Clinical Policy: Tazemetostat (Tazverik)

Reference Number: CP.PHAR.452
Effective Date: 03.01.20
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Tazemetostat (Tazverik™) is a methyltransferase inhibitor.

FDA Approved Indication(s)

Tazverik is indicated for the treatment of:

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

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Tazverik is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Epithelioid Sarcoma (must meet all)**:**

1. Diagnosis of ES;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 16 years;
4. For brand Tazverik requests, member must use generic tazemetostat, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Disease is metastatic or locally advanced, and not amenable to complete resection;
6. Tumor demonstrates loss of INI1 gene expression through inactivation, deletion, or mutation of the INI1 (SMARCB-1) gene;
7. Tazemetostat is prescribed as monotherapy;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,600 mg (8 tablets) per day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Follicular Lymphoma (must meet all)**:**

1. Diagnosis of FL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand Tazverik requests, member must use generic tazemetostat, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Relapsed/refractory disease after ≥ 2 prior therapies (*see Appendix B for examples*);*
   **Prior authorization may be required.*
6. If EZH2 mutation status is negative or unknown, failure of at least one of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Aliqopa™, Copiktra™, Zydelig®;*
   **Prior authorization may be required.*
7. Member does not have a history of or current CNS metastases;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,600 mg (8 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Tazverik for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Tazverik requests, member must use generic tazemetostat, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 1,600 mg (8 tablets) per day ;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ES: epithelioid sarcoma
EZH2: enhancer of zeste homolog 2
FDA: Food and Drug Administration
FL: follicular lymphoma
NCCN: National Comprehensive Cancer Network

STS: soft tissue sarcoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Follicular Lymphoma *Examples of first-line, second-line and subsequent therapies:* • bendamustine + Gazyva® or rituximab • CHOP (cyclophosphamide, doxorubicin, vincristine, predenisone) + Gazyva® or rituximab • CVP (cyclophosphamide, vincristine, prednisone) + Gazyva® or rituximab • Revlimid® + rituximab • Revlimid® + Gazyva® • Single-agent examples: rituximab; Gazyva®; Revlimid®	Varies	Varies
Zydelig® (idelalisib)	FL (third-line and subsequent therapy): 150 mg PO BID	300 mg/day
Copiktra® (duvelisib)	FL (third-line and subsequent therapy): 25 mg PO BID	50 mg/day
Aliqopa® (copanlisib)	FL (third-line and subsequent therapy): 60 mg IV on days 1, 8, and 15 of a 28-day treatment cycle	60 mg/dose/ week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
Not reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ES, FL	800 mg PO BID until disease progression or unacceptable toxicity	1,600 mg/day

VI. Product Availability

Tablet: 200 mg

VII. References

1. Tazverik Prescribing Information. Cambridge, MA: Epizyme, Inc., June 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213400s000lbl.pdf. Accessed November 24, 2021.
2. Tazemetostat. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 24, 2021.
3. National Comprehensive Cancer Network. B-cell Lymphomas – Follicular Lymphoma. Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed November 24, 2021.
4. National Comprehensive Cancer Network. Soft Tissue Sarcoma. Version 2.2021. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed November 24, 2021.
5. Stacchiotti S, Schoffski P, Jones R, et al. Safety and efficacy of tazemetostat, a first-in-class EZH2 inhibitor, in patients (pts) with epithelioid sarcoma (ES) (NCT02601950). Presented at the 2019 American Society of Clinical Oncology (ASCO) annual meeting. DOI: 10.1200/JCO.2019.37.15_suppl.11003 *Journal of Clinical Oncology* 37, no. 15_suppl (May 20, 2019) 11003-11003. Available at https://ascopubs.org/doi/abs/10.1200/JCO.2019.37.15_suppl.11003.
6. Italiano A, Soria JC, Toulmonde M, et al. Tazemetostat, an EZH2 inhibitor, in relapsed or refractory B-cell non-Hodgkin lymphoma and advanced solid tumours: a first-in-human, open-label, phase 1 study. Lancet Oncol 2018; 19:649-59.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	12.10.19	02.20
Drug is now FDA approved - criteria updated per FDA labeling: age is reduced to 16 years; prior therapeutic trial removed; references reviewed and updated.	03.03.20	05.20
RT2: added criteria set for two new FDA approved FL indications; references reviewed and updated.	06.22.20	08.20
1Q 2021 annual review: oral oncology generic redirection language added; for FL, EZH2 wild type mutation status clarified as negative, and unknown mutation status added for completeness; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.05.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.16.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
Template changes applied to other diagnoses/indications.	09.28.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.