Clinical Policy: Tazemetostat (Tazverik)

Reference Number: ERX.SPA.367
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, 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.*

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*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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 expression through inactivation, deletion, or mutation of the INI1 (SMARCB-1) gene;
7. Tazverik 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:
Commercial – Length of Benefit
Medicaid – 6 months

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 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:
   Commercial – Length of Benefit
   Medicaid – 6 months

C. **Other diagnoses/indications**
   1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. **All Indications in Section I** (must meet all)**:**
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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:
   Commercial – Length of Benefit
   Medicaid – 12 months

B. **Other diagnoses/indications** (must meet 1 or 2)**:**
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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
None 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.	01.17.20	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 new FDA approved FL indication; references reviewed and updated.	06.22.20	08.20
1Q 2021 annual review: for FL, EZH2 wild type mutation status clarified as negative, and unknown mutation status added for completeness; references reviewed and updated.	11.05.20	02.21
1Q 2022 annual review: no significant changes; oral oncology generic redirection language added; references reviewed and updated.	11.16.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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