Indication	For the treatment of either metastatic or locally advanced and inoperable adenocarcinoma of the colon or rectum in adults who have had previous treatments of fluoropyrimidine, oxaliplatin or irinotecan based chemotherapy and anti-EGFR agents or when these therapies are not suitable. The third (or more) line of systemic therapy for locally advanced or metastatic adenocarcinoma of the stomach or gastro-oesophageal junction. NB no previous treatment with trifluridine and tipiracil for either indication is permitted.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days. Continue until disease progression or unmanageable toxicity or patient choice. A formal medical review as to whether treatment should continue or not should occur no later than by the end of the 2nd cycle of therapy.
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 for proteinuria by dipstick urinalysis prior to starting and before each cycle. • FBC, U&Es, LFTs Day 1 of every cycle. Neutrophils should be >/=1.5 and platelets >/=100. • **Management of toxicity and dose modifications** (see table 3 and also table 2 for patients with severe renal impairment) • Neutrophils 0.5 – 1.49 or Platelets 50-100. Delay treatment until recovered, then restart treatment at same dose. • Neutrophils < 0.5 or platelets <50. Delay treatment until recovered. If the delay is more than 1 week, or febrile neutropenia observed, or non-haematological Grade 3 or Grade 4 adverse reaction (except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or diarrhoea responsive to antidiarrhoeals) dose reduce as follows, o Interrupt dosing until toxicity resolves to Grade 1 or baseline. o When resuming dosing, decrease the dose level by 5mg/m^2/dose from the previous dose level. o A maximum of 3 dose reductions are permitted to a minimum dose of 20mg/m^2 (or 15 mg/m^2/dose twice daily in severe renal impairment) twice daily. Dose level reduction is to 30mg/m^2 bd, 25mg/m^2 bd and 20mg/m^2 bd as appropriate. • Dose escalation is not permitted after it has been reduced. • **Renal Impairment:** • No dose adjustment in mild or moderate renal impairment (30-89ml/min). • In severe renal impairment (15-29ml/min) a starting dose of 20 mg/m^2 is recommended. One dose reduction to a minimum dose of 15 mg/m^2 twice daily is permitted (see table 2). Dose escalation is not permitted after it has been reduced. Not recommended in end stage renal disease (CrCl<15ml/min). • **Hepatic Impairment:** • No dose adjustment in mild hepatic impairment. Not recommended in moderate or severe hepatic impairment (total bilirubin > 1.5 x ULN) as a higher incidence of

	Grade 3 or 4 hyperbilirubinaemia is observed in patients with baseline moderate hepatic impairment (limited data). • **Common drug/food interactions (for comprehensive list refer to BNF/SPC):** • Antivirals which are human thymidine kinase substrates (e.g. zidovudine) may have a reduced anti-viral effect. • **Driving and using machinery**: There may be a minor influence on the ability to drive and use machines. Fatigue, dizziness or malaise may occur during treatment. • **For oral self-administration**: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	ARIA regimen COL-039 v2 SPC accessed online 14.11.22 CDF v1.238

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

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**TRIFLURIDINE & TIPIRACIL** **(Lonsurf®)**	**35mg/m² (Max.80mg/dose)**	PO	BD on Days 1 to 5 and Days 8 to 12 Swallow whole with water within one hour after completion of morning and evening meals. Available as 15mg (+ 6.14 mg tipiracil) and 20mg (+ 8.19 mg tipiracil) trifluridine tablets. See table 1 for starting dose calculation. If doses are missed or withheld, they should be omitted.
	Metoclopramide	10mg	PO	10mg up to 3 times a day as required. Do not take for more than 5 days continuously. (dispense on cycle 1 then only if required)
	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if required.

Table 1 - Starting dose calculation according to BSA

Starting dose	BSA (m^2)	Dose in mg (2x daily)	Tablets per dose (2x daily)		Total daily dose (mg)
			15 mg/6.14 mg	20 mg/8.19 mg	
35 mg/m^2	< 1.07	35	1	1	70
	1.07 - 1.22	40	0	2	80
	1.23 - 1.37	45	3	0	90
	1.38 - 1.52	50	2	1	100
	1.53 - 1.68	55	1	2	110
	1.69 - 1.83	60	0	3	120
	1.84 - 1.98	65	3	1	130
	1.99 - 2.14	70	2	2	140
	2.15 - 2.29	75	1	3	150
	≥ 2.30	80	0	4	160

Table 2 – Starting dose and dose reduction in patients with severe renal impairment according to BSA

Reduced dose	BSA (m^2)	Dose in mg (2x daily)	Tablets per dose (2x daily)		Total daily dose (mg)
			15 mg/6.14 mg	20 mg/8.19 mg	
Starting dose					
20 mg/m^2	< 1.14	20	0	1	40
	1.14 – 1.34	25[a]	2[a]	1[a]	50[a]
	1.35 – 1.59	30	2	0	60
	1.60 – 1.94	35	1	1	70
	1.95 – 2.09	40	0	2	80
	2.10 – 2.34	45	3	0	90
	≥ 2.35	50	2	1	100
Dose reduction: From 20 mg/m^2 to 15 mg/m^2					
15 mg/m^2	< 1.15	15	1	0	30
	1.15 – 1.49	20	0	1	40
	1.50 – 1.84	25[a]	2[a]	1[a]	50[a]
	1.85 – 2.09	30	2	0	60
	2.10 – 2.34	35	1	1	70
	≥ 2.35	40	0	2	80

Table 3 - Dose reductions according to BSA

Reduced dose	BSA (m^2)	Dose in mg (2x daily)	Tablets per dose (2x daily)		Total daily dose (mg)
			15 mg/6.14 mg	20 mg/8.19 mg	
Level 1 dose reduction: From 35 mg/m^2 to 30 mg/m^2					
30 mg/m^2	< 1.09	30	2	0	60
	1.09 - 1.24	35	1	1	70
	1.25 - 1.39	40	0	2	80
	1.40 - 1.54	45	3	0	90
	1.55 - 1.69	50	2	1	100
	1.70 - 1.94	55	1	2	110
	1.95 - 2.09	60	0	3	120
	2.10 - 2.28	65	3	1	130
	≥ 2.29	70	2	2	140
Level 2 dose reduction: From 30 mg/m^2 to 25 mg/m^2					
25 mg/m^2	< 1.10	25[a]	2[a]	1[a]	50[a]
	1.10 - 1.29	30	2	0	60
	1.30 - 1.49	35	1	1	70
	1.50 - 1.69	40	0	2	80
	1.70 - 1.89	45	3	0	90
	1.90 - 2.09	50	2	1	100
	2.10 - 2.29	55	1	2	110
	≥ 2.30	60	0	3	120
Level 3 dose reduction: From 25 mg/m^2 to 20 mg/m^2					
20 mg/m^2	< 1.14	20	0	1	40
	1.14 – 1.34	25[a]	2[a]	1[a]	50[a]
	1.35 – 1.59	30	2	0	60
	1.60 – 1.94	35	1	1	70
	1.95 – 2.09	40	0	2	80
	2.10 – 2.34	45	3	0	90
	≥ 2.35	50	2	1	100

[a] At a total daily dose of 50 mg, patients should take 1 x 20 mg/8.19 mg tablet in the morning and 2 x 15 mg/6.14 mg tablets in the evening.