Niraparib

Indication

Treatment of relapsed, platinum sensitive high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in patients who have responded to the most recent course of platinum based chemotherapy if they:

- have a documented germline BRCA mutation and have had 2 (and only 2) courses of platinum based chemotherapy

or

- have had a BRCA test that shows they do not have a germline BRCA mutation and have had 2 or more courses of platinum based chemotherapy.

(NICE TA 528 – cancer drugs fund)

ICD-10 codes

Codes with a pre fix C48, 56, 57

Regimen details

Day	Drug	Dose	Route
Daily (28-day cycle)	Niraparib	300mg OD	PO

If patient weighs <58kg use 200mg OD as starting dose due to increased risk of adverse effects. If the patient weighs <77kg and has platelets <150x10^9/L, consider starting at 200mg od and escalation to 300mg if no significant toxicity.

Cycle frequency

4 weeks

Number of cycles

Continuous until disease progression or unacceptable toxicity.

Administration

Niraparib is available as 100mg capsules. Patients should be advised to take the dose at approximately the same time each day. The capsules should be swallowed whole with water and should not be crushed or chewed.

Administration at bedtime may reduce nausea.

If a dose is missed, it should be omitted and the next dose taken as planned.

Pre-medication

Nil

Emetogenicity

This regimen has mild emetic potential.

Additional supportive medication

Antiemetics 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
Blood pressure*	Baseline
Pregnancy test (women of child bearing potential)	Baseline

* Blood pressure should be adequately controlled prior to commencing treatment.

Investigations – pre subsequent cycles

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

* Haematological toxicity is common during the initial phase of treatment. FBC should be monitored weekly until stable dose for 4 weeks, then monthly for 12 months, then every 2-3 months.

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 – see below
Platelets	> 100 x 10^9/L
Haemoglobin	> 90g/L
CrCl	≥ 30 mL/min
Bilirubin	See below
ALT/AST	See below

Dose modifications

Adverse reactions should initially be managed by maximal supportive measures. If the patient recovers within 28 days, treatment may be recommenced at the same dose. Treatment interruptions are required for haematological toxicities and treatment resumed on recovery, usually at a lower dose level (see below). If the reaction persists beyond 28 days, treatment should be discontinued.

If the adverse reaction recurs then the dose should be reduced as below:

Dose level	Niraparib dose
Full dose	300mg OD
First dose reduction	200mg OD
Second dose reduction	100mg OD

If the adverse reaction cannot be managed with dose interruption and subsequent dose reduction, treatment should be discontinued.

- **Haematological toxicity**

Haematological adverse reactions have been observed with Niraparib, especially during the initial phase of treatment.

Platelets:

Platelet level		Management
< 100 x 10^9/L	First occurrence	Withhold (maximum of 28 days) and monitor weekly FBC Once resolved resume at same dose or with one dose reduction (clinician decision). If platelets < 75 x 10^9/L at any time resume with reduced dose on recovery.
	Second occurrence	Withhold (maximum of 28 days) and monitor weekly FBC Once resolved resume with reduced dose.

If platelet count dose not recover within 28 days or if the dose has been reduced to 100mg OD discontinue treatment.

If platelets < 10 x 109/L consider platelet transfusion. On recovery resume with reduced dose.

Neutrophils and haemoglobin:

If neutrophils < 1.0 x 10^9/L and/or haemoglobin < 80g/L:

- Withhold (maximum of 28 days) and monitor weekly FBC until neutrophils ≥ 1.5 x 10^9/L and haemoglobin ≥ 90g/L.
- Once resolved resume with reduced dose.
- If counts do not recover within 28 days or if the dose has been reduced to 100mg OD discontinue treatment.

If counts do not recover, consider myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML). Permanently discontinue treatment and refer to haematology.

- **Renal impairment**

No dose adjustment is necessary for patients with mild (CrCl < 90 - ≥ 60 mL/min) to moderate (CrCl < 60 - ≥ 30 mL/min) renal impairment. There is no data in patients with severe renal impairment or end stage renal disease undergoing haemodialysis therefore use with caution.

- **Hepatic impairment**

No dose adjustment is necessary for patients with mild to moderate hepatic impairment. There is no data in patients with severe hepatic impairment therefore use with caution.

- **Other toxicities**

Hypertension

Hypertension and hypertensive crisis have been reported in patients taking niraparib. Blood pressure should be adequately controlled prior to commencing treatment. Blood pressure should be monitored as above. Hypertension should be controlled adequately using standard antihypertensive treatment, rarely are dose modifications required. Treatment should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.

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

- **Serious side effects**

Myelodysplastic syndrome and AML (approx. 0.5% increase over placebo)
Myelosuppression

- **Frequently occurring side effects**

Nausea and vomiting
Abdominal pain
Diarrhoea
Dyspepsia
Hypertension
Urinary tract infections
Myelosuppression
Insomnia
Anxiety, depression
Fatigue
Stomatitis

- **Other side effects**

Peripheral oedema
Decreased appetite
Deranged LFTs
Rash

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

Caution is recommended when niraparib is used concomitantly with medicinal products where their active products are **metabolised by CYP3A4**-dependent mechanisms, particularly those with a narrow therapeutic range (e.g. ciclosporin, tacrolimus, alfentanil, ergotamine, pimozide, quetiapine, and halofantrine).

Caution is recommended when niraparib is used concomitantly with medicinal products where their active products are **metabolised by CYP1A2**-dependent mechanism, particularly those with a narrow therapeutic range (e.g. clozapine, theophylline, and ropinirole).

Caution is recommended when niraparib is combined with **substrates of BCRP** (irinotecan, rosuvastatin, simvastatin, atorvastatin, and methotrexate).

Increased plasma concentrations of co-administered medicinal products that are **substrates of MATE 1 and MATE** 2 (e.g. metformin) cannot be excluded.

Caution is recommended when niraparib is combined with active substances that undergo an uptake transport by OCT1 such as metformin.

Additional comments

Women of childbearing potential should not become pregnant while on treatment and should not be pregnant at the beginning of treatment. A pregnancy test should be performed on all women of childbearing potential prior to treatment. Women of childbearing potential must use effective contraception during therapy and for 1 month after receiving the last dose of niraparib.

References

- Summary of Product Characteristics Niraparib (Tesaro) accessed 5 December 2018 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA 528) accessed 5 December 2018 via www.nice.org.uk
- Oza AM, editor Quality of Life in Patients with Recurrent Ovarian Cancer (OC) Treated with Niraparib: Results from the ENGOT-OV16/NOVA Trial. ESMO; 2017; Madrid, Spain.
- Mirza. M.R., et al Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer December 1, 2016. N Engl J Med 2016; 375:2154-2164

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