

Medication Guide
NILOTINIB (nye loe' ti nib)
CAPSULES

Medication Guide is available at <https://www.apotex.com/products/us/mg.asp>

What is the most important information I should know about nilotinib capsules?

Nilotinib capsules can cause a possible life-threatening heart problem called QTc prolongation. QTc prolongation causes an irregular heartbeat, which may lead to sudden death.

Your healthcare provider should check the electrical activity of your heart with a test called an electrocardiogram (ECG):

- before starting nilotinib capsules
- 7 days after starting nilotinib capsules
- with any dose changes
- regularly during nilotinib treatment

You may lower your chances for having QTc prolongation with nilotinib capsules if you:

- **Take nilotinib capsules on an empty stomach:**
 - Avoid eating food for at least 2 hours before the dose is taken, and
 - Avoid eating food for at least 1 hour after the dose is taken.
- Avoid grapefruit, grapefruit juice, and any supplement containing grapefruit extract during treatment with nilotinib capsules. Food and grapefruit products increase the amount of nilotinib in your body.
- Avoid taking other medicines or supplements with nilotinib capsules that can also cause QTc prolongation.
- Nilotinib capsules can interact with many medicines and supplements and increase your chance for serious and life-threatening side effects.
- Do not take any other medicine during treatment with nilotinib capsules unless your healthcare provider tells you it is okay to do so.
- If you cannot swallow nilotinib capsules whole, you may open the nilotinib capsule and sprinkle the contents of each capsule in 1 teaspoon of applesauce (puréed apple). Swallow the mixture right away (within 15 minutes). For more information, see “How should I take nilotinib capsules?”

Call your healthcare provider right away if you feel lightheaded, faint, or have an irregular heartbeat during treatment with nilotinib capsules. These can be symptoms of QTc prolongation.

What are nilotinib capsules?

Nilotinib capsules are a prescription medicine used to treat:

- adults and children who have been newly diagnosed with a certain type of leukemia called Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- adults with chronic phase Ph+ CML or accelerated phase Ph+ CML who:
 - are no longer benefiting from other treatments, including imatinib (Gleevec), **or**
 - have taken other treatments, including imatinib (Gleevec), and cannot tolerate them.
- Children with chronic phase Ph+ CML or accelerated phase Ph+ CML who:
 - are no longer benefiting from treatment with a tyrosine-kinase inhibitor medicine, **or**
 - have taken a tyrosine-kinase inhibitor medicine and cannot tolerate it.

It is not known if nilotinib capsules are safe and effective in children younger than 1 year of age with newly diagnosed, resistant, or intolerant Ph+ CML in chronic phase.

The long-term effects of treating children with nilotinib capsules for a long period of time are not known.

Who should not take nilotinib capsules?

Do not take if you have:

- low levels of potassium or magnesium in your blood
- long QTc syndrome

Before taking nilotinib capsules, tell your healthcare provider about all of your medical conditions, including if you:

- have heart problems
- have had a stroke or other problems due to decreased blood flow to the brain
- have problems with decreased blood flow to your legs
- have irregular heartbeat
- have QTc prolongation or a family history of it
- have liver problems
- have had pancreatitis
- have low blood levels of potassium or magnesium in your blood
- have a severe problem with lactose (milk sugar) or other sugars. Nilotinib capsules contain lactose. Most people who have mild or moderate lactose intolerance can take nilotinib capsules.
- have bleeding problems
- had a surgical procedure involving the removal of the entire stomach (total gastrectomy)
- are pregnant or plan to become pregnant. Nilotinib can harm your unborn baby. Tell your healthcare provider right away if you are pregnant, or if you become pregnant during treatment with nilotinib capsules.

In females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start treatment with nilotinib capsules.
- Use effective birth control (contraception) during treatment with nilotinib capsules and for 14 days after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if nilotinib passes into your breast milk. Do not breastfeed during treatment and for 14 days after your last dose of nilotinib capsules.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

If you need to take antacids (medicines to treat heartburn) do not take them at the same time that you take nilotinib capsules. If you take:

- **a medicine to block the amount of acid produced in the stomach (H2 blocker):** Take these medicines **about 10 hours before** you take nilotinib capsules, **or about 2 hours after** you take nilotinib capsules.
- **an antacid that contains aluminum hydroxide, magnesium hydroxide, and simethicone to reduce the amount of acid in the stomach:** Take these medicines **about 2 hours before or about 2 hours after** you take nilotinib capsules.

Nilotinib capsules can interact with many medicines and supplements and increase your chance for serious and life-threatening side effects. See **“What is the most important information I should know about nilotinib capsules?”**

How should I take nilotinib capsules?

- Take nilotinib capsules exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking nilotinib capsules unless your healthcare provider tells you.
- Nilotinib capsules are a long-term treatment.
- Your healthcare provider will tell you how many nilotinib capsules to take and when to take them.

- If your child takes nilotinib capsules, your healthcare provider will change the dose as your child grows.
- **Nilotinib capsules must be taken on an empty stomach.**
 - **Avoid eating food for at least 2 hours before the dose is taken, and**
 - **Avoid eating food for at least 1 hour after the dose is taken.**
- Swallow nilotinib capsules whole with water. If you cannot swallow nilotinib capsules whole, tell your healthcare provider.
- **If you cannot swallow nilotinib capsules whole:**
 - **Open the nilotinib capsules and sprinkle the contents in 1 teaspoon of applesauce (puréed apple).**
 - **Do not use more than 1 teaspoon of applesauce.**
 - **Only use applesauce. Do not sprinkle nilotinib capsules onto other foods.**
 - **Swallow the mixture right away (within 15 minutes).**
- Do not drink grapefruit juice, eat grapefruit, or take supplements containing grapefruit extract at any time during treatment. See **“What is the most important information I should know about nilotinib capsules?”**
- If you miss a dose, just take your next dose at your regular time. Do not take 2 doses at the same time to make up for a missed dose.
- If you take too much nilotinib capsules, call your healthcare provider or go to the nearest hospital emergency room right away. Symptoms may include vomiting and drowsiness.
- During treatment with nilotinib capsules your healthcare provider will do tests to check for side effects and to see how well nilotinib capsules are working for you. The tests will check your:
 - heart
 - blood cells (white blood cells, red blood cells, and platelets). Your blood cells should be checked every 2 weeks for the first 2 months and then monthly.
 - electrolytes (potassium, magnesium)
 - pancreas and liver function
 - bone marrow samples

Your healthcare provider may change your dose. Your healthcare provider may have you stop nilotinib capsules for some time or lower your dose if you have side effects with it.

- Your healthcare provider will monitor your CML during treatment with nilotinib capsules to see if you are in a remission. After at least 3 years of treatment with nilotinib capsules, your healthcare provider may do certain tests to determine if you continue to be in remission. Based on your test results, your healthcare provider may decide if you may be eligible to try stopping treatment with nilotinib capsules. This is called Treatment Free Remission (TFR).
- Your healthcare provider will carefully monitor your CML during and after you stop taking nilotinib capsules. Based on your test results, your healthcare provider may need to re-start your nilotinib capsules if your CML is no longer in remission.
- It is important that you are followed by your healthcare provider and undergo frequent monitoring to find out if you need to re-start your nilotinib capsules treatment because you are no longer in TFR. Follow your healthcare provider’s instructions about re-starting nilotinib capsules if you are no longer in TFR.

What are the possible side effects of nilotinib capsules?

Nilotinib capsules may cause serious side effects, including:

- See **“What is the most important information I should know about nilotinib capsules?”**

- **Low blood cell counts.** Low blood cell counts (red blood cells, white blood cells, and platelets) are common with nilotinib capsules, but can also be severe. Your healthcare provider will check your blood counts regularly during treatment with nilotinib capsules. Call your healthcare provider or get medical help right away if you develop any signs or symptoms of low blood counts including:
 - fever
 - chills or other signs of infection
 - unexplained bleeding or bruising
 - unexplained weakness
 - shortness of breath
- **Decreased blood flow to the leg, heart, or brain.** People who have recently been diagnosed with Ph+ CML and take nilotinib capsules may develop decreased blood flow to the leg, the heart, or brain. Get medical help right away if you suddenly develop any of the following symptoms:
 - chest pain or discomfort
 - numbness or weakness
 - problems walking or speaking
 - leg pain
 - your leg feels cold
 - change in the skin color of your leg
- **Pancreas inflammation (pancreatitis).** Tell your healthcare provider right away if you develop any symptoms of pancreatitis including sudden stomach area pain with nausea and vomiting.
- **Liver problems.** Nilotinib capsules can increase your risk of liver problems. People who have had liver problems in the past may be at risk for getting liver problems with nilotinib capsules. Call your healthcare provider or get medical help right away if you develop any symptoms of liver problems including:
 - stomach area (abdominal) pain
 - yellow skin and eyes
 - dark-colored urine
- **Tumor Lysis Syndrome (TLS).** TLS is caused by a fast breakdown of cancer cells. Your healthcare provider may do blood tests to check you for TLS. TLS can cause you to have:
 - **kidney failure and the need for dialysis treatment**
 - **an abnormal heart beat**
- **Bleeding problems.** Serious bleeding problems and death have happened during treatment with nilotinib capsules. Tell your healthcare provider right away if you develop any signs and symptoms of bleeding during treatment with nilotinib capsules.
- **Fluid retention.** Your body may hold too much fluid (fluid retention). Symptoms of fluid retention include shortness of breath, rapid weight gain, and swelling.
- **Abnormal growth or development in children.** Effects on growth and development have happened in children with chronic phase Ph+ CML during treatment with nilotinib capsules. Some children and adolescents may have slower than normal growth during treatment with nilotinib capsules.

The most common side effects of nilotinib capsules in adults include:

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|-------------|---|
| • nausea | • diarrhea |
| • rash | • cough |
| • headache | • constipation |
| • tiredness | • muscle and joint pain |
| • itching | • runny or stuffy nose, sneezing, sore throat |
| • vomiting | • fever |
| | • night sweats |

Sides effects in adult patients attempting treatment free remission:

If you and your healthcare provider decide that you can stop taking nilotinib capsules and try treatment free remission (TFR), you may have more muscle and bone (musculoskeletal) symptoms than before you stopped treatment. Symptoms may include:

- muscle pain
- arm and leg pain
- joint pain
- bone pain
- spine pain

Tell your healthcare provider if you have any side effect that bothers you or does not go away. These are not all of the possible side effects of nilotinib capsules.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store nilotinib capsules?

- Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].
- Safely throw away medicine that is out of date or no longer needed.

Keep nilotinib capsules and all medicines out of the reach of children.

General information about the safe and effective use of nilotinib capsules.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use nilotinib capsules for a condition for which it was not prescribed. Do not give nilotinib capsules to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about nilotinib capsules that is written for health professionals.

For more information, call Apotex Corp. at 1-800-706-5575.

What are the ingredients in nilotinib capsules?

Active ingredient: nilotinib

Inactive ingredients: colloidal silicon dioxide, crospovidone, lactose monohydrate, magnesium stearate and poloxamer. The capsule shells contain gelatin, iron oxide red (50 mg and 150 mg), iron oxide yellow and titanium dioxide.

The capsules are imprinted with edible black ink or maroon ink. The black ink is comprised of ammonium hydroxide, iron oxide black, propylene glycol and shellac. The maroon ink is comprised of ammonia solution, D&C Red #7 calcium lake, FD&C Blue #2 aluminum lake, FD&C Red # 40 aluminum lake, propylene glycol and shellac.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

APOTEX INC.

Nilotinib Capsules

50 mg, 150 mg and 200 mg

Manufactured by:
Apotex Inc.
Toronto, Ontario
Canada M9L 1T9

Manufactured for:
Apotex Corp.
Weston, Florida
USA 33326

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