Indication	Bevacizumab with fluoropyrimidine-based chemotherapy for metastatic colorectal carcinoma as **first**- or **second**-line treatment only, when: • targeted treatments or immunotherapy are unsuitable, and • chemotherapy would otherwise be offered. Fluoropyrimidine based chemotherapy options: • FOLFIRI • FOLFOX • FOLFOXIRI • Single agent capecitabine or single agent 5FU • Or alternative fluoropyrimidine based regimen. Note: patients may also/additionally have received neoadjuvant systemic therapy for non-metastatic disease and/or adjuvant chemotherapy after surgery.
Treatment Intent	Palliative
Frequency and number of cycles	There are 2 dosing schedules: Schedule 1 Bevacizumab 5mg/kg every 2 weeks Schedule 2 Bevacizumab 7.5mg/kg every 3 weeks For chemotherapy frequency and number of cycles refer to the relevant KMCC protocol. Continue bevacizumab until disease progression, unacceptable toxicity or patient choice. NB Patients who move to **2nd line** fluoropyrimidine based chemotherapy may continue to receive bevacizumab with this 2nd line chemotherapy, see form BEV12. Patients who move to **3rd line** treatment may continue to receive bevacizumab with trifluridine plus tipiracil if this is the most appropriate third line regimen, and the patient meets all commissioning criteria, see form TRI3.

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.
	• Monitor FBC, LFT's and U&E's at each cycle. See chemotherapy protocol for haematological parameters.
	• **Blood pressure (BP)**
	  ○ Check BP prior to starting treatment, any pre-existing hypertension should be adequately controlled prior to initiating treatment.
	  ○ Monitor BP at each cycle. Report to consultant if BP >/= 140/90. Reference should be made to KMCC guidelines for bevacizumab induced hypertension, https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/ . See table 1 for guidance on proteinuria.
	  ○ Monitor for **proteinuria** by dipstick urinalysis to starting and before each cycle.
	• **Hepatic impairment and Renal impairment:** no dose recommendations.
	• **Bevacizumab 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.
	• Bevacizumab should not be administered as an intravenous push or bolus.
	• **Bevacizumab monitoring and guidance:**
	  ○ 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). • **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. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ Bevacizumab: Caution when used with drugs known to cause bleeding, concurrent use may increase risk. • **Pregnancy and Contraception:** Women of childbearing potential should use effective contraception during treatment and for 6 months after the last dose of bevacizumab. • **Driving:** There may be a minor influence on the ability to drive and use machines. Patients should be advised not to drive or operate machinery if they experience symptoms that effect their vison, concentration or reaction time (NB consider effect of concomitant chemotherapy).
References	CDF list accessed online 31.12.25 V1.381 SPC accessed online 02.01.2025 KMCC protocol COL-044 V2 Colorectal NOG 10.02.2026 agreed to use only 5mg/kg and 7.5mg/kg as standard for this protocol and remove CEA Consultant approved V0.4.

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.

Schedule 1: Repeat every 14 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**BEVACIZUMAB**	**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				
TTO	Drug	Dose	Route	Directions	
Day 1	**When given in conjunction with chemotherapy, give antiemetics as per chemotherapy protocol**				

Schedule 2: 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				
TTO	Drug	Dose	Route	Directions	
Day 1	**When given in conjunction with chemotherapy, give antiemetics as per chemotherapy protocol**				