Fruquintinib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with available standard therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents, and who have progressed on or are intolerant to treatment with either trifluridine-tipiracil or regorafenib.	C18	00890a	CDS 01/04/2025

* This applies to post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Fruquintinib is taken orally once daily for 21 consecutive days, followed by a 7-day rest period to comprise a complete cycle of 28 days.

Treatment should be continued until disease progression or unacceptable toxicity occurs.

Day	Drug	Dose	Route	Cycle
1-21	Fruquintinib	5mg once daily	PO	Repeat every 28 days
Fruquintinib should be taken at approximately the same time each day. The capsules can be taken with or without food and should be swallowed whole. The capsules should not be chewed, dissolved, or opened, as the potential effects of these alterations are unknown.				
If a dose is missed by less than 12 hours, it should be taken, and the next dose should be taken as scheduled. If a dose is missed by more than 12 hours, it should be skipped, and the next dose should be taken as scheduled. If a patient vomits after taking a dose, the patient should not repeat the dose on the same day but resume the usual dosing as prescribed on the following day.				

ELIGIBILITY:

- Indications as above
- ECOG status 0-2
- Adequate bone marrow, renal and liver function

CAUTIONS:

- Pre-existing hypertension
- Bleeding / clotting disorders

EXCLUSIONS:

- Hypersensitivity to fruquintinib or to any of the excipients
- Severe hepatic impairment
- History of thromboembolic events (within past 6 months)
- History of stroke and/or transient ischemic attack (within last 12 months)
- Pregnancy / breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Dipstick urinalysis for protein
- Blood pressure
- INR if clinically indicated*

Regular tests:

- FBC, renal and liver profile
- Dipstick urinalysis for protein
- Blood pressure
- INR if clinically indicated*

*(For patients on warfarin, weekly INR until stable warfarin dose established, then INR prior to each cycle)

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- The dose of fruquintinib should be modified based on safety and tolerability
- Fruquintinib should be permanently discontinued in patients unable to tolerate a dose of 3mg once daily
- The recommended dose reduction schedule for adverse reactions is provided in Table 1

Table 1: Recommended fruquintinib dose reduction schedule

Dose reduction schedule	Dose and schedule	Number and strength of capsules
First dose reduction	4mg once daily	Four 1mg capsules once daily
Second dose reduction	3mg once daily	Three 1mg capsules once daily

Renal and Hepatic Impairment:

Table 2: Dose modification of fruquintinib in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No dose adjustment is required for patients with mild, moderate, or severe renal impairment.	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.
Recommendations for fruquintinib from SmPC.	

Management of adverse events:

Table 3: Recommended dose modification of fruquintinib for adverse reactions

Adverse reactions	Severity[a]	Dose modification
Hypertension	Grade 3	• Withhold if Grade 3 hypertension persists despite initiation or modification of antihypertensive treatment. • If hypertension recovers to Grade 1 or baseline, resume at a reduced dose as per Table 1. If the patient still experiences Grade 3 hypertension after taking 3 mg daily, permanently discontinue.
	Grade 4	Permanently discontinue.
Haemorrhagic events	Grade 2	• Withhold until bleeding fully resolves or recovers to Grade 1. • Resume at a reduced dose as per Table 1. If the patient still experiences Grade 2 haemorrhagic events after taking 3 mg daily, permanently discontinue.
	Grade ≥3	Permanently discontinue.
Proteinuria	≥ 2 g / 24 hours	• Withhold until proteinuria fully resolves or is < 1 g / 24 hours (Grade 1). • Resume at a reduced dose as per Table 1. If the patient still experiences ≥ 2 g / 24 hours proteinuria after taking 3 mg daily, permanently discontinue. Permanently discontinue for nephrotic syndrome.
Liver function test abnormalities	Grade 2 or 3 liver function test abnormalities	• Withhold until liver function test abnormality recovers to Grade 1 or baseline. • Resume at a reduced dose as per Table 1.

		If the patient still experiences Grade 2 or Grade 3 liver function test abnormalities after taking 3 mg daily, permanently discontinue.
	Grade ≥ 2 elevation (> 3 x ULN) of either Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) with concurrent total bilirubin elevation > 2 x ULN in the absence of cholestasis; Grade 4 liver function test Abnormalities	Permanently discontinue.
Palmar-plantar erythrodysaesthesia 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 Table 1. If the patient still experiences Grade 3 PPES after taking 3 mg daily, permanently discontinue.
Other adverse reactions	Grade 3	• Withhold until the reaction recovers to Grade 1 or baseline. • Resume at a reduced dose as per Table 1. If the patient still experiences Grade 3 other adverse reactions after taking 3 mg daily, permanently discontinue.
	Grade 4	Discontinue. Consider resuming at a reduced dose as per Table 1 if the toxicity recovers to Grade 1 or baseline and the potential benefit outweighs the risks.
[a] Graded per national cancer institute common terminology criteria for adverse events, version 5.0 (NCI CTCAE v5)		

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting – Available on NCCP website

Minimal to low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on NCCP website

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

- Refer to local skin care policy for management of skin adverse reactions.
- Women of childbearing potential/Contraception in females: Women of childbearing potential should be advised to use highly effective contraception during treatment and for at least 2 weeks following the last dose of fruquintinib.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Dasari A et al; FRESCO-2 Study Investigators. Fruquintinib versus placebo in patients with refractory metastatic colorectal cancer (FRESCO-2): an international, multicentre, randomised, double-blind, phase 3 study. Lancet. 2023 Jul 1;402(10395):41-53. doi: 10.1016/S0140-6736(23)00772-9. Epub 2023 Jun 15. PMID: 37331369.
2. Dasari A et al. FRESCO-2: a global Phase III study investigating the efficacy and safety of fruquintinib in metastatic colorectal cancer. Future Oncol. 2021 Aug; 17(24):3151-3162. doi: 10.2217/fon-2021-0202. Epub 2021 May 17. PMID: 33993740.
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
4. Fruquintinib (Fruzaqla®) Summary of Product Characteristics. Last updated: 27/11/2024. Accessed December 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/fruzaqla-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	07/02/2025		Prof. Maccon Keane
1a	01/04/2025	Updated reimbursement status	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.