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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	February 28, 2020
Subject:	Tazverik	**Page:**	1 of 5

Last Review Date: December 13, 2024

Tazverik

Description

Tazverik (tazemetostat)

Background
Tazverik (tazemetostat) is an inhibitor of the methyltransferase, EZH2, and some EZH2 gain-of-function mutations including Y646X and A687V. The most well-characterized function of EZH2 is as the catalytic subunit of the polycomb repressive complex 2 (PRC2), catalyzing mono-, di-, and trimethylation of the lysine 27 of the histone H3. Trimethylation of histone H3 leads to transcriptional repression. SWItch/Sucrose Non-Fermentable (SWI/SNF) complexes can antagonize PRC2 function in the regulation of the expression of certain genes. The loss or dysfunction of certain SWI/SNF complex members can lead to aberrant EZH2 activity or expression and a resulting oncogenic dependence on EZH2 (1).

Regulatory Status
FDA-approved indications: Tazverik is a methyltransferase inhibitor indicated for the treatment of: (1)

1. Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
2. Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
3. Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.

The risk of developing secondary malignancies is increased following treatment with Tazverik. Across clinical trials of 668 adults who received Tazverik 800 mg twice daily, myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) occurred in 0.6% of patients (1).

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

The safety and effectiveness of Tazverik in pediatric patients less than 16 years of age with epithelioid sarcoma have not been established. The safety and effectiveness of Tazverik in pediatric patients less than 18 years of age with follicular lymphoma have not been established (1).

Related policies

Policy

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

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

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

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Metastatic or locally advanced epithelioid sarcoma
    a. 16 years of age or older
    b. **NOT** eligible for complete resection
2. Relapsed or refractory follicular lymphoma

a. 18 years of age or older
b. Patient must have **ONE** of the following:
    i. Tumors are positive for an EZH2 mutation as detected by an FDA-approved test **AND** patient has received at least 2 prior systemic therapies
    ii. Patient has no satisfactory alternative treatment options

AND ALL of the following:

a. Prescriber agrees to monitor for the development of secondary malignancies
b. Females of reproductive potential **only**: patient will be advised to use effective non-hormonal contraception during treatment with Tazverik and for 6 months after the final dose
c. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Tazverik and for 3 months after the final dose

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Metastatic or locally advanced epithelioid sarcoma
    a. 16 years of age or older
2. Relapsed or refractory follicular lymphoma
    a. 18 years of age or older

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor for the development of secondary malignancies
c. Females of reproductive potential **only**: patient will be advised to use effective non-hormonal contraception during treatment with Tazverik and for 6 months after the final dose
d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Tazverik and for 3 months after the final dose

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Quantity 720 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

Rationale

Summary
Tazverik (tazemetostat) is an inhibitor of the methyltransferase, EZH2, and some EZH2 gain-of-function mutations including Y646X and A687V. The most well-characterized function of EZH2 is as the catalytic subunit of the polycomb repressive complex 2 (PRC2), catalyzing mono-, di-, and trimethylation of the lysine 27 of the histone H3. Trimethylation of histone H3 leads to transcriptional repression. SWItch/Sucrose Non-Fermentable (SWI/SNF) complexes can antagonize PRC2 function in the regulation of the expression of certain genes. The loss or dysfunction of certain SWI/SNF complex members can lead to aberrant EZH2 activity or expression and a resulting oncogenic dependence on EZH2. The safety and effectiveness of Tazverik in pediatric patients less than 16 years of age with epithelioid sarcoma have not been established. The safety and effectiveness of Tazverik in pediatric patients less than 18 years of age with follicular lymphoma have not been established (1).

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

References
1. Tazverik [package insert]. Cambridge, MA: Epizyme, Inc.; August 2024.
2. NCCN Drugs & Biologics Compendium® Tazemetostat 2024. National Comprehensive Cancer Network, Inc. Accessed on October 7, 2024.

Policy History

Date	Action
February 2020	Addition to PA
March 2020	Annual review
June 2020	Annual review. Addition of indication: relapsed or refractory follicular lymphoma. Revised female contraception requirements to say “effective non-hormonal contraception”
September 2020	Annual review
June 2021	Annual review and reference update
December 2022	Annual review and reference update
June 2023	Annual review and reference update
September 2023	Annual review and reference update
March 2024	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.