Pharmacy Medical Necessity Guidelines: Zolinza™ (vorinostat)

Effective: July 11, 2017

Prior Authorization Required | ✓ | Type of Review – Care Management
Not Covered | | Type of Review – Clinical Review | ✓
Pharmacy (RX) or Medical (MED) Benefit | RX | Department to Review | RXUM

This Pharmacy Medical Necessity Guideline applies to the following:

Tufts Health Plan Commercial Plans
✓ Tufts Health Plan Commercial Plans – large group plans
✓ Tufts Health Plan Commercial Plans – small group and individual plans

Tufts Health Public Plans
✓ Tufts Health Direct – Health Connector
✓ Tufts Health Together – A MassHealth Plan
✓ Tufts Health RITogether – A Rite Care + Rhody Health Partners Plan

Tufts Health Freedom Plan products
✓ Tufts Health Freedom Plan - large group plans
✓ Tufts Health Freedom Plan - small group plans

Fax Numbers:
RXUM: 617.673.0988

Note: For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Health Plan Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

OVERVIEW
Cutaneous T-cell lymphoma (CTCL) is a malignancy of the T-helper (CD4+) cells and includes variants such as mycosis fungoides and Sézary syndrome. It may mimic many benign processes, such as eczema, psoriasis, and contact dermatitis. Early in the course of the disease, the clinical and histologic diagnosis of CTCL is difficult. The diagnosis may be missed and the patient left untreated for years because of the benign appearance of this disorder. Close follow-up with multiple biopsies over time may help with the diagnosis. Once the disease becomes systemic, the prognosis is significantly worse. A variety of treatments for CTCL exist, with overall good patient response when treatment is started early.

Every year in the United States, about three in every one million people are diagnosed with CTCL. The majority of people with CTCL are men with an average age of 50 years. It is twice as common in black persons as in white persons, but CTCL may affect persons in any age or ethnic group. A recent series noted that between 4 and 5 percent of patients with CTCL had the disease by 20 years of age.

Zolinza (vorinostat) is a histone deacetylase (HDAC) inhibitor. Acetylation of histones affects the regulation of gene expression, and inhibitors of HDACs have been found to cause growth arrest, differentiation and/or apoptosis of many tumor cells by altering the transcription of a small number of genes. The antineoplastic mechanism of Zolinza (vorinostat) has not been fully characterized. Zolinza (vorinostat) inhibits the enzymatic activity of HDAC1, HDAC2, HDAC3 (Class I) and HDAC6 (Class II). These enzymes catalyze the removal of acetyl groups from the lysine residues of proteins, such as histones and transcription factors, which play an important role in the regulation of gene transcription. Zolinza (vorinostat) is believed to decrease the activity of HDAC thereby allowing for the activation of genes that may help to slow or stop the growth of cancer cells.

FDA-APPROVED INDICATIONS
Zolinza (vorinostat) is indicated for treatment of cutaneous manifestations in patients with CTCL who have progressive, persistent or recurrent disease on or following two systemic therapies.

COVERAGE GUIDELINES
The plan may authorize coverage of Zolinza (vorinostat) for Members when all of the following criteria are met:

1. Documented diagnosis of advanced cutaneous T-cell lymphoma (Stage IIB and higher)

2. Documentation the Member has progressive, persistent or recurrent disease

3. Documentation of current or prior treatment or treatment failure with at least one systemic chemotherapeutic agent for cutaneous T-cell lymphoma
4. The prescribing physician is an oncologist or hematologist

**Off-label Use Coverage for Other Cancer Diagnoses**

Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia, or in the medical literature, or by the Massachusetts commissioner of Insurance (commissioner) under the provisions of the "Sullivan Law": (M.G.L. c.175, s.47K).

The plan may authorize coverage for use for other cancer diagnoses provided effective treatment with such drug is recognized as a “Medically Accepted Indication” according to the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium as indicated by a Category 1 or 2A for quality of evidence and level of consensus.

**Note:** The plan requires prescribers to submit clinical documentation supporting the drug's effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s).

In cases where the requested off-label use for the diagnosis is not recognized by the NCCN Drugs and Biologics Compendium, the plan will follow the Centers for Medicare and Medicaid Services (CMS) guidance, unless otherwise directed by the commissioner, and accept clinical documentation referenced in one of the other "Standard Reference Compendia" noted below or supported by clinical research that appears in a regular edition of a "Peer-Reviewed Medical Literature" noted below.

**"Standard Reference Compendia"**

1. American Hospital Formulary Service – Drug Information (AHFS-DI)
2. Thomson Micromedex DrugDex
3. Clinical Pharmacology (Gold Standard)
4. Wolters Kluwer Lexi-Drugs

**"Peer Reviewed Medical Literature"**

- American Journal of Medicine
- Annals of Internal Medicine
- Annals of Oncology
- Annals of Surgical Oncology
- Biology of Blood and Marrow Transplantation
- Blood
- Bone Marrow Transplantation
- British Journal of Cancer
- British Journal of Hematology
- British Medical Journal
- Cancer
- Clinical Cancer Research
- Drugs
- European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)
- Gynecologic Oncology
- International Journal of Radiation, Oncology, Biology, and Physics
- The Journal of the American Medical Association
- Journal of Clinical Oncology
- Journal of the National Cancer Institute
- Journal of the National Comprehensive Cancer Network (NCCN)
- Journal of Urology
- Lancet
- Lancet Oncology
- Leukemia
- The New England Journal of Medicine
- Radiation Oncology

When the plan evaluates the evidence in published, peer-reviewed medical literature, consideration will be given to the following:

1. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
4. Whether the study is appropriate to address the clinical question.
   - whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (e.g., in some clinical studies it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover);
   - that non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,
c. that case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

**LIMITATIONS**

1. The plan will not authorize the use of Zolinza (vorinostat) for conditions other than those listed above without appropriate documentation.

**CODES**

None

**REFERENCES**


**APPROVAL HISTORY**

March 13, 2007: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
- January 15, 2008: No changes
- January 13, 2009: Inserted updated language for Off-label Use Coverage for Other Cancer Diagnoses
- January 1, 2010: Removed Medicare Preferred language (separate criteria has been created specifically for Medicare Preferred).
- January 12, 2010: No changes
- January 11, 2011: Removed requirement of documented contraindication or treatment failure of radiotherapy, total skin electron beam therapy, PUVA, or extracorporeal photopheresis. Changed requirement of current or prior treatment or treatment failure from at least two to at least one systemic chemotherapeutic agents for cutaneous T-cell lymphoma.
- January 11, 2011: Administrative Update: Effective 4/1/2011, Off-label Use Coverage for Other Cancer Diagnoses language updated. Tufts Health Plan requires prescribers to submit clinical documentation supporting the drug's effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s)
- January 10, 2012: No changes
- January 15, 2013: No changes
- November 5, 2013: No changes
- November 4, 2014: No changes
- November 10, 2015: No changes
- January 1, 2016: Administrative change to rebranded template applicable to Tufts Health Direct.
- July 12, 2016: Added the criterion that the prescribing physician must be an oncologist or a hematologist for all approvable diagnoses. Effective October 10, 2016 Medical Necessity Guideline applies to Tufts Health Together.
- July 11, 2017: No changes

**BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION**

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage
decisions are made. They are used in conjunction with a Member’s benefit document and in
coordination with the Member’s physician(s). The plan makes coverage decisions on a case-by-case
basis considering the individual Member’s health care needs. Pharmacy Medical Necessity Guidelines
are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in
a limited, defined population of patients or clinical circumstances. They include concise clinical
coverage criteria based on current literature review, consultation with practicing physicians in the
service area who are medical experts in the particular field, FDA and other government agency
policies, and standards adopted by national accreditation organizations. The plan revises and updates
Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes
available that suggests needed revisions.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan
Members or to certain delegated service arrangements. Unless otherwise noted in the Member’s
benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity
Guidelines do not apply to CareLink™ Members. For self-insured plans, drug coverage may vary
depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline
and a self-insured Member’s benefit document, the provisions of the benefit document will govern.
Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior
Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of
this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be
adjudicated. Claims payment is subject to Member eligibility and benefits on the date of service,
coordination of benefits, referral/authorization and utilization management guidelines when applicable,
and adherence to plan policies and procedures and claims editing logic.