Indication	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 SECOND line 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. 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. OR 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 SECOND or SUBSEQUENT line chemotherapy with PS 0-1 and who **do not have** a deleterious or suspected deleterious germline and/or somatic BRCA mutation. 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. 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.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days. Continuous until disease progression or unacceptable toxicity or patient choice. 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.
Monitoring parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • 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. • U&Es and LFTs prior to each cycle. • 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. • **Missed doses:** If a patient misses a dose, take next dose at usual time. • **Adverse reactions:** 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. • **Dose reductions:** Starting dose level **300mg**, 1st dose reduction should be to 200mg OD, and 2nd dose reduction to 100mg OD. No further dose reduction recommended and treatment should be discontinued.

	Starting dose level **200mg,** 1st dose reduction should be to 100mg OD, no further dose reduction recommended and treatment should be discontinued. • **Renal impairment:** 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. • **Hepatic impairment:** No dose adjustment is needed in patients with mild hepatic impairment. In moderate hepatic impairment (any AST and Bilirubin > 1.5 x - 3 x ULN) the recommended starting dose is 200mg once daily. Use with caution in patients with severe hepatic impairment, no data available. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** 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. • **Posterior Reversible Encephalopathy Syndrome (PRES):** has been reported in patients receiving niraparib. In patients developing suspected or confirmed PRES, treatment should be discontinued. • **Driving & using machines:** Caution, niraparib may cause asthenia, fatigue, dizziness or difficulties concentrating.
Reference(s)	SPC accessed online 13.09.2023 KMCC protocol GYN-038 V4

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

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

Table 2: Dose modifications for haematologic adverse reactions	
Haematologic adverse reaction requiring transfusion or haematopoietic growth factor support	For patients with platelet count ≤ 10 x 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 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 based on clinical evaluation. 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 each day.
Neutrophil < 1 x 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 ≥ 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 each day.
Confirmed diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML)	Permanently discontinue niraparib.

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**NIRAPARIB**	**300mg***	PO	Swallow whole once daily with water at the same time each day, preferably at night. Do not crush or chew. Available as 100mg tablets.
	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.			