PDL DRUG REVIEW

Proprietary Name: Rubraca®
Common Name: rucaparib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Lynparza	Non-Recommended with Conditions

Summary

Pharmacology/Usage: Rucaparib, the active ingredient of Rubraca®, is an inhibitor of the mammalian polyadenosine 5'-diphosphoribose polymerase (PARP) enzyme, including PARP-1, PARP-2, and PARP-3 which play a role in DNA repair. Rucaparib has been shown to decrease tumor growth in animal models of human cancer with or without deficiencies in the Breast Cancer susceptibility genes (BRCA). *In vitro* studies have shown that rucaparib-induced cytotoxicity may result in DNA damage, apoptosis, and cell death.

Indications: As monotherapy for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. 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.

There is no pregnancy category associated with this medication; however, the risk summary indicates that based on findings from animal studies and its mechanism of action, Rubraca® use can cause fetal harm if administered to a pregnant woman. Thera are no data on use in pregnant women to inform the drug-associated risk. It is recommended to advise pregnant women of the potential risk to a fetus. Pregnancy testing is recommended for females of reproductive potential prior to starting treatment. It is recommended to advise females of reproductive potential to use effective contraception during treatment and for 6 months after the last dose. The safety and efficacy of use in the pediatric population below 18 years of age have not been established.

Dosage Forms: Immediate-release, film-coated Tablets: 200mg, 250mg, 300mg

Recommended Dosage: Information on the FDA-approved test for the detection of a tumor BRCA mutation in patients with ovarian cancer is available at: http://www.fda.gov/CompanionDiagnostics.

Take 600mg (two 300mg tablets) by mouth twice daily with or without food until disease progression or unacceptable toxicity. It is recommended to consider interruption of treatment or dose reduction to manage adverse events. Information on recommended dose reductions can be found in the prescribing information.

Dose adjustments are not required with mild to moderate renal impairment, but there are no recommended starting doses for those with CrCl <30ml/min or those on dialysis. Dose adjustments are not required with mild hepatic impairment; however, there are no recommended starting doses for moderate to severe hepatic impairment.

Drug Interactions: There are currently no drug interactions listed with this product.

Common Adverse Drug Reactions: *There was no placebo data to compare with Rubraca®.* The most frequently reported adverse events with Rubraca® of all ovarian cancer patients (N=377) of grades 1-4 included nausea (77%), vomiting (46%), constipation (40%), diarrhea (34%), abdominal pain (32%), asthenia/fatigue (77%), anemia (44%), thrombocytopenia (21%), dysgeusia (39%), decreased appetite (39%), and dyspnea (21%). Adverse reactions reported in <20% of patients included dizziness (17%), neutropenia (15%), rash (13%), pyrexia (11%), photosensitivity reaction (10%), pruritus (9%), Palmar-plantar erythrodysesthesia syndrome (2%), and febrile neutropenia (1%). Reported lab abnormalities included increase in creatinine (92%), increase in ALT (74%), increase in AST (73%), increase in cholesterol (40%), decrease in hemoglobin (67%), decrease in lymphocytes (45%), decrease in platelets (39%), and decrease in absolute neutrophil count (35%).

Myelodysplastic syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 0.5% (N=2/377) of those treated with Rubraca®. It is recommended to monitor complete blood count testing at baseline and monthly thereafter. Rubraca® treatment should be discontinued if MDS/AML is confirmed.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: Clovis Oncology, Inc

Analysis: The efficacy of Rubraca® was assessed in 2 multicenter, single-arm, open-label studies that included patients (N=106) with advanced BRCA-mutant ovarian cancer who had progressed after ≥2 prior chemotherapies. All patients received Rubraca® as monotherapy until disease progression or unacceptable toxicity. The median age of the patients was 59 years, and most were Caucasian (78%). Objective response rate (ORR) and duration of response (DOR) were assessed by the investigator and independent radiology review (IRR). Results can be found in the table below, which was adapted from the prescribing information.

	Investigator-assessed (N=106)
Objective Response Rate	54%
Complete Response	9%
Partial Response	45%
Median DOR in months	9.2

Response assessment by IRR was 42%, with a median DOR of 6.7 months. In addition, investigator-assessed ORR was 66% in platinum-sensitive patients, 25% in platinum-resistant patients, and 0% in platinum-refractory patients. ORR was similar for patients with a BRCA1 gene mutation or BRCA2 gene mutation.

Place in Therapy: Rubraca® is indicated as monotherapy for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. 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.

It is recommended that Rubraca® be added to the Recommended Drug List as non-recommended and require clinical prior authorization to verify diagnosis and prior trial/failure with at least 2 chemotherapies.

PDL Placement:
- ☐ **Preferred**
- ☒ **Non-Recommended with Conditions**

References

[1] Rubraca [package insert]. Boulder, CO: Clovis Oncology, Inc; 2017.