Indication	In combination with 1st line carboplatin and paclitaxel AS INDUCTION TREATMENT for patients with stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma. NB: A dose of 7.5mg/Kg or 15mg/kg of bevacizumab may be used. As MAINTENANCE monotherapy for patients with stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma after completion of 1st line induction chemotherapy in combination with bevacizumab 7.5mg/Kg for previously untreated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer. NB: Bevacizumab should be given at a dose of 7.5mg/Kg NB: Neither a dose of 7.5mg/kg bevacizumab nor its use in the neoadjuvant setting, nor its use in stage IIIA disease is licensed in ovarian cancer, this use of bevacizumab must be within the treating Trust's governance framework. NB Maintenance bevacizumab 7.5mg/Kg is NOT commissioned for patients with stage I-III disease who have had optimal debulking
Treatment Intent	Palliative/neo-adjuvant/ adjuvant
Frequency and number of cycles	Repeat every 21 days **Induction:** A maximum of 6 cycles of bevacizumab will be given as part of induction chemotherapy. The bevacizumab should start: • with the 1st or 2nd cycle of chemotherapy following primary debulking surgery OR • with the 1st or 2nd cycle of chemotherapy following interval debulking surgery performed after 3 – 4 cycles of non-bevacizumab-containing neoadjuvant chemotherapy OR • with the 1st or 2nd cycle of chemotherapy for those patients who have inoperable stage IV disease or inoperable stage III disease or who are unable to undergo surgery due to increased risk during COVID19 OR • with the 1st or 2nd cycle of neo-adjuvant chemotherapy **Maintenance:** A maximum of 18 cycles in total to include doses given as part of induction 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, LFT's, U&E's and CA125 at each cycle. Dipstick urine for proteinurea and test BP each cycle. Report to consultant if BP >/= 140/90. Reference should be made to KMCC guidelines for bevacizumab induced hypertension. See table 1 for guidance on proteinuria. • **Hepatic impairment and Renal impairment:** no dose recommendations. • **Infusion-related reactions:** If a patient experiences a mild infusion-related reaction, give the next infusion over 60 - 90 minutes +/- chlorphenamine cover. If this is tolerated, reduce the infusion time for the next doses in a step-wise fashion to a minimum of 30 minutes, and maintain that infusion time for all remaining doses.

	• **Dose Modification:** Dose reduction for adverse reactions is not recommended. If indicated, therapy should either be permanently discontinued or temporarily suspended. If chemotherapy is delayed, bevacizumab should also be delayed. In the event chemotherapy is permanently discontinued continue with bevacizumab only. • 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 at least 28 days prior to elective surgery. • 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. Patients with thromboembolic reactions </= Grade 3 need to be closely monitored. • Bevacizumab should be discontinued in patients with life-threatening (Grade 4) thromboembolic reactions, including pulmonary embolism (refer to SPC for management). • Interactions Caution when used with drugs known to cause bleeding, concurrent use may increase risk.
References	SPC accessed online 25.01.2022 BT form accessed online 25.01.2022 KMCC proforma GYN-023 v4 ARIA regimen GYN-023 Reidy, DL et al; JCO 2007; 25 (19): 2691 – 2695 (infusion rates)

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

Table 1: Proteinuria

1+ or 2+ on dipstick (0.3 – 2.9g/L)	**3+ on dipstick (3 - 19g/L):**	**4+ on dipstick (≥20g/L)**
Continue with bevacizumab. No additional evaluation required	May have dose of bevacizumab as scheduled, but will need 24-hour urine collection to measure protein 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.	**Withhold bevacizumab**. 24-hour urine collection required. Follow 24-hour urine monitoring and guidance as for 3+ on dipstick.

Induction treatment with 1st line carboplatin and paclitaxel and maintenance monotherapy:
NB alternatively, eligible patients may continue on to olaparib and bevacizumab 15mg/kg following 1st line induction.
Repeat every 21 days:

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**BEVACIZUMAB**	**7.5mg/kg**	IV	15mins*	In a total of 100mls sodium chloride 0.9% Flush line with sodium chloride 0.9%
	If a patient experiences a mild infusion-related reaction, give the next infusion over 60 - 90 minutes +/- chlorphenamine cover. If this is tolerated, reduce the infusion time for the next doses in a step-wise fashion to a minimum of 30 minutes, and maintain that infusion time for all remaining doses. *unlicensed rate of infusion				

Induction treatment with 1st line carboplatin and paclitaxel:
NB patients may then continue on to olaparib and bevacizumab 15mg/kg where appropriate.
Repeat every 21 days:

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**BEVACIZUMAB**	**15mg/kg**	IV	30min	In a total of 100mls sodium chloride 0.9% Flush line with sodium chloride 0.9%
	If a patient experiences a mild infusion-related reaction, give the next infusion over 60 - 90 minutes +/- chlorphenamine cover. If this is tolerated, reduce the infusion time for the next doses in a step-wise fashion to a minimum of 30 minutes, and maintain that infusion time for all remaining doses.				