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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 19, 2025
Subject:	Komzifti	**Page:**	1 of 4

Last Review Date: March 6, 2026

Komzifti

Description

Komzifti (ziftomenib)

Background
Komzifti (ziftomenib) is a menin inhibitor that blocks the interaction of menin and lysine [K]-specific methyltransferase 2A (KMT2A). Acute leukemias can be driven by mutations in nucleophosmin 1 (*NPM1*) that recruit the wild-type menin-KMT2A complex to promoters of leukemogenic genes. Susceptible *NPM1* mutations are defined as those that result in loss of the nucleolar localization signal and the insertion of a new nuclear export signal leading to cytoplasmic accumulation of mutant NPM1 protein that disrupts normal cell function and drives leukemogenesis through altered gene expression. Pharmacologic disruption of the menin-KMT2A protein-protein interaction by Komzifti blocks oncogenic activity of mutant NPM1, which induces differentiation of leukemic cells as evidence by increased expression of differentiation markers. Komzifti demonstrated in vitro and in vivo antitumor activity in models of *NPM1*-mutant leukemia (1).

Regulatory Status
FDA-approved indication: Komzifti is a menin inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible nucleophosmin 1 (*NPM1*) mutation who have no satisfactory alternative treatment options (1).

Komzifti has a boxed warning for differentiation syndrome, which can be fatal. 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 (1).

Komzifti also carries a warning for QTc interval prolongation. Monitor electrocardiograms and electrolytes. Correct hypokalemia and hypomagnesemia prior to treatment. Interrupt Komzifti if the QTc interval is >500 ms or the change from baseline is >60 ms (1).

Komzifti can cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to use effective contraception during treatment with Komzifti and for 6 months after the last dose. Males with female partners of reproductive potential should be advised to use effective contraception during treatment with Komzifti and for 3 months after the last dose (1).

The safety and effectiveness of Komzifti in pediatric patients less than 18 years of age have not been established (1).

Related policies
Revuforj

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Komzifti may be considered **medically necessary** if the conditions indicated below are met.

Komzifti may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)
    a. Susceptible nucleophosmin 1 (*NPM1*) mutation
    b. Patient has no satisfactory alternative treatment options

AND ALL of the following:

a. Prescriber agrees to correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to treatment
b. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
c. Prescriber agrees to monitor for QTc interval prolongation
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Komzifti and for 6 months after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Komzifti and for 3 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
c. Prescriber agrees to monitor for QTc interval prolongation
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Komzifti and for 6 months after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Komzifti and for 3 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 600 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Komzifti is a menin inhibitor indicated for the treatment of relapsed or refractory AML with a susceptible *NPM1* mutation. Komzifti has a boxed warning regarding differentiation syndrome. The safety and effectiveness of Komzifti in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Komzifti while maintaining optimal therapeutic outcomes.

References

1. Komzifti [package insert]. San Diego, CA: Kura Oncology, Inc.; November 2025.
2. NCCN Drugs & Biologics Compendium® Ziftomenib 2026. National Comprehensive Cancer Network, Inc. Accessed on February 2, 2026.

Policy History

Date	Action
December 2025	Addition to PA
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.