Clinical Policy Title:	tazemetostat
Policy Number:	RxA.629
Drug(s) Applied:	Tazverik™
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Tazverik™ is a methyltransferase inhibitor indicated for

- The treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
- The treatment of 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
- Adult patients with relapsed or refractory follicular lymphoma 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 these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
tazemetostat (Tazverik™)	Epithelioid Sarcoma	800 mg taken orally twice daily with or without food.	1,600 mg daily
	Relapsed or Refractory Follicular Lymphoma	800 mg taken orally twice daily with or without food.	1,600 mg daily

Dosage Forms

- tazemetostat (Tazverik™): 200 mg oral tablets

Clinical Policy

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

I. Initial Approval Criteria

A. Epithelioid Sarcoma (must meet all):

1. Member is 16 years or older;

2. Prescribed by or in consultation with an oncologist;
3. The member has metastatic or locally advanced epithelioid sarcoma that is not eligible for complete resection;
4. The member has histologically confirmed metastatic or locally advanced disease;
5. The member has loss of INI1 expression or mutation of INI1 gene (SMARCB-1) detected using local tests;
6. Tazverik is prescribed as monotherapy;
7. Meets one of the following (a or b)*:
   a. Dose does not exceed 1,600 mg 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 dosing regimen must be FDA-approved or recommended by NCCN guidelines.

Approval Duration:
Commercial: 6 months
Medicaid: 6 months

B. Relapsed or Refractory Follicular Lymphoma (must meet all):
1. Member is 18 years or older;
2. Prescribed for the treatment of (a or b):
   a. EZH2 mutation positive relapsed/refractory disease as detected by FDA-approved test, after at least two prior systemic therapies (prescriber must provide supporting documentation of previous therapies)
   b. EZH2 wild-type or unknown relapsed/refractory disease and no satisfactory alternative treatment options as evidenced by supporting documentation;
3. Prescribed by or in consultation of oncologist;
4. Meets one of the following (a or b)*:
   a. Dose does not exceed 1,600 mg 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 dosing regimen must be FDA-approved or recommended by NCCN guidelines.

Approval Duration:
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that the member has received this medication for at least 30 days for an FDA-approved indication or an indication that has NCCN level 2A recommendation;
2. Member is responding positively to therapy.
3. Meets one of the following (a or b)*:
   a. Dose does not exceed 1,600 mg 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 dosing regimen must be FDA-approved or recommended by NCCN guidelines.

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

INI1: Integrase interactor 1
NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration
ES: Epithelioid Sarcoma
FL: Follicular Lymphoma

APPENDIX B: Therapeutic Alternatives

- There are no oncology medications that have been specifically approved for epithelioid sarcoma. Votrient (pazopanib) and doxorubicin are approved for soft-tissue sarcomas and are used in patients with epithelioid sarcomas.

  Other medications used for sarcomas, including epithelioid sarcoma, include but are not limited to ifosfamide, gemcitabine, docetaxel, Lartruvo (olaratumab), Sutent (sunitinib malate), dacarbazine, epirubicin, and temozolomide.
- The optimal chemotherapy regimen for relapsed FL is unknown and practice varies. Other medications used for follicular lymphomas combination of bendamustine plus obinutuzumab (BO) or bendamustine plus rituximab (BR), CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) plus obinutuzumab (O-CHOP) or rituximab (R-CHOP), idelalisib, copanlisib

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

APPENDIX D: General Information

Soft Tissue Sarcoma (Version 6.2019). NCCN Clinical Practice Guidelines in Oncology. Tazemetostat was added as category 2A recommendation for epithelioid sarcoma for metastatic or locally advanced disease not eligible for complete resection.
A lack of INI1 expression enables the epigenetic modifier EZH2 to act as an oncogenic driver in tumor cells.

References

1. Tazverik™ (tazemetostat) [prescribing information]. Cambridge, MA: Epizyme Inc.; July 2020. Available at: https://www.tazverik.com/ .Accessed on January 22, 2021.
2. Soft Tissue Sarcoma (Version 1.2021). NCCN Clinical Practice Guidelines in Oncology. National Comprehensive Cancer Network (NCCN).Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf . Accessed on January 22, 2021.
3. B-Cell Lymphomas - Follicular Lymphoma.(Version 1.2021). NCCN Clinical Practice Guidelines in Oncology. National Comprehensive Cancer Network (NCCN). Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on January 22, 2021.
4. Epizyme Announces U.S. FDA Accelerated Approval of TAZVERIK™™ (tazemetostat) for the Treatment of Patients with Epithelioid Sarcoma. BusinessWire. 2020. Available at: https://www.businesswire.com/news. Accessed on January 22, 2021.
5. Agulnik M, Tannir N, Pressey J, et al. A phase II, multicenter study of the EZH2 inhibitor tazemetostat in adult subjects with INI1-negative tumors or relapsed/refractory synovial sarcoma. TPS11071 Journal of Clinical Oncology 34, no. 15_suppl. Published online May 11, 2017. Accessed on January 22, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	5/2020	5/21/2020
Policy was reviewed: 1) Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy. 2) Continued therapy criteria was updated: added “If request is for dose increase…”. 3) Background New indication added: relapsed or refractory Follicular lymphoma. 4) Dosing Information-dosing regimen added for relapsed or refractory Follicular lymphoma. 5) Removed hydrobromide from Dosage forms. 6) Continued therapy approval duration updated from 1 year to 12 months. 7) References were updated and point 3 reference added 8) Added initial approval criteria for new indication of relapsed or refractory follicular lymphoma 9) Updated Appendix A, abbreviations 10) Added dosing criteria under continued therapy approval Section II	01/22/2020	03/09/2021