FRUQUINTINIB (Fruzaqla)

INDICATION (ICD10) C18, C20

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (FRU1)

1. Fruquintinib monotherapy for patients with either metastatic or locally advanced and inoperable adenocarcionama colorectal cancer who have received 2 or more prior anticancer treatment regimens including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies with or without anti-VEGF agents and/or anti-EGFR-based agents AND for whom the combination of trifluridine plus tipiracil and bevacizumab is unsuitable (FOLFIRINOX or FOLFOXIRI can be counted as 2 chemotherapy regimens). The concomitant use of fruquintinib with strong or moderate CYP3A inducers should be avoided. Iin the view of the risk of arterial thromboembolic events, starting treatment with fruquintinib is avoided in patients with a history of thromboembolic events (including a DVT or PE) within the past 6 months or if they have a history of stroke and/or TIA within the last 12 months. PS 0 or 1. (TA1079)

REGIMEN

Days 1 to 21	**FRUQUINTINIB**	5mg	oral	once daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression (formal medical review by end of 2nd cycle)

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Fruquintinib	-

ADMINISTRATION

Fruquintinib	-

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils ≥1.5x10^9/L (and see dose modifications) Platelets ≥100x10^9/L (and see dose modifications)	baseline and every cycle (day 1)
Serum creatinine (and calculated CrCl)	baseline and every cycle (day 1)
Blood pressure (pre-existing hypertension should be adequately controlled before starting fruquintinib treatment)	baseline and every cycle (day 1)
Urine protein (dipstick)	baseline and every cycle (day 1)
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Fruquintinib	Dermatological toxicities Fatigue – may affect ability to drive Haemorrhagic events Hypertension Hypothyroidism Liver function test abnormalities Proteinuria

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Fruquintinib	Concomitant use of fruquintinib with strong or moderate CYP3A inducers should be avoided. Substrates of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) may affect levels of substrates of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP).

DOSE MODIFICATIONS
Fruquintinib

Dose level	Dose
Full dose	5mg
First dose reduction	4mg
Second dose reduction	3mg

Haematological
Fruquintinib
Haemorrhagic events

Grade 2	First occurrence • Withhold until bleeding recovers to grade 1 or baseline. • Resume at the next lower dose level. Recurrence • Withhold until bleeding recovers to grade 1 or baseline. • Resume at the next lower dose level. If the patient still experiences bleeding after taking 3mg daily, permanently discontinue.
Grade ≥3	Permanently discontinue.

Non-haematological

Fruquintinib

Dermatological toxicities

Grade 2	First occurrence • Administer supportive treatment. • Withhold until skin reaction recovers to grade 1 or baseline. • Resume at the same dose level. Recurrence • Administer supportive treatment. • Withhold until skin reaction recovers to grade 1 or baseline. • Resume at the same dose level.
Grade 3	First occurrence • Administer supportive treatment. • Withhold until skin reaction recovers to grade 1 or baseline. • Resume at the next lower dose level. Recurrence • Administer supportive treatment. • Withhold until skin reaction recovers to grade 1 or baseline. • Resume at the next lower dose level. If the patient still experiences toxicity after taking 3 mg daily, permanently discontinue.
Grade 4	Discontinue and only resume if the potential benefit outweighs the risks.

Hypertension

Pre-existing hypertension should be adequately controlled before starting fruquintinib treatment

Grade 3	First occurrence • Withhold if blood pressure at grade 3 worsens despite initiation or modification of antihypertensive treatment. • If hypertension recovers to grade 1 or baseline, resume at the next lower dose level. Recurrence • Withhold if blood pressure at grade 3 worsens despite initiation or modification of antihypertensive treatment. • If hypertension recovers to grade 1 or baseline, resume at the next lower dose level. If the patient still experiences hypertension after taking 3mg daily, permanently discontinue.
Grade 4	Permanently discontinue.

Liver function test abnormalities

Grade 2 or 3 (ALT or AST <3xULN or bilirubin <2xULN or alk phos <2xULN (biochemical criteria for Hy's Law are not met)	First Occurrence • Withhold until the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin (TB) return to grade 1 or baseline. • Resume at the next lower dose level. Recurrence • Withhold until the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin (TB) return to grade 1 or baseline. • Resume at the next lower dose level. If the patient still experiences toxicity after taking 3mg daily, permanently discontinue.
Grade 2 or 3 (biochemical criteria for Hy's Law are met (ALT or AST >3xULN or bilirubin >2xULN or alk phos >2xULN) or grade 4	Permanently discontinue.

Other adverse reactions

Grade 3	First occurrence • Withhold until the reaction recovers to grade 1 or baseline. • Resume at the next lower dose level. Recurrence • Withhold until the reaction recovers to grade 1 or baseline. • Resume at the next lower dose level. If the patient still experiences toxicity after taking 3mg daily, permanently discontinue.
Grade 4	Discontinue and only resume if the potential benefit outweighs the risks.

Palmar-plantar erythrodysesthia syndrome (PPES)

Grade 2	• Administer supportive treatment. • Withhold until PPES recovers to grade 1 or baseline. • Resume at the same dose level.
Grade 3	• Administer supportive treatment. • Withhold until PPES recovers to grade 1 or baseline. • Resume at a reduced dose as per dose modification table. If the patient still experiences Grade 3 PPES after taking 3mg daily, permanently discontinue.

Proteinuria

≥2g/24 hours	First Occurrence • Withhold until proteinuria <1g/24 hours or recovers to baseline. • Resume at the next lower dose level. Recurrence • Withhold until proteinuria <1g/24 hours or recovers to baseline. • Resume at the next lower dose level. If the patient still experiences proteinuria after taking 3mg daily, permanently discontinue. Permanently discontinue for nephrotic syndrome.

Hepatic impairment
Fruquintinib
See dose modification section too.
No dose adjustment is required for patients with mild or moderate hepatic impairment.
Fruquintinib is not recommended for use in patients with severe hepatic impairment as fruquintinib has not been studied in this population.

Renal impairment
Fruquintinib
No dose adjustment is required for patients with mild, moderate, or severe renal impairment

REFERENCES
1. SPC

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed consent	x				
Clinical assessment	x		Pre-C2		Alternate cycles, or at clinician's discretion
SACT assessment (PS and toxicities)	x	x	x	x	Every cycle
FBC	x	x	x	x	Every cycle
U&E & LFTs (including AST and ALP) & magnesium	x	x	x	x	Every cycle
Blood pressure	x	x	x	x	Every cycle
Urine protein (dipstick)	x	x	x	x	Every cycle
CrCl	x	x	x	X	Every cycle
CT scan	x				At baseline, then CT-restaging at 3 cycles, or at clinician's discretion
Weight recorded	x	x	x	x	Every cycle
Height	x	x	x	x	Every cycle