Clinical Policy: Vorinostat (Zolinza)

Reference Number: PA.CP.PHAR.83
Effective Date: 01/18
Last Review Date: 07/17/19 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness ® clinical policy for vorinostat (Zolinza®).

FDA Approved Indication(s)
Zolinza 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.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Zolinza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CTCL;
2. Prescribed by or in consultation with an oncologist;
3. Dose does not exceed 400 mg/day (4 capsules per day).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. No disease progression or unacceptable toxicity.
3. If request is for a dose increase, new dose does not exceed 400 mg/day (4 capsules per day).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background
Description/Mechanism of Action:

Vorinostat inhibits the enzymatic activity of histone deacetylases HDAC1, HDAC2 and HDAC3 (Class I) and HDAC6 (Class II) at nanomolar concentrations (IC50<86 nM). These enzymes catalyze the removal of acetyl groups from the lysine residues of proteins, including histones and transcription factors. In some cancer cells, there is an overexpression of HDACs, or an aberrant recruitment of HDACs to oncogenic transcription factors causing hypoacetylation of core nucleosomal histones. Hypoacetylation of histones is associated with a condensed chromatin structure and repression of gene transcription. Inhibition of HDAC activity allows for the accumulation of acetyl groups on the histone lysine residues resulting in an open chromatin structure and transcriptional activation. In vitro, vorinostat causes the accumulation of acetylated histones and induces cell cycle arrest and/or apoptosis of some transformed cells. The mechanism of the antineoplastic effect of vorinostat has not been fully characterized.

Formulations:
Each 100 mg Zolinza capsule for oral administration contains 100 mg vorinostat.

Appendices

Appendix A: Abbreviation Key

ALCL: anaplastic large cell lymphoma
ATLL: adult T-cell leukemia/lymphoma
CTCL: cutaneous T-cell lymphoma
HDAC: histone deacetylase
MF: mycosis fungoides
NHL: non-Hodgkin's lymphoma
PTCL-NOS: pimary cutaneous peripheral T-cell lymphoma, unspecified

Appendix B: World Health Organization-European Organization for Research and Treatment of Cancer Classification of Cutaneous T-Cell Lymphomas* (CTCL) with Primary Cutaneous Manifestations[4]

- Mycosis fungoides
  - 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
- Primary cutaneous peripheral T-cell lymphoma, unspecified (PTCL-NOS)
  - 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

**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.*

Appendix C: Examples of Systemic Antineoplastic Agents for Cutaneous T-Cell Lymphomas (CTCL)

- Histone deacetylase (HDAC) inhibitors (romidepsin, vorinostat)
- Monoclonal antibodies (brentuximab vedotin)
- Systemic retinoids (bexarotene, all-trans retinoic acid, isotretinoin, acitretin)
- Interferons (IFN-alpha, IFN-gamma)
- Extracorporeal photopheresis
- Other chemotherapeutic agents (bortezomib, chlorambucil, cyclophosphamide, etoposide, gemcitabine, liposomal doxorubicin, methotrexate, pentostatin, pralatrexate, temozolomide)

Reviews, Revisions, and Approvals	Date	Approval Date
3Q 2018 annual review: specialist requirements added; continuation of care statement added; NCCN and FDA-approved uses summarized for improved clarity (criteria limited to CTLC diagnosis); references reviewed and updated.	05.18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

References

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vi. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. May 2005; 105(10): 3768-85.