Pay $0 out-of-pocket drug costs with the Rubraca $0 Co-Pay Program

If you have private/commercial insurance, you may qualify to receive Rubraca™ (rucaparib) at no cost.

Rubraca Connections is a patient support program designed to help you start, afford, and continue to take Rubraca as directed by your doctor. One of the financial support programs Rubraca Connections provides is the Rubraca $0 Co-Pay Program.

If you have private/commercial insurance and qualify for this co-pay program, 100% of your out-of-pocket drug costs are covered—which means you pay $0 for Rubraca.*

To see if you qualify and to enroll in the Rubraca $0 Co-Pay Program, please call **1-844-779-7707**, Monday through Friday 8 AM to 8 PM EST, or visit RubracaConnections.com

If you qualify for and enroll into the Rubraca $0 Co-Pay Program, use the space below to log your personal co-pay information. Then, detach and keep with your important medical/health insurance records.

*The program does not cover costs for any other medication, procedure, office visit, or diagnostic test. Please see back page for Terms and Conditions.

<table>
<thead>
<tr>
<th>What does the Rubraca $0 Co-Pay Program cover?</th>
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<tbody>
<tr>
<td>Co-pay program covers*</td>
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<tr>
<td>You pay</td>
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</table>
$0 Co-Pay Q&A

How do I know if I qualify for the Rubraca $0 Co-Pay Program?

Call 1-844-779-7707 to speak with a Rubraca Connections Access Specialist who will help you determine if you qualify. When you speak to your Access Specialist, make sure you have the following information on hand:

- Your doctor’s name, address, and phone number
- Private/commercial insurance information (insurance type, group number, and member ID)
- Your insurance card (if you have more than one insurer, please have all information available)

Is there a maximum or minimum income requirement to qualify?

There is no income requirement. If you are eligible, the Rubraca $0 Co-Pay Program will pay 100% of your out-of-pocket drug costs for Rubraca™ (rucaparib) for up to $24,000 per calendar year, regardless of income.

How do I know if I have private/commercial insurance?

You probably have private/commercial insurance if you get your insurance through your work or if you buy insurance privately or through a healthcare exchange.

How do I know if I have federal or state-backed insurance?

You probably have government-backed insurance if your healthcare is covered by programs or organizations such as Medicaid, Medicare, TRICARE, Veterans Affairs (VA), or the Department of Defense (DoD).

Terms and Conditions

- Commercially insured patients are eligible to participate in the Rubraca $0 Co-Pay Program for as long as they are treated with Rubraca and do not have government insurance. Patients can receive support of up to $24,000 per calendar year.
- The Rubraca $0 Co-Pay Program is available for patients residing in the US, Puerto Rico, or US territories.
- The card may only be used for co-pays associated with the payment for Rubraca. The card is limited to one patient and is not transferable and cannot be used retroactively for Rubraca prescriptions already purchased. No substitutions are permitted.
- The card is not insurance and patients must have existing insurance that covers Rubraca.
- Patient is responsible for reporting receipt of co-pay assistance to any insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the card, as may be required.
- The card is valid only for patients with commercial insurance (includes healthcare exchanges) and not for patients who have government insurance to access Rubraca (Medicare, Medicaid, TRICARE, VA, DoD, or any other federal or state-funded healthcare benefit program).
- The card is not valid for cash-paying patients who do not have commercial insurance.
- The card is not valid where otherwise prohibited, taxed, or otherwise restricted.
- The Rubraca $0 Co-Pay Program is valid for the calendar year and will automatically renew upon verification that the patient still meets the eligibility criteria.
- The offer cannot be combined with other offers. The card has no cash value. No other purchase is necessary.
- Clovis reserves the right to change the terms and conditions of the program or terminate the program without notice.
- Patients may be enrolled by calling 1-844-779-7707 or by going online and providing valid commercial insurance and patient information (name and address).

To enroll in Rubraca Connections, or if you have any questions or would like more information, please call 1-844-779-7707 Monday through Friday 8 AM to 8 PM EST, or visit RubracaConnections.com.

The Rubraca $0 Co-Pay Program does not cover costs for any other medication, procedure, office visit, or diagnostic test. Commercially insured patients are eligible to participate in the Rubraca $0 Co-Pay Program for as long as they are treated with Rubraca. Patients will receive support up to $24,000 per calendar year. The Rubraca $0 Co-Pay Program is available for patients residing in the US, Puerto Rico, or US territories.

For questions about benefits, call 1-844-779-7707 or visit RubracaConnections.com.

See RubracaConnections.com for complete Terms and Conditions and eligibility criteria.
17 PATIENT COUNSELING INFORMATION

Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION: CONTENTS

1 INDICATIONS AND USAGE

Rubraca™ is indicated as monotherapy for the treatment of patients with deleterious (germline and/or somatic) 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 [See Dosage and Administration (2.1)].

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of advanced ovarian cancer with Rubraca based on the presence of a deleterious BRCA mutation (germline and/or somatic) [See Indications and Usage (1) and Clinical Pharmacology (15)]. Information on the FDA-approved test for detection of a known BRCA mutation in patients with ovarian cancer is available at: http://www.fda.gov/CompanionDiagnoses.

2.2 Recommended Dose

The recommended dose of Rubraca is 600 mg (two 300 mg tablets) taken orally twice daily with or without food. (2.3)

2.3 Dose Modifications for Adverse Reactions

To manage adverse reactions, consider interruption of treatment or dose reduction. Recommended dose modifications are included in Table 1.

Table 1. Recommended Dose Adjustments

| Dose Reduction | Dose
<table>
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<tr>
<td>Reduced Dose</td>
<td>450 mg twice daily (two 300 mg tablets)</td>
</tr>
<tr>
<td>Second Dose</td>
<td>300 mg twice daily (two 300 mg tablets)</td>
</tr>
<tr>
<td>First Dose</td>
<td>600 mg twice daily (two 300 mg tablets)</td>
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2.4 Administration

Rubraca tablets should be swallowed whole. Rubraca tablets can be taken with or without food with a glass of water. Tablets should be taken at the same time each day. (2.4)

3 CONTRAINDICATIONS

None. (4)

4 WARNINGS AND PRECAUTIONS

4.1 Myelodysplastic Syndrome/Acute Myeloid Leukemia

Myelodysplastic syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 2 of 377 patients (0.5%) with ovarian cancer treated with Rubraca. MDS/AML was diagnosed 57 days and 539 days after Rubraca treatment prior to the diagnosis of MDS/AML. In 2 of 5 patients with ovarian cancer treated with Rubraca, MDS/AML was diagnosed 57 days and 539 days after Rubraca treatment. In the 3 patients, Rubraca was the last chemotherapy received before the diagnosis of MDS/AML. In the 5 patients, Rubraca was received prior to treatment with platinum and other DNA damaging agents. MDS/AML was reported in the setting of platinum and other DNA damaging agents.

4.2 Embryo-Fetal Toxicity

Rubraca can cause fetal harm when administered to a pregnant woman based on animal reproduction studies. (4.2)

4.3 Lactation

It is not known whether Rubraca is excreted in human milk, or if it can cause fetal harm to a nursing infant. (4.3)

4.4 Pediatric Use

The safety and effectiveness of Rubraca in pediatric patients have not been established. (4.4)

4.5 Geriatric Use

One hundred and sixty (42%) of the 377 ovarian cancer patients in clinical trials of Rubraca were 65 years of age or older. No overall differences in safety were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. (4.5)

4.6 Renal Impairment

No starting dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance [CLcr] between 30 and 89 mL/min, as estimated by Cockcroft-Gault method). There was no recommendation for starting dose adjustment is available for patients with moderate to severe hepatic impairment (total bilirubin >1.5 times ULN) due to a lack of data. (4.6)

5 ADVERSE REACTIONS

9% of patients experienced at least one adverse reaction during clinical trials. The most common adverse reactions (≥35%) were increase in creatinine, increase in AST, ALT, increase in hemoglobin, decreases in lymphocytes, decreases in platelets, and decreases in platelet count (≥35%). (5)

3.1 Clinical Trials Experience

In the randomized phase 3 clinical trial, the median duration of treatment with Rubraca was 5.5 months (range 0.1 to 28.0). The median duration of treatment with Rubraca was 5.5 months (range 0.1 to 28.0). 14% of patients discontinued Rubraca due to adverse reactions. The most common adverse reactions (≥10%) were increased creatinine (35%), increase in AST (22%), increase in ALT (15%), decrease in hemoglobin (23%), decrease in lymphocytes (15%), decrease in platelets (67%), decrease in platelets (67%), and increase in AST (73%). (3.1)

3.2 Agency-Reported Adverse Reactions

The following serious adverse reactions are discussed elsewhere in the labeling: 

3.3 Laboratory Abnormalities

The following laboratory abnormalities have been identified in ≥2% of patients treated with Rubraca: 

3.4 Overdose

In the event of suspected overdose, physicians should consult the Poison Control Center for treatment advice. (3.4)

6 CLINICAL PHARMACOLOGY

6.1 Clinical Trials Experience

The following serious adverse reactions are discussed elsewhere in the labeling:

6.2 Preclinical Pharmacology

Rubraca pharmacokinetics have not been characterized. (6.2)

7 CLINICAL PHARMACOLOGY

7.1 Mechanism of Action

Rubraca is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3. (7.1)

7.2 Pharmacokinetics

The effect of multiple doses of Rubraca on CYP2C9 and CYP3A4 activity was evaluated in an open-label single-arm study of up to 100 mg Rubraca administered to patients with solid tumors who were administered concomitant chemotherapy. (7.2)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Rubraca is a pregnancy category D medication. Women of reproductive potential should use effective contraceptive measures during treatment with Rubraca. (8.1)

8.2 Lactation

Rubraca is not recommended for use in breastfeeding mothers. (8.2)

8.3 Females and Males of Reproductive Potential

Rubraca is a pregnancy category D medication. Women of reproductive potential should use effective contraceptive measures during treatment with Rubraca. (8.3)

8.4 Pediatric Use

The safety and effectiveness of Rubraca in pediatric patients have not been established. (8.4)

8.5 Geriatric Use

One hundred and sixty (42%) of the 377 ovarian cancer patients in clinical trials of Rubraca were 65 years of age or older. No overall differences in safety were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. (8.5)

8.6 Renal Impairment

No starting dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance [CLcr] between 30 and 89 mL/min, as estimated by Cockcroft-Gault method). (8.6)

8.7 Renal Impairment

No starting dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance [CLcr] between 30 and 89 mL/min, as estimated by Cockcroft-Gault method). (8.7)

10 OVERDOSAGE

There were no specific treatment in the event of Rubraca overdose, and symptoms of overdose are not established. In the event of unexpected overdose, physicians should follow general supportive measures and should treat symptomatically. (10)

11 HOW SUPPLIED/STORAGE AND HANDLING

Rubraca tablets contain 30 mg and 60 mg capsules as the active ingredient. 120 mg of rucaparib as the active ingredient. 160 mg of rucaparib as the active ingredient. (11)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

14.1 Ca ncers

Rucaparib capsules are white to pale yellow powder, formulated into a tablet for oral use. Rucaparib capsules are white to pale yellow powder, formulated into a tablet for oral use. (14)

14.2 Pharmacodynamics

The effect of multiple doses of Rubraca on CYP2C9 and CYP3A4 activity was evaluated in an open-label single-arm study of up to 100 mg Rubraca administered to patients with solid tumors who were administered concomitant chemotherapy. (14.2)

14.3 Females and Males of Reproductive Potential

Rubraca is a pregnancy category D medication. Women of reproductive potential should use effective contraceptive measures during treatment with Rubraca. (14.3)

14.4 Lactation

Rubraca capsules contain 30 mg and 60 mg capsules as the active ingredient. 120 mg of rucaparib as the active ingredient. 160 mg of rucaparib as the active ingredient. (14.4)

14.5 Geriatric Use

One hundred and sixty (42%) of the 377 ovarian cancer patients in clinical trials of Rubraca were 65 years of age or older. No overall differences in safety were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. (14.5)

14.6 Renal Impairment

No starting dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance [CLcr] between 30 and 89 mL/min, as estimated by Cockcroft-Gault method). (14.6)

14.7 Clinical Pharmacology

12.1 Mechanism of Action

Rubraca is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3. (12.1)

12.2 Pharmacokinetics

The effect of multiple doses of Rubraca on CYP2C9 and CYP3A4 activity was evaluated in an open-label single-arm study of up to 100 mg Rubraca administered to patients with solid tumors who were administered concomitant chemotherapy. (12.2)
12.3 Pharmacokinetics
All pharmacokinetics of rucaparib were characterized in patients with cancer. Rucaparib is metabolized by cytochrome P450 enzymes to its active metabolite, PARP inhibitor PARP-1. PARP inhibition results in tumor cell death. The mean terminal half-life of rucaparib immediate-release tablet was 16 hours with a range from 30% to 40%.

Food effects: The Tmax in rucaparib was increased by 20% and AUC by increased, and Tmax was delayed by 2 hours, as compared to dosing without fasting conditions [see Dosage and Administration (2.2)].

Distribution
Rucaparib had a steady-state volume of distribution of 113.1 to 262.1 following a single intravenous dose of 12 mg of rucaparib.

In vitro, the binding of rucaparib was 70% in human plasma at therapeutic concentrations. Rucaparib preferentially distributed to red blood cells with a blood-to-plasma concentration ratio of 1.83.

Elimination
The mean terminal T1/2 of rucaparib was 17 hours to follow a single oral dose of 600 mg rucaparib. The apparent clearance ranged from 15.3 to 79.2 L/hour, following continuous 600 mg rucaparib orally twice daily. The clearance ranged from 13.9 to 18.4 L/hour, following a single intravenous dose of 12 mg of rucaparib.

Metabolism
In vitro, metabolism was predominantly by CYP2D6 and to a lesser extent by CYP1A2 and CYP3A4.

Specific Populations
Age, Race, and Body Weight
Based on population pharmacokinetic analyses, age, race, and body weight did not have a clinically significant effect on rucaparib exposure.

Renal Impairment
In patients who received Rubraca 600 mg twice daily, those with mild renal impairment (N=148; CLcr between 60 and 89 mL/min, as estimated by the Cockcroft-Gault method) and those with moderate renal impairment (N=72; CLcr between 30 and 59 mL/min) showed approximately a 50% increase in AUC compared to patients with normal renal function (N=143; CLcr greater than or equal to 90 mL/min). The pharmacokinetics characteristics of rucaparib in patients with CLcr less than or equal to 60 mL/min or patients on dialysis are unknown.

Hepatic Impairment
Based on population pharmacokinetic analyses, no apparent pharmacokinetic difference was observed in patients with mild hepatic impairment (total bilirubin less than or equal to ULN and AST greater than ULN, or total bilirubin between 1.0 to 3.0 x ULN and AST greater than ULN), and those with moderate hepatic impairment (total bilirubin greater than or equal to 3.0 x ULN and AST greater than or equal to 5.0 x ULN). The pharmacokinetics characteristics of rucaparib in patients with moderate severe hepatic impairment (total bilirubin greater than or equal to 5.1 x ULN) are unknown.

CYP Enzyme Polymorphism
In vitro, based on population pharmacokinetic analyses, rucaparib is a substrate of P-gp and BCRP, but not a substrate of CYP3A4, CYP2D6 or CYP2C9.

Drug Interaction Studies
Effects of Other Drugs on Rucaparib
In vitro, rucaparib had a low metabolic turnover rate in human liver microsomes, and rucaparib was not a substrate of CYP3A4, CYP2D6 or CYP2C9.

Effects of Other Drugs on Rucaparib
In vitro, rucaparib was shown to be a substrate of P-gp and BCRP, but not a substrate of CYP3A4, CYP2D6 or CYP2C9.

In vivo, rucaparib had a low metabolic turnover rate in human liver microsomes, and rucaparib was not a substrate of CYP3A4, CYP2D6 or CYP2C9.