

## Niraparib maintenance after 2<sup>nd</sup> line (or 2nd and subsequent line if no BRCA mutation) platinum based chemotherapy

<b>Indication</b>	<p>Maintenance treatment in patients with relapsed, platinum-sensitive and high grade serous ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based <u>SECOND line</u> chemotherapy with PS 0-1 and have a deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour or in both.</p> <p>NB The patient should be less than 8 weeks since the date of the last infusion of the last cycle of the recent 2nd line chemotherapy.</p> <p>OR</p> <p>Maintenance treatment in patients with relapsed, platinum-sensitive and high grade serous ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based <u>SECOND or SUBSEQUENT line</u> chemotherapy with PS 0-1 and who <b>do not have a deleterious or suspected deleterious germline and/or somatic BRCA mutation.</b></p> <p>NB The patient should be less than 8 weeks since the date of the last infusion of the last cycle of the recent 2nd or subsequent line chemotherapy.</p> <p>NB No previous treatment with a PARP inhibitor, unless rucaparib or olaparib (where appropriate) has had to be stopped within 3 months of starting, solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.</p>
<b>Treatment Intent</b>	Palliative
<b>Frequency and number of cycles</b>	<p>Repeat every 28 days</p> <p>Continuous until disease progression or unacceptable toxicity or patient choice.</p> <p>NB A formal medical review as to whether maintenance treatment with niraparib should continue or not and at what dose will be scheduled to occur at least by the start of the second cycle of treatment</p>
<b>Monitoring parameters pre-treatment</b>	<ul style="list-style-type: none"> <li>• Monitor FBC at baseline and every week during cycle 1, thereafter FBC prior to each of cycles 2-11 or more frequently if clinically indicated. Thereafter as clinically indicated.</li> <li>• U&amp;Es and LFTs prior to each cycle.</li> <li>• Monitor BP at baseline and weekly for the first 2 cycles, then prior to each cycle for the next 10 cycles then as clinically indicated. Hypertension should be adequately controlled before starting niraparib. Niraparib should be discontinued if hypertension cannot be adequately controlled.</li> <li>• <b>Missed doses:</b> If a patient misses a dose, take next dose at usual time.</li> <li>• <b>Adverse reactions:</b> See tables 1 and 2 below. Treatment should be interrupted (but for no longer than 28 consecutive days) to allow the patient to recover from the adverse reaction and then restart at the same dose (unless otherwise stated in tables below). In the case that the adverse reaction recurs, it is recommended to interrupt treatment and then to reduce the dose. If adverse reactions persist beyond a 28-day dose interruption, or interruption with dose reduction are insufficient to manage adverse reactions, discontinue niraparib.</li> <li>• <b>Dose reductions:</b>  <u>Starting dose level 300mg</u>, 1<sup>st</sup> dose reduction should be to 200mg OD, and 2<sup>nd</sup> dose reduction to 100mg OD. No further dose reduction recommended and treatment should be discontinued.  <u>Starting dose level 200mg</u>, 1<sup>st</sup> dose reduction should be to 100mg OD, no further dose reduction recommended and treatment should be discontinued.</li> <li>• <b>Renal impairment:</b> No dose adjustment for patients with mild to moderate renal impairment. Use with caution in patients with severe renal impairment or end stage renal disease undergoing haemodialysis, no data available.</li> <li>• <b>Hepatic impairment:</b> No dose adjustment is needed in patients with mild to moderate hepatic impairment. Use with caution in patients with severe hepatic impairment, no data available.</li> <li>• <b>Common drug interactions (for comprehensive list refer to BNF/SPC):</b>                      Anticoagulants and drugs that reduce the platelet count should be used with caution. Interaction is unlikely but give with caution with drugs metabolised by CYP3A4 particularly if they have a narrow therapeutic range (e.g ciclosporin, tacrolimus, alfentanil), drugs metabolised by CYP1A2 particularly if they have a narrow therapeutic range (e.g clozapine, theophylline), substrates of BCRP (e.g. simvastatin, methotrexate, atorvastatin) and substances that undergo an uptake transport by OCT1 such as metformin.</li> <li>• <b>Posterior Reversible Encephalopathy Syndrome (PRES):</b> has been reported in patients receiving niraparib. In patients developing suspected or confirmed PRES, treatment should be discontinued.</li> </ul>

Protocol No	GYN-038	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	3	Written by	M.Archer
Supersedes version	2	Checked by	C.Waters E.Parry
Date	26.02.21	Authorising consultant (usually NOG Chair)	J.Waters

	<ul style="list-style-type: none"> <li><b>Driving &amp; using machines:</b> Caution, niraparib may cause asthenia, fatigue and dizziness.</li> </ul>
<b>Reference(s)</b>	SPC accessed online 20.01.21 KMCC protocol GYN-038 v2

NB For funding information; refer to CDF and NICE Drugs Funding List

<b>Table 1: Dose modifications for non-haematologic adverse reactions</b>	
≥ Grade 3 where prophylaxis is not considered feasible or adverse reaction persists despite treatment	<p>First occurrence: Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. Resume niraparib at a reduced dose level.</p> <p>Second occurrence: Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. Resume niraparib at a reduced dose level or discontinue.</p>
≥ Grade 3 adverse reaction lasting more than 28 days while patient is administered Niraparib 100 mg/day	Discontinue treatment.

<b>Table 2: Dose modifications for haematologic adverse reactions</b>	
Haematologic adverse reaction requiring transfusion or haematopoietic growth factor support	For patients with platelet count $\leq 10 \times 10^9/L$ platelet transfusion should be considered. If there are other risk factors for bleeding such as co-administration of anticoagulation or antiplatelet medicinal products, consider interrupting these substances and/or transfusion at a higher platelet count. Resume niraparib at a reduced dose.
Platelet count $< 100 \times 10^9/L$	<p>First occurrence: Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to <math>\geq 100 \times 10^9/L</math> Resume Niraparib at same or reduced dose based on clinical evaluation. If platelet count is <math>&lt; 75 \times 10^9/L</math> at any time, resume at a reduced dose.</p> <p>Second occurrence: Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to <math>\geq 100 \times 10^9/L</math> 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 each day.</p>
Neutrophil $< 1 \times 10^9/L$ or Haemoglobin $< 80g/L$	Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until neutrophil counts return to $\geq 1.5 \times 10^9/L$ or haemoglobin returns to $\geq 90 g/L$ . 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 each day.
Confirmed diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML)	Permanently discontinue niraparib.

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platinum based chemotherapy**

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
1	<b>NIRAPARIB</b>	<b>300mg*</b>	po	Swallow whole once daily with water at the same time each day, preferably at night. Do not crush or chew.  Available as 100mg capsules.
	Metoclopramide	10mg	po	up to 3 times a day as required. Do not take for more than 5 days continuously.
	*Patients <58kg: Consider a starting dose of 200mg daily.			

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