects with confirmed BRCA-mutated ovarian cancer who had received at least three prior lines of chemotherapy. The median number of prior treatments was five.

* Objective response rate (ORR) was evaluated as the outcome of interest. An ORR of 34% was reported for patients receiving treatment with olaparib.

* The lack of randomization and comparator make it difficult to quantify any potential for benefit, or to determine whether the benefit of therapy with olaparib outweighs the risks.

- ORR has not been shown to be an accurate predictor of clinically important outcomes (e.g. improved symptom control, quality of life, or survival) in advanced ovarian cancer.

- There is currently no evidence comparing olaparib with any other advanced ovarian cancer therapy in the fourth-line setting.

- The evidence is evolving for the use of olaparib in other treatment settings for ovarian cancer. There is insufficient evidence at this time to support the use of olaparib in other settings, such as in combination with cytotoxic chemotherapy than as maintenance therapy. [4]

- The National Comprehensive Cancer Network (NCCN) ovarian cancer guideline was recently updated to include recommendations for olaparib in the recurrent setting. Olaparib is listed as a preferred single agent for platinum-sensitive and platinum-resistant disease in patients with deleterious germline BRCA-mutated advanced ovarian cancer who have been treated with three or more lines of chemotherapy. The NCCN does not recommend the use of olaparib as maintenance therapy after cytotoxic chemotherapy. [5]

- Olaparib is actively being studied in many different cancers. Ongoing areas of research for olaparib include use in other ovarian cancer settings (e.g. maintenance or postremission), breast cancer, pancreatic cancer, head and neck cancer, Ewing’s Sarcoma, NSCLC, and prostate cancer. [3,6] Whether olaparib provides clinical benefit in these settings is still under investigation.

OmedaRx performs independent analyses of oncology medications. The OmedaRx analysis and coverage policy may differ from NCCN clinical practice guidelines.

**Safety** [1]

- Common (incidence ≥ 20%) adverse reactions with olaparib include: anemia, nausea, vomiting, diarrhea, fatigue, dysgeusia, dyspepsia, headache, decreased appetite, upper respiratory infection/cough, musculoskeletal pain, rash, and abdominal pain.

- Notable serious adverse events include myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) and pneumonitis.

- Olaparib should not be used concomitantly with strong and moderate CYP3A inhibitors or inducers. Dose reductions may be required if concomitant use cannot be avoided. Additionally, if concomitant CYP3A inducer use cannot be avoided, there is potential for decreased efficacy of olaparib.
Dosing [1]

- The recommended dose of olaparib is 400 mg orally twice daily until disease progression or unacceptable toxicity. A total of eight 50 mg capsules are given twice daily.
- Dose interruptions or dose reductions should be considered to manage adverse reactions or for renal impairment.

Cross References

| Genetic Testing for Hereditary Breast and/or Ovarian Cancer, Medical Policy Manual, Policy No. 02 |
| Avastin®, bevacizumab, Medication Policy Manual, Policy No. 215 |
| Doxil®, doxorubicin liposomal injection, Medication Policy Manual, Policy No. 239 |

References


Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
<tr>
<td>2/17/2017</td>
<td>- Clarify BRCA mutation testing criteria (simplify)</td>
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<td></td>
<td>- Add criteria for no prior PARP therapy [such as rucaparib (Rubraca)] and documented disease progression</td>
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<tr>
<td>2/12/2016</td>
<td>No coverage criteria changes.</td>
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