



Intended for Irish healthcare professionals
with an interest in oncology only.

A practical guide for FRUZAQLA[®]▼ (fruquintinib)

FRUZAQLA as monotherapy is indicated 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.

▼ This medicinal product is subject to additional monitoring.

Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Reporting forms and information can be found at: www.hpra.ie. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com.

Prescribing information is available at the end of this booklet.

EGFR = epidermal growth factor receptor; mCRC = metastatic colorectal cancer;
VEGF = vascular endothelial growth factor.

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 **Fruzaqla[®]**▼
(fruquintinib) capsules

Indication

FRUZAQLA as monotherapy is indicated 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.¹

Contraindication

FRUZAQLA is contraindicated in patients with hypersensitivity to the active substance or any of the excipients listed in the Summary of Product Characteristics (SmPC).

For special warnings and precautions for use before starting FRUZAQLA, please see pages 4–7.

Special populations

FRUZAQLA is not recommended for use in patients with severe hepatic impairment as FRUZAQLA has not been studied in this population.¹



What is FRUZAQLA?

FRUZAQLA is a selective tyrosine kinase inhibitor of VEGFR-1, -2, and -3 with antitumor effects resulting from suppression of tumour angiogenesis.¹

Communicating the mode of action of FRUZAQLA to your patients

If your patients ask how FRUZAQLA works and the potential benefits of their treatment. We recommend using the following language to explain:

“This medicine stops tumours from making new blood vessels and therefore slows down the growth of cancer.”²



Patients should refer to the Patient Information Leaflet for more details on how FRUZAQLA works and what to expect during treatment.

How is FRUZAQLA dosed?

FRUZAQLA is for oral use and can be taken with or without food. It should be swallowed as a whole capsule.¹

The recommended dose is 5 mg (one 5 mg capsule) once daily at approximately the same time each day for 21 consecutive days, followed by a 7-day rest period to comprise a complete cycle of 28 days.¹

Treatment with FRUZAQLA should be continued until disease progression or unacceptable toxicity occurs.¹



There are two tablet formulations of FRUZAQLA

- **5 mg:** The 5 mg capsules are red and white
- **1 mg:** A 1 mg dose is also available.¹ The 1 mg capsules are yellow and white



Missed doses or vomiting

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.¹

Dose reductions can help manage adverse events

The dose should be modified based on safety and tolerability. The recommended dose reduction schedule for adverse reactions is provided below. The recommended dose modifications for certain adverse reactions can be found on pages 4-7 of this material.

Recommended FRUZAQLA dose reduction schedule¹

Dose reduction schedule	Dose and schedule	Number and strength of capsules
First dose reduction	4 mg once daily	Four 1 mg capsules / once daily
Second dose reduction	3 mg once daily	Three 1 mg capsules / once daily
FRUZAQLA should be permanently discontinued in patients unable to tolerate a dose of 3 mg once daily.		

EGFR = epidermal growth factor receptor; VEGF = vascular endothelial growth factor.

Key considerations when treating with FRUZAQLA

What are the most common adverse reactions associated with FRUZAQLA?

The safety profile of FRUZAQLA is based on data from 911 patients with mCRC who received at least one dose of FRUZAQLA in clinical studies (5 mg once daily 3 weeks on/1 week off each 28-day cycle).¹

In this patient population, the most common adverse reactions of any grade (incidence $\geq 20\%$) were:

- Hypertension (49.3%)
- Anorexia (35.6%)
- Proteinuria (35.5%)
- Palmar-plantar erythrodysesthesia syndrome (34.6%)
- Hypothyroidism (32.4%)
- Dysphonia (28.6%)
- Diarrhoea (26.3%)
- Asthenia (24.5%)

The most common adverse reactions of Grade ≥ 3 are hypertension (19.1%) and PPES (8.3%).¹

The most common serious adverse reactions are gastrointestinal haemorrhage (1.5%), pneumonia (1.5%), hypertension (1.5%), and gastrointestinal perforation (1.3%).¹

The frequency of treatment discontinuation due to adverse reactions is 7.6%. The most common adverse reaction leading to treatment discontinuation is proteinuria (1.6%).

Refer to SmPC for full table of adverse events

Recommended dose modification for FRUZAQLA for specific adverse reactions



Hypertension

Hypertension, including hypertensive crisis, has been reported in patients treated with FRUZAQLA. Considerations for hypertension management with FRUZAQLA include:¹

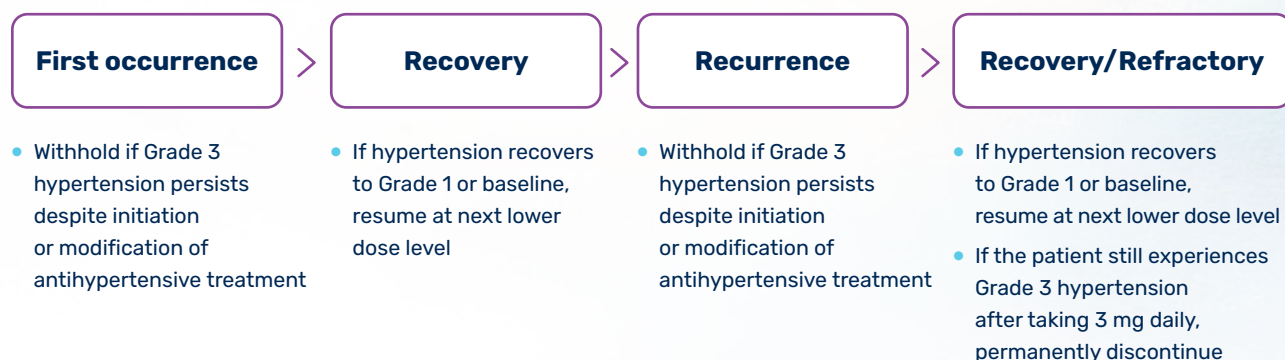
Before starting FRUZAQLA

- Pre-existing hypertension should be monitored and adequately controlled in accordance with standard medical practices before starting FRUZAQLA treatment

During treatment with FRUZAQLA

- Hypertension should be medically managed with antihypertensive medicinal products
- FRUZAQLA's dose can be adjusted to manage hypertension (next page)

Grade 3 hypertension



Grade 4 hypertension

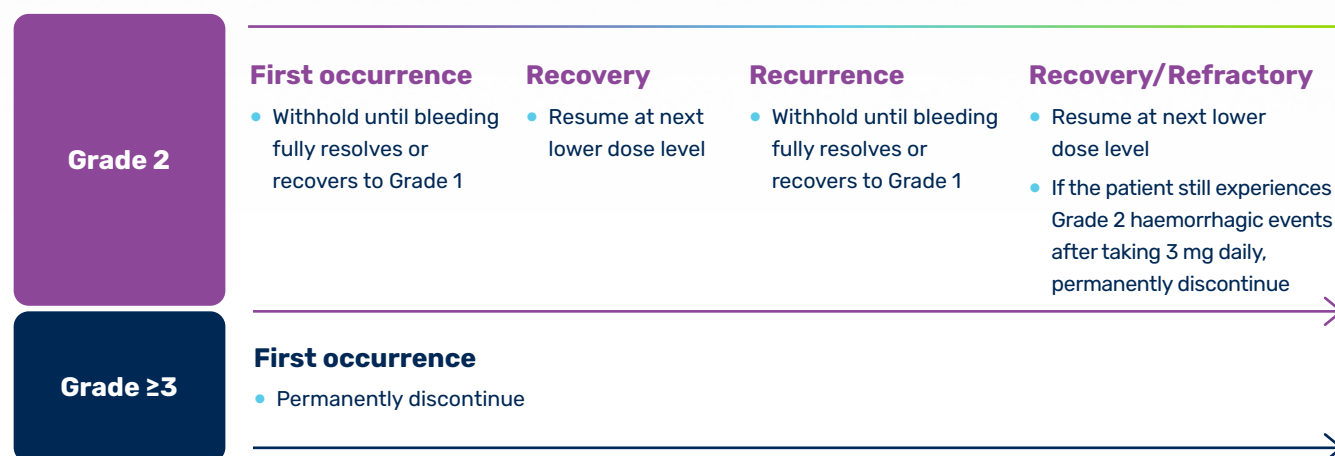
- Permanently discontinue

Haemorrhagic events

Haemorrhagic events have been reported in patients treated with FRUZAQLA, including gastrointestinal (GI) tract events. Serious and sometimes fatal bleeding events have been reported in patients after treatment with FRUZAQLA.¹

Haematologic and coagulation profiles should be monitored in accordance with standard medical practices in patients at risk for bleeding, including those treated with anticoagulants or other concomitant medicinal products that increase the risk of bleeding. In the event of severe bleeding requiring immediate medical intervention, FRUZAQLA should be permanently discontinued.¹

Haemorrhagic events Grade ≥2



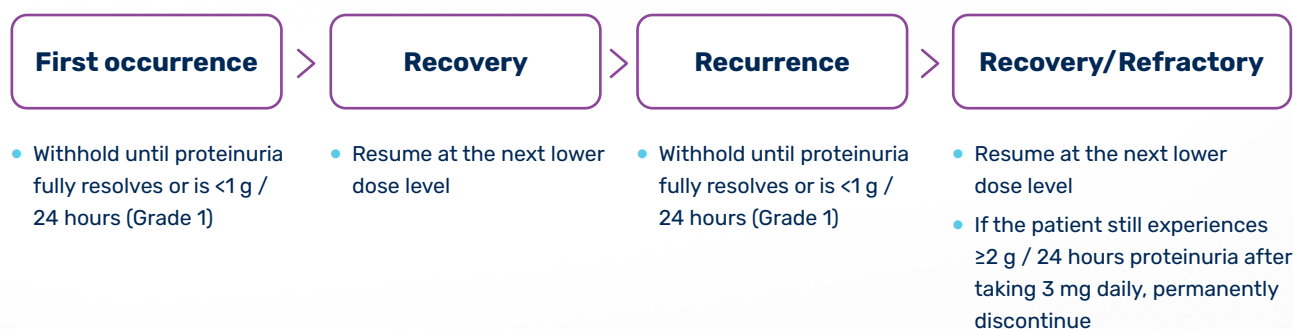
mCRC = metastatic colorectal cancer; PPES = palmar-plantar erythrodysaesthesia syndrome; SmPC = summary of product characteristics.



Proteinuria

Proteinuria events have occurred in patients treated with FRUZAQLA. Proteinuria should be monitored before initiation and during treatment with FRUZAQLA in accordance with standard medical practices. If urine dipstick proteinuria ≥ 2 g / 24 hours is detected, dose interruptions, adjustments, or discontinuation may be necessary. See dosing guidance below:¹

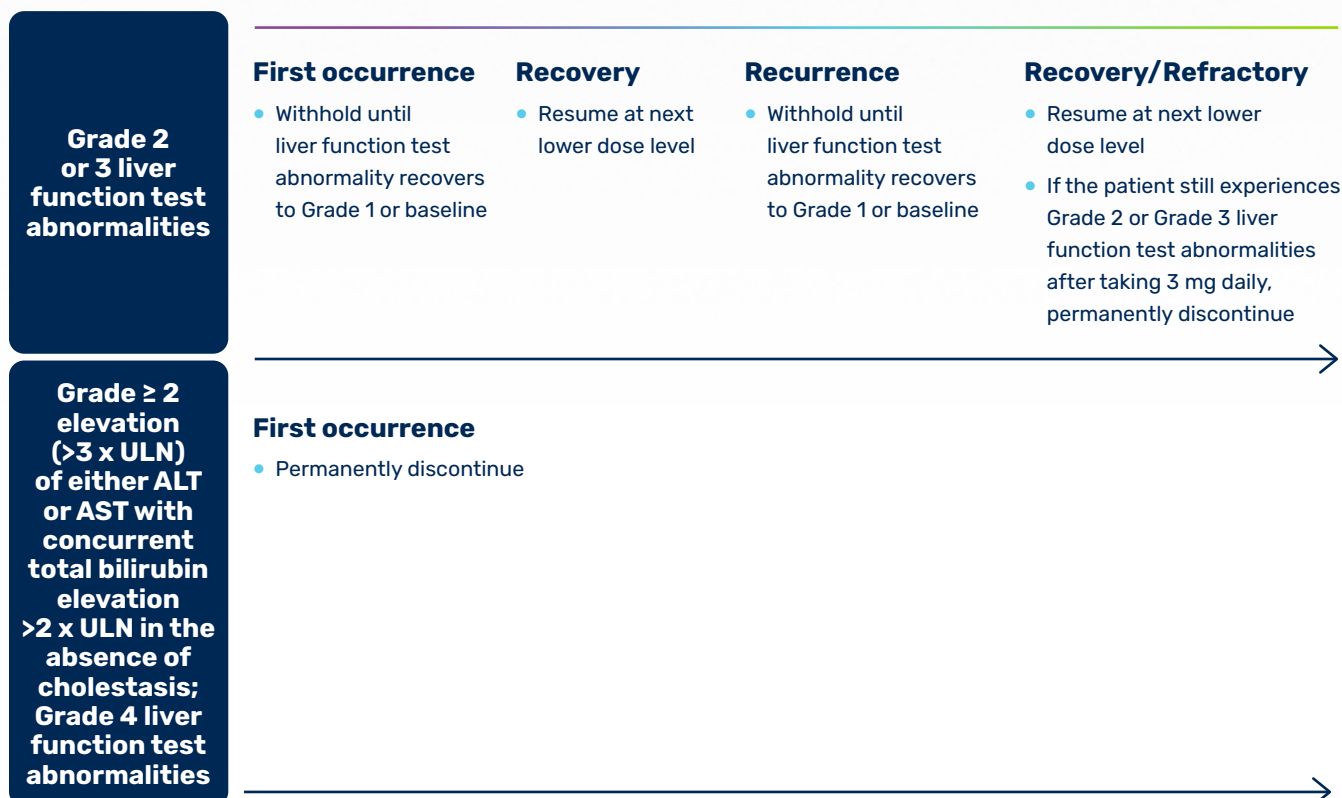
Proteinuria ≥ 2 g / 24 hours



Nephrotic syndrome

- Permanently discontinue

Liver function test abnormalities





Palmar-plantar erythrodysaesthesia syndrome (PPES)

PPES is the most frequently reported dermatological adverse reaction. If Grade ≥ 2 skin reactions are detected, dose interruptions, adjustments, or discontinuation may be necessary. Please see guidance below on managing adverse reactions for PPES.¹

PPES

Grade 2

First occurrence

- Administer supportive treatment
- Withhold until PPES recovers to Grade 1 or baseline

Recovery

- Resume at same dose level

Grade 3

First occurrence

- Administer supportive treatment
- Withhold until PPES recovers to Grade 1 or baseline

Recovery

- Resume at the next lower dose level

Recurrence

- Administer supportive treatment
- Withhold until PPES recovers to Grade 1 or baseline

Recovery/Refractory

- Resume at the next lower dose level
- If the patient still experiences Grade 3 PPES after taking 3 mg daily, permanently discontinue

Other special warnings and precautions for use include **gastrointestinal perforation, posterior reversible encephalopathy syndrome (PRES), impaired wound healing, arterial and venous thromboembolic events and excipients**.¹

Refer to Table 2 of the SmPC for recommended dose modifications for 'Other adverse reactions'.

PLEASE REFER TO THE FULL SUMMARY OF PRODUCT CHARACTERISTICS BEFORE PRESCRIBING FOR THE FULL LIST OF POTENTIAL ADVERSE EVENTS AND FOR MORE INFORMATION REGARDING SPECIAL WARNINGS AND PRECAUTIONS FOR FRUZAQLA.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal; PPES = posterior reversible encephalopathy syndrome.

Prescribing information

FRUZAQLA®▼ (fruquintinib) PRESCRIBING INFORMATION FOR REPUBLIC OF IRELAND

Refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentation: Fruquintinib 1mg and 5mg hard capsules. Indication: FRUZAQLA as monotherapy is indicated 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. **Dosage and administration:** FRUZAQLA should be initiated by a physician experienced in the administration of anticancer therapy. The recommended dose is 5 mg (one 5 mg capsule) once daily at approximately the same time each day 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. FRUZAQLA is for oral use and 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. **Renal impairment:** No dose adjustment is required for patients with mild, moderate, or severe renal impairment. **Hepatic impairment:** No dose adjustment is required for patients with mild or moderate hepatic impairment. FRUZAQLA is not recommended for use in patients with severe hepatic impairment as FRUZAQLA has not been studied in this population. **Elderly population:** No dose adjustment is required in patients aged 65 years or above. **Paediatric population:** There is no relevant use of FRUZAQLA in the paediatric population for the indication of metastatic colorectal cancer. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Warnings and precautions:** **Hypertension:** Hypertension, including hypertensive crisis, has been reported with FRUZAQLA. Pre existing hypertension should be monitored and adequately controlled in accordance with standard medical practices before starting FRUZAQLA treatment. Hypertension should be medically managed with antihypertensives and adjustment of the FRUZAQLA dose, if necessary. Permanently discontinue FRUZAQLA for hypertension that cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis. **Haemorrhagic events:** Haemorrhagic events have been reported with FRUZAQLA, including gastrointestinal (GI) tract events. Serious and sometimes fatal bleeding events have been reported after treatment with FRUZAQLA. Monitor haematologic and coagulation profiles more frequently in patients at risk for bleeding, including those treated with anticoagulants or other concomitant medicinal products that increase the risk of bleeding. In the event of severe bleeding requiring immediate medical intervention, permanently discontinue FRUZAQLA. **GI perforation:** GI perforation events, including fatal events, have been reported with FRUZAQLA. Symptoms of GI perforation should be periodically monitored during treatment. Permanently discontinue FRUZAQLA in patients developing GI perforation. **Proteinuria:** Proteinuria events have occurred with FRUZAQLA. Proteinuria should be monitored before initiation and during treatment. If urine dipstick proteinuria ≥ 2 g / 24 hours is detected, dose interruptions, adjustments, or discontinuation may be necessary. FRUZAQLA should be permanently discontinued in patients developing nephrotic syndrome. **Palmar-plantar erythrodysesthesia syndrome (PPES):** PPES is the most frequently reported dermatological adverse reaction. If Grade ≥ 2 skin reactions are detected, dose interruptions, adjustments, or discontinuation may be necessary. **Posterior reversible encephalopathy syndrome (PRES):** PRES has been reported in 1 patient (0.1%) with FRUZAQLA. PRES can present with headache, seizure, lethargy, confusion, altered mental function, blindness, and other visual or neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain

imaging, preferably magnetic resonance imaging (MRI). In patients developing PRES, discontinuation of FRUZAQLA, along with control of hypertension and supportive medical management of other symptoms, are recommended. **Impaired wound healing:** Impaired wound healing has been reported in 1 patient (0.1%) treated with FRUZAQLA. Patients are recommended to withhold FRUZAQLA for at least 2 weeks prior to surgery. FRUZAQLA should not be resumed for at least 2 weeks after surgery as clinically indicated when there is evidence of adequate wound healing. **Arterial and venous thromboembolic events:** It is recommended to avoid starting treatment with FRUZAQLA in patients with a history of thromboembolic events (including deep vein thrombosis and pulmonary embolism) within the past 6 months or if they have a history of stroke and/or transient ischemic attack within the last 12 months. If arterial thrombosis is suspected, FRUZAQLA should be discontinued immediately. **Excipients:** FRUZAQLA 1 mg capsules contain tartrazine (E102) and sunset yellow FCF (E110) and FRUZAQLA 5 mg capsules contain Allura red AC (E129), which may cause allergic reactions. **Interactions:** The concomitant use of FRUZAQLA with strong and moderate CYP3A inducers should be avoided. **Fertility, pregnancy and lactation:** Women of childbearing potential should be advised to use highly effective contraception during and for at least 2 weeks following the last dose of FRUZAQLA. There are no clinical data available on the use of FRUZAQLA in pregnant women. Based on its mechanism of action, FRUZAQLA has the potential to cause foetal harm. FRUZAQLA should not be used during pregnancy unless the woman's clinical condition requires treatment with FRUZAQLA. The safe use of FRUZAQLA during breast feeding has not been established. It is not known whether FRUZAQLA or its metabolites are excreted in human milk. There are no animal data on the excretion of FRUZAQLA in animal milk. A risk to newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with FRUZAQLA and for at least 2 weeks after the last dose. There are no data on the effects of FRUZAQLA on human fertility. Results from animal studies indicate that FRUZAQLA may impair male and female fertility. **Effects on ability to drive and use machines:** FRUZAQLA has minor influence on the ability to drive and use machines. Fatigue may occur following administration of FRUZAQLA. **Undesirable effects (all grades):** **Very common ($\geq 1/10$):** Thrombocytopenia, hypothyroidism, anorexia, hypertension, dysphonia, diarrhoea, stomatitis, aspartate aminotransferase increased, total bilirubin increased, alanine aminotransferase increased, palmar-plantar erythrodysesthesia syndrome, musculoskeletal discomfort, arthralgia, proteinuria, asthenia and fatigue. **Common ($\geq 1/100$ to $< 1/10$):** Pneumonia, upper respiratory tract infection, bacterial infections, leukopenia, neutropenia, hypokalaemia, epistaxis, throat pain, GI haemorrhage, GI perforation, pancreatic enzymes increased, oral pain, rash and mucosal inflammation. **Other serious undesirable effects:** **Uncommon ($\geq 1/1000$ to $< 1/100$):** PRES, pancreatitis, cholecystitis and impaired wound healing. **Refer to the SmPC for details on full side effect profile and interactions. Legal classification:** POM. **Marketing authorisation (MA) number(s):** EU/1/24/1827/001; EU/1/24/1827/002. **Name and address of MA holder:** Takeda Pharmaceuticals International AG Ireland Branch, Block 2 Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, D02 HW68, Ireland. Additional information is available on request at: medinfoemea@takeda.com. **PI approval code:** pi-03530. Date of preparation: February 2025.

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Reference: 1. FRUZAQLA Summary of Product Characteristics. Available at: <https://www.medicines.ie/medicines/fruzaqla-1-mg-5mg-hard-capsules-36443/spc> (Accessed: May 2025). **2.** FRUZAQLA Patient Information Leaflet. Available at: <https://www.medicines.ie/medicines/fruzaqla-1-mg-5mg-hard-capsules-36443/patient-info> (Accessed: May 2025).

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