In patients with *RAS* WT, HER2+ disease

# COLORECTAL CANCER TREATMENT SCENARIOS[1-5]

TUKYSA® tucatinib
50 mg | 150 mg tablets

**TUKYSA is the first FDA-approved HER2-directed therapy in 2L+ *RAS* WT, HER2+ mCRC[1,6]**

| TREATMENT SCENARIOS[1-5]* | ADJUVANT SETTING | ADVANCED/METASTATIC SETTING | | |
|---|---|---|---|---|
| | | 1ST LINE | 2ND LINE | 3RD LINE |
| SCENARIO 1 | Oxaliplatin-based therapy | FOLFIRI ± biologic | PROGRESSED → TUKYSA + trastuzumab | |
| SCENARIO 2 | | FOLFOXIRI | PROGRESSED → TUKYSA + trastuzumab | |
| SCENARIO 3 | | FOLFOX ± biologic | FOLFIRI ± biologic | PROGRESSED → TUKYSA + trastuzumab |
| SCENARIO 4 | | FOLFIRI ± biologic | FOLFOX ± biologic | PROGRESSED → TUKYSA + trastuzumab |

*These are specific treatment scenarios for illustrative purposes only and not an exhaustive list. Please visit asco.org/gastrointestinal-cancer-guidelines for the full set of treatment recommendations.[2]

## Indication

TUKYSA is indicated in combination with trastuzumab for the treatment of adult patients with *RAS* wild-type, HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

## Select Important Safety Information

- **The labeling for TUKYSA contains warnings and precautions** for diarrhea, hepatotoxicity, and embryo-fetal toxicity, some of which may be severe or fatal. Please see the full Prescribing Information for management and dose modification information specific to adverse reactions.
- **The most common serious adverse reactions** in ≥2% of patients who received TUKYSA in combination with trastuzumab were intestinal obstruction, urinary tract infection, pneumonia, abdominal pain, and rectal perforation.
- **The most common adverse reactions** in ≥20% of patients who received TUKYSA in combination with trastuzumab were diarrhea, fatigue, rash, nausea, abdominal pain, infusion-related reactions, and pyrexia.

FOLFIRI = folinic acid, 5-fluorouracil, and irinotecan; FOLFOX = folinic acid, 5-fluorouracil, and oxaliplatin; FOLFOXIRI = folinic acid, 5-fluorouracil, oxaliplatin, and irinotecan.

**Please see additional Important Safety Information on the next page and the accompanying full Prescribing Information.**

# Important Safety Information

## Warnings and Precautions

- **Diarrhea:** TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

  In MOUNTAINEER, when TUKYSA was given in combination with trastuzumab, diarrhea occurred in 64% of patients, including Grade 3 (3.5%), Grade 2 (10%), and Grade 1 (50%).

- **Hepatotoxicity:** TUKYSA can cause severe hepatotoxicity. Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatotoxicity, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

  In MOUNTAINEER, 6% of patients had a bilirubin increase > 3 × ULN (Grade ≥3), 6% had an AST increase > 5 × ULN, and 4.7% had an ALT increase > 5 × ULN. Hepatotoxicity led to dose reduction of TUKYSA in 3.5% of patients and discontinuation of TUKYSA in 2.3% of patients.

- **Embryo-Fetal Toxicity:** TUKYSA can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential, and male patients with female partners of reproductive potential, to use effective contraception during TUKYSA treatment and for 1 week after the last dose.

## Adverse Reactions

Serious adverse reactions occurred in 22% of patients; the most common (in ≥2% of patients) were intestinal obstruction (7%), urinary tract infection (3.5%), pneumonia, abdominal pain, and rectal perforation (2.3% each).

Adverse reactions leading to permanent discontinuation of TUKYSA occurred in 6% of patients; the most common (in ≥2% of patients) was increased ALT (2.3%). Adverse reactions leading to dosage interruption occurred in 23% of patients; the most common (in ≥3% of patients) were increased ALT and diarrhea (3.5% each). Adverse reactions leading to dose reduction occurred in 9% of patients; the most common (in ≥2% of patients) were increased ALT and diarrhea (2.3% each).

The most common adverse reactions (≥20%) in patients treated with TUKYSA and trastuzumab were diarrhea, fatigue, rash, nausea, abdominal pain, infusion-related reactions, and pyrexia.

Other adverse reactions (<10%) include epistaxis (7%), weight decreased (7%), oropharyngeal pain (5%), oral dysesthesia (1%), and stomatitis (1%).

## Lab Abnormalities

In MOUNTAINEER, Grade ≥3 laboratory abnormalities reported in ≥5% of patients who received TUKYSA were decreased lymphocytes and decreased sodium.

The mean increase in serum creatinine was 32% within the first 21 days of treatment with TUKYSA. The serum creatinine increases persisted throughout treatment and were reversible in 87% of patients with values outside normal lab limits upon treatment completion. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

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## Drug Interactions

- **Strong CYP3A/Moderate CYP2C8 Inducers:** Concomitant use may decrease TUKYSA activity. Avoid concomitant use of TUKYSA.
- **Strong or Moderate CYP2C8 Inhibitors:** Concomitant use of TUKYSA with a strong CYP2C8 inhibitor may increase the risk of TUKYSA toxicity; avoid concomitant use. Increase monitoring for TUKYSA toxicity with moderate CYP2C8 inhibitors.
- **CYP3A Substrates:** Concomitant use may increase the toxicity associated with a CYP3A substrate. Avoid concomitant use of TUKYSA with a CYP3A substrate, where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, decrease the CYP3A substrate dosage.
- **P-gp Substrates:** Concomitant use may increase the toxicity associated with a P-gp substrate. Consider reducing the dosage of P-gp substrates, where minimal concentration changes may lead to serious or life-threatening toxicities.

## Use in Specific Populations

- **Lactation:** Advise women not to breastfeed while taking TUKYSA and for 1 week after the last dose.
- **Hepatic Impairment:** Reduce the dose of TUKYSA for patients with severe (Child-Pugh C) hepatic impairment.

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**Please see the accompanying full Prescribing Information.**

Learn more at
TUKYSAhcp.com


**References:**

**1.** TUKYSA [Prescribing Information]. Bothell, WA: Seagen Inc. January 2023. **2.** Morris VK, Kennedy EB, Baxter NN, et al. Treatment of metastatic colorectal cancer: ASCO guideline. *J Clin Oncol.* 2023;41(3):678-700. doi:10.1200/JCO.22.01690 **3.** Cremolini C, Loupakis F, Antoniotti C, et al. FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study. *Lancet Oncol.* 2015;16(13):1306-1315. doi:10.1016/S1470-2045(15)00122-9 **4.** Cervantes A, Adam R, Roselló S, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2023;34(1):10-32. doi:10.1016/j.annonc.2022.10.003 **5.** McCleary NJ, Benson AB III, Dienstmann R. Personalizing adjuvant therapy for stage II/III colorectal cancer. *Am Soc Clin Oncol Educ Book.* 2017;37:232-245. doi:10.1200/EDBK_175660 **6.** Strickler JH, Cercek A, Siena S, et al; MOUNTAINEER investigators. Tucatinib plus trastuzumab for chemotherapy-refractory, HER2-positive, RAS wild-type unresectable or metastatic colorectal cancer (MOUNTAINEER): a multicentre, open-label, phase 2 study. *Lancet Oncol.* 2023;24(5):496-508. doi:10.1016/S1470-2045(23)00150-X


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