Systemic Anti Cancer Treatment Protocol

Niraparib (maintenance) Gynaecological Cancer

PROTOCOL REF: MPHANIRMA
(Version No: 1.1)

Approved for use in:

- Patients with relapsed, platinum-sensitive and high grade serous ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based SECOND line chemotherapy and who HAVE a germline BRCA mutation

- Patients with relapsed, platinum-sensitive and high grade serous ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based SECOND OR LATER line chemotherapy and who DO NOT HAVE a germline BRCA mutation

Treatment needs to start within 12 weeks of completing their previous course of chemotherapy.

Patient must NOT have received previous therapy with a PARP inhibitor

Blueteq registration required

Dosage:

Drug	Dosage	Route	Frequency
Niraparib	300mg	PO	Once daily at night, until disease progression

Treatment will be supplied every 28 days, each capsule contains 100mg.

For patients weighing less than 58kg, a starting dose of 200mg may be considered.

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 niraparib with or without food at approximately the same time each day, preferably at night. Capsules must be swallowed whole.

Not to be used in pregnant or breast-feeding women. For patients of child-bearing potential, ensure appropriate contraception is discussed.

Interactions:

Niraparib has a minimal likelihood of drug interactions.

Caution is recommended when niraparib is used alongside CYP1A2 metabilosed drugs with a narrow therapeutic window (clozapine, theophylline and ropinirole)

Caution is recommended when niraparib is used alongside CYP3A4 metabolised drugs with a narrow therapeutic window (ciclosporin, tacrolimus, alfentanil, ergotamine, pimozide, quetiapine and halofantrine)

Caution is recommended when niraparib is used alongside substrates of BCRP transporters (irinotecan, statins and methotrexate)

Main Toxicities:

Niraparib	
Haematological toxicity	Very common - anaemia, neutropenia and thrombocytopenia, leukopenia
Gastrointestinal disorders	Very common- nausea, vomiting, constipation, abdominal pain, mucositis, diarrhea, dyspepsia, dry mouth
General disorders	Very common – fatigue/asthenia, decreased appetite, headache, insomnia, urinary tract infections, rash
Hypertension and tachycardia	Common, but can be managed with anti-hypertensives and dose reduction of niraparib
Embryo-foetal toxicity	Niraparib should not be used during pregnancy and in women of childbearing potential not using reliable contraception during therapy and for 1 month after receiving the last dose of niraparib.
Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML)	Occurred in 0.9% of patients in clinical trials taking Niraparib. Monitor patients for signs of weakness, fatigue, fever, weight loss, infections, bleeding/bruising, breathlessness and haematological toxicities.

Management of hypertension:

Treat patients according to the following NICE guidance and refer follow up monitoring and dose adjustment to the GP. https://www.nice.org.uk/guidance/CG127

Investigations:

	Pre	Cycle 1				Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
		D1	D8	D15	D22						
Medical Assessment	X					X			X		Before cycle 2 and then every 3 cycles thereafter
SACT Assessment	X	X				X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	X	X	X	Every cycle for the first year then every 3 cycles thereafter
U&E & LFT	X	X				X	X	X	X	X	Every cycle for the first year then every 3 cycles thereafter
CA125	X	X				X	X	X	X	X	Every cycle
BP and HR	X	X				X	X	X	X	X	Every cycle for the first year then every 3 cycles thereafter
CT scan	X										If clinically indicated
Informed Consent	X										
PS recorded	X	X				X	X	X	X	X	Every cycle
Toxicities documented	X	X				X	X	X	X	X	Every cycle
Weight recorded	X	X				X	X	X	X	X	

Dose Modifications and 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 weekly.
- 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, Niraparib 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 adjustments	
Initial dose	300mg once daily
First dose reduction	200mg once daily
Second dose reduction	100mg* once daily

*If further dose reduction below 100mg daily is required, discontinue niraparib

FBC needed weekly for 4 weeks after each dose reduction

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) or end stage renal disease undergoing haemodialysis therefore use with caution in these patients

Hepatic impairment
No dose adjustment is needed in patients with mild or moderate hepatic impairment. There are no data in patients with severe hepatic impairment, use with caution in these patients.

References

Zejula 100mg hard capsules, Summary of Product Characteristics, Tesaro UK Limited, 16/11/2017. Available from https://www.medicines.org.uk/emc/product/8828 Last updated 04/01/2018

CDF criteria on blueteq forms