



CIGNA PHARMACY COVERAGE POLICY

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

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Coverage Policy Number 8009

Subject **Nilotinib (Tasigna®)**

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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. 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 nilotinib (Tasigna®) as medically necessary for the treatment of EITHER of the following conditions:

- Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in an adult
- gastrointestinal stromal tumors (GIST) when there is failure, contraindication, or intolerance to imatinib (Gleevec®) or sunitinib (Sutent®)

FDA Approved Indications

Treatment of newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase. Treatment of chronic phase (CP) and accelerated phase (AP) Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib.

FDA Recommended Dosing

Newly Diagnosed Ph+ CML-CP

The recommended dose of Tasigna is 300 mg orally twice daily.

Resistant or Intolerant Ph+ CML-CP and CML-AP

The recommended dose of Tasigna (nilotinib) is 400 mg orally twice daily.

Black Box Warning

Tasigna prolongs the QT interval. Sudden deaths have been reported in patients receiving nilotinib. Tasigna should not be used in patients with hypokalemia, hypomagnesemia, or long QT syndrome. Hypokalemia or hypomagnesemia must be corrected prior to Tasigna administration and should be periodically monitored. Drugs known to prolong the QT interval and strong CYP3A4 inhibitors should be avoided. Patients should avoid food 2 hours before and 1 hour after taking dose. A dose reduction is recommended in patients with hepatic impairment. ECGs should be obtained to monitor the QTc at baseline, seven days after initiation, and periodically thereafter, as well as following any dose adjustments.

Drug Availability

Tasigna (nilotinib) capsules are light yellow opaque hard gelatin capsules, size 0 with the red axial imprint "NVR/TKI." Tasigna capsules are supplied in blister packs as cartons of 4 blister pack or blisters of 28 capsules. Each blister pack contains one folded blister card of 28 capsules each, for dosing two in the morning and two in the evening at 12 hour intervals over a 7 day period.

General Background

Pharmacology/Disease Overview

Nilotinib binds to the inactive Bcr-Abl protein, blocking Bcr-Abl mediated proliferation of leukemic cells. Nilotinib possesses an in vitro Bcr-Abl binding potency 30 times greater than imatinib in imatinib-resistant cells, and 5-7 times greater than imatinib in imatinib-susceptible leukemic cells. The clinical importance of nilotinib's greater binding affinity is not established in patients with imatinib-susceptible disease. Nilotinib absorption greatly decreases with increasing dose above 400 mg. Absorption increases significantly in the presence of food.

The clinical course of CML begins with an indolent chronic phase, but can quickly progress to the more aggressive accelerated, then blast phases if left untreated. Disease classification is based on the degree of cell abnormality in the blood and bone marrow. Nearly 85% of patients are diagnosed during the chronic stage, when treatment is most effective. Diagnosis is often made from a routine blood test wherein leukocytosis (up to $1000 \times 10^9/L$) is found. Disease staging is primarily based on percent of blasts in the blood and bone marrow. Staging criteria vary between guidelines. Most CML studies follow criteria established at M.D. Anderson Cancer Center. The World Health Organization (WHO) guidelines propose a lower threshold for the acute and blastic phases of CML. Other criteria such as clonal evolution and platelet abnormalities also contribute to disease staging. Patients in the blastic phase with symptoms of malaise, fever, and worsening splenomegaly are considered to be in blast crisis.

Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN recommends Tasigna for the following:

CML

Grade 1

Primary treatment for patients with newly diagnosed CML (Philadelphia chromosome or BCR-ABL positive).

Grade 2A

Initial-dose nilotinib for follow-up therapy after primary treatment in patients with complete hematologic remission at 3 months; complete, partial, or minor cytogenetic response at 6 months; complete or partial cytogenetic response at 12 months; complete cytogenetic response at 18 months.

Follow-up therapy after primary treatment with imatinib or dasatinib in patients with less than complete hematologic response at 3 months; no cytogenetic response at 6 months; minor or no cytogenetic response or in cytogenetic relapse at 12 months; partial cytogenetic response or in cytogenetic relapse at 18 months.

Treatment of patients with disease progression as a single agent for accelerated phase; single agent or in combination with induction chemotherapy for blast crisis. Acute lymphocytic leukemia-type induction

chemotherapy is recommended for lymphoid blast crisis. Acute myeloid leukemia (AML)-type induction chemotherapy is recommended for myeloid blast crisis. Posttransplant follow-up treatment in patients with molecular relapse (polymerase chain reaction positive) following complete cytogenetic remission cytogenetic relapse or those who are not in cytogenetic remission.

Alternative treatment for patients with severe hepatotoxicity due to imatinib therapy or severe nonhematologic toxicity due to imatinib or dasatinib therapy.

Gastrointestinal Stromal Tumors (GIST)

Grade 2A

Treatment for progressive disease when patient is no longer receiving benefit from imatinib or sunitinib.

Adverse Reactions

The most common drug related adverse effects include rash, pruritus, constipation, nausea, vomiting, diarrhea, thrombocytopenia, and neutropenia. Other serious adverse events with nilotinib include elevated lipase and liver function tests, and electrolyte abnormalities. Nilotinib is a competitive inhibitor of CYP3A4, CYP2C8, CYP2C9, and CYP2D6. Nilotinib is also metabolized by the hepatic enzyme CYP3A4 and is transported through the P-glycoprotein efflux system. Drugs that are substrates, inducers, or inhibitors of these enzymes may have significantly interacted with nilotinib.

Coding/Billing Information

Note: This section is not in use.

References

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7. Novartis Pharmaceuticals. Tassigna (nilotinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation. Jan 2011.
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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	7/15/2008	8009	Nilotinib (Tasigna [®])
Great-West Healthcare	12/2007	P07.102	Tasigna

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