Rucaparib

Indication
Maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

(NICE TA 611)

ICD-10 codes
Codes with a pre fix C48, 56, 57

Regimen details

Day	Drug	Dose	Route
Daily (28-day cycle)	Rucaparib	600mg BD	PO

Patients should start the maintenance treatment no later than 8 weeks after completion of their final dose of the platinum-based chemotherapy.

Cycle frequency
4 weeks

Number of cycles
Continuous until disease progression or unacceptable toxicity.

Administration
Rucaparib is available as 200mg, 250mg and 300mg tablets. The doses should be taken approximately 12 hours apart and tablets should be swallowed whole with water and should not be crushed or chewed. They may be taken with or without food.

If a dose is missed, it should be omitted and the next dose taken as planned. If a patient vomits after taking the dose they should not retake the dose and should take the next scheduled dose as planned.

Pre-medication
Nil

Emetogenicity
This regimen has mild emetic potential.

Additional supportive medication
Antiemetics if required.
Loperamide if required.

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U + Es (including creatinine)	14 days
LFTs	14 days
CA 125	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC*	Monthly
U + Es (including creatinine)	Monthly
LFTs	Monthly
CA 125	3 monthly

* Haematological toxicity is common during first 8-10 weeks of treatment.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	> 1.5 x 10^9/L – prior to commencing treatment, then see below for subsequent cycles
Platelets	> 100 x 10^9/L
Haemoglobin	> 90g/L
CrCl	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
ALT/AST	See below
Alkaline Phosphatase	See below

Dose modifications

Doses should be reduced as below:

Dose level	Rucaparib dose
Full dose	600mg BD
First dose reduction	500mg BD
Second dose reduction	400mg BD
Third dose reduction	300mg BD

- **Haematological toxicity**

For any Grade 3 or 4 toxicity:
Neutrophils < 1.0 x 10^9/L
Platelets < 100 x 10^9/L
Haemoglobin < 80g/L

Delay treatment check FBC weekly and on recovery continue with one dose level reduction.

If counts do not recover to ≤Grade 1 after 4 weeks, discontinue treatment and refer to haematology for further investigation.

- **Renal impairment**

No dose adjustment is necessary for patients with mild to moderate renal impairment. There are no data in patients with severe renal impairment. Rucaparib is not recommended if CrCl < 30mL/min

- **Hepatic impairment**

No dose adjustment is necessary for patients with mild hepatic impairment. There are no data in patients with moderate-severe hepatic impairment. Rucaparib is not recommended if bilirubin > 1.5 x ULN.

- **Other toxicities**

Photosensitivity

Photosensitivity has been observed in patients treated with rucaparib. Patients should avoid spending time in direct sunlight because they may burn more easily during rucaparib treatment; when outdoors, patients should wear a hat and protective clothing, and use sunscreen and lip balm with sun protection factor (SPF) of 50 or greater.

ALT/AST elevations

Grade	Management
Grade 3 without signs of liver dysfunction	Monitor LFTs weekly until ≤ Grade 2 Continue if bilirubin < ULN and ALP < 3 x ULN Withhold if ALT/AST does not improve within 2 weeks and when ≤ Grade 2 resume at same dose or with one dose level reduction.
Grade 4	Withhold until ≤ Grade 2. Then resume with one dose level reduction and monitor LFTs weekly for 3 weeks.

Any other Grade 3-4 reactions should be managed with dose interruptions and dose reductions as necessary.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelodysplastic syndrome (MDS) and AML
Myelosuppression

- **Frequently occurring side effects**

Nausea and vomiting
Abdominal pain
Diarrhoea
Constipation
Dyspepsia
Fatigue
Dizziness
Myelosuppression
Insomnia
Photosensitivity

- **Other side effects**

Deranged LFTs
Rash, pruritis

Significant drug interactions – for full details consult product literature/ reference texts

Caution if concomitant use of **strong CYP3A4 inhibitors or inducers.**

Caution if concomitant use of **strong inhibitors of P-gp.**

If concomitant use of **medicinal products metabolized by CYP1A2**, particularly medicines which have a narrow therapeutic index (e.g., tizanidine, theophylline), dose adjustments may be considered.

If concomitant use of **medicinal products that are CYP2C9 substrates with a narrow therapeutic index** (e.g., warfarin, phenytoin), dose adjustments may be considered, if clinically indicated.
Warfarin: monitor INR closely
Phenytoin: therapeutic drug level monitoring required.

Caution if concomitant use of **medicinal products that are CYP3A substrates with a narrow therapeutic index** (e.g., alfentanil, astemizole, cisapride, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus, terfenadine).

Interactions between rucaparib and **oral contraceptives** have not been studied.

Rucaparib has potential to increase **metformin** renal elimination and decrease liver uptake of metformin, caution is advised when metformin is co-administered.

Caution if concomitant use of **BCRP substrates** (e.g., rosuvastatin).

Additional comments

Women of childbearing potential must use effective contraception during therapy and for 6 months after last dose.

References

- Summary of Product Characteristics Rucaparib (Clovis) accessed December 2019 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA611) accessed December 2019 via www.nice.org.uk
- Coleman, R et al; Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3). Lancet 2017; 390 (10106): 1949 – 1961

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