CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
1Q17 January – February

BRAND NAME
Rubraca®

GENERIC NAME
rucaparib

MANUFACTURER
Clovis Oncology, Inc.

DATE OF APPROVAL
December 19, 2016

PRODUCT LAUNCH DATE
December 19, 2016

REVIEW TYPE

☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☒ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

FDA-APPROVED INDICATION(S)[1]
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.

OFF-LABEL USES

CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
1Q17 January – February

Rubraca is currently being evaluated in clinical trials in pancreatic cancer, breast cancer, solid tumors.

CLINICAL EFFICACY[2]
The Assessment of Rucaparib In Ovarian CancEr TriaL (ARIEL2) is an international, multicenter, two-part, phase 2, open-label study that enrolled 206 patients with recurrent, platinum-sensitive, high-grade ovarian carcinomas. [3] Patients received oral rucaparib 600 mg twice a day for 28 day cycles until disease progression or discontinuation. The primary endpoint was progression-free survival. In ARIEL2 Part 1, patients were classified into one of three predefined homologous recombination deficiency subgroups on the basis of tumor mutational analysis: 1) breast cancer susceptibility gene (BRCA) mutant (deleterious germline or somatic), 2) BRCA wild-type (loss of heterozygosity) and LOH high (14% or more genomic LOH), or 3) BRCA wild-type and LOH low.

One hundred and ninety-two patients could be classified into one of the three predefined homologous recombination deficiency subgroups: BRCA mutant (n=40), LOH high (n=82), or LOH low (n=70). Tumors from 12 patients were established as BRCA wildtype, but could not be classified for LOH because of insufficient neoplastic nuclei in the sample. The median duration of treatment for the 204 patients was 5.7 months (IQR 2.8–10.1). Median progression-free survival after rucaparib treatment was 12.8 months (95% CI 9.0–14.7) in the BRCA mutant subgroup, 5.7 months (5.3–7.6) in the LOH high subgroup, and 5.2 months (3.6–5.5) in the LOH low subgroup. Progression-free survival was significantly longer in the BRCA mutant (hazard ratio 0.27, 95% CI 0.16–0.44, $p<0.0001$) and LOH high (0.62, 0.42–0.90, $p=0.011$) subgroups compared with the LOH low subgroup. The most common grade 3 or worse treatment-emergent adverse events were anemia or decreased hemoglobin (22%), and elevations in alanine aminotransferase or aspartate aminotransferase (12%).

CONTRAINDICATIONS
None reported

BLACK BOX WARNINGS
None reported

DRUG INTERACTIONS
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.

ADVERSE REACTIONS
Myelodysplastic Syndrome/Acute Myeloid Leukemia: Myelodysplastic syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 2 of 377 (0.5%) patients with ovarian cancer treated with Rubraca. If MDS/AML is confirmed, discontinue Rubraca.

CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
1Q17 January – February

Embryo-Fetal Toxicity: Rubraca can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings from animal studies.

All Ovarian Cancer Patients (N = 377) %	**Grades 1-4**	**Grades 3-4**
Nausea	77	5
Asthenia/Fatigue	77	11
Anemia	44	25
Thrombocytopenia	21	5
Increase in ALT	74	13
Increase in AST	73	5
Decrease in hemoglobin	67	23
Decrease in lymphocytes	45	7
Decrease in platelets	39	6
Decrease in absolute neutrophil count	35	10

The following adverse reactions have been identified in < 20% of the 377 patients treated with Rubraca 600 mg twice daily: dizziness (17%), neutropenia (15%), rash (includes rash, rash erythematous, rash maculopapular and dermatitis) (13%), pyrexia (11%), photosensitivity reaction (10%), pruritus (includes pruritus and pruritus generalized) (9%).

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

Dose Reduction	**Dose**
Starting Dose	600 mg twice daily (two 300 mg tablets)
First Dose Reduction	500 mg twice daily (one 300 mg tablet and one 200 mg tablet)
Second Dose Reduction	400 mg twice daily (two 200 mg tablets)
Third Dose Reduction	300 mg twice daily (one 300 mg tablet)

PRODUCT AVAILABILITY
Tablets: 200 mg, 300 mg

THERAPEUTIC ALTERNATIVES

DRUG NAME	**USAGE REGIMEN**	**COMMENTS**

CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
1Q17 January – February

	(route of admin/frequency of use)	
carboplatin (Paraplatin®)	Varies	
cisplatin (Platinol-AQ®)	Varies	

Boldface indicates generic availability

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s): (1) To prevent inappropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes. (2) Rubraca is being evaluated in clinical trials for pancreatic cancer, breast cancer, solid tumors ii) Recommended utilization management tool(s): (check all that apply) (1) ☒ Prior authorization (2) ☐ Quantity limits (3) ☐ Provider newsletter (4) ☐ Hard block (plan exclusion) (5) ☐ Messaging (6) ☐ Electronic step therapy (7) ☐ Clinical Program
Product Comparison
• Only available third line therapy for ovarian cancer (Not scored) • It would be clinically appropriate to require a trial of two or more prior chemotherapies, including platinum agents.

©2017 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.

CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
1Q17 January – February

REFERENCES

[1] Rubraca [Prescribing Information] Clovis Oncology, Inc., Boulder, CO. December 2016.
[2] Swisher EM, Lin KK, Oza AM, et al. Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicenter, open-label, phase 2 trial. The Lancet 2016; 16:30559-9.