

Protocol Contains CHECKPOINT INHIBITOR IMMUNOTHERAPY	
Indication	For the treatment of persistent, recurrent or metastatic cervical cancer in patients whose tumour PD-L1 expression test results have a combined positive score ≥ 1 and who have not been previously treated with any systemic chemotherapy or have only received chemotherapy which has been used as a radio-sensitising agent or as neo adjuvant chemotherapy prior to chemoradiotherapy. The patient cannot have received prior treatment with an anti PD-1 or anti PD-L1 or anti PD-L2 or CD137 or OX40 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) unless the patient has received pembrolizumab via the MSD company early access scheme.
Treatment Intent	Palliative
Frequency and number of cycles	Pembrolizumab subcutaneous with paclitaxel & carboplatin with or without bevacizumab repeated every 21 days for 6 cycles, followed by Pembrolizumab subcutaneous with or without bevacizumab continuing until progressive disease or unacceptable toxicity or withdrawal of patient consent or a maximum duration of 2 years (35 x 21 day cycles or its equivalent if 6 weekly pembrolizumab is used, including the initial 6 cycles), whichever occurs first. Patients who have completed 2 years of bevacizumab and pembrolizumab and are still benefitting from treatment can continue with bevacizumab monotherapy until disease progression. NB Patients can switch to between SC and IV therapy if the clinical need arises, the switch takes place at the next scheduled dose at a dose of pembrolizumab 400mg IV every 42 days or pembrolizumab 200mg IV every 21 days A formal medical review must be scheduled to occur by the end of the first 6 weeks of treatment to assess tolerance and whether to continue with treatment or not.
Monitoring Parameters	• 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. • Blood parameters: ○ Monitor FBC, U&Es, LFTs, LDH, Ca++ and glucose at each cycle. ○ Cycles 1-6: If neuts < 1.5 and/or PLT < 100 defer treatment by one week and consider dose reduction of paclitaxel and carboplatin on subsequent cycles. ○ Cycles 7 onwards: If PLT < 75 or neuts < 1.0 d/w consultant. • Pre-treatment cardiac assessment: ○ ECG baseline and as clinically indicated. ○ Check BNP, and Troponin T prior to treatment. ○ Undertake ECHO/MUGA at baseline if clinically indicated. • Thyroid function must be assessed at baseline then every 6 weeks or as clinically indicated. • Cortisol monitoring should be undertaken in line with ESMO immunotherapy toxicity guidance available on KMCC website (see link below). Cortisol level should not be taken within 24 hours of the last steroid dose. • EDTA should be used to measure GFR prior to cycle 1. C+G to estimate CrCl may only be used before CYCLE 1 when there is a delay in obtaining EDTA result. • Bevacizumab specific monitoring: ○ Monitor blood pressure at each cycle. Pre-existing hypertension should be adequately controlled before starting treatment. Report to consultant if BP $\geq 140/90$. Reference should be made to KMCC guidelines for bevacizumab induced hypertension.

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V4	Written by	M. Archer
Supersedes version	V3	Checked by	C. Waters O. Adebayo
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat

	○ Dipstick urine for proteinuria at each cycle. See table 1 for guidance on proteinuria. ○ Monitor for signs and symptoms of myocarditis. Carry out ECG 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. ● Hepatic impairment: ○ Pembrolizumab ○ Prior to treatment: No dose adjustment is needed for patients with mild or moderate hepatic impairment. Pembrolizumab has not been studied in patients with severe hepatic impairment d/w consultant. ○ During treatment: For immune related hepatitis see immune related toxicity guidance below. ○ Bevacizumab: no dose recommendations. ○ Paclitaxel: If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction, not recommended in severe hepatic impairment. ○ Carboplatin: no dose recommendations. ● Renal impairment: ○ Pembrolizumab: No specific dose adjustment is necessary in patients with mild to moderate renal impairment. Severe renal impairment (CrCl<30ml/min) d/w consultant. ○ Bevacizumab: no dose recommendations. ○ Paclitaxel: no dose reduction necessary. ○ Carboplatin: Discuss with consultant if creatinine clearance drops by 25%. Stop if CrCl<30ml/min. ● Dose Modification ○ Paclitaxel: Dose reduce by 20% in the event of grade $\geq$ 2 neuropathy and consider delay until recovery to $\leq$ grade 1. Consider omitting paclitaxel in event of recurrent grade $\geq$ 3 neuropathy OR recurrent or persistent $\geq$ grade 2 neuropathy following a dose reduction. ○ Dose reduction of carboplatin and paclitaxel should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to $\leq$ grade 1. ○ Pembrolizumab: dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. If chemotherapy is delayed, pembrolizumab should also be delayed. ○ Bevacizumab: 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. ● Pembrolizumab Sub cutaneous administration: ○ If SC Injection is being prepared on the ward Trust SOP should be followed. ○ Remove from fridge and allow to reach room temperature for at least 30minutes before administration. ○ Withdraw the required volume either 2.4 mL (395 mg) or 4.8 mL (790 mg) using a sterile syringe and a transfer needle (18-21G recommended), according to the recommended dosage. To avoid needle clogging, change the needle to a 25-30G, 13 mm hypodermic injection needle immediately prior to subcutaneous injection. ○ Inject into the subcutaneous tissue of the thigh or abdomen, avoiding 5cm area around the naval. ○ Rotate injection sites for subsequent injection, selecting a site that is 2.5 cm from the previous injection site. ○ Do not inject into areas where the skin is damaged, sore, bruised, scarred, scaly, or has red patches. ○ During the treatment other medicinal products for subcutaneous administration should be injected at different sites. ● Infusion / injection related reactions: If the reaction can be attributed to a particular agent, treat as follows: ○ Pembrolizumab: Severe infusion / injection-related reactions have been reported in patients receiving pembrolizumab.
--	--

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V4	Written by	M. Archer
Supersedes version	V3	Checked by	C. Waters O. Adebayo
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat

	○ For severe infusion/ injection reactions (grade 3-4), treatment should be stopped and pembrolizumab permanently discontinued. Patients with mild or moderate reactions may continue to receive pembrolizumab with close monitoring; premedication with antipyretic and antihistamine may be considered. ○ Bevacizumab: 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. ○ Paclitaxel: Patients developing hypersensitivity reactions may be re-challenged with full dose paclitaxel following prophylactic medication (e.g. famotidine 40mg po given 4 hours prior to treatment plus hydrocortisone 100mg iv and chlorphenamine 10mg iv 30 minutes prior to treatment), then give paclitaxel over 3-6 hours (i.e. starting at over 6 hours and gradually increase rate if possible). ○ Carboplatin: Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate. If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be re-challenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider desensitisation regimen. Severe (grade 3): Do not restart infusion. Consider re-challenge with carboplatin desensitisation regimen. Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. ● Management of adverse reactions: ● Pembrolizumab: Immune related reactions. ○ Immune-related adverse reactions may appear during or after treatment. The most common immune-related reactions are: pneumonitis, colitis, nephritis, hepatitis, symptomatic hypophysitis, hyperthyroidism, hypothyroidism and type 1 diabetes. The following additional, immune related adverse reactions have been reported in patients receiving pembrolizumab: uveitis, arthritis, myositis, pancreatitis, severe skin reactions, myasthenic syndrome, encephalitis, Guillian-Barre syndrome, optic neuritis, rhabdomyolysis, sarcoidosis, myocarditis, haemolytic anaemia and partial seizures arising in a patient with inflammatory foci in brain parenchyma. ○ See guidelines for management of immune-related adverse reactions following immunotherapy: https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/ ○ Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some with fatal outcome, have been reported. For signs or symptoms of SJS or TEN, pembrolizumab should be withheld and the patient should be referred to a specialised unit for assessment and treatment. If SJS or TEN is confirmed, pembrolizumab should be permanently discontinued. ○ Pembrolizumab may be restarted within 12 weeks after last dose, if an adverse reaction remains at <= Grade 1 and corticosteroid dose has been reduced to <= 10 mg prednisone or equivalent per day. ● Bevacizumab: ○ 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.
--	---

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V4	Written by	M. Archer
Supersedes version	V3	Checked by	C. Waters O. Adebayo
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat

	○ 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 $\leq$ Grade 3 need to be closely monitored. ○ Bevacizumab should be discontinued in patients with life-threatening (Grade 4) thromboembolic reactions, including pulmonary embolism or (refer to spc for management). • Common drug interactions (for comprehensive list refer to BNF/SPC): ○ Pembrolizumab: The use of systemic corticosteroids or immunosuppressants before starting pembrolizumab should be avoided; dexamethasone is permitted as prescribed within this protocol. Systemic corticosteroids or other immunosuppressants can be used after starting pembrolizumab to treat immune-related adverse reactions. ○ Vaccines should only be given where the benefit outweighs the risk and after discussion between consultant and patient. ○ Bevacizumab: Caution when used with drugs known to cause bleeding, concurrent use may increase risk. ○ Paclitaxel: Avoid concomitant use of paclitaxel with CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin) and inhibitors (e.g. ketoconazole erythromycin, fluoxetine, gemfibrozil, clopidogrel, cimetidine, ritonavir, nelfinavir). ○ Carboplatin: Caution with other nephrotoxic drugs. • Delayed or missed dose: If a planned dose is missed, the next dose should be administered as soon as possible. The administration schedule must be adjusted to maintain a 3-week interval between doses. Treatment breaks of up to 12 weeks beyond the expected 3-weekly cycle length are allowed but solely to allow any immune toxicities to settle. • Driving & using machines: Pembrolizumab may have a minor influence on the ability to drive and use machines. Fatigue has been reported following administration of pembrolizumab. • Pregnancy and Contraception: Women of childbearing potential should use effective contraception during treatment with pembrolizumab and bevacizumab, for at least 4 months after the last dose of pembrolizumab and for 6 months after the last dose of bevacizumab. • Women of childbearing potential should use effective contraception and not consider pregnancy during treatment and men should be advised to use effective contraception and not to conceive children during treatment, please refer to the brand specific SPC for carboplatin and paclitaxel for further guidance. • Each patient should be given a copy of the relevant Keytruda[®] patient alert card at each cycle. Patients must be advised to contact the oncology team or the 24-hour hot-line immediately if they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment.
References	KMCC protocol GYN-046 V1 CDF list V1.284 SPC accessed online 17.06.2026

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

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V4	Written by	M. Archer
Supersedes version	V3	Checked by	C. Waters O. Adebayo
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat

Table 1: Bevacizumab induced 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.

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V4	Written by	M. Archer
Supersedes version	V3	Checked by	C. Waters O. Adebayo
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat

CYCLES 1-6 subcutaneous administration: Repeat every 21 days

NB Pembrolizumab may alternatively be given at a dose of 790mg SC every 6 weeks where clinically appropriate.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	10mg	PO		Stat
	PEMBROLIZUMAB	395mg	SC	1 min	Inject into the subcutaneous tissue of the left or right thigh or abdomen, avoiding 5cm area around the naval. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Give pre-meds 30 minutes prior to paclitaxel				
	Dexamethasone	16mg*	IV		
	Chlorphenamine	10mg	IV	bolus	
	Ondansetron	< 75yrs 16mg ≥75yrs 8mg	IV	15min	In 50ml sodium chloride 0.9%
	PACLITAXEL	175mg/m²	IV	Over 3 hours	Diluted in 500ml sodium chloride 0.9% (Use non-PVC bag and non-PVC administration set) Via in-line 0.22micron filter Doses <150mg in 250ml 0.9% sodium chloride.
	CARBOPLATIN	(AUC 5) Dose = AUC X (GFR + 25) (dose capped at 790mg on epx system)	IV	30min	500ml glucose 5% In clinical practice the dose is usually capped at either 700mg OR for a maximum calculated dose of GFR 125ml/min
	(+/-) BEVACIZUMAB	15mg/kg	IV	30min	In a total of 100mls sodium chloride 0.9% Flush the line with sodium chloride 0.9% for injection at the end of the infusion.
*From 3rd infusion dexamethasone may be reduced to 12mg IV					
TTO	Drug	Dose	Route	Directions	
Day 1	Dexamethasone	6mg	PO	OD for 3 days starting on day 2.	
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required (max. 30mg per day including 10mg pre-chemo dose) Do not take for more than 5 days continuously.	

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.		
Version	V4	Written by	M. Archer	
Supersedes version	V3	Checked by	C. Waters O. Adebayo	
Date	05.10.2026	Authorising consultant (usually NOG Chair)	L. Kviat	

Cycle 7- 35 sub-cutaneous administration: repeat every 21 days

NB Pembrolizumab may alternatively be given at a dose of 790mg SC every 6 weeks.

Switch patients to 6 weekly dosing where clinically appropriate

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	10mg	PO		Stat
	PEMBROLIZUMAB	395mg	SC	1 min	Inject into the subcutaneous tissue of the left or right thigh or abdomen, avoiding 5cm area around the naval. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	(+/-) BEVACIZUMAB	15mg/kg	IV	30min	In a total of 100mls sodium chloride 0.9% Flush the line with sodium chloride 0.9% for injection at the end of the infusion.
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	10mg up to 3 times a day as required (max. 30mg per day including 10mg pre-chemo dose) Do not take for more than 5 days continuously.	

Cycle 36 onwards - ONLY for patients receiving bevacizumab as part of regimen**Repeat every 21 days**

Day	Drug	Dose	Route	Infusion Duration	Administration
1	BEVACIZUMAB	15mg/kg	IV	30 min	In a total of 100mls sodium chloride 0.9% Flush the line with sodium chloride 0.9% for injection at the end of the infusion.

Protocol No	GYN-046	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.			
Version	V4	Written by		M. Archer	
Supersedes version	V3	Checked by		C. Waters O. Adebayo	
Date	05.10.2026	Authorising consultant (usually NOG Chair)		L. Kviat	