Indication	For maintenance treatment in patients with high grade epithelial stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma who are in response following platinum-based FIRST line chemotherapy AND who have either a deleterious or suspected deleterious BRCA 1/2 germline and/or somatic mutation or has had a Myriad homologous recombination deficiency (HRD) test which has shown genomic instability. Treatment with olaparib and bevacizumab must commence no more than 9 weeks from the date of the last infusion of the last cycle of 1st line chemotherapy. Patients must have received a minimum of 4 cycles of platinum-based treatment with complete or partial response. Patients must not have previously received any PARP inhibitor.
Treatment Intent	Disease modification
Frequency and number of cycles	**Combination therapy cycle 1 to 11:** Olaparib and bevacizumab repeat every 42 days. **Monotherapy cycle 12 onwards:** Repeat every 42 days. Olaparib should be continued until disease progression or unacceptable toxicity or patient choice to stop treatment or for a maximum total treatment duration of 2 calendar years (combination or monotherapy), whichever is the sooner. Bevacizumab to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment or for a maximum total bevacizumab treatment duration of 15 calendar months, whichever is sooner. **NB** 15 calendar months should be measured from the start of bevacizumab-containing treatment, whether this was with chemotherapy or as maintenance therapy. Equivalent to 22 doses if there are no treatment breaks. A formal medical review as to whether maintenance treatment with olaparib in combination with bevacizumab should continue or not will be scheduled to occur at least by the start of the third cycle of treatment.
Monitoring Parameters pre-treatment	• **NB: Olaparib tablets should not be substituted for olaparib capsules due to differences in the dosing and bioavailability of each formulation.** • **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, LFT's and U&E's prior to each cycle and prior to day 22 during combination therapy and for at least 12 months, and then every 6 weeks. • Commence treatment if neuts >/=1.5 x10^9/l, PLT >/=75x 10^9/l, WBC >/=3x10^9/l and Hb>/= 100g/l. • Monitor blood pressure at each cycle. Pre-existing hypertension should be adequately controlled before starting treatment. • **ECG** at first cycle and then as clinically indicated. Caution should be exercised when treating patients with clinically significant cardiovascular disease such as pre-existing coronary artery disease, or congestive heart failure.

- Dipstick urine for proteinurea at each cycle. Report to consultant if protein 2+ (equivalent to 1g/l) and/or BP >/= 140/90 respectively. Reference should be made to KMCC guidelines for bevacizumab induced hypertension.
- **Renal impairment:**
  - Olaparib: The recommended dose for patients with moderate impairment (CrCl 31-50 ml/min) is 200mg twice a day. Not recommended to be used in patients with severe or end stage renal disease, clinician's decision.
  - Bevacizumab: no dose recommendations.
- **Hepatic Impairment:**
  - Olaparib can be administered to patients with mild or moderate hepatic impairment (Child-Pugh classification A or B) with no dose adjustment. Not recommended for use in patients with severe hepatic impairment (Child-Pugh classification C).
  - Bevacizumab: no dose recommendations.
- **Dose Modifications to manage adverse reactions:**
  - **Olaparib:** The recommended dose reduction is to 250mg twice daily (equivalent to a total daily dose of 500 mg). If a further final dose reduction is required, then reduction to 200mg twice daily (equivalent to a total daily dose of 400 mg) is advised. *NB see **below for dose adjustment when co-administered with CYP3A inhibitors.***
  - **Bevacizumab:** Dose reduction for adverse reactions is not recommended. If indicated, therapy should either be permanently discontinued or temporarily suspended.
- **Management of adverse reactions:**
- **Olaparib guidance:**
  - **Pneumonitis:** If patients present with new or worsening respiratory symptoms such as dyspnoea, cough and fever, or a radiological abnormality occurs, treatment with olaparib should be interrupted and prompt investigation initiated. If pneumonitis is confirmed, treatment with olaparib should be discontinued and the patient treated appropriately.
  - **Hepatotoxicity:** Cases of hepatotoxicity have been reported in patients treated with olaparib. If drug-induced liver injury is suspected, treatment should be interrupted, or if severe, consider discontinuing treatment.
  - Monitor patients for clinical signs and symptoms of venous **thrombosis and pulmonary** embolism and treat as medically appropriate. Patients with a prior history of VTE may be more at risk of a further occurrence and should be monitored appropriately.
  - **Haematological toxicity for Olaparib:**
  - If neuts 1.0-1.4 and/or WBC 2-2.9 and/ or PLT 50-74 and /or Hb 80-100 d/w consultant.
  - If neuts <1 and/or WBC <2 and/or PLT <50 and/or Hb <80 delay until neuts >/=1.5, WBC >/=3, PLT >/=75 and Hb >/= 90 and consider dose reduction.
  - If reoccurrence interrupt and dose reduce.
  - Treatment must be interrupted if any grade 3 or 4 **non-haematological toxicity.**
- **Bevacizumab Guidance:**
  - Use with caution in patients with any history of or concurrent brain metastases, active autoimmune disease, or medical conditions requiring systemic immunosuppression, after careful consideration of the potential risk-benefit. No symptomatically active brain metastases or leptomeningeal metastases allowed under BT criteria.
  - Infusion-related reactions: If a reaction occurs, the infusion should be discontinued and appropriate medical therapies should be administered.
  - Patients may be at an increased risk for the development of gastrointestinal perforation and gall bladder perforation with bevacizumab. Therapy should be permanently discontinued in patients who develop gastrointestinal perforation. It is recommended an OGD is undertaken in patients at high risk of variceal bleeding and that all sizes of varices be assessed and treated as per local standard of care prior to treatment.
  - Patients may be at increased risk for the development of fistulae when treated with bevacizumab.

	○ Posterior Reversible Encephalopathy Syndrome (PRES) has been reported with bevacizumab. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of bevacizumab. ○ Caution should be exercised when bevacizumab and intravenous bisphosphonates are administered simultaneously or sequentially, as cases of osteonecrosis of the jaw have been reported. A dental examination and appropriate preventive dentistry should be considered prior to starting the treatment with bevacizumab. In patients who have previously received or are receiving intravenous bisphosphonates invasive dental procedures should be avoided, if possible. ○ Any suspected thrombosis and/or haemorrhage d/w consultant. ○ Patients with a history of arterial thromboembolism, diabetes or >65 years old should be treated with caution. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** ○ Avoid concomitant treatment of olaparib with strong or moderate CYP3A inhibitors (e.g ketoconazole, itraconazole, clarithromycin, and erythromycin). If a strong CYP3A inhibitor must be given, the recommended dose reduction is to 100 mg taken twice daily. If a moderate CYP3A inhibitor must be given, the recommended dose reduction is to 150 mg taken twice daily. ○ Avoid grapefruit and grapefruit juice throughout the course of treatment. ○ Co-administration of olaparib with strong or moderate CYP3A inducers is not recommended. In the event that a patient requires treatment with a strong (e.g phenytoin, rifampicin, carbamazepine) or moderate (e.g rifabutin, efavirenz) CYP3A inducer, the prescriber should be aware that the efficacy of olaparib may be substantially reduced. ○ Caution and appropriate monitoring when olaparib is administered with sensitive CYP3A substrates or substrates with a narrow therapeutic margin (e.g. simvastatin, cisapride, and ciclosporin). ○ Co-administration of olaparib may reduce the exposure to substrates of the CYP2C9, CYP2C19 and P-gp; the efficacy of some hormonal contraceptives may be reduced. ○ Olaparib may increase exposure to substrates of BCRP, OATP1B1, OCT1, OCT2, OAT3, MATE1 and MATE2K. Caution should be exercised if olaparib is administered in combination with any statin. ○ Live vaccines should not be administered whilst the patient is receiving olaparib and for 30 days after treatment stops. • **Missed doses:** If a patient misses a dose of olaparib, they should take their next normal dose at its scheduled time. • **Surgery and Wound healing:** ○ Olaparib should be stopped 3 days prior to surgery and restarted when the wound has healed. Treatment should be discontinued for a minimum of 3 days prior any radiation treatment. ○ Bevacizumab may adversely affect wound healing. Do not give bevacizumab if patient has undergone major surgery within the last 28 days. Treatment should be stopped prior to elective surgery. • **Driving and operating machinery:** Olaparib may cause drowsiness and dizziness, patients should be made aware and advised if affected to not drive or operate machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed online 06.10.2025 KMCC protocol GYN-044 V1.

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

Repeat every 42 days: *Maximum bevacizumab treatment duration is 15 calendar months (from the start of bevacizumab-containing treatment, whether this was with chemotherapy or as maintenance therapy).*

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1 and 22	**BEVACIZUMAB**	**15mg/kg**	IV	30min	The final concentration must be between 1.4 and 16.5 mg/ml. In 100ml 0.9% sodium chloride. If the patient >/= 110kg give in total of 250mls sodium chloride 0.9%
TTO	Drug	Dose	Route	Directions	
Day 1 and Day 22	**OLAPARIB tablets**	**300mg**	PO	BD, 12 hours apart, to be taken as continuous treatment. Do not take with grapefruit juice. Swallow whole do not crush/chew or dissolve. Available as 150mg and 100mg tablets	
	Metoclopramide	10mg	PO	TDS PRN Do not take for more than 5 days continuously. (dispense 28 tablets on cycle 1, then only if specified)	
	Loperamide	2-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) (dispense 1x op on cycle 1, then when required)	

Repeat every 42 days: *Olaparib to continue for up to 2 years (combination or monotherapy).*

TTO	Drug	Dose	Route	Directions
Day 1	**OLAPARIB tablets**	**300mg**	PO	BD, 12 hours apart, to be taken as continuous treatment. Do not take with grapefruit juice. Swallow whole do not crush/chew or dissolve. Available as 150mg and 100mg tablets Dispense 6 weeks supply.
	Metoclopramide	10mg	PO	TDS PRN Do not take for more than 5 days continuously. (dispense 28 tablets on cycle 1, then only if specified)
	Loperamide	2-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) (dispense 1x op on cycle 1, then when required)