BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TAZVERIK™ (tazemetostat) oral tablet
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for TAZVERIK (tazemetostat)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Metastatic or locally advanced epithelioid sarcoma not eligible for complete resection
- Relapsed or refractory follicular lymphoma in an adult (18 years of age or older) whose tumors are positive for an enhancer of zeste homolog 2 (EZH2) mutation and who have received at least two prior systemic therapies

ORIGINAL EFFECTIVE DATE: 02/13/2020 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

- Relapsed or refractory follicular lymphoma in adult (18 years of age or older) who have no satisfactory alternative treatment options
- Other oncologic direct treatment uses listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 16 years of age or older for epithelioid sarcoma
- 18 years of age or older for follicular lymphoma

Baseline Clinical Evaluation
- For relapsed or refractory follicular lymphoma there is documentation of presence of enhancer of zeste homolog 2 (EZH2) mutation of codons Y646, A682, or A692 in tumor specimens
- Negative pregnancy test in a woman of childbearing potential
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No concomitant use with strong or moderate cytochrome P450 3A (CYP3A) inducers (see Definitions section)

Additional Requirements
- Will not be used in moderate (total bilirubin greater than 1.5 times upper limit of normal) or severe (total bilirubin greater than 3 times upper limit of normal) hepatic impairment

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (EZH2 mutation testing, pregnancy test, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist

Clinical Response
- Documented evidence of efficacy, disease stability, and/or improvement

- No evidence of significant unacceptable adverse drug reactions

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No significant adverse drug effects such as:
  - Fourth occurrence of neutropenia (count less than 1 x 10^9/L) despite dose reduction
  - Third occurrence of thrombocytopenia (count less than 50 x 10^9/L) despite dose reduction
  - Third occurrence of any other severe toxicity despite dose reduction
  - Second occurrence of any other life threatening toxicity despite dose reduction
  - Moderate (total bilirubin greater than 1.5 times upper limit of normal) or severe (total bilirubin greater than 3 times upper limit of normal) hepatic impairment
- No concomitant use with strong or moderate cytochrome P450 3A (CYP3A) inducers (see Definitions section)

Additional Requirements
- Requested dose is at least 400 mg twice daily or 200 mg twice daily if there is concurrent use of a moderate inhibitor of metabolism
- Will not be used in moderate (total bilirubin greater than 1.5 times upper limit of normal) or severe (total bilirubin greater than 3 times upper limit of normal) hepatic impairment

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

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Description:

Tazverik (tazemetostat) is indicated for the treatment of:

- Metastatic or locally advanced epithelioid sarcoma not eligible for complete resection in adults and adolescents ≥ 16 years of age.
- Relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test who have received at least 2 prior systemic therapies in adults
- Relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options in adults.

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Tazverik (tazemetostat) is a potent and selective inhibitor of histone methyltransferase EZH2 (enhancer of zeste homolog 2); it also inhibits some EZH2 gain-of-function mutations (including Y646X and A687V), as well as EZH1. 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 lysine 27 of 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. Preclinical in vitro and in vivo models with the loss or dysfunction of certain SWI/SNF complex members (e.g., integrase interactor 1 [INI1/SNF5/SMARCB1/BAF47], SMARCA4 and SMARCA2) can lead to aberrant EZH2 activity or expression and a resulting oncogenic dependence on EZH2.

INI1 (is also known as hSNF5, BAF47, and SMARCB1) is a member of SWI/SNF multi subunit chromatin remodeling complex located on the long arm of chromosome 22 (22q11.2). The loss of INI1 gene has been shown in more than 80% of patients with epithelioid sarcoma.

EZH2 is overexpressed or mutated in many cancer types and plays a role in tumor proliferation. SWI/SNF complex aids in facilitating gene expression and terminal differentiation; altered EZH2 upregulation and loss-of-function mutations in SWI/SNF are oncogenic in many human cancers; tazemetostat has antitumor activity in EZH2-mutant cell lines.

Epithelioid sarcoma is a rare, slow-growing type of soft tissue cancer. Most cases begin in the soft tissue under the skin of a finger, hand, forearm, lower leg or foot.

It starts as a small firm painless growth or lump. It appears as a single growth, but multiple growths may occur. The sarcoma may appear as ulcers that don't heal, looking like open wounds over the growths. Epithelioid sarcomas have a high rate of recurrence and can metastasize.

Treatment includes surgical resection, radiation prior to surgery to shrink large tumor size or for metastatic disease or for inoperable patients, and chemotherapy. Chemotherapy appears to be less effective in treating epithelioid sarcomas compared to surgery and radiation, but it is used in combination to surgery or for metastatic disease. Chemotherapy has consisted of doxorubicin, Ifosfamide, etoposide, vincristine, dactinomycin, and cyclophosphamide. Gemcitabine, pazopanib, cixutumumab, temozolomide, dasatinib, bevacizumab, taxanes, and vinorelbine have been tried also.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

CYP 3A4 inducers (not a complete listing):

Moderate inducers	bosentan, efavirenz, etravirine, modafinil and nafcillin
Strong inducers	carbamazepine, phenytoin, rifampin and St. John's Wort

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status (also known as Zubrod Score)	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Symptomatic, fully ambulatory, restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Symptomatic, ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Symptomatic, capable of only limited self-care, confined to bed or chair more than 50% of waking hours but not bedridden
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Activities of daily living (ADL):

Instrumental ADL:
Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.
Self-care ADL:
Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

Response Evaluation Criteria in Solid Tumors (RECIST):

- Complete response – disappearance of all target lesions
- Partial response – 30% decrease in the sum of the longest diameter of target lesions

- Progressive disease – 20% increase in the sum of the longest diameter of target lesions or the appearance of one or more new lesions
- Stable disease – small changes that so not meet the above criteria of PR and PD

Revised Response Evaluation Criteria in Solid Tumors (RECIST) for assessing clinical tumor response:

Response assessment	RECIST guideline, version 1.1[1]
Target lesions	
CR	Disappearance of all target lesions and reduction in the short axis measurement of all pathologic lymph nodes to ≤10 mm
PR	≥30 percent decrease in the sum of the longest diameter of the target lesions compared with baseline
PD	≥20 percent increase of at least 5 mm in the sum of the longest diameters of the target lesions compared with the smallest sum of the longest diameter recorded **OR** The appearance of new lesions including those detected by FDG-PET
SD	Neither PR nor PD
Non-target lesions	
CR	Disappearance of all non-target lesions and normalization of tumor marker levels
IR, SD	Persistence of one or more non-target lesions and/or the maintenance of tumor marker levels above normal limits
PD	The appearance of one of more new lesions or unequivocal progression. If patient has measurable disease, an increase in the overall level, or substantial worsening in non-target lesions, such that tumor burden has increased, even if there is a SD or PR in target lesions. If no measurable disease, an increase in the overall tumor burden comparable in magnitude to the increase that would be required to declare PD in measurable disease (e.g., an increase in pleural effusions from trace to large, or an increase in lymphangitic disease from localized to widespread).

CR: complete response; PR: partial response; PD: progressive disease; IR: incomplete response; SD: stable disease.
Reference: Eisenhauer E, et al. Eur J Cancer 2009; 45:228.

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

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Resources:

Tazverik (tazemetostat) tab product information, revised by Epizyme, Inc. 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 24, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 3.2025 – Updated August 18, 2025. Available at https://www.nccn.org. Accessed November 09, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 1.2025 – Updated May 02, 2025. Available at https://www.nccn.org. Accessed November 09, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.