Clinical Policy Title:	Vorinostat
Policy Number:	RxA.578
Drug(s) Applied:	Zolinza®
Original Policy Date:	03/06/2020
Last Review Date:	10/19/2022
Line of Business Policy Applies to:	All lines of business

Background

Vorinostat (Zolinza®) is a histone deacetylase (HDAC) inhibitor. It is indicated for the treatment of cutaneous manifestations in patients with cutaneous T- cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
vorinostat (Zolinza®)	CTCL	400 mg orally once daily. If patient is intolerant to therapy, reduce the dose to 300 mg orally once daily. If necessary, reduce the dose further to 300 mg once daily for 5 consecutive days each week. **For Hepatic Impairment:** Reduce the starting dose to 300 mg orally once daily with food in patients with mild to moderate hepatic impairment (bilirubin 1 to 3 x ULN or AST greater than ULN)	400 mg/day

Dosage Forms

- Capsules: 100 mg

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. **Initial Approval Criteria**

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Diagnosis of CTCL;
2. Disease is progressive, persistent or recurrent on or following two systemic therapies (e.g., bexarotene, romidepsin, etc) unless contraindicated or clinically significant adverse effects are experienced;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b): *
   a. Dose does not exceed 400 mg (4 capsules) 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: 6 months
Medicaid: 6 months

II. **Continued Therapy Approval**

A. Cutaneous T-Cell Lymphoma (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b): *
   a. New dose does not exceed 400 mg (4 capsules) 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: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

CTCL: Cutaneous T-cell lymphoma
FDA: Food and Drug Administration
HDAC: Histone Deacetylase
MF: Mycosis fungoides
SS: Sezary syndrome
ATLL: Adult T-cell leukemia/lymphoma
ALCL: anaplastic large cell lymphoma
NHLs: Non-Hodgkin's lymphomas

APPENDIX B: Therapeutic Alternatives

- Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

World Health Organization-European Organization for Research and Treatment of Cancer Classification of CTCL* with Primary Cutaneous Manifestations:

- Mycosis fungoides (MF)
  - MF variants and subtypes
    - Folliculotropic MF
    - Pagetoid reticulosis
    - Granulomatous slack skin
- Sezary syndrome (SS)
- Adult T-cell leukemia/lymphoma (ATLL)
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma (ALCL)
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK**/T-cell lymphoma, nasal type
- Chronic active EBV infection
- Primary cutaneous peripheral T-cell lymphoma, NOS
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma
  - Cutaneous ϒ/δ (gamma/delta) T-cell lymphoma
  - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma
  - Primary cutaneous acral CD8+ T-cell lymphoma

*Non-Hodgkin's lymphomas (NHLs) include lymphoproliferative disorders originating in B-lymphocytes, T-lymphocytes, and natural killer cells. Cutaneous T-cell lymphomas (CTCLs) are a subset of NHLs characterized by skin involvement and the potential to progress to lymph nodes, blood, and visceral organs. Mycosis fungoides, the most common CTCL, is an extranodal NHL of mature T-cells with primary skin involvement.
Sezary syndrome, a less common CTCL, is characterized by significant blood involvement and lymphadenopathy.
**Extranodal NK-cell lymphoma is considered a CTCL subtype under the policy criteria.

References

1. Zolinza® Prescribing Information. Whitehouse Station, NJ: Merck and Company, Inc.; July 2022. Available at: https://www.merck.com/product/usa/pi_circulars/z/zolinza/zolinza_pi.pdf . Accessed July 28, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/. Accessed July 28, 2022.
3. National Comprehensive Cancer Network. Primary Cutaneous Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed July 28, 2022.
4. National Comprehensive Cancer Network. T-Cell Lymphomas Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed July 28, 2022.
5. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. May 2005; 105(10): 3768-85. Available at: https://pubmed.ncbi.nlm.nih.gov/15692063/. Accessed July 28, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020

Policy was reviewed: 1. Clinical Policy Title Table was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Dosing information was updated to include the information for dose reduction. 5. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 6. Initial Approval criteria: Commercial and Medicaid approval duration were updated from length of benefit to 6 months. 7. Continued Approval criteria: Commercial and Medicaid approval duration were updated from length of benefit to 12 months. 8. References were updated.	10/01/2020	12/07/2020
Policy was reviewed: 1. Dosing information table was updated to add dosing regimen for hepatic impairment. 2. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3. Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Appendix A was updated to include SS, MF, ATLL, ALCL & NHL. 5. References were reviewed and updated.	10/11/2021	12/07/2021
PA policy was reviewed: 1. Initial Approval Criteria, I.A.2: Updated to include new disease progression criteria Disease is progressive, persistent or recurrent on or following two systemic therapies (e.g., bexarotene, romidepsin, etc) unless contraindicated or clinically significant adverse effects are experienced. 2. Initial Approval Criteria, I.A.5.b:	7/28/2022	10/19/2022

Updated to include new dosing criteria 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. 3. Continued Therapy Approval Crtieria, II.A.3.b: Updated to include new dosing criteria 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. 4. Appendix D, General Information: Updated to include new information regarding Chronic active EBV infection, Primary cutaneous peripheral T-cell lymphoma, NOS, Primary cutaneous acral CD8+ T-cell lymphoma.		