



Prior Authorization Approval Criteria
Department of Pharmacy Services

Generic Name: Nilotinib

Brand Name: Tasigna

Medication Class: Antineoplastic agent (Tyrosine kinase inhibitor)

FDA Approved Uses: Chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia resistant to or intolerant to prior therapy that includes imatinib.

Available Dosage Forms: Capsule-200mg

Usual Dose: 400 mg orally twice daily.

Duration of Therapy: Treatment should continue as long as the patient does not show evidence of progression or unacceptable toxicity.

Approximate monthly cost (based on AWP 2008): \$6,000.00

Criteria for Use: *(bullet points below are all inclusive unless otherwise noted)*

- Clinically diagnosed with chronic phase or accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia
- Must be 18 years of age or older.
- Failed or intolerant to therapy with imatinib (Gleevec)

Criteria for Continuation of Therapy:

- Patient responding to treatment without disease progression

Cautions:

- Capsules contain lactose- do not use in patients with galactose intolerance, severe lactase deficiency, or glucose-galactose malabsorption syndromes
- Caution should be exerted when patients are on concurrent drugs that prolong the QT interval as Tasigna can also prolong the QT interval resulting in Torsades de pointes, which can result in seizure, syncope, and death
- Use in caution in patients with pancreatitis as Tasigna may cause dose limiting elevations of serum lipase and amylase
- Tasigna may cause hepatotoxicity and dose-limiting elevations in bilirubin, AST, ALT, and phosphatase
- Tasigna should be used in caution in patients with hepatic impairment as metabolism of the drug is mostly hepatic (Tasigna has not been studied in patients that have AST or ALT levels greater than 2.5 times the upper limit of normal or greater than 5 times the upper limit of normal if disease related or in patients with bilirubin greater than 1.5 times the upper limit of normal



- Myelosuppression (grade 3 or 4 thrombocytopenia, neutropenia, or anemia) may occur with treatment
- Electrolyte abnormalities (hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, hyponatremia) may occur with treatment

Monitoring and does adjustments:

- CBC with differential (every 2 weeks for the first 2 months and then monthly thereafter)
- Electrolytes (baseline and periodic)
- Hepatic function- AST, ALT, bilirubin, and alkaline phosphatase should be monitored at baseline and periodically thereafter
- Serum lipase (baseline and periodic)
- Bone marrow assessments
- ECG (baseline, 7 days after initiation of treatment or dosage adjustments, then periodic)

- **Dose Adjustments for QT Prolongation**

ECGs with a QTc > 480 msec

1. Withhold Tasigna, and perform an analysis of serum potassium and magnesium, and if below lower limit of normal, correct with supplements to within normal limits. Concomitant medication usage must be reviewed.
2. Resume within 2 weeks at prior dose if QTcF returns to <450msec and to within 20 msec of baseline.
3. If QTcF is between 450 msec and 480 msec after 2 weeks reduce the dose to 400 mg once daily.
4. If, following dose-reduction to 400 mg once daily, QTcF returns to >480 msec, Tasigna should be discontinued.
5. An ECG should be repeated approximately 7 days after any dose adjustment.

- **Dose Adjustments for Neutropenia and Thrombocytopenia**

Chronic Phase or Accelerated Phase CML at 400 mg twice daily

ANC* < 1.0 x 10⁹/L and/or platelet counts < 50 x 10⁹/L

1. Stop Tasigna, and monitor blood counts
2. Resume within 2 weeks at prior dose if ANC >1.0 x 10⁹/L and platelets >50 x 10⁹/L
3. If blood counts remain low for > 2 weeks, reduce the dose to 400 mg once daily

Contraindications:

- Do not use in patients with hypokalemia, hypomagnesemia, or long QT syndrome.

Not Approved if:

- Does not meet the above stated criteria
- Have any contraindications to the use of nilotinib.
- Patients with the BCR-ABL mutation T315I, as data suggests that Tasigna is not effective against this mutation
- Patients with galactose intolerance, severe lactase deficiency, or glucose-galactose malabsorption syndromes
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Special Considerations:

- FDA's approval of Tasigna includes a black box warning for possible life-threatening heart problems that may lead to an irregular heartbeat and possible sudden death.
- The effectiveness of Tasigna is based on hematological and cytogenetic (chromosome related) response rates. So far, no controlled trials have shown a clinical benefit, such as improvement in disease related symptoms or increased survival.

Imatinib Resistance/failure

- Failure to achieve a complete hematologic response (CHR) after 3 months or loss of CHR, or a failure to achieve a cytogenetic response (CyR) after 6 months or loss of CyR, or a failure to achieve a major cytogenetic response (MCyR) after 12 months of treatment or loss of MCyR

Imatinib Intolerance

- Grade 3 or 4 adverse events that persist despite optimal supportive care, or grade 2 or higher adverse events that persist for longer than a month, or grade 2 or higher adverse events that recur more than 3 times despite optimal supportive care

P&T Approval: _____ Date: _____