

**Regence BlueCross BlueShield of Oregon · Regence BlueShield  
Regence BlueCross BlueShield of Utah · Regence BlueShield of Idaho  
Independent licensees of the Blue Cross and Blue Shield Association**

**Medication Policy Manual**

**Policy No:** dru151

**Topic:** Tasigna<sup>®</sup>, nilotinib

**Date of Origin:** November 9, 2007

**Revised/Effective Date:** November 14, 2008

**Next Review Date:** November 2009

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Nilotinib (Tasigna<sup>®</sup>) is an oral cancer medication used to treat a certain type of leukemia.

## **Policy/Criteria**

**I.** Most contracts require prior authorization approval of nilotinib prior to coverage. Nilotinib may be considered medically necessary when all of the following criteria A, B, and C below are met.

**A.** Documentation of chronic or accelerated phase Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML).

**AND**

**B.** Resistance or intolerance to treatment with imatinib (Gleevec<sup>®</sup>).

**AND**

**C.** A hematologist or oncologist prescribes nilotinib.

**II.** Administration and Authorization Period

**A.** Regence considers nilotinib to be a self-administered medication.

**B.** When prior authorization is approved, up to 120 nilotinib 200 mg capsules may be authorized per month. Quantities exceeding 120 capsules per month are considered not medically necessary.

**C.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

**III.** Nilotinib is considered investigational when used for all other conditions, including, but not limited to:

**A.** Gastrointestinal stromal tumor (GIST).

**B.** Other leukemias/blood cancers.

## Position Statement

- Several tyrosine kinase inhibitor medications have shown benefit in treating blood cancers, such as chronic myeloid leukemia (CML), that are associated with the Philadelphia chromosome.
- Imatinib (Gleevec<sup>®</sup>), a tyrosine kinase inhibitor medication, was the first new therapy found to be more effective than other kinds of medication treatment for CML. <sup>[8]</sup>
- Dasatinib (Sprycel<sup>®</sup>) and nilotinib (Tasigna<sup>®</sup>), also tyrosine kinase inhibitor medications, have demonstrated possible benefit in the small proportion of patients in whom imatinib stops working or is not tolerated. <sup>[1,17]</sup>
- There is no reliable information that shows how well any single tyrosine kinase inhibitor medication works relative to another.
- There are many studies looking to see if these medications work in other kinds of cancer; however, more information is needed before it is known whether they work in these cancers.

### *Background on CML treatment*

- CML is a blood disease that is caused by a specific gene mutation that leads to the formation of the Philadelphia chromosome. Confirmation of the Philadelphia chromosome along with the presence of specific immature cells in the blood establishes a diagnosis of CML.
- Several medications belonging to the protein kinase inhibitor class (dasatinib, imatinib, and nilotinib) have been found to prevent the formation of the Philadelphia chromosome which prevents progression of CML and improves survival of patients when compared with patients who had CML before these medications became available.

### *Clinical Efficacy*

- A single clinical trial studied nilotinib in the treatment of CML, a blood cancer associated with formation of the Philadelphia chromosome. <sup>[1, 4-5]</sup>
- In this study, nilotinib was found to lower the amount of Philadelphia chromosome present in the cells (cytogenetic response) and return blood counts to normal (hematologic response) in patients with either the chronic or accelerated phases of CML. <sup>[1, 4-5]</sup>

- Patients in the nilotinib studies either experienced resistance to imatinib therapy (they did not achieve a hematologic or cytogenetic response or had progression of disease after an initial response) or discontinued imatinib because they could not tolerate it. <sup>[1]</sup>
- There is no reliable information directly comparing nilotinib with other therapies so it is not known how well it works relative to other medications (e.g., dasatinib).
- It is not known how much nilotinib will benefit patients with CML.

### *Safety*

- Package labeling for nilotinib contains a Box Warning regarding the potential for QTc prolongation and sudden death. <sup>[1]</sup>
- Other serious adverse events observed during the nilotinib clinical trial include thrombocytopenia, neutropenia, pneumonia, intracranial hemorrhage, elevated lipase, and pyrexia. <sup>[1]</sup>
- Less serious adverse events commonly reported with nilotinib include rash, pruritus, nausea, fatigue, headache, constipation, diarrhea, and vomiting. <sup>[1]</sup>
- The incidence and severity of adverse effects may increase when nilotinib is given in combination with strong CYP3A4 inhibitors, such as clarithromycin or ketoconazole. <sup>[1]</sup>

### *Dosing and administration*

- The safety and efficacy of nilotinib in doses exceeding 800 mg per day has not been established. <sup>[1]</sup>
- Nilotinib should be administered on an empty stomach. Food increases absorption and may increase the risk of potentially serious adverse effects. <sup>[1]</sup>
- Dose modifications are recommended for QTc prolongation, neutropenia and thrombocytopenia, elevated lipase and/or amylase, and elevated hepatic enzymes. <sup>[1]</sup>

### *Other Conditions*

- The nilotinib clinical trials included a small proportion of patients with blast phase CML and Philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ ALL).<sup>[6]</sup> Preliminary results appear promising, however, studies in larger populations of patients are necessary to establish the safety and efficacy of nilotinib in these conditions.
- Nilotinib is also being studied in gastrointestinal stromal tumor and other blood cancers.<sup>[3]</sup> However, there is currently no evidence available for either of these conditions.

### **References**

1. Tasigna (nilotinib) Prescribing Information. Novartis Pharmaceuticals Corporation; East Hanover, NJ, October 2007.
2. U.S. National Institute of Health clinical trials registry. Available at: <http://www.clinicaltrials.gov/>.
3. National Comprehensive Cancer Network (NCCN); Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia – v.2.2008. Available at: [http://www.nccn.org/professionals/physician\\_gls/PDF/cml.pdf](http://www.nccn.org/professionals/physician_gls/PDF/cml.pdf). Accessed on 10/30/2007.
4. le Coutre P, Ottmann OG, Giles F, Kim DW, Cortes J, et al. Nilotinib (formerly AMN107), a highly selective BCR-ABL tyrosine kinase inhibitor, is active in patients with imatinib-resistant or –intolerant accelerated-phase chronic myelogenous leukemia. *Blood*. 2008 Feb 15;111(4):1834-9. Epub 2007 Nov 29.
5. Kantarjian HM, Giles F, Gattermann N, Bhalla K, Alimena G, et al. Nilotinib (formerly AMN107), a highly selective BCR-ABL tyrosine kinase inhibitor, is effective in patients with Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase following imatinib resistance and intolerance. *Blood*. 2007 Nov 15;110(10):3540-6. Epub 2007 Aug 22.
6. Kantarjian H, Giles F, Wunderle L, Bhalla K, O'Brien S, et al. Nilotinib in imatinib-resistant CML and Philadelphia chromosome-positive ALL. *N Engl J Med*. 2006 Jun 15;354(24):2542-51.

<b>Cross References</b>
Gleevec <sup>®</sup> , imatinib dru043
Sprycel <sup>®</sup> , dasatinib dru137

<b>Codes</b>	<b>Number</b>	<b>Description</b>
HCPCS	J8999	Oral chemotherapeutic drug, not otherwise classified