Niraparib

Indication

Maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy

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

Regimen details

Niraparib 200mg orally daily.
Consider a starting dose of 300 mg daily for patients weighing more than 77 kg and with platelet count over 150

Cycle frequency

Continuous treatment, dispense monthly

Number of cycles

Until disease progression

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

N/A

Emetogenicity

Mild

Additional supportive medication

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
CA125	14 days
Blood pressure	Baseline
Pregnancy test (women of child bearing potential)	Baseline

FBC should be taken weekly for the 6 weeks and monthly whilst on treatment. Any change in dose will necessitate checking FBC weekly x 6 weeks.
Blood pressure should be adequately controlled prior to commencing treatment
Blood pressure should be monitored weekly for the first two months, monthly afterwards during treatment with niraparib. Home monitoring of BP is allowed in reliable patients.

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), CA125, Blood pressure

Standard limits for administration to go ahead

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

Investigation	**Limit**
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Hb	≥ 90g/L
Blood pressure	See below

Hypertension should be medically managed with antihypertensive medicinal products as well as adjustment of the niraparib dose, if necessary. In most cases, hypertension was controlled adequately using standard antihypertensive treatment with or without niraparib dose adjustment. Niraparib should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy

Dose modifications

May be implemented at any time for any grade of adverse events, when deemed in the best interest of the patient. Not all AEs require dose modification. Use best clinical judgment for AE management. No more than 2 dose reductions will be allowed based on treatment side effects. If further dose reduction below 100mg/day is required, niraparib treatment needs to be discontinued

Dose Modification Guidelines for Haematological Adverse Events

Platelet count < 100 x 10^9/L	First occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥ 100 x 10^9/L • Resume niraparib at same or reduced dose • If platelet count is < 75 x 10^9/L at any time, resume at a reduced dose
	Second occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥ 100 x 10^9/L • Resume niraparib at a reduced dose • Discontinue niraparib if the platelet count has not returned to acceptable levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100 mg*
Neutrophil < 1.0 x 10^9/L or Haemoglobin < 80 g/L	• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until neutrophil counts return to ≥ 1.5 x 10^9/L or haemoglobin returns to ≥ 90 g/L. • Resume niraparib at a reduced dose • Discontinue niraparib if neutrophils and/or haemoglobin have not returned to acceptable

	levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100 mg*

***If myelodysplastic syndrome or acute myeloid leukaemia (MDS/AML) is confirmed, discontinue niraparib**

Renal and Hepatic Impairment
There are no data in patients with severe renal impairment or end stage renal disease undergoing haemodialysis; niraparib should be used with caution in these patients. No dosage adjustment is needed with mild to moderate hepatic impairment. There are no data in patients with severe hepatic impairment, use with caution in these patients

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

Posterior Reversible Encephalopathy Syndrome (PRES)
There have been reports of Posterior Reversible Encephalopathy Syndrome (PRES) in patients receiving niraparib. PRES is a rare, reversible, neurological disorder which can present with rapidly evolving symptoms including seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI).
In case of PRES, it is recommended to discontinue niraparib permanently and to treat specific symptoms including hypertension.

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 6 months after receiving the last dose of niraparib

References

Zejula SPC - https://www.medicines.org.uk/emc/product/8828

SWCN protocols - http://www.swscn.org.uk/guidance-protocols/cancer-protocols/

THIS PROTOCOL HAS BEEN DIRECTED BY DR YIANNAKIS, DESIGNATED LEAD CLINICIAN FOR GYNAE CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: May 2022
Review: May 2024
VERSION: 5