



# CIGNA MEDICAL 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.

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Coverage Policy Number ..... 8006

Subject            **Vorinostat (Zolinza™)**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant'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 participant'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 participant'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 group 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. Proprietary information of CIGNA. Copyright ©2009 CIGNA

## Coverage Policy

**CIGNA covers vorinostat (Zolinza™) as medically necessary for treatment of cutaneous T-cell lymphoma (CTCL) when there is progressive, persistent, or recurrent disease while on or following two systemic therapies.**

## General Background

### 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 with food. 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 with food. The dose may be further reduced to 300 mg once daily with food for 5 consecutive days each week, as necessary.

Cutaneous T-cell lymphoma (CTCL) is classified as a non-Hodgkin's lymphoma. CTCL presents as a variety of primary T-lymphocyte malignancies all having skin-invasive tendency, the subtype mycosis fungoides (MF) represents nearly half of all CTCL cases with the remaining half being composed of a dozen different subtypes. The majority of research involving CTCL diagnosis, prognosis, and treatment is directed at the most common subtype MF and the most aggressive subtype Sezary syndrome (SS).

While the National Comprehensive Cancer Network (NCCN) has not yet developed specific guidelines for CTCL, they do recommend vorinostat for use of MF and SS as follows: primary treatment as systemic biologic therapy for patients with stage IA to IIA with blood involvement, stage IIB to IV MF and SS. Used as a single agent or in combination therapy as indicated below: single agent for stage IA to IIA and stage III MF with blood involvement or single agent for stage IA to IIB with large cell transformed MF, stage IIB MF (generalized tumor disease or limited-extent tumor disease with blood involvement), stage IV MF with bulky lymph nodes or visceral disease or SS or single agent or in combination with skin-directed therapies (corticosteroids, carmustine, or mechlorethamine hydrochloride) for stage III MF with no blood involvement; may be used as adjuvant systemic biologic therapy after total skin electron beam therapy for stage IIB MF generalized tumor disease or limited tumor disease with blood involvement or large cell transformation or after chemotherapy for stage IV MF with bulky lymph nodes or visceral disease; systemic biologic therapy for patients with stage IA to IIA or stage IIB (patch or plaque) MF that is refractory to skin-directed therapies.

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.

Researchers have investigated the efficacy of vorinostat as a treatment for CTCL in two open-label experimental trials. All patients were refractory or intolerant to prior therapies for CTCL. The studies reported an objective response rate (partial + complete response rate) ranging from 24.2% to 29.7%. Only 1 patient from both studies achieved a complete response.

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.

Vorinostat is routinely not a first line agent for CTCL. Vorinostat is generally an alternative treatment option in patients who continue to experience progressive, persistent or recurrent CTCL following two systemic therapies.

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## Coding/Billing Information

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

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## References

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## 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

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