Systemic Anti Cancer Treatment Protocol

Rucaparib
Gynaecological Cancer

PROTOCOL REF: MPHARUCGY
(Version No: 1.0)

Approved for use in:

Patients with relapsed, platinum sensitive and high grade serous ovarian, fallopian tube or primary peritoneal cancer, who have responded following a second line or subsequent platinum based chemotherapy and who have a germline and/or somatic BRCA mutation and need **MAINTENANCE** therapy.

OR

Patients with relapsed, platinum sensitive and high grade serous ovarian, fallopian tube or primary peritoneal cancer, who have responded to second or subsequent platinum based chemotherapy who do not have a germline and/or somatic BRCA mutation and need **MAINTENANCE** therapy.

Treatment needs to start within 8 weeks of completing their previous course of chemotherapy.

Patient must NOT have received previous therapy with a PARP inhibitor unless it has been stopped within 3 months of its start solely as a consequence of toxicity in the absence of disease progression.

Blueteq registration required: see Blueteq for full eligibility criteria

Dosage:

Drug	Dosage	Route	Frequency
Rucaparib	600mg	PO	TWICE a day, until disease progression or unacceptable toxicity

Treatment will be supplied every 28 days, each capsule contains 300mg.

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Not applicable - Oral agent

Administration:

- Patients can take rucaparib with or without food TWICE daily. Tablets must be swallowed whole.
- If a dose is missed, the patient should resume taking rucaparib with the next scheduled dose.
- Not to be used in pregnant or breast-feeding women. For patients of child-bearing potential, ensure appropriate contraception is discussed and used for 6 months after receiving the last dose of rucaparib.

Interactions:

Effect of other medicinal products on rucaparib:

- Caution should be used for concomitant use of strong CYP3A4 inhibitors or inducers.
- Caution is recommended when rucaparib is co-administered with medicinal products that are strong inhibitors of P-gp.

Effects of rucaparib on other medicinal products:

- CYP1A2 substrates: When co-administering medicinal products metabolized by CYP1A2, particularly medicines which have a narrow therapeutic index (e.g. tizanidine, theophylline), dose adjustments may be considered based on appropriate clinical monitoring.
- CYP2C9 substrates: When co-administering medicinal products that are CYP2C9 substrates with a narrow therapeutic index (e.g., warfarin, phenytoin), dose adjustments may be considered, if clinically indicated. Caution should be exercised and additional International Normalised Ratio (INR) monitoring with co-administration of warfarin and therapeutic drug level monitoring of phenytoin should be considered, if used concomitantly with rucaparib.

- Caution is advised when co-administering 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). Dose adjustments may be considered, if clinically indicated based on observed adverse reactions.

Please refer to the summary of product characteristics for further information: https://www.medicines.org.uk/emc

Main Toxicities:

Rucaparib	
Haematological toxicity	Very common - anaemia, neutropenia and thrombocytopenia
Gastrointestinal disorders	Very common- nausea, vomiting, constipation, abdominal pain, diarrhea, dyspepsia
General disorders	Very common – fatigue/asthenia, dizziness, headache, back pain, peripheral edema, pyrexia, upper respiratory tract infections, insomnia, pruritus, rash
ALT and AST	Rucaparib can increase these liver enzymes in approximately 1 in 3 patients
Embryo-foetal toxicity	Rucaparib should not be used during pregnancy and in women of childbearing potential not using reliable contraception during therapy and for 6 months after receiving the last dose of rucaparib.
Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML)	Occurred in 0.5% of patients in clinical trials taking Rucaparib. Monitor patients for signs of weakness, fatigue, fever, weight loss, infections, bleeding/bruising, breathlessness and haematological toxicities.

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical Assessment	X				X	Every 3 cycles
SACT Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
CA125	X	X	X	X	X	Every cycle
CT scan	X					If clinically indicated
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Height recorded	X					
Weight recorded	X	X	X	X	X	Every cycle

Toxicity Management:

Haematological toxicities

Proceed with treatment if:

Hb ≥ 80g/L	ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Stop treatment if:

Hb < 80g/L	ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/L

- Recheck FBC monthly
- Treatment should be discontinued and restarted at a reduced dose when toxicity returns to the thresholds above.
- If delayed for more than 28 days to recover, Rucaparib should be discontinued permanently.

Non-haematological toxicities

Treatment must be interrupted for any patient who experiences an intolerable grade 2 or any grade 3 or 4 adverse event using the CTCAE V3/4, treatment can be restarted at a reduced dose when the toxicity returns to grade 1 or less.

Dose Modifications

Dose adjustments	
Initial dose	600mg TWICE daily
First dose reduction	500mg TWICE daily
Second dose reduction	400mg TWICE daily
Third dose reduction	300mg TWICE daily

Renal and hepatic impairment

Renal impairment
Treatment can be administered in patients with mild or moderate renal impairment (creatinine clearance > 30 mL/min). There is limited data in patients with severe impairment (creatinine clearance < 30 mL/min) therefore; rucaparib is not recommended for use in these patients.

Hepatic impairment
No dose adjustment is needed in patients with mild hepatic impairment (total bilirubin <ULN and AST>ULN, or total bilirubin between 1.0-1.5 times ULN and any AST). The safety of rucaparib in patients with moderate to severe hepatic impairment is unknown and therefore not recommended.

References:

1. Summary of Product Characteristics, Rubraca 300mg film coated tablets, Clovis Oncology UK ltd. www.medicines.org.uk [accessed on 18th October 2019]
2. NICE FAD document: Rucaparib for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian tube or peritoneal cancer. Published September 2019