

# Facilitating Rubraca® (rucaparib) tablets delivery to your patients where and when they need it

Our integrated support program coordinates with providers and patients to facilitate delivery of Rubraca in 2 ways:

## 1 Specialty Pharmacies

Rubraca® (rucaparib) tablets ship to the patient's home or preferred location directly from one of our network specialty pharmacies.\* You have the option to send your patient's Rubraca Connections Prescription Form directly to your network specialty pharmacy of choice:



[www.avella.com](http://www.avella.com) | 877-546-5779



[www.biologicsinc.com](http://www.biologicsinc.com) | 800-850-4306



[www.cvsspecialty.com](http://www.cvsspecialty.com) | 800-259-1783



[www.usbioservices.com](http://www.usbioservices.com) | 877-757-0667

## 2 Wholesalers

If your practice/institution has an in-office pharmacy, you can order Rubraca directly from one of our wholesalers:



The choice of delivery will not impact the support offered by Rubraca Connections

\*Rubraca cannot be delivered to a PO Box.

# Along with multiple delivery options, Rubraca Connections links patients to a range of support programs

## Reimbursement support

Assistance with benefits investigation, prior authorization, and appeals

## Rubraca financial support programs

Co-pay support and limited supply of free drug during coverage delays for eligible patients

## Adherence support

Patient education and resources to help patients follow their care plans

## To get started with Rubraca Connections:



**Complete the Rubraca Prescription Form** (available at [RubracaConnections.com](http://RubracaConnections.com)) and fax to Rubraca Connections at **1-844-779-7717** or to a network specialty pharmacy

OR



Visit **Rubraca eRx and eSupport Solutions** at [RubracaConnections.com/iAssist](http://RubracaConnections.com/iAssist) to submit online

OR



Call **Rubraca Connections** at **1-844-779-7707**

To get patients started with 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 ET, or visit [RubracaConnections.com](http://RubracaConnections.com)



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### 12.3 Pharmacokinetics

All pharmacokinetics of rucaparib were characterized in patients with cancer. Rucaparib demonstrated linear pharmacokinetics over a dose range from 240 to 840 mg twice daily with time-independence and dose-proportionality. The mean steady-state rucaparib *C*<sub>max</sub> was 1940 ng/mL (54% coefficient of variation [CV]) and AUC<sub>0-12h</sub> was 16900 h·ng/mL (54% CV) at the approved recommended dosage. Accumulation was 3.5 to 6.2 fold. Median terminal half-life (T<sub>1/2</sub>) was 17 hours following a single intravenous dose of 12 to 40 mg rucaparib.

**Absorption**

The median T<sub>max</sub> was 1.9 hours at the approved recommended dosage. The mean absolute bioavailability of rucaparib immediate-release tablet was 36% with a range from 30% to 45%.

Following a high-fat meal, the *C*<sub>max</sub> was increased by 20% and AUC<sub>0-24h</sub> was increased by 38%, and T<sub>max</sub> was delayed by 2.5 hours, as compared to dosing under fasted conditions *[see Dosage and Administration (2.2)]*.

**Distribution**

Rucaparib had a steady-state volume of distribution of 113 L to 262 L following a single intravenous dose of 12 mg to 40 mg rucaparib.

*In vitro*, the protein 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 T<sub>1/2</sub> of rucaparib was 17 to 19 hours, following 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 rucaparib 12 mg to 40 mg.

**Metabolism**

*In vitro*, rucaparib was metabolized primarily 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 15% and 32% higher steady-state AUC, respectively, compared to patients with normal renal function (N=143; CLcr greater than or equal to 90 mL/min). The pharmacokinetic characteristics of rucaparib in patients with CLcr less than 30 mL/min or patients on dialysis are unknown.

**Hepatic Impairment**

Based on population pharmacokinetic analyses, no apparent pharmacokinetic difference was observed in 34 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 1.5 times ULN and any AST) who received Rubraca 600 mg twice daily as compared to patients with normal hepatic function (N=337). The pharmacokinetic characteristics of rucaparib in patients with moderate to severe hepatic impairment (total bilirubin greater than 1.5 times ULN) are unknown.

*CYP Enzyme Polymorphism*

Based on population pharmacokinetic analyses, steady-state concentrations following rucaparib 600 mg twice daily did not differ significantly across CYP2D6 or CYP1A2 genotype subgroups.

**Drug Interaction Studies**

*Effects of Other Drugs on Rucaparib*

*In vitro*, rucaparib had a low metabolic turnover rate in human liver microsomes, and was metabolized primarily by CYP2D6 and to a lesser extent by CYP1A2 and CYP3A4. *In vitro*, rucaparib was shown to be a substrate of P-gp and BCRP, but not a substrate of renal uptake transporters OAT1, OAT3, and OCT2, or hepatic transporters OATP1B1 and OATP1B3.

Concomitant treatment with proton pump inhibitors has no clinically meaningful change in steady-state exposures.

*Effect of Rucaparib on Other Drugs*

Effect of rucaparib on other drugs has not been studied in humans. Rucaparib reversibly inhibited CYP1A2, CYP2C19, CYP2C9, and CYP3A, and to a lesser extent CYP2C8, CYP2D6, and UGT1A1. Rucaparib induced CYP1A2, and down regulated CYP2B6 and CYP3A4 in human hepatocytes at clinically relevant exposures. Rucaparib was a potent inhibitor of MATE1 and MATE2-K, and a moderate inhibitor of OCT1. Weak inhibition was observed at ultra-therapeutic concentration (300 μM) of rucaparib for MRP4, OATP1B1, OATP1B3, OAT1, and OAT3. No inhibition was observed for MRP2, MRP3, or BSEP. Rucaparib was an inhibitor of BCRP and P-gp efflux transporters with IC<sub>50</sub> of 55 μM and 283 μM, respectively.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with rucaparib.

Rucaparib was mutagenic in a bacterial reverse mutation (Ames) test, and clastogenic in an *in vitro* chromosomal aberration assay in cultured human lymphocytes. The clastogenic response in mitotically-stimulated cells was anticipated based on the mechanism of action of rucaparib and indicates potential genotoxicity in humans.

Fertility studies with rucaparib have not been conducted. In 3-month repeat-dose general toxicology studies, rucaparib had no effects on male and female reproductive organs at doses up to 100 mg/kg/day and 20 mg/kg/day in rats and dogs, respectively. These dose levels resulted in systemic exposures of approximately 0.3 and 0.09 times the human exposure (AUC<sub>0-24h</sub>), respectively, at the recommended dose.

### 14 CLINICAL STUDIES

The efficacy of Rubraca was investigated in 106 patients in two multicenter, single-arm, open-label clinical trials, Study 1 and Study 2, in patients with advanced *BRCA*-mutant ovarian cancer who had progressed after 2 or more prior chemotherapies. All 106 patients received Rubraca 600 mg orally twice daily as monotherapy until disease progression or unacceptable toxicity. Objective response rate (ORR) and duration of response (DOR) were assessed by the investigator and independent radiology review (IRR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

The median age of the patients was 59 years (range 33 to 84), the majority were Caucasian (78%), and 100% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. All patients had received at least two prior platinum-based chemotherapies and 43% had received 3 or more prior lines of chemotherapy. There were 18/106 patients (17%) who had deleterious *BRCA* mutations detected in tumor tissue and not in whole blood specimens. Tumor *BRCA* mutation status was verified retrospectively in 96% (64/67) of the patients for whom a tumor tissue sample was available by the companion diagnostic FoundationFocus™ CDx*BRCA* test, which is FDA approved for selection of patients for Rubraca treatment.

Efficacy results are summarized in Table 4.

	Investigator-assessed N=106
Objective Response Rate (95% CI)	54% (44, 64)
Complete Response	9%
Partial Response	45%
Median DOR in months (95% CI)	9.2 (6.6,11.6)

Response assessment by independent radiology review was 42% (95% CI [32, 52]), with a median DOR of 6.7 months (95% CI [5.5, 11.1]). Investigator-assessed ORR was 66% (52/79; 95% CI [54, 76]) in platinum-sensitive patients, 25% (5/20; 95% CI [9, 49]) in platinum-resistant patients, and 0% (0/7; 95% CI [0, 41]) in platinum-refractory patients. ORR was similar for patients with a *BRCA1* gene mutation or *BRCA2* gene mutation.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

#### 16.1 How Supplied

Rubraca is available as 200 mg, 250 mg, and 300 mg tablets.

200 mg Tablets:

- Blue, round, and debossed with “C2” on one side
- Supplied in bottles of 60 tablets (NDC: 69660-201-91)

250 mg Tablets:

- White, diamond, and debossed with “C25” on one side
- Supplied in bottles of 60 tablets (NDC: 69660-202-91)

300 mg Tablets:

- Yellow, oval, and debossed with “C3” on one side
- Supplied in bottles of 60 tablets (NDC: 69660-203-91)

#### 16.2 Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) *[see USP Controlled Room Temperature]*.

### 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

**MDS/AML:** Advise patients to contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. These may be signs of hematological toxicity or a more serious uncommon bone marrow problem called ‘myelodysplastic syndrome’ (MDS) or ‘acute myeloid leukemia’ (AML) which have been reported in patients treated with Rubraca *[see Warnings and Precautions (5.1)]*.

**Embryo-Fetal Toxicity:** Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of the pregnancy *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after receiving the last dose of Rubraca *[see Warnings and Precautions (5.2) and Use in Specific Populations (8.1, 8.3)]*.

**Photosensitivity:** Advise patients to use appropriate sun protection due to the increased susceptibility to sunburn while taking Rubraca *[see Adverse Drug Reactions (6.1)]*.

**Lactation:** Advise females not to breastfeed during treatment and for 2 weeks after the last dose of Rubraca *[see Use in Specific Populations (8.2)]*.

**Dosing Instructions:** Instruct patients to take Rubraca orally twice daily with or without food. Doses should be taken approximately 12 hours apart. Advise patients that if a dose of Rubraca is missed or if the patient vomits after taking a dose of Rubraca, patients should not take an extra dose, but take the next dose at the regular time *[see Dosage and Administration (2.1)]*.

<p>Distributed by: Clovis Oncology, Inc. Boulder, CO 80301 1-844-258-7662</p>
<p>Rubraca is a trademark of Clovis Oncology, Inc.</p>

<p><b>PATIENT INFORMATION</b> <b>Rubraca™ (roo-brah´-kah)</b> <b>(rucaparib)</b> <b>tablets</b></p>
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<p><b>What is the most important information I should know about Rubraca?</b> <b>Rubraca may cause serious side effects including:</b> <b>Bone marrow problems called Myelodysplastic Syndrome (MDS) or a type of cancer of the blood called Acute Myeloid Leukemia (AML).</b> Some people who have ovarian cancer and who have received previous treatment with chemotherapy or certain other medicines for their cancer have developed MDS or AML during or after treatment with Rubraca. MDS or AML may lead to death. If you develop MDS or AML, your healthcare provider will stop treatment with Rubraca.</p>
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Symptoms of low blood cell counts are common during treatment with Rubraca, but can be a sign of serious problems, including MDS or AML. Tell your healthcare provider if you have any of the following symptoms during treatment with Rubraca:

- weakness
- weight loss
- fever
- frequent infections
- blood in urine or stool
- shortness of breath
- feeling very tired
- bruising or bleeding more easily

Your healthcare provider will do blood tests to check your blood cell counts:

- before treatment with Rubraca.
- every month during treatment with Rubraca.
- weekly if you have low blood cell counts for a long time. Your healthcare provider may stop treatment with Rubraca until your blood cell counts improve.

**See “What are possible side effects of Rubraca?” for more information about side effects.**

<p><b>What is Rubraca?</b> Rubraca is a prescription medicine used to treat people with advanced ovarian cancer who:</p> <ul style="list-style-type: none"><li>have certain “<i>BRCA</i>” gene mutations, either inherited (germline) or acquired (somatic), and</li> <li>have received previous treatment with 2 or more prior chemotherapy medicines for their cancer.</li></ul> <p>Your healthcare provider will perform a test to make sure Rubraca is right for you. It is not known if Rubraca is safe and effective in children.</p>
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**What should I tell my healthcare provider before taking Rubraca?**  
**Before you take Rubraca, tell your healthcare provider about all of your medical conditions, including if you:**

- are pregnant or plan to become pregnant. Rubraca can harm your unborn baby and may cause loss of pregnancy (miscarriage). You should not become pregnant during treatment with Rubraca.
    - If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with Rubraca.
    - Females who are able to become pregnant should use effective birth control during treatment and for 6 months after the last dose of Rubraca. Talk to your healthcare provider about birth control methods that may be right for you.
    - Tell your healthcare provider right away if you become pregnant.
  - are breastfeeding or plan to breastfeed. It is not known if Rubraca passes into your breast milk. Do not breastfeed during treatment and for 2 weeks after the last dose of Rubraca.
- Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

<p><b>How should I take Rubraca?</b></p> <ul style="list-style-type: none"><li>Take Rubraca exactly as your healthcare provider tells you.</li> <li>Your healthcare provider may temporarily stop treatment with Rubraca or change your dose of Rubraca if you have side effects. Do not change your dose or stop taking Rubraca unless your healthcare provider tells you to.</li> <li>Take Rubraca 2 times a day. Each dose should be taken about 12 hours apart.</li> <li>Take Rubraca with or without food.</li> <li>If you miss a dose of Rubraca, take your next dose at your usual scheduled time. Do not take an extra dose to make up for a missed dose.</li> <li>If you vomit after taking a dose of Rubraca, do not take an extra dose. Take your next dose at your usual time.</li> <li>If you take too much Rubraca, call your healthcare provider or go to the nearest emergency room right away.</li></ul>
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<p><b>What should I avoid while taking Rubraca?</b> Avoid spending time in sunlight. Rubraca can make your skin sensitive to the sun (photosensitivity). You may sunburn more easily during treatment with Rubraca. You should wear a hat and clothes that cover your skin and use sunscreen to help protect against sunburn if you have to be in the sunlight.</p>
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<p><b>What are the possible side effects of Rubraca?</b> <b>Rubraca may cause serious side effects.</b> <b>• See “What is the most important information I should know about Rubraca?”</b> The most common side effects of Rubraca include:</p> <ul style="list-style-type: none"><li>nausea</li> <li>fatigue</li> <li>vomiting</li> <li>stomach-area pain</li> <li>changes in how food tastes</li> <li>constipation</li> <li>decreased appetite</li> <li>diarrhea</li> <li>shortness of breath</li> <li>decrease in hemoglobin (anemia)</li> <li>low blood cell counts</li> <li>changes in liver or kidney function blood tests</li> <li>increased cholesterol levels</li></ul> <p>These are not all of the possible side effects of Rubraca. For more information, ask your healthcare provider or pharmacist.</p> <p>Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.</p>
<p><b>How should I store Rubraca?</b> • Store Rubraca at room temperature at 68°F to 77°F (20°C to 25°C).</p> <p><b>Keep Rubraca and all medicines out of the reach of children.</b></p>
<p><b>General information about the safe and effective use of Rubraca</b> Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Rubraca for a condition for which it was not prescribed. Do not give it to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about Rubraca.</p>
<p><b>What are the ingredients in Rubraca?</b> <b>Active ingredient:</b> rucaparib <b>Inactive ingredients:</b> microcrystalline cellulose, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate. The film coating contains polyvinyl alcohol, titanium dioxide, polyethylene glycol/macrogol, and talc. The blue film coating contains brilliant blue aluminum lake and indigo carmine aluminum lake. The yellow film coating contains yellow iron oxide.</p> <p>Distributed by: Clovis Oncology, Inc. Boulder, Colorado 80301</p> <p>For more information, go to www.Rubraca.com or call 1-844-258-7662.</p>

<p>This Patient Information has been approved by the U.S. Food and Drug Administration.</p> <p>Issued: February 2017</p> <p>PP-RUCA-US-0424 07/2017</p>
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