DOSING & ADMINISTRATION GUIDE

komzifti™
(ziftomenib)
200 mg capsules

For your adult patients without satisfactory alternative treatments,

THINK BRIGHTER

R/R *NPM1*-m AML is actionable WITH KOMZIFTI™ [1]

Remission is possible

21.4%[a] of patients achieved CR[b]/CRh[c] with KOMZIFTI in a Ph1b/2 open-label, single-arm study (KOMET-001).[1]

KOMET-001 is the largest pivotal monotherapy study of an approved menin inhibitor in adults with R/R *NPM1*-m AML[1,2]

Actor portrayal.

[a] (n=24/112; 95% CI: 14.2–30.2).[1]
[b] CR is defined as bone marrow blasts <5%, ANC >1.0 x 10^9/L, and platelet count >100 x 10^9/L.[1]
[c] CRh is defined as bone marrow blasts <5%, ANC >0.5 x 10^9/L, and platelet count >50 x 10^9/L.[1]

INDICATION

KOMZIFTI is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (R/R AML) with a susceptible nucleophosmin 1 (*NPM1*) mutation who have no satisfactory alternative treatment options.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME

Differentiation syndrome, which can be fatal, has occurred with KOMZIFTI. Signs and symptoms may include fever, joint pain, hypotension, hypoxia, dyspnea, rapid weight gain or peripheral edema, pleural or pericardial effusions, pulmonary infiltrates, acute kidney injury, and rashes. If differentiation syndrome is suspected, interrupt KOMZIFTI, and initiate oral or intravenous corticosteroids with hemodynamic and laboratory monitoring until symptom resolution; resume KOMZIFTI upon symptom improvement.

Please see Important Safety Information throughout and full Prescribing Information, including **Boxed WARNING**.

The *first and only* oral menin inhibitor approved for *once daily* use[1]

Straightforward dosing
3 x 200 mg capsules (600 mg), once per day, regardless of weight

No dose adjustments required for concomitant CYP3A4 inhibitors

Concomitant use of KOMZIFTI with strong or moderate CYP3A4 inhibitors may increase the risk of adverse reactions such as QT prolongation.

Prior to starting treatment with KOMZIFTI, reduce the WBC counts to less than 25 x 10^9/L

Patients should

- Take KOMZIFTI on an empty stomach, at least 1 hour before or 2 hours after a meal[a]
- Take KOMZIFTI at about the same time each day
- Swallow capsules whole. They should not open, break, or chew the capsules

If patients miss a dose

- Instruct them to take their dose as soon as possible on the same day, ≥12 hours prior to their next dose
- Patients can return to their normal dosing schedule the following day. Do not administer 2 doses within 12 hours

For patients without confirmed disease progression or unacceptable toxicity
Treatment for a minimum of 6 months is recommended to allow time for a clinical response

[a] Following administration with a high-fat meal (approximately 1,000 calories, 60% fat, 25% carbohydrates, 15% protein), AUC and C_{max} increased 4-fold compared with fasting. T_{max} was 4.1 hours (median range: 0.5–8.15).

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS

Drug interactions may occur when KOMZIFTI is concomitantly used with:

- Strong or Moderate CYP3A4 Inhibitors: Monitor patients more frequently for KOMZIFTI-associated adverse reactions.
- Strong or Moderate CYP3A4 Inducers: Avoid concomitant use of KOMZIFTI.
- Gastric Acid Reducing Agents: Avoid concomitant use of KOMZIFTI with proton pump inhibitors (PPIs), H2 receptor antagonists (H2RAs), or locally acting antacids. If concomitant use with H2RAs or locally acting antacids cannot be avoided, modify KOMZIFTI administration time.
  - Take KOMZIFTI 2 hours before or 10 hours after administration of an H2 receptor antagonist.
  - Take KOMZIFTI 2 hours before or 2 hours after administration of a locally acting antacid.
- Drugs that Prolong the QT Interval: Avoid concomitant use of KOMZIFTI. If concomitant use cannot be avoided, obtain ECGs when initiating, during concomitant use, and as clinically indicated. Interrupt KOMZIFTI if the QTc interval is > 500 ms or the change from baseline is > 60 ms.

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Proactive identification and management protocol for differentiation syndrome[1]

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Signs and symptoms may include fever, joint pain, hypotension, hypoxia, dyspnea, rapid weight gain or peripheral edema, pleural or pericardial effusions, pulmonary infiltrates, acute kidney injury, and rashes.

Differentiation syndrome in R/R *NPM1*-m AML

- Differentiation syndrome occurred in 26% (n=29/112) of patients
- Grade 3 differentiation syndrome occurred in 13% of patients
- Differentiation syndrome was fatal in 2 patients
- Differentiation syndrome was observed with and without concomitant hyperleukocytosis in as early as 3 days and up to 46 days after KOMZIFTI initiation
- The median time to onset was 15 days
- 2 patients experienced more than 1 differentiation syndrome event
- 13% of patients interrupted and resumed treatment
- 2% of patients permanently discontinued due to differentiation syndrome

In broader evaluation of all patients with any genetic form of AML treated with KOMZIFTI monotherapy in clinical trials, differentiation syndrome occurred in 25% of patients. Four fatal cases of differentiation syndrome occurred out of 39 patients with *KMT2A*-rearranged AML treated with KOMZIFTI. **KOMZIFTI is not approved for use in patients with *KMT2A*-rearranged AML.**

Prior to starting treatment with KOMZIFTI, reduce the WBC counts to less than 25 x 10^9/L

If differentiation syndrome is suspected:

1. **Interrupt dosing of KOMZIFTI**
2. **Initiate oral or intravenous corticosteroids**
   (eg, dexamethasone 10 mg every 12 hours) for a minimum of 3 days with hemodynamic and laboratory monitoring.
3. **Resume treatment with KOMZIFTI at the same dose**
   when signs and symptoms improve to Grade 2 or lower. Taper corticosteroids over a minimum of 3 days after adequate control or resolution of symptoms. Symptoms may recur with premature discontinuation of corticosteroids.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Differentiation Syndrome

KOMZIFTI can cause fatal or life-threatening differentiation syndrome (DS). DS is associated with rapid proliferation and differentiation of myeloid cells. Symptoms of DS, including those seen in patients treated with KOMZIFTI, may include fever, hypoxia, joint pain, hypotension, dyspnea, rapid weight gain or peripheral edema, pleural or pericardial effusions, acute kidney injury, and rashes.

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Recommended management and dose modifications for adverse reactions[1]

Adverse reaction[a]	Recommended action
Differentiation syndrome	• Interrupt KOMZIFTI if differentiation syndrome is suspected • Administer systemic corticosteroids and initiate hemodynamic monitoring until symptom resolution and for a minimum of 3 days and provide supportive care • Resume KOMZIFTI at the same dose level when signs and symptoms improve to Grade ≤2[b]
Noninfectious leukocytosis[c]	• Evaluate for differentiation syndrome • Initiate treatment with hydroxyurea, as per standard institutional practices, and leukapheresis if clinically indicated • Taper hydroxyurea only after leukocytosis improves or resolves • Interrupt KOMZIFTI if leukocytosis is not controlled with hydroxyurea within 48 hours. If interrupted, resume KOMZIFTI at the same daily dose once WBC counts are controlled
Nonhematological adverse reactions Grade ≥3[b]	• Interrupt KOMZIFTI until recovery to Grade ≤2[b] • Resume KOMZIFTI at the same dose level • If the same Grade ≥3 toxicity recurs, interrupt KOMZIFTI until recovery to Grade ≤2[b] • Restart KOMZIFTI at a reduced dose

Recommended dosage reductions for KOMZIFTI adverse reactions

- First dose reduction: 400 mg once daily
- Second dose reduction: 200 mg once daily
- Permanently discontinue KOMZIFTI in patients unable to tolerate 200 mg once daily following second dose reduction

[a] Cancer Institute Common Terminology for Adverse Events version 5.0.
[b] Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.
[c] Defined as sudden or significant WBC increase, including WBC doubling within the first 2 weeks of administration or an absolute increase of 10 x 10^9/L.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Differentiation Syndrome (cont'd)

In the clinical trial, DS occurred in 29 (26%) of 112 patients with R/R AML with an *NPM1* mutation who were treated with KOMZIFTI at the recommended dosage. DS was Grade 3 in 13% and fatal in two patients. In broader evaluation of all patients with any genetic form of AML treated with KOMZIFTI monotherapy in clinical trials, DS occurred in 25% of patients. Four fatal cases of DS occurred out of 39 patients with *KMT2A*-rearranged AML treated with KOMZIFTI. KOMZIFTI is not approved for use in patients with *KMT2A*-rearranged AML.

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Drug interactions with KOMZIFTI[1]

Drug class and use with KOMZIFTI	Effect
Strong or moderate CYP3A4 inhibitors **Monitor patients more frequently for KOMZIFTI-associated adverse reactions**	Concomitant use of KOMZIFTI increases KOMZIFTI exposure, which **may increase the risk of adverse reactions such as QT prolongation**
Strong or moderate CYP3A4 inducers **Avoid concomitant use**	Concomitant use of KOMZIFTI decreases KOMZIFTI exposure, which **may reduce the efficacy of KOMZIFTI**
Gastric Acid Reducing agents PPIs: **avoid concomitant use** H2 receptor antagonists or locally acting antacids: **avoid concomitant use** If concomitant use with H2RAs or locally acting antacids cannot be avoided, modify KOMZIFTI administration time • Take KOMZIFTI 2 hours before or 10 hours after administration of an H2 receptor antagonist • Take KOMZIFTI 2 hours before or 2 hours after administration of a locally acting antacid	Concomitant administration of KOMZIFTI with PPIs may decrease KOMZIFTI exposure, which **may reduce the efficacy of KOMZIFTI**
Drugs that prolong the QT interval **Avoid concomitant use** • If concomitant use cannot be avoided, obtain ECGs when initiating, during concomitant use, and as clinically indicated • Interrupt KOMZIFTI if the QTc interval is >500 milliseconds or if the change from baseline is >60 milliseconds	**KOMZIFTI causes QTc interval prolongation** • Concomitant use of KOMZIFTI with other products that prolong the QTc interval may result in a greater increase in QTc interval and adverse reactions associated with QTc interval prolongation, including Torsades de pointes, other serious arrhythmias, and sudden death

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Differentiation Syndrome (cont'd)

In the 112 patients with an *NPM1* mutation, DS was observed with and without concomitant hyperleukocytosis, in as early as 3 days and up to 46 days after KOMZIFTI initiation. The median time to onset was 15 days. Two patients experienced more than one DS event. Treatment was interrupted and resumed in 15 (13%) patients, while it was permanently discontinued in 2 (2%) patients.

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Steps to fulfill a KOMZIFTI prescription

KOMZIFTI is available through a tailored oncology distribution network

3 steps to Rx fulfillment

1 Send the prescription

KOMZIFTI is available through a limited distribution network (LDN). Send the prescription to one of the Specialty Pharmacies in our LDN or to your Medically Integrated Dispensing pharmacy.

2 Confirmation

Prior Authorization (PA) will likely be required. Be sure to submit a complete PA.

3 Shipping

Oral Oncolytics are typically shipped directly to patients. Remind them to answer or return the call from the fulfilling pharmacy.

Flexibility that supports patient access to medicine

Fulfilling pharmacies	Phone	Fax
Biologics	1-800-850-4306	1-800-823-4506
Onco360	1-877-662-6633	1-877-622-6355
Specialty distributors	**Phone**	**Fax**
ASD Healthcare	1-800-746-6273	1-800-547-9413
Cardinal Health	1-855-855-0708	1-614-553-6301
McKesson Plasma and Biologics	1-877-625-2566	1-888-752-7626
McKesson Specialty Health	1-800-482-6700	1-855-824-9489
Oncology Supply	1-800-633-7555	1-800-248-8205

KURA RxKONNECT

Kura is here to support you and your patients when needed

- Financial assistance is available to eligible patients
- Navigating access challenges
- Free product for uninsured/underinsured eligible patients

For more information visit **KuraRxKonnect.com**

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Differentiation Syndrome (cont'd)

Prior to starting treatment with KOMZIFTI, reduce the WBC counts to less than 25 x 109/L. If DS is suspected, interrupt KOMZIFTI, initiate oral or intravenous corticosteroids (e.g., dexamethasone 10 mg every 12 hours) for a minimum of 3 days with hemodynamic and laboratory monitoring. Resume treatment with KOMZIFTI at the same dose level when signs and symptoms improve and are Grade 2 or lower. Taper corticosteroids over a minimum of 3 days after adequate control or resolution of symptoms. Symptoms of DS may recur with premature discontinuation of corticosteroid treatment.

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Eligible commercially insured patients may pay as little as

$0 per month

Prescriber's office or the pharmacy can help enroll eligible patients.

For more information and details on patient eligibility, scan to visit

komzifti.com/copay

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WARNINGS AND PRECAUTIONS

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In the clinical trial, DS occurred in 29 (26%) of 112 patients with R/R AML with an *NPM1* mutation who were treated with KOMZIFTI at the recommended dosage. DS was Grade 3 in 13% and fatal in two patients. In broader evaluation of all patients with any genetic form of AML treated with KOMZIFTI monotherapy in clinical trials, DS occurred in 25% of patients. Four fatal cases of DS occurred out of 39 patients with *KMT2A*-rearranged AML treated with KOMZIFTI. KOMZIFTI is not approved for use in patients with *KMT2A*-rearranged AML.

In the 112 patients with an *NPM1* mutation, DS was observed with and without concomitant hyperleukocytosis, in as early as 3 days and up to 46 days after KOMZIFTI initiation. The median time to onset was 15 days. Two patients experienced more than one DS event. Treatment was interrupted and resumed in 15 (13%) patients, while it was permanently discontinued in 2 (2%) patients.

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QTc Interval Prolongation

KOMZIFTI can cause QTc interval prolongation. In the clinical trial, QTc interval prolongation was reported as an adverse reaction in 12% of 112 patients treated with KOMZIFTI at the recommended dosage for R/R AML with an *NPM1* mutation. QTc interval prolongation was Grade 3 in 8% of patients. The heart-rate corrected QT interval (using Fridericia's method) (QTcF) was greater than 500 msec in 9% of patients, and the increase from baseline QTcF was greater than 60 msec in 12% of patients. KOMZIFTI dose reduction was required for 1% of patients due to QTc interval prolongation. QTc prolongation occurred in 14% of the 42 patients less than 65 years of age and in 10% of the 70 patients 65 years of age or older.

Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to treatment with KOMZIFTI. Perform an ECG prior to initiation of treatment with KOMZIFTI, and do not initiate KOMZIFTI in patients with QTcF > 480 msec. Perform an ECG at least once weekly for the first four weeks on treatment, and at least monthly thereafter. Interrupt KOMZIFTI if the QTc interval is > 500 ms or the change from baseline is > 60 ms (Grade 3). In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval, more frequent ECG monitoring may be necessary. Concomitant use of KOMZIFTI with drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation, result in a greater increase in the QTc interval and adverse reactions associated with QTc interval prolongation, including Torsades de pointes, other serious arrhythmias, and sudden death.

Please see additional Important Safety Information on page 8 and full Prescribing Information, including Boxed WARNING.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, KOMZIFTI can cause embryo-fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with KOMZIFTI and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with KOMZIFTI and for 3 months after the last dose.

ADVERSE REACTIONS

Fatal adverse reactions occurred in 4 (4%) patients who received KOMZIFTI, including 2 with differentiation syndrome, 1 with infection, and 1 with sudden death. Serious adverse reactions were reported in 79% of patients who received KOMZIFTI. Serious adverse reactions occurring in ≥ 5% of patients included infection without an identified pathogen (29%), febrile neutropenia (18%), bacterial infection (16%), differentiation syndrome (16%), and dyspnea (6%).

Dosage interruption of KOMZIFTI due to an adverse reaction occurred in 54% of patients. Adverse reactions that required dose interruption in ≥ 2% of patients included infection without an identified pathogen (15%), differentiation syndrome (13%), febrile neutropenia (5%), pyrexia (4%), electrocardiogram QT prolonged (4%), leukocytosis (4%), bacterial infection (3%), cardiac failure (2%), cholecystitis (2%), diarrhea (2%), pruritus (2%), and thrombosis (2%). Dose reduction of KOMZIFTI due to an adverse reaction occurred in 4% of patients. Permanent discontinuation of KOMZIFTI due to an adverse reaction occurred in 21% of patients. Adverse reactions that required permanent discontinuation of KOMZIFTI in ≥ 2% of patients were infection without an identified pathogen (8%), bacterial infection (4%), cardiac arrest (2%), and differentiation syndrome (2%).

Most common (≥ 20%) adverse reactions, including laboratory abnormalities, were aspartate aminotransferase increased (53%), infection without an identified pathogen (52%), potassium decreased (52%), albumin decreased (51%), alanine aminotransferase increased (50%), sodium decreased (49%), creatinine increased (45%), alkaline phosphatase increased (41%), hemorrhage (38%), diarrhea (36%), nausea (35%), fatigue (34%), edema (30%), bacterial infection (28%), musculoskeletal pain (28%), bilirubin increased (27%), potassium increased (26%), differentiation syndrome (26%), pruritus (23%), febrile neutropenia (22%), and transaminases increased (21%).

DRUG INTERACTIONS

Drug interactions may occur when KOMZIFTI is concomitantly used with:

- Strong or Moderate CYP3A4 Inhibitors: Monitor patients more frequently for KOMZIFTI-associated adverse reactions.
- Strong or Moderate CYP3A4 Inducers: Avoid concomitant use of KOMZIFTI.
- Gastric Acid Reducing Agents: Avoid concomitant use of KOMZIFTI with proton pump inhibitors (PPIs), H2 receptor antagonists (H2RAs), or locally acting antacids. If concomitant use with H2RAs or locally acting antacids cannot be avoided, modify KOMZIFTI administration time.
  - Take KOMZIFTI 2 hours before or 10 hours after administration of an H2 receptor antagonist.
  - Take KOMZIFTI 2 hours before or 2 hours after administration of a locally acting antacid.
- Drugs that Prolong the QT Interval: Avoid concomitant use of KOMZIFTI. If concomitant use cannot be avoided, obtain ECGs when initiating, during concomitant use, and as clinically indicated. Interrupt KOMZIFTI if the QTc interval is > 500 ms or the change from baseline is > 60 ms.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on findings in animals and its mechanism of action, KOMZIFTI can cause embryo-fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to starting KOMZIFTI.

Lactation: Because of the potential for adverse reactions in the breastfed child, advise women not to breastfeed during treatment with KOMZIFTI and for 2 weeks after the last dose.

Infertility: Based on findings in animals, KOMZIFTI may impair fertility in females and males of reproductive potential.

Please see full Prescribing Information, including **Boxed WARNING**, for additional information.

AML, acute myeloid leukemia; ANC, absolute neutrophil count; CI, confidence interval; CR, complete remission; CRh, complete remission with partial hematologic recovery; CYP3A4, cytochrome P450 3A4; ECG, electrocardiogram; H2, histamine 2; H2RA, histamine 2 receptor antagonist; *KMT2A*, lysine [k]-specific methyltransferase 2A; *NPM1*-m, mutated nucleophosmin 1; Ph, phase; PPI, proton pump inhibitor; QTc, corrected QT interval; R/R, relapsed or refractory; Rx, prescription; WBC, white blood cell.

References: 1. KOMZIFTI [Prescribing information]. San Diego, CA; Kura Oncology, Inc.
2. Wang ES et al. *J Clin Oncol.* 2025 Nov;43(31):3381-3390.

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