**nilotinib** (ni-lo-tin-ib)

**Table**

**Pharmacokinetics**

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>3 hr</td>
<td>12 hr</td>
<td></td>
</tr>
</tbody>
</table>

**Indications**

- Newly diagnosed Philadelphia chromosome positive (Ph1+) chronic myelogenous leukemia (CML) in chronic phase.
- Chronic or accelerated phase Ph1 - CML that has not responded to prior treatment, including imatinib.

**Action**

Inhibits kinases which may be produced by malignant cell lines.

**Indications**

- Chronic or accelerated phase Ph1 - CML that has not responded to other treatment, including imatinib.
- Newly diagnosed Philadelphia chromosome positive (Ph1+) chronic myelogenous leukemia (CML) in chronic phase.

**Contraindications/Precautions**

- Hypokalemia or hypomagnesemia; Long QT syndrome; Concurrent use of medications known to prolong QT interval; Concurrent use of strong inhibitors of the CYP3A enzyme system (e.g. dexamethasone, phenytoin, carbamazepine, rifampin, erlotinib, gefitinib, phenobarbital, St John's wort, irtraconazole, voriconazole); Concurrent use of medications that prolong QT interval; Concurrent use of potent inhibitors of the cytochrome P450 (CYP) isoenzymes CYP1A2, CYP2C8, CYP2C9, CYP2D6, and CYP3A4.

**Adverse Reactions/Side Effects**

- **CNS:** Headache, dizziness; EENT: Vertigo; CV: Torsades de Pointes, hyperkalemia.
- **Resp:** Hypersensitivity, non-hypersensitivity.
- **Gastrointestinal:** Diarrhea, nausea.
- **Metab:** Hypocalcemia, hypokalemia, hyponatremia, hypophosphatemia.
- **Hemat:** Neutropenia, anemia.
- **Misc:** Myalgia, myopathy, rash, vomiting, vision disturbances.

**Drug Interactions**

- Strong CYP3A4 inhibitors including ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin, atazanavir, ritonavir, saquinavir, phenobarbital, phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital, St John's wort; Concurrent use of other drugs that prolong QT interval; Concurrent use of strong inducers of the CYP3A4 enzyme system (e.g. dexamethasone, phenytoin, carbamazepine, rifampin, erlotinib, gefitinib, phenobarbital, St John's wort, irtraconazole, voriconazole); Concurrent use of medications known to prolong QT interval; Concurrent use of potent inhibitors of the cytochrome P450 (CYP) isoenzymes CYP1A2, CYP2C8, CYP2C9, CYP2D6, and CYP3A4.

**Pharmacology**

**Antineoplastics**

**Therapeutic:**

- Classification: enzyme inhibitors, kinase inhibitors
- Action: Inhibits production of malignant cells lines with decreased proliferation of leukemic cells.

**Half-life:** 17 hr.

**Distribution:** Unknown.

**Metabolism and Excretion:** Mostly metabolized by the liver; metabolites are not active.

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**PO (Adults):** Hepatic Impairment

**Resistance or Intolerant Ph**

PO (Adults):

**NURSING IMPLICATIONS**

**Assessment**

- Monitor ECG to assess the QTc interval at baseline, 7 days after initiation of therapy, and periodically thereafter. For ECGs with QTc >480 msec, withhold nilotinib and check serum potassium and magnesium. If below lower limit of normal, correct to normal with supplements. Review concomitant medications for effects on electrolytes. If QTc returns to <450 msec and within 20 msec of baseline within 2 wk, return to prior dose. If QTc is <440 msec and >450 msec after 2 wk, reduce nilotinib dose to 400 mg once daily. Following dose reduction to 400 mg once daily, if QTc return to >440 msec, discontinue nilotinib. Repeat ECG approximately 7 days after any dose adjustment.

- Monitor for myelosuppression. Assess for bleeding (bleeding gums, bruising, petechiae, blood in stools, urine, emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture sites for at least 10 min. Assess for signs of infection during neutropenia. Anemia may occur. Monitor for fatigue, dyspnea, and electrocardiographic changes.

- Monitor for tumor lysis syndrome (malignant disease progression, high WBC counts, hyperuricemia, hypercalcemia, hyperphosphatemia, hypocalcemia, and/or dehydration). Prevent by maintaining adequate hydration and correcting uric acid levels prior to starting nilotinib.

- Lab Test Considerations: Monitor serum electrolytes prior to and periodically during therapy. May cause hypocalcemia, hypomagnesemia, hyperphosphatemia, hyperuricemia, hyperkalemia, and/or dehydration. Prevent by maintaining adequate hydration and correcting electrolyte levels prior to starting nilotinib.

- Monitor CBC every 2 wk for first 2 mo and monthly thereafter or as indicated. May cause Grade 3/4 thrombocytopenia, neutropenia, and anemia. If ANC <1.0 x 10^9/L and/or platelet counts <50 x 10^9/L, stop nilotinib and monitor blood counts. Resume within 2 wk at prior dose if ANC >1.0 x 10^9/L and platelet >50 x 10^9/L. If blood counts remain low for >2 wk, reduce dose to 400 mg once daily. Myelosuppression is generally reversible.

- May cause hyperbilirubinemia. If bilirubin >3 mg/dL, withhold nilotinib and monitor serum bilirubin. Resume treatment at 400 mg once daily if serum bilirubin or amylase return to <Grade 1.

- May cause transaminase elevations. If AST or ALT >5 times upper limit of normal and monitor serial AST, ALT, and alkaline phosphatase. Resume treatment at 400 mg once daily if serum bilirubin or amylase returns to <Grade 1.

- Monitor hepatic transaminases. If AST or ALT >5 times upper limit of normal and monitor serum AST, ALT, and alkaline phosphatase. Resume treatment at 400 mg once daily if serum bilirubin or amylase returns to <Grade 1.

- May cause hyperglycemia. If hyperglycemia >125 mg/dL, withhold nilotinib and monitor blood sugars. Resume treatment at 400 mg once daily if serum bilirubin or amylase returns to <Grade 1.

- **Potential Nursing Diagnoses**

  Deficient knowledge, related to medication regimen (Patient/Family Teaching)

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Nilotinib

Implementation
- Correct hypokalemia and hypomagnesemia prior to beginning therapy.
- PO: Administer twice daily at 12-hour intervals on an empty stomach, at least 1 hour before and 2 hours after food. Do not open capsule.
- Patients unable to swallow capsule may open capsule and sprinkle contents of each capsule in 1 teaspoon of applesauce. Swallow mixture within 15 minutes. Do not use more than 1 teaspoon of applesauce and lose with applesauce.
- Avoid arthralgia less than 2 hours before or after and GI antagoassia less than 10 hours before or less than 2 hours after administration.

Patient/Family Teaching
- Instruct patient to take nilotinib as directed, approximately 12 hours apart. If a dose is missed, skip dose and resume taking prescribed dose. Nilotinib is a long-term treatment; do not stop medication or change dose without consulting health care professional. Advise patient to read the Medication Guide before starting and with each Rx refill or changes.
- Advise patient to avoid grapefruit, grapefruit juice, or products with grapefruit extract during therapy; may cause toxicity.
- May cause dizziness. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.
- Instruct patient not to receive any vaccinations without advice of health care professional.
- Instruct patient to notify health care professional promptly if fever; chills; cough; hoarseness; signs of infection; lower back or side pain; difficult urination; bleeding gums; bruising; petechiae; blood in stools, urine, or emesis; increased fatigue; dyspnea; or orthostatic hypotension occurs. Caution patient to avoid crowds and persons with known infections. Instruct patients to use a soft toothbrush and electric razor and to avoid falls. Caution patient not to drink alcoholic beverages or take medication containing aspirin or NSAIDs; may precipitate bleeding.
- Instruct patient not to receive any vaccinations without advice of health care professional.
- Discuss the possibility of hair loss with patient. Explore methods of coping. Regrowth usually occurs 2–3 months after discontinuation of therapy. Advise women of childbearing potential to use highly effective contraception during therapy and to avoid breast-feeding.
- Why was this drug prescribed for your patient?