Indication	Fruquintinib monotherapy for the treatment of metastatic or locally advanced and inoperable colorectal cancer in patients who have received 2 or more lines of treatment including fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapies with or without anti-VEGF agents and/or anti-EGFR-based agents AND where the combination of trifluridine plus tipiracil and bevacizumab is unsuitable. NB FOLFIRINOX or FOLFOXIRI can be counted as 2 chemotherapy regimens
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. • BP should be checked prior to treatment, weekly for the first month of treatment, and at each cycle. If clinically indicated BP should be monitored more closely. Pre-existing hypertension should be well controlled before the start of treatment. • Monitor for proteinuria by dipstick urinalysis prior to starting treatment and at each cycle. • If urine dipstick 2+ protein, continue treatment but arrange a 24hr urine protein within the week. If proteinuria >/=2 g / 24 hours is detected withhold treatment, see table 1 for guidance. If urine dipstick 3+ protein withhold fruquintinib and arrange 24hr urine protein. • FBC, U&Es and LFTs baseline and at each cycle. • **Hepatic impairment:** no dose adjustment in mild or moderate impairment. Not recommended for use in severe hepatic impairment. • **Renal impairment:** no dose adjustment required. • **Dose Modification:** Dose modification may be required based on safety and tolerability. If a dose reduction is required the first dose reduction should be to 4mg OD, second dose reduction to 3mg OD. If 3mg OD cannot be tolerated fruquintinib should be permanently discontinued. • **Management of adverse reactions and dose adjustments:** • See table 1 for recommended dose modification for adverse reactions. • **Haemorrhagic events** - Monitor haematologic and coagulation profiles more frequently in patients at risk for bleeding. • **Arterial thromboembolic events:** Due to the risk of arterial thromboembolism, starting treatment with fruquintinib is not recommended for patients with a history of thromboembolic events (including DVT and PE) within the last 6 months or a history of stroke and/or transient ischemic attack within the last 12 months. If arterial thrombosis is suspected fruquintinib should be discontinued immediately. • **Wound Healing:** Fruquintinib may adversely affect wound healing. Treatment should be withheld at least 7 days prior to surgery and resumed post-surgery as clinically indicated when there is adequate wound healing. • **Gastrointestinal events**: Patients may be at an increased risk for the development of gastrointestinal perforation and symptoms of GI perforation should be periodically monitored throughout treatment. Treatment should be permanently discontinued in patients who develop gastrointestinal perforation.

	• **Posterior Reversible Encephalopathy Syndrome (PRES)** has been reported with fruquintinib. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of fruquintinib. • The use of VEGF pathway may promote the formation of aneurysms and/or artery dissections. Before initiating fruquintinib, this risk should be carefully considered in patients with a history of risk factors such as hypertension or aneurysm. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** • The concomitant use of fruquintinib with strong (e.g. apalutamide, enzalutamide, rifampicin, carbamazepine, phenytoin, and St. John's wort) and moderate (e.g. dabrafenib, lorlatinib, modafinil, phenobarbital, primidone) CYP3A inducers should be avoided. • Fruquintinib may increase or decrease exposure of drugs that are substrates of P-gp and BCRP, if co-administered with substrates with a narrow therapeutic range, monitor closely. • Monitor haematologic and coagulation profiles more frequently in patients treated with anticoagulants or other concomitant medicinal products that increase the risk of bleeding. • **Missed dose:** If a dose is missed by less than 12 hours it should be taken as soon as possible, treatment should then resume with the next scheduled dose, if missed by more than 12 hours the dose should be omitted and then resume with the next scheduled dose. Additional tablets should not be taken if the patient vomits after their dose. • **Contraception:** Women of childbearing potential and male patients with female partners of childbearing potential should be advised to use effective contraception during treatment and for at least 2 weeks following the last dose of fruquintinib. • **Driving and Machinery:** Fruquintinib may cause fatigue, patients should be made aware and advised if affected to not drive or operate machinery. • **For oral self-administration:** refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	SPC accessed online 09.07.2025 and 21.07.2025. CDF list V1.368 accessed online 09.07.2025 BlueTeq form accessed online 09.07.2025

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

Table 1 Recommended dose modification for adverse reactions

Adverse reaction	Severity[1]	Dose modification
Hypertension	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 3 mg daily, permanently discontinue.
	Grade 4	Permanently discontinue.
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 3 mg daily, permanently discontinue.
	Grade ≥3	Permanently discontinue.
Proteinuria	≥2 g / 24 hours	First Occurrence • Withhold until proteinuria <1 g / 24 hours or recovers to baseline. • Resume at the next lower dose level. Recurrence • Withhold until proteinuria <1 g / 24 hours or recovers to baseline. • Resume at the next lower dose level. If the patient still experiences proteinuria after taking 3 mg daily, permanently discontinue. Permanently discontinue for nephrotic syndrome.
Liver Function Test Abnormalities	Grade 2 or 3 (biochemical criteria for Hy's Law are not met)[2]	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 3 mg daily, permanently discontinue.
	Grade 2 or 3 (biochemical criteria for Hy's Law are met)[2] or Grade 4	Permanently discontinue.

Table 1 continued Recommended dose modification for adverse reactions

Adverse reaction	Severity[1]	Dose modification
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.
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 3 mg daily, permanently discontinue.
	Grade 4	Discontinue and only resume if the potential benefit outweighs the risks.
[1]Graded per national cancer institute common terminology criteria for adverse events. Version 5.0 (NCI CTCAE v5). [2]Hy's Law is an increase in serum AST or ALT ≥3 × ULN together with total bilirubin ≥2 × ULN, without findings of cholestasis, and no other reason can be found to explain the biochemical changes.		

Repeat every 28 days.

TTO	Drug	Dose	Route	Directions
Day 1	**FRUQUINTINIB**	**5mg**	PO	OD for 21 consecutive days followed by a 7 day break. Swallow whole. Available as 1mg and 5mg capsules
	Metoclopramide	10mg	PO	10mg up to three times a day PRN. Do not take for more than 5 days continuously. Dispense on Cycle 1 only, then only if required
	Loperamide	2mg-4mg	PO	Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day). Dispense on Cycle 1 only, then only if required.