



# CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date ..... 6/15/2011  
Next Review Date..... 6/15/2012  
Coverage Policy Number ..... 8006

Subject Vorinostat (Zolinza™)

## Table of Contents

Coverage Policy .....	1
General Background .....	2
Coding/Billing Information .....	2
References .....	2
Policy History.....	3

## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers vorinostat (Zolinza™) as medically necessary for the treatment of cutaneous T-cell lymphoma (CTCL).**

### FDA Approved Indications

Zolinza is indicated for the treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma who have progressive, persistent or recurrent disease on or following two systemic therapies.

### FDA Recommended Dosing

The recommended dose is 400 mg orally once daily. Treatment may be continued as long as there is no evidence of progressive disease or unacceptable toxicity. If a patient is intolerant to therapy, the dose may be reduced to 300 mg orally once daily. The dose may be further reduced to 300 mg once daily for 5 consecutive days each week, as necessary.

### Drug Availability

Zolinza capsules, 100 mg, are white, opaque hard gelatin capsules with "568" over "100 mg" printed within the radial bar in black ink on the capsule body. They are supplied in bottles of 120 capsules.

## General Background

### Pharmacology

Vorinostat inhibits the enzyme histone deacetylase. Some cancer cells overexpress these enzymes resulting in condensed DNA. Prevention of DNA condensation may allow transcription of cell-cycle regulatory genes leading to apoptosis. Peak concentration is achieved approximately 4 hours after dosing with food. Cytochrome P450 metabolism was negligible during in vitro studies. The primary route of vorinostat metabolism is through glucuronidation and hydrolysis with subsequent beta-oxidation. Vorinostat has not been studied in patients having hepatic or renal impairment.

### Guidelines

While the National Comprehensive Cancer Network (NCCN) has not yet developed specific guidelines for CTCL, they do recommend vorinostat for use of Mycosis Fungoides (MF) and Sezary Syndrome (SS) as follows:

#### Grade 2A

Systemic biologic therapy as a single agent or in combination with skin-directed therapy for stage I-IIA and stage III MF with blood involvement; single agent or in combination with skin-directed therapies for stage I-IIA MF with histologic evidence of folliculotropic or large cell transformed or stage IIB MF with limited extent tumor disease; single agent or in combination with denileukin diftitox, systemic retinoids, interferons, or photopheresis for stage IA-IIB with histologic evidence of folliculotropic or large cell transformed MF, stage IIB MF with generalized extent tumor, transformed, and/or folliculotropic disease, or SS

May be used as adjuvant systemic biologic therapy after total skin electron beam therapy for stage IIB MF generalized extent tumor, transformed, and/or folliculotropic disease or after chemotherapy for stage IV non-Sezary or visceral disease

Systemic biologic therapy for refractory or progressive stage IA-IIA or stage IIB (patch or plaque) MF

#### Ongoing Studies

There is a completed phase 1 study for the use of vorinostat in combination with bortezomib for relapsed and refractory multiple myeloma. The promising antimyeloma activity of this regimen merits further evaluation.

#### Adverse Reactions

The most common adverse effects of vorinostat are diarrhea, fatigue, nausea, dysgeusia, and thrombocytopenia. Serious adverse effects include pulmonary embolism, squamous cell carcinoma, and anemia. Some patients receiving vorinostat along with warfarin demonstrate a prolonged prothrombin time and International Normalized Ratio. Patients receiving vorinostat along with valproic acid may develop gastrointestinal bleeding and severe thrombocytopenia. As vorinostat may prolong QTc, concomitant medications which also affect QTc should be used cautiously.

---

## Coding/Billing Information

**Note:** This section is not in use.

---

## References

1. Badros A, Burger AM, Philip S, Niesvizky R, Kolla SS, Golubeva O, Harris C, Zwiebel J, Wright JJ, Espinoza-Delgado I, Baer MR, Holleran JL, Egorin MJ, Grant S. Phase I study of vorinostat in combination with bortezomib for relapsed and refractory multiple myeloma. *Clin Cancer Res*. 2009 Aug 15;15(16):5250-7. Epub 2009 Aug 11.
2. Demierre MF, Kim YH, Zackheim HS. Prognosis, clinical outcomes and quality of life issues in cutaneous T-cell lymphoma. *Hematol Oncol Clin North Am*. Dec 2003;17(6):1485-1507.

3. Duvic M, Talpur R, Ni X, et al. Phase 2 trial of oral vorinostat (suberoylanilide hydroxamic acid, SAHA) for refractory cutaneous T-cell lymphoma (CTCL). *Blood*. Jan 1 2007;109(1):31-3
4. Kim EJ, Hess S, Richardson SK, et al. Immunopathogenesis and therapy of cutaneous T cell lymphoma. *J Clin Invest*. Apr 2005;115(4):798-812.
5. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2011.
6. Merck & Co., Inc. Zolinza (vorinostat) package insert. Whitehouse Station, NJ: Merck & Co., Inc. Oct 2010.
7. NCCN Drugs & Biologics Compendium. Zolinza™ (vorinostat). Copyright 2011, National Comprehensive Cancer Network.
8. Office of Orphan Products Development. List of Orphan Designations and Approvals. Available online at: <http://www.fda.gov/orphan/designat/list.htm>. Accessed on January 31, 2007. Rockville, MD: Food and Drug Administration; 2007.
9. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. May 15 2005;105(10):3768-3785.
10. Wilson LD, Jones GW, Girardi M, Edelson RL, Heald PW. Book Chapter - Cutaneous T-Cell Lymphomas. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: principles and practice of oncology*. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005:1998-2011.
11. Zhang C, Richon V, Ni X, Talpur R, Duvic M. Selective induction of apoptosis by histone deacetylase inhibitor SAHA in cutaneous T-cell lymphoma cells: relevance to mechanism of therapeutic action. *J Invest Dermatol*. Nov 2005;125(5):1045-1052.

---

## Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	6/15/2008	8006	Vorinostat (Zolinza™)
Great-West Healthcare	12/2006	P06.112	Zolinza

“CIGNA”, “CIGNA HealthCare” and the “Tree of Life” logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Health and Life Insurance Company, CIGNA Behavioral Health, Inc., CIGNA Health Management, Inc., and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company or CIGNA Health and Life Insurance Company.