Indication	For first-line or subsequent line treatment of metastatic colorectal cancer.
Treatment Intent	Palliative.
Frequency and number of cycles	Repeat every 14 days Continue until disease progression or unacceptable toxicity or patient choice to stop treatment. Review after 12 weeks. NB note that patients may have breaks from treatment where clinically appropriate.
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, U&Es and LFT's at each cycle. • Neuts <1.5 and/ or PLT<100 delay one week. • If neuts >/=1.5 and/ or Plts >/=100 continue with treatment. • **DPD testing** must be undertaken in all patients before starting treatment; the result must be checked before treatment is started. • **ECG** prior to cycle 1. • **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris. • **Hepatic impairment:** o Fluorouracil: In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%. If the bilirubin is >85umol/L and / or AST >180 fluorouracil is contra-indicated. o Irinotecan: Consider dose reduction if bilirubin >/= 26µmol/L. Bilirubin >51µmol/L clinical decision. • **Renal impairment:** o Fluorouracil: consider dose reduction in severe impairment. • **Management of adverse reactions and dose adjustments:** • Patients with persistent diarrhoea for >/= 24hrs should have an FBC and if neutropenic start a broad-spectrum antibiotic in line with Trust antibiotic policy. • Dose reduction should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** o **5FU** o 5FU must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC. Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants. o Monitor phenytoin levels with concomitant use. o Caution with folinic acid or folic acid – potential for increased toxicity. o I**rinotecan**: St. John's Wort should not be administered with irinotecan. o Concurrent administration with strong inhibitors (e.g. ketoconazole, itraconazole, clar-ithromycin) or inducers (e.g. phenytoin, rifampicin, carbamazepine, phenobarbital) of cytochrome P450 3A4 (CYP3A4) may alter the metabolism of irinotecan and should be avoided.

	• **Driving:** Patients should be warned about the potential for dizziness or visual disturbances which may occur within 24 hours following treatment, and advised not to drive or operate machinery if these symptoms occur.
References	ARIA regimen COL-016 KMCC proforma COL-016 V4 SPC irinotecan accessed online 17.01.2024 Colorectal NOG 23.01.2023

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

Repeat every 14 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	Dexamethasone	8mg	PO		
	Atropine	0.25mg	S/C	bolus	if required for acute cholinergic syndrome.
	IRINOTECAN	**180mg/m²**	IV	30 min	In 250ml NaCl 0.9% or glucose 5% with a final volume of 180ml-240ml (pre-made bag) Can be run concurrently with Calcium folinate infusion
	CALCIUM FOLINATE (calcium leucovorin)	**350mg**	IV	2 hrs	Sodium chloride 0.9% 500ml Can be run concurrently with Irinotecan infusion
	5-FLUOROURACIL	**400mg/m²**	IV	slow bolus	Through the side of a fast running Sodium chloride 0.9% intravenous infusion
Day 1-2	**5-FLUOROURACIL**	**2400mg/m²/over 46 hrs**	IV	46 hr pump	continuous infusion
TTO	Drug	Dose	Route	Directions	
Day 1	Loperamide	2mg	PO	Take TWO capsules (4mg) after first loose stool, then ONE capsule every 2 hrs for at least 12 hrs or until 12 hrs after last loose stool (for max. of 48hrs)	
	Dioralyte Sachets	1 sachet	PO	Take the contents of ONE sachet dissolved in 200mls of water after each loose stool	
	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg 3 times a day for 3 days, then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.	