

Flexibility, convenience, and proven efficacy in mCRC¹

FRUZAQLA VIRTUOUS

Understanding FRUZAQLA® (fruquintinib)—
a guideline-supported, oral, non-chemotherapy¹⁻⁴

In FRESCO, FRUZAQLA + BSC significantly improved overall survival vs placebo + BSC
(9.3 months vs 6.6 months, a 2.7-month difference); HR=0.65 (95% CI: 0.51-0.83); $P<0.001$ ¹

BSC=best supportive care; CI=confidence interval; HR=hazard ratio.

INDICATION

FRUZAQLA is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type and medically appropriate, an anti-EGFR therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Hypertension** occurred in 49% of 911 patients with mCRC treated with FRUZAQLA, including Grade 3-4 events in 19%, and hypertensive crisis in three patients (0.3%). Do not initiate FRUZAQLA unless blood pressure is adequately controlled. Monitor blood pressure weekly for the first month and at least monthly thereafter as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue FRUZAQLA based on severity of hypertension.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

 **Fruzaqla**®
(fruquintinib) capsules
5 mg • 1 mg

While treatment-related ARs in mCRC may be manageable, their impact on patients should not be overlooked⁵⁻⁸

Day-to-day living becomes increasingly important as patients advance through multiple lines of treatment⁸⁻¹⁰



86% of patients experience 1 or more ARs in 3L mCRC treatment.⁵

Repeated use of chemotherapy often leads to myelosuppression and other hematologic ARs that can negatively impact daily living^{8,9}



88% of patients* reported moderate to major overall impact on daily life due to myelosuppression and related ARs.¹¹

Many patients with mCRC say that the most common factors in their treatment decisions are impact on day-to-day living and physical health¹²

3L=third-line; AR=adverse reaction; IV=intravenous; OS=overall survival.

*The results came from a 2019 online survey involving 301 US patients with breast, lung, or colorectal cancer who had received chemotherapy in the prior 12 months and experienced at least 1 episode of chemotherapy-induced myelosuppression.¹¹

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hemorrhagic Events** including serious, fatal events can occur with FRUZAQLA. In 911 patients with mCRC treated with FRUZAQLA, 6% of patients experienced gastrointestinal hemorrhage, including 1% with a Grade ≥ 3 event and 2 patients with fatal hemorrhages. Permanently discontinue FRUZAQLA in patients with severe or life-threatening hemorrhage. Monitor the International Normalized Ratio (INR) levels in patients receiving anticoagulants.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

Inpatient IV treatment can be time-consuming for patients and caregivers¹³

Potential considerations when helping patients choose their next treatment



IV therapies

- Increase chair time, travel, and port-related complications
- Reduce flexibility of patient lifestyle
- Require more clinic staffing and monitoring for infusion reactions



Oral therapies

- Increase patient autonomy and dosing convenience
- Reduce institutional burden
- Decrease caregiver time spent transporting patients to and from treatment

Talk with your patients about their IV treatment experiences

- One study showed patients can spend nearly 4 hours on a trip to an infusion center¹³
- Some patients have said they would accept small reductions in OS if it meant switching to an oral therapy¹⁴



“My life as I knew it was put on hold, and I could not make plans because I never knew how I would feel.”

—Former chemotherapy patient

IV=intravenous; OS=overall survival.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Infections.** FRUZAQLA can increase the risk of infections, including fatal infections. In 911 patients with mCRC treated with FRUZAQLA, the most common infections were urinary tract infections (6.8%), upper respiratory tract infections (3.2%) and pneumonia (2.5%); fatal infections included pneumonia (0.4%), sepsis (0.2%), bacterial infection (0.1%), lower respiratory tract infection (0.1%), and septic shock (0.1%). Withhold FRUZAQLA for Grade 3 or 4 infections, or worsening infection of any grade. Resume FRUZAQLA at the same dose when the infection has resolved.

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Repeated chemotherapy could lead to myelosuppression and treatment delays¹⁵



Many chemotherapy regimens can suppress bone marrow, leading to low blood counts¹⁵



Low blood counts may require dose delays, dose reductions, or treatment holds¹⁵



Treatment holds, dose delays, or reductions can cause patients to feel anxious, but there are options you can discuss with them during this time¹¹

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Gastrointestinal Perforation** occurred in patients treated with FRUZAQLA. In 911 patients with mCRC treated with FRUZAQLA, 1.3% experienced a Grade ≥ 3 gastrointestinal perforation, including one fatal event. Permanently discontinue FRUZAQLA in patients who develop gastrointestinal perforation or fistula.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

Consider alternatives to chemotherapy when discussing treatment options



When chemotherapy is delayed, patients may ask about enrolling in a clinical trial or switching to a different treatment^{11,16}



Depending on your patient's clinical picture, it may be appropriate to discuss non-chemotherapy options that come with a lower risk of myelosuppression^{17,18}



Many clinical trials establish blood count thresholds as eligibility criteria, so severe cytopenias may lead to delays or disqualifications from enrollment^{19,20}



Patients need later-line therapies that balance efficacy and tolerability¹⁰

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hepatotoxicity.** FRUZAQLA can cause liver injury. In 911 patients with mCRC treated with FRUZAQLA, 48% experienced increased ALT or AST, including Grade ≥ 3 events in 5%, and fatal events in 0.2% of patients. Monitor liver function tests (ALT, AST, and bilirubin) before initiation and periodically throughout treatment with FRUZAQLA. Temporarily hold and then reduce or permanently discontinue FRUZAQLA depending on the severity and persistence of hepatotoxicity as manifested by elevated liver function tests.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.



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In a study of FRUZAQLA + BSC vs placebo + BSC in patients with previously treated mCRC

Clinical efficacy of FRUZAQLA established in FRESCO¹

9.3 MOS
OVERALL
SURVIVAL

Significant median OS benefit¹

9.3 months with FRUZAQLA + BSC (95% CI: 8.2–10.5) vs **6.6 months** with placebo + BSC (95% CI: 5.9–8.1), a 2.7-month difference; **HR=0.65** (95% CI: 0.51–0.83); $P<0.001$

3.7 MOS
PROGRESSION-FREE
SURVIVAL

More than doubled median PFS¹

3.7 months with FRUZAQLA + BSC (95% CI: 3.7–4.6) vs **1.8 months** with placebo + BSC (95% CI: 1.8–1.8), a 1.9-month difference; **HR=0.26** (95% CI: 0.21–0.34)

62%
DISEASE CONTROL
RATE

Better disease control rate^{1,21*}

62% of patients with FRUZAQLA + BSC vs **12%** with placebo + BSC

Higher OS at 6 and 9 months^{18†‡}

69.5% alive at 6 months with FRUZAQLA + BSC (95% CI: 64.0–74.9) vs **54.1%** with placebo + BSC (95% CI: 45.7–62.5)

51.3% alive at 9 months with FRUZAQLA + BSC (95% CI: 45.4–57.3) vs **34.7%** with placebo + BSC (95% CI: 26.5–42.9)

Study design: FRESCO was a single-country (China), multicenter, randomized, double-blind, placebo-controlled, phase 3 study of 416 patients with mCRC who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan-based chemotherapy. Patients were randomized 2:1 to receive either FRUZAQLA 5 mg orally once daily + BSC (3 weeks on, 1 week off) (n=278) or placebo + BSC (3 weeks on, 1 week off) (n=138). Treatment continued until disease progression, death, unacceptable toxicity, or withdrawal. Primary efficacy outcome measure was OS. Secondary efficacy outcome measures were PFS, objective response rate, disease control rate, duration of response, and safety.^{1,21}

Neither FRESCO nor FRESCO-2 was powered to show statistical significance in OS or PFS across prespecified subgroups or in disease control rate.

BSC=best supportive care; CI=confidence interval; HR=hazard ratio; OS=overall survival; PFS=progression-free survival.

*Disease control was defined as a complete response, partial response, or stable disease for ≥ 8 weeks.²¹

¹OS rates with FRUZAQLA + BSC vs placebo + BSC at 3, 12, and 18 months (95% CI) were 90.6% (87.1–94.0) vs 80.8% (74.1–87.4); 34.3% (28.1–40.4) vs 18.0% (10.5–25.4); and 18.3% (11.8–24.9) vs 9.0% (2.1–15.9), respectively.¹⁸

^{†‡}The landmark OS analyses at 3, 6, 9, 12, and 18 months were prespecified endpoints of the FRESCO trial.¹⁸

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Proteinuria.** FRUZAQLA can cause proteinuria. In 911 patients with mCRC treated with FRUZAQLA, 36% experienced proteinuria and 2.5% of patients experienced Grade ≥ 3 events. Monitor for proteinuria before initiation and periodically throughout treatment with FRUZAQLA. For proteinuria ≥ 2 g/24 hours, withhold FRUZAQLA until improvement to $\leq$ Grade 1 proteinuria and resume FRUZAQLA at a reduced dose. Discontinue FRUZAQLA in patients who develop nephrotic syndrome.

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In a study of FRUZAQLA + BSC vs placebo + BSC in patients with previously treated mCRC

Results from FRESCO were confirmed in FRESCO-2^{1,22}

7.4 MOS
OVERALL
SURVIVAL

Significant median OS benefit¹

7.4 months with FRUZAQLA + BSC (95% CI: 6.7–8.2) vs **4.8 months** with placebo + BSC (95% CI: 4.0–5.8), a 2.6-month difference; **HR=0.66** (95% CI: 0.55–0.80); $P<0.001$

3.7 MOS
PROGRESSION-FREE
SURVIVAL

More than doubled median PFS^{1,22}

3.7 months with FRUZAQLA + BSC (95% CI: 3.5–3.8) vs **1.8 months** with placebo + BSC (95% CI: 1.8–1.9), a 1.9-month difference; **HR=0.32** (95% CI: 0.27–0.39); $P<0.001$

56%
DISEASE CONTROL
RATE

Better disease control rate^{1,22}

56% of patients with FRUZAQLA + BSC vs **16%** with placebo + BSC

Higher OS at 6 and 9 months^{18§||}

60.4% alive at 6 months with FRUZAQLA + BSC (95% CI: 55.9–64.9) vs **41.5%** with placebo + BSC (95% CI: 35.0–48.0)

41.1% alive at 9 months with FRUZAQLA + BSC (95% CI: 36.4–45.8) vs **28.2%** with placebo + BSC (95% CI: 22.1–34.3)

Study design: FRESCO-2 was a global, multicenter, randomized, double-blind, placebo-controlled, phase 3 study that enrolled 691 patients with mCRC who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if RAS wild type, an anti-EGFR biological therapy, and trifluridine-tipiracil, regorafenib, or both.¹ Patients were randomized 2:1 to receive either FRUZAQLA 5 mg orally once daily + BSC[§] (3 weeks on, 1 week off) (n=461) or placebo + BSC (3 weeks on, 1 week off) (n=230). Treatment continued until disease progression, death, or unacceptable toxicity. Primary efficacy outcome measure was OS. Secondary efficacy outcome measures were PFS, objective response rate, disease control rate,¹ duration of response, and safety.^{1,22}

In FRESCO and FRESCO-2, OS and PFS benefits were consistent across prespecified subgroups, including duration of metastatic disease and prior types of therapy^{1,22}

BSC=best supportive care; CI=confidence interval; EGFR=epidermal growth factor receptor; HR=hazard ratio; PFS=progression-free survival; OS=overall survival.

[§]OS rates with FRUZAQLA + BSC vs placebo + BSC at 3, 12, and 18 months (95% CI) were 88.1% (85.1–91.1) vs 68.8% (62.8–74.9); 27.8% (23.0–32.6) vs 23.2% (17.1–29.2); and 8.3% (2.3–14.2) vs 10.3% (3.9–16.8), respectively.¹⁸

^{||}The landmark OS analyses at 3, 6, 9, 12, and 18 months were prespecified endpoints of the FRESCO-2 trial.¹⁸

[†]To prevent unintentional enrichment, the number of patients treated with previous regorafenib was limited to 50% of the total randomly assigned patients.²²

^{*}BSC was determined by local clinical practice.²²

^{**}Disease control was defined as the proportion of patients with a best overall response of confirmed complete response, partial response, or stable disease for ≥ 7 weeks.²²

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Palmar-Plantar Erythrodysesthesia (PPE)** occurred in 35% of 911 patients treated with FRUZAQLA, including 8% with Grade 3 events. Based on severity of PPE, withhold FRUZAQLA and then resume at the same or reduced dose.

Please see additional **Important Safety Information** throughout, and full **Prescribing Information** for FRUZAQLA.

 **Fruzaqla**[®]
(fruquintinib) capsules
5 mg • 1 mg

Once-daily, oral dosing with FRUZAQLA¹

Flexible, convenient administration that helps patients spend more time with loved ones

Available dose strengths¹

**FRUZAQLA 5 mg
(starting dose)**



or

FRUZAQLA 1 mg



Once-daily treatment

Patients should take one 5-mg capsule orally every day for the first 21 days, followed by 7 days off treatment. This should be repeated during each 28-day cycle.¹



With or without food

Patients should swallow the capsules whole. Patients should not chew, dissolve, or open the capsules.^{1,23}



About the same time each day

Patients should take a missed dose if <12 hours have passed since the missed scheduled dose.¹ Patients can take their dose at home or on the go.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Posterior Reversible Encephalopathy Syndrome (PRES)**, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in one of 911 patients treated with FRUZAQLA. Perform an evaluation for PRES in any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue FRUZAQLA in patients who develop PRES.

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Getting patients started on their routine with FRUZAQLA¹

Recommended dosage for FRUZAQLA (5 mg)

28-day cycle	Week 1 Days 1-7	Week 2 Days 8-14	Week 3 Days 15-21	Week 4 Days 22-28	Subsequent cycles
FRUZAQLA	✓	✓	✓	—	 Repeat new 28-day cycle

After Day 28, patients should begin a new treatment cycle with the same schedule

Important reminders to ensure patients stay on FRUZAQLA

- Patients should not take 2 doses on the same day to make up for a missed dose
- Patients should not take an additional dose if vomiting occurs after taking FRUZAQLA, but they should continue with the next scheduled dose
- Patients should continue treatment until disease progression or unacceptable toxicity occurs
- Prescribers may recommend taking FRUZAQLA in the evening to help ease symptoms



FRUZAQLA is not chemotherapy and does not require time at an infusion center¹

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Impaired Wound Healing.** In 911 patients with mCRC treated with FRUZAQLA, 1 patient experienced a Grade 2 event of wound dehiscence. Do not administer FRUZAQLA for at least 2 weeks prior to major surgery. Do not administer FRUZAQLA for at least 2 weeks after major surgery and until adequate wound healing. The safety of resumption of FRUZAQLA after resolution of wound healing complications has not been established.

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(fruquintinib) capsules
5 mg • 1 mg

Clear, on-label dose reductions can help patients stay on FRUZAQLA¹

Simple dose reductions can help manage ARs

Dose level	FRUZAQLA dose	Number and strength of capsules
Recommended dose	5 mg orally once daily	One 5-mg capsule once daily
First dose reduction	4 mg orally once daily	Four 1-mg capsules once daily
Second dose reduction	3 mg orally once daily	Three 1-mg capsules once daily
Permanently discontinue FRUZAQLA in patients unable to tolerate 3 mg orally once daily		

Dose reductions for special populations

Special population	Dose adjustment
Renal impairment	
Mild	None required
Moderate	None required
Severe	None required
Hepatic impairment	
Mild	None required
Moderate	None required
Severe	FRUZAQLA is not recommended for use, as it has not been studied in this population



Dose reductions are a normal management tool used over the course of treatment¹

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Arterial Thromboembolic Events.** In 911 patients with mCRC treated with FRUZAQLA, 0.8% of patients experienced an arterial thromboembolic event. Initiation of FRUZAQLA in patients with a recent history of thromboembolic events should be carefully considered. In patients who develop arterial thromboembolism, discontinue FRUZAQLA.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.



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Across FRESCO and FRESCO-2, the majority of patients were able to stay on therapy with FRUZAQLA^{22,24}



Low rate of discontinuations due to ARs^{1,21,22}

FRESCO: 15% with FRUZAQLA + BSC vs 6% with placebo + BSC

FRESCO-2: 20% with FRUZAQLA + BSC vs 21% with placebo + BSC



Dose interruptions due to ARs^{1,21,22}

FRESCO: 35% with FRUZAQLA + BSC vs 10% with placebo + BSC

FRESCO-2: 47% with FRUZAQLA + BSC vs 27% with placebo + BSC



Dose reductions due to ARs^{1,21,22}

FRESCO: 24% with FRUZAQLA + BSC vs 4% with placebo + BSC

FRESCO-2: 24% with FRUZAQLA + BSC vs 4% with placebo + BSC

- Serious ARs occurred in 15% of patients treated with FRUZAQLA + BSC in FRESCO and 38% of patients treated with FRUZAQLA + BSC in FRESCO-2¹
 - **FRESCO:** Serious ARs in ≥2% of patients included intestinal obstruction (2.9%) and hemorrhage (2.2%)
 - **FRESCO-2:** Serious ARs in ≥2% of patients included hemorrhage (2.2%) and gastrointestinal perforation (2.0%)
- Fatal ARs occurred in 7 (2.5%) patients treated with FRUZAQLA + BSC in FRESCO and 14 (3.1%) patients with FRUZAQLA + BSC in FRESCO-2¹
 - **FRESCO:** Fatal ARs included cerebral infarction (n=1), gastrointestinal hemorrhage (n=1), hemoptysis (n=1), bacterial infection (n=1), lung/lower respiratory infection (n=2), and multiple organ dysfunction (n=1)
 - **FRESCO-2:** Fatal ARs occurring in ≥2 patients included pneumonia (n=3), sepsis/septic shock (n=2), and hepatic failure/encephalopathy (n=2)

ARs=adverse reactions; BSC=best supportive care.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Allergic Reactions to FD&C Yellow No. 5 (Tartrazine) and No. 6 (Sunset Yellow FCF).** FRUZAQLA 1 mg capsules contain FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. FRUZAQLA 1 mg contains FD&C Yellow No. 6 (sunset yellow FCF), which may cause allergic reactions.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

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Across trials, the majority of ARs were predictable and manageable^{1,21,22,25}

ARs occurring in ≥10% of patients in FRESCO¹

AR	FRUZAQLA + BSC (n=278)		Placebo + BSC (n=137)	
	All grades (%)	Grades 3/4 (%)	All grades (%)	Grades 3/4 (%)
Hypertension ^a	61	23	17	2.2
Proteinuria ^a	55	4.7	30	0
Palmar-plantar erythrodysesthesia	49	11	2.9	0
Dysphonia ^a	38	0	1.5	0
Stomatitis ^a	33	0.7	2.9	0
Abdominal pain ^a	29	4	17	1.5
Hemorrhage ^a	28	1.1	14	0
Diarrhea ^a	25	3.6	5	0
Fatigue ^a	25	2.5	13	1.5
Musculoskeletal pain ^a	22	2.2	6	1.5
Anorexia ^a	21	1.4	9	0
Hypothyroidism	17	0	2.2	0
Back pain	15	1.8	7	0
Arthralgia	13	0.4	2.2	0
Throat pain	10	0	1.5	0

^aRepresents a composite of multiple related terms.

- “Predictable” refers to ARs consistent with inhibition of VEGF and VEGFR^{25*}
- In FRESCO-2, ARs remained generally consistent with FRESCO. ARs that were higher in prevalence included fatigue (53% for FRUZAQLA, 39% for placebo) and hypothyroidism (21% for FRUZAQLA, 0.4% for placebo)¹

AR=adverse reaction; VEGFR=vascular endothelial growth factor receptor.

*Despite predictability, individual patient experiences may vary.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Embryo-Fetal Toxicity.** Based on findings in animal studies and its mechanism of action, FRUZAQLA can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

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Improve outcomes for patients with mCRC through early detection of side effects



Fatigue

What to do: Encourage patients to monitor and record bouts of fatigue.

Why: Fatigue is one of the main ARs associated with FRUZAQLA—and mCRC in general. Tracking it can guide timely interventions. Fatigue associated with **FRUZAQLA is typically Grade 1 or 2**, which means patients may experience moderate tiredness that can affect daily activities.¹ The severity and duration of fatigue can differ from patient to patient.

Managing treatment-related fatigue

- Consider taking FRUZAQLA in the evening or before bedtime, if appropriate
- Encourage consistent hydration, including fluids with electrolytes
- Suggest staying lightly active, such as taking short walks, to support energy levels



Blood pressure

What to do: Check blood pressure at each clinic visit, and also encourage patients to measure it at home 2 to 3 times per week.

Why: Hypertension may occur with FRUZAQLA; early detection prevents complications.



Skin changes (palms/soles)

What to do: Inspect palms and soles weekly; ask patients to report redness, pain, or swelling.

Why: Hand-foot syndrome may occur with FRUZAQLA; early recognition allows timely dose adjustments and supportive care.



Bowel habits and hydration

What to do: Track frequency and consistency of stools; monitor fluid intake.

Why: Diarrhea is common with FRUZAQLA; dehydration can lead to dose interruptions or hospitalizations.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 20\%$) following treatment with FRUZAQLA included hypertension, palmar-plantar erythrodysesthesia (hand-foot skin reactions), proteinuria, dysphonia, abdominal pain, diarrhea, and asthenia.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

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Recommended strategies to help manage potential ARs¹

Adverse reaction	Severity ^a	FRUZAQLA dosage modification
Hypertension	Grade 3	- Withhold if Grade 3 hypertension persists despite optimal antihypertensive treatment - If hypertension fully resolves or recovers to Grade 1, resume at the next lower dose level
	Grade 4	Permanently discontinue
Proteinuria	≥2 g/24 hours	- Withhold until proteinuria fully resolves or is <1 g/24 hours - Upon recovery, resume at the next lower dose level - Permanently discontinue for nephrotic syndrome or if proteinuria does not recover to <1 g/24 hours

^aGraded per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0.

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS: Avoid concomitant administration of FRUZAQLA with strong or moderate CYP3A inducers.

USE IN SPECIFIC POPULATIONS

- **Lactation:** Advise women not to breastfeed during treatment with FRUZAQLA and for 2 weeks after the last dose.
- **Females and Males of Reproductive Potential**
 - **Pregnancy Testing:** Verify pregnancy status of females of reproductive potential prior to initiating FRUZAQLA.

Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.


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Adverse reaction	Severity	FRUZAQLA dosage modification
Palmar-plantar erythrodysesthesia	Grade 2	- Administer supportive treatment (eg, moisturizing creams or lotions that contain urea or steroids)²⁶ - If toxicity fully resolves or recovers to Grade 1, resume at the same dose level¹
	Grade 3	- Administer supportive treatment (eg, moisturizing creams or lotions that contain urea or steroids)²⁶ - Withhold and initiate supportive treatment¹ - If toxicity fully resolves or recovers to Grade 1, resume at the next lower dose level¹
Other ARs	Grade 3	- Withhold until the reaction fully resolves or recovers to Grade 1¹ - If toxicity fully resolves or recovers to Grade 1, resume at the next lower dose level¹
	Grade 4	- Discontinue - Consider resuming at the next lower dose level if the toxicity is non-life threatening and fully resolves or recovers to Grade 1 and the potential benefit outweighs the risks¹

IMPORTANT SAFETY INFORMATION (continued)

USE IN SPECIFIC POPULATIONS (continued)

- **Contraception:** Females of childbearing potential and males with female partners of childbearing potential should use effective contraception during treatment and for 2 weeks after the last dose of FRUZAQLA.
- **Infertility:** Advise females of reproductive potential that FRUZAQLA may cause post-implantation loss.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals at 1-844-662-8532 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional **Important Safety Information** throughout, and full **Prescribing Information** for FRUZAQLA.

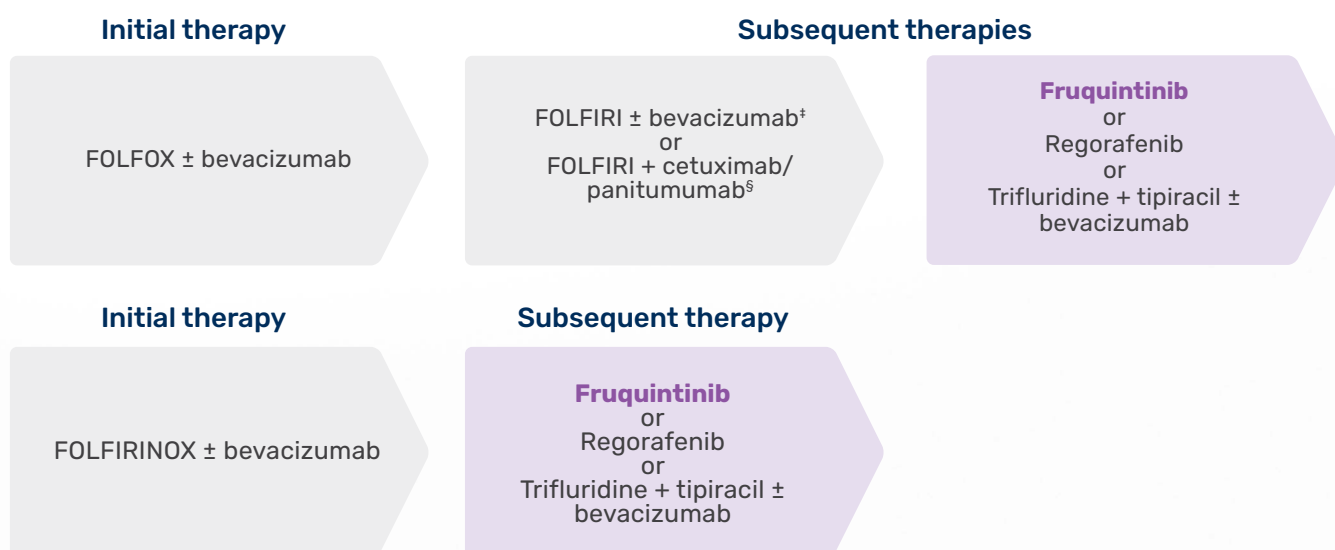

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**National Comprehensive Cancer Network®
(NCCN®) recommends fruquintinib (FRUZAQLA)
as a potential treatment option for patients
with previously treated mCRC, regardless of
mutation status^{2,3}**

Fruquintinib (FRUZAQLA) is indicated for the treatment of adult patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type and medically appropriate, an anti-EGFR therapy.¹

Potential treatment algorithms^{2,3*†}



FOLFIRI=leucovorin, fluorouracil, and irinotecan; FOLFIRINOX=leucovorin, fluorouracil, oxaliplatin, and irinotecan; FOLFOX=leucovorin, fluorouracil, and oxaliplatin; HER2=human epidermal growth factor receptor 2; MSS=microsatellite stable; NTRK=neurotrophic tyrosine receptor kinase; pMMR=proficient mismatch repair.

*Other permutations and combinations are also recommended in NCCN guidelines.

[†]These examples are for *BRAF* and HER2 wild type, pMMR/MSS, and *NTRK* gene fusion negative disease, unless otherwise noted.

[‡]If RAS mutant.

[§]If RAS wild type.

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Please see additional [Important Safety Information](#) throughout, and full [Prescribing Information](#) for FRUZAQLA.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hypertension** occurred in 49% of 911 patients with mCRC treated with FRUZAQLA, including Grade 3-4 events in 19%, and hypertensive crisis in three patients (0.3%). Do not initiate FRUZAQLA unless blood pressure is adequately controlled. Monitor blood pressure weekly for the first month and at least monthly thereafter as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue FRUZAQLA based on severity of hypertension.

Please see additional **Important Safety Information** throughout, and full **Prescribing Information** for FRUZAQLA.

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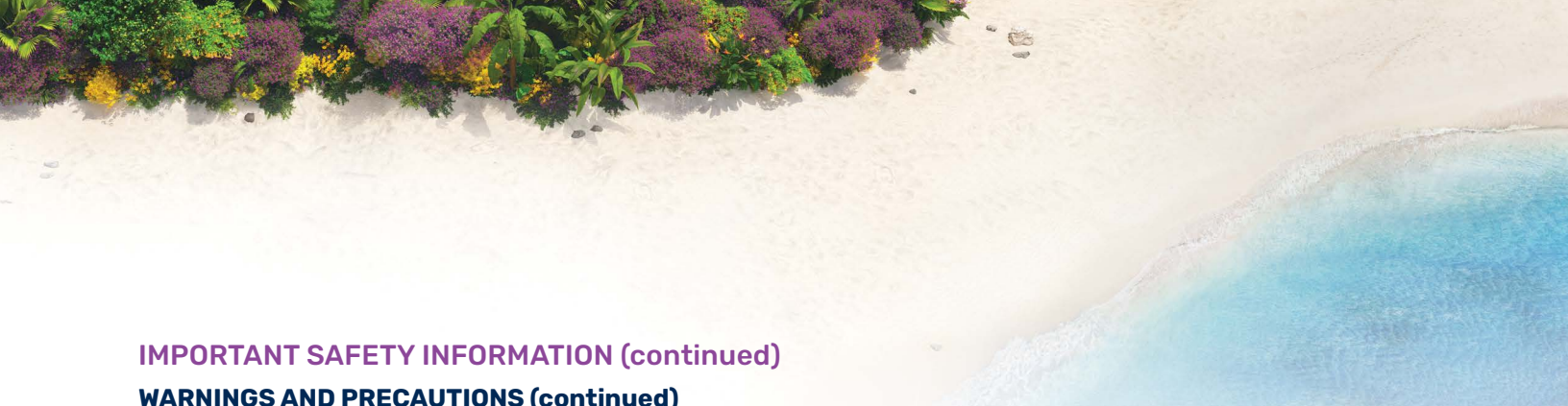


Important Safety Information

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Hypertension** occurred in 49% of 911 patients with mCRC treated with FRUZAQLA, including Grade 3–4 events in 19%, and hypertensive crisis in three patients (0.3%). Do not initiate FRUZAQLA unless blood pressure is adequately controlled. Monitor blood pressure weekly for the first month and at least monthly thereafter as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue FRUZAQLA based on severity of hypertension.
- **Hemorrhagic Events** including serious, fatal events can occur with FRUZAQLA. In 911 patients with mCRC treated with FRUZAQLA, 6% of patients experienced gastrointestinal hemorrhage, including 1% with a Grade ≥ 3 event and 2 patients with fatal hemorrhages. Permanently discontinue FRUZAQLA in patients with severe or life-threatening hemorrhage. Monitor the International Normalized Ratio (INR) levels in patients receiving anticoagulants.
- **Infections.** FRUZAQLA can increase the risk of infections, including fatal infections. In 911 patients with mCRC treated with FRUZAQLA, the most common infections were urinary tract infections (6.8%), upper respiratory tract infections (3.2%) and pneumonia (2.5%); fatal infections included pneumonia (0.4%), sepsis (0.2%), bacterial infection (0.1%), lower respiratory tract infection (0.1%), and septic shock (0.1%). Withhold FRUZAQLA for Grade 3 or 4 infections, or worsening infection of any grade. Resume FRUZAQLA at the same dose when the infection has resolved.
- **Gastrointestinal Perforation** occurred in patients treated with FRUZAQLA. In 911 patients with mCRC treated with FRUZAQLA, 1.3% experienced a Grade ≥ 3 gastrointestinal perforation, including one fatal event. Permanently discontinue FRUZAQLA in patients who develop gastrointestinal perforation or fistula.
- **Hepatotoxicity.** FRUZAQLA can cause liver injury. In 911 patients with mCRC treated with FRUZAQLA, 48% experienced increased ALT or AST, including Grade ≥ 3 events in 5%, and fatal events in 0.2% of patients. Monitor liver function tests (ALT, AST, and bilirubin) before initiation and periodically throughout treatment with FRUZAQLA. Temporarily hold and then reduce or permanently discontinue FRUZAQLA depending on the severity and persistence of hepatotoxicity as manifested by elevated liver function tests.
- **Proteinuria.** FRUZAQLA can cause proteinuria. In 911 patients with mCRC treated with FRUZAQLA, 36% experienced proteinuria and 2.5% of patients experienced Grade ≥ 3 events. Monitor for proteinuria before initiation and periodically throughout treatment with FRUZAQLA. For proteinuria $\geq 2\text{g}/24$ hours, withhold FRUZAQLA until improvement to $\leq$ Grade 1 proteinuria and resume FRUZAQLA at a reduced dose. Discontinue FRUZAQLA in patients who develop nephrotic syndrome.
- **Palmar-Plantar Erythrodysesthesia (PPE)** occurred in 35% of 911 patients treated with FRUZAQLA, including 8% with Grade 3 events. Based on severity of PPE, withhold FRUZAQLA and then resume at the same or reduced dose.
- **Posterior Reversible Encephalopathy Syndrome (PRES),** a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in one of 911 patients treated with FRUZAQLA. Perform an evaluation for PRES in any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue FRUZAQLA in patients who develop PRES.



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Impaired Wound Healing.** In 911 patients with mCRC treated with FRUZAQLA, 1 patient experienced a Grade 2 event of wound dehiscence. Do not administer FRUZAQLA for at least 2 weeks prior to major surgery. Do not administer FRUZAQLA for at least 2 weeks after major surgery and until adequate wound healing. The safety of resumption of FRUZAQLA after resolution of wound healing complications has not been established.
- **Arterial Thromboembolic Events.** In 911 patients with mCRC treated with FRUZAQLA, 0.8% of patients experienced an arterial thromboembolic event. Initiation of FRUZAQLA in patients with a recent history of thromboembolic events should be carefully considered. In patients who develop arterial thromboembolism, discontinue FRUZAQLA.
- **Allergic Reactions to FD&C Yellow No. 5 (Tartrazine) and No. 6 (Sunset Yellow FCF).** FRUZAQLA 1 mg capsules contain FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. FRUZAQLA 1 mg contains FD&C Yellow No. 6 (sunset yellow FCF), which may cause allergic reactions.
- **Embryo-Fetal Toxicity.** Based on findings in animal studies and its mechanism of action, FRUZAQLA can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus.

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 20\%$) following treatment with FRUZAQLA included hypertension, palmar-plantar erythrodysesthesia (hand-foot skin reactions), proteinuria, dysphonia, abdominal pain, diarrhea, and asthenia.

DRUG INTERACTIONS: Avoid concomitant administration of FRUZAQLA with strong or moderate CYP3A inducers.

USE IN SPECIFIC POPULATIONS

- **Lactation:** Advise women not to breastfeed during treatment with FRUZAQLA and for 2 weeks after the last dose.
- **Females and Males of Reproductive Potential**
 - **Pregnancy Testing:** Verify pregnancy status of females of reproductive potential prior to initiating FRUZAQLA.
 - **Contraception:** Females of childbearing potential and males with female partners of childbearing potential should use effective contraception during treatment and for 2 weeks after the last dose of FRUZAQLA.
 - **Infertility:** Advise females of reproductive potential that FRUZAQLA may cause post-implantation loss.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals at 1-844-662-8532 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



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Significant median OS benefit¹

9.3 months median OS with FRUZAQLA + BSC vs **6.6 months** with placebo + BSC in FRESCO, a 2.7-month difference; **HR=0.65** (95% CI: 0.51–0.83); $P<0.001$



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Manageable safety profile^{1,21}

- **15%** discontinuation rate due to ARs with FRUZAQLA + BSC vs **6%** with placebo + BSC in FRESCO



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3L=third line; AR=adverse reaction; BSC=best supportive care; CI=confidence interval; HR=hazard ratio; OS=overall survival.

INDICATION

FRUZAQLA is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type and medically appropriate, an anti-EGFR therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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