OLAPARIB (Lynparza) BEVACIZUMAB

INDICATION (ICD10) C56, C57

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (OLAP4)

1. As 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 whose cancer has a positive status for homologous recombination deficiency as defined by the presence of either a deleterious or suspected deleterious BRCA 1/2 germline and/or somatic mutation or genomic instability. Has just completed 1st line platinum-based chemotherapy and received a minimum of 4 cycles of platinum-based treatment and has achieved a complete or partial response. Has not previously received a PARP inhibitor. PS 0 or 1. (TA946)

REGIMEN

For calendar months 1 to 15 after initiation

Day 1	**BEVACIZUMAB**	15mg/kg	IV infusion	#ml sodium chloride 0.9%
Days 1 to 21	**OLAPARIB**	300mg	oral	twice daily

For calendar months 16 to 24 after initiation of olaparib bevacizumab

Days 1 to 21	**OLAPARIB**	300mg	oral	twice daily

Bevacizumab - The initial dose should be administered over 90 minutes, if tolerated well the second infusion may be administered over 60 minutes.
If the 60 minute infusion is well tolerated all subsequent infusions may be administered over 30 minutes.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Calendar years or months - maximum duration of treatment from initiation of the treatment, the treatment must stop at that maximum time duration irrespective of any breaks in treatment.
A first 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 3-weekly cycle of treatment

Bevacizumab every 21 days to stop 15 **calendar** months after 1st dose (irrespective of number of doses received ie stop 15 months after initiation even if there have been treatment delays)

Olaparib continuously to stop 2 **calendar** years after 1st dose (irrespective of number of doses received ie stop 2 years after initiation even if there have been treatment delays)

ANTI-EMETICS

Low emetic risk all days

CONCURRENT MEDICATION REQUIRED

Bevacizumab	None

EXTRAVASATION AND TYPE OF LINE / FILTERS

Bevacizumab – neutral

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils $x10^9$/L ≥1.0 Platelets ≥$100x10^9$/L	baseline and every cycle minimum for 15 months then alternate months
GFR assessed using EDTA result (BMI <19 or >30) or calculated creatinine clearance at the Consultant's discretion	baseline and every cycle
Serum creatinine	baseline and every cycle minimum for 15 months then alternate months
CA125	baseline and day 1 every cycle
Blood pressure	baseline and before every bevacizumab dose
Urinalysis for proteinuria	baseline and before every bevacizumab dose
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Bevacizumab	Arterial thromboembolism Gastrointestinal perforation Haemorrhage Hypertension Wound healing complications
Olaparib	Diarrhoea Myelosuppression Nausea, vomiting Raised creatinine

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Olaparib	Concomitant use of strong or moderate CYP3A inhibitors is not recommended and alternative agents should be considered. If a strong CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 100mg twice daily. If a moderate CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 150mg twice daily.

DOSE MODIFICATIONS

Non-haematological

Bevacizumab

Hypertension

Baseline blood pressure should be <150/100mmHg.

Diastolic increase >20mmHg above baseline or BP rises to >150/100mmHg	Antihypertensive therapy may be required.
Blood pressure >180/110mmHg	It is advised that bevacizumab therapy is withheld until blood pressure controlled.

Proteinuria

Urine dipstick result. 1+ or 2+ on dipstick (0.3–2.9g/L)	Continue with bevacizumab. No additional evaluation required.
3+ on dipstick (3-19g/L)	May have dose of bevacizumab as scheduled, but 24 hour urine to measure 24 hour protein to be done a few days before next cycle due. If 24hr protein result <2g, continue with bevacizumab, with continued proteinuria monitoring via 24 hour urine before each dose. If the 24 hour protein level falls to <1g/24hr, return to dipstick analysis. If ≥2g, withhold bevacizumab until repeat 24 hour urine collection shows <2g protein. Then re-introduce bevacizumab, with continued proteinuria monitoring via 24 hour urine.
4+ on dipstick (≥20g/L)	Withhold bevacizumab. 24 hour urine required. Follow 24 hour urine monitoring and guidance as for 3+ on dipstick.

Wound healing

Bevacizumab may adversely affect the wound healing process. Therapy should not be initiated for at least 28 days following major surgery or until the surgical wound is fully healed. Therapy should also be withheld for at least 28–60 days before elective surgery.

Olaparib

When dose reduction is necessary, the olaparib dose may be reduced to 250mg twice daily and further to 200mg twice daily.

Hepatic impairment

Bevacizumab

No need for dose adjustment

Olaparib

No dose adjustment required for patients with mild or moderate hepatic impairment (Child-Pugh A or B).

Olaparib is not recommended for use in patients with severe hepatic impairment.

Renal impairment

Bevacizumab

No need for dose adjustment

Olaparib
No dose adjustment is necessary for patient with CrCl >50ml/minute.
The recommended starting dose is 200mg twice daily for patients with CrCl 31–50ml/minute.
Olaparib is not recommended for patients with CrCl ≤30ml/min.

REFERENCES
CDF list

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Pre-C2, then every 6 weeks (every 2 cycles), or team discretion
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle for 15 months then alternate months
U&E, calcium, & LFT	X	X	X	X	X	Every cycle for 15 months then alternate months
CrCl	X	X	X	X	X	Every cycle for 15 months then alternate months
Blood pressure	X	X	X	X	X	Every cycle
Urine protein	X	X	X	X	X	Every cycle
CT scan	X					At clinician's discretion, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle