

**IMPORTANT
CORRECTION
OF DRUG
INFORMATION
about
Gleevec®
(imatinib mesylate)
Tablets for Oral Use**

September 2010

Dear Patient or Caregiver:

Recently Novartis Pharmaceuticals Corporation received a Warning Letter from the US Food and Drug Administration (FDA) stating that our www.cmlalliance.com website contained misleading information about Gleevec because the website did not contain any information about the serious risks of using Gleevec.

As someone registered to receive information from the program, this letter is being sent to you at FDA's request to provide important information about these serious risks and to correct the messages and presentations that you may have seen on this website about Gleevec that the FDA considered to be misleading.

Novartis takes the FDA Warning Letter very seriously and as a result has suspended this website and all related materials. Novartis values the safety of patients and believes that providing patients access to accurate, timely and relevant disease information on rare diseases is important.

As always, your physician is the best resource for information about your treatment. For general information, you may contact our Customer Interaction Center at 1-888-NOW-NOVARTIS (1-888-669-6682). We encourage you to read the following information which includes the approved indications for CML and the Important Safety Information for Gleevec. This information is meant to fully clarify the risks associated with Gleevec use and not to announce new safety information for Gleevec. There is no change in the risk information regarding the use of Gleevec in CML.

About Gleevec:

Gleevec is indicated, among other things, for:

- Newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML) in the chronic phase.
- Patients with Philadelphia chromosome positive chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

Important Safety Information for Use of Gleevec in CML

Who should NOT take Gleevec

- Women who are or could be pregnant. Fetal harm can occur when administered to pregnant women; therefore, woman should not become pregnant, as well as be advised of the potential risk to the unborn child if Gleevec is used during pregnancy.
- Women who are breast-feeding should not take Gleevec because of the potential for serious adverse reactions in nursing infants.
- Sexually active females should use adequate birth control while taking Gleevec.
- Be sure to talk to your doctor and/or nurse about these issues before taking Gleevec.

Warnings and precautions

- Gleevec is often associated with edema (swelling) and serious fluid retention. It is important that patients be weighed and monitored regularly for signs and symptoms of serious fluid retention, or unexpected weight gain. Patients experiencing unexpected rapid weight gain should speak to their doctor about appropriate supportive care treatment. Studies have shown that edema (swelling) tended to occur more often among patients who are 65 and older or those taking higher doses of Gleevec. If you experience severe fluid retention your doctor may stop your treatment with Gleevec until the fluid retention has been managed.
- Cytopenias (reduction or lack of certain cell elements in blood circulation) such as anemia, have occurred. Your doctor will perform complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter. In most cases, your doctor will reduce or interrupt your Gleevec therapy; in rare cases, your doctor may

discontinue treatment. If the cytopenia is severe your doctor may reduce your dose or temporarily stop your treatment with Gleevec.

- Severe congestive heart failure and left ventricle dysfunction have been reported, particularly in patients with other health issues and risk factors. Patients with heart disease or risk factors will be monitored and treated for the condition.
- In patients with hypereosinophilic syndrome (a condition with increased eosinophils which are a type of white blood cell) and heart involvement, cases of heart disease (cardiogenic shock/left ventricular dysfunction) have been associated with the initiation of Gleevec therapy. Speak to your doctor regarding appropriate supportive care or discontinuing Gleevec.
- Severe liver problems (hepatotoxicity) may occur. Your doctor will check your liver function before beginning treatment and continue to monitor liver function as needed. If you experience severe liver problems your doctor may stop your treatment with Gleevec until the liver problem has been managed.
- Bleeding may occur. Severe gastrointestinal (GI) bleeding has been reported in patients with newly diagnosed Ph+CML.
- GI perforation (small holes or tears in the walls of the stomach or intestine), in some cases fatal, has been reported.
- Skin reactions, such as fluid filled blisters, have been reported with the use of Gleevec.
- Clinical cases of hypothyroidism (reduction in thyroid hormones) have been reported in patients taking levothyroxine replacement during treatment with Gleevec. Your doctor should closely monitor your thyroid hormone levels.
- Long-term use may result in potential liver, kidney, and/or heart toxicities; immune system suppression may also result from long-term use.
- Gleevec can cause fetal harm when administered to a pregnant woman. Women should be aware of the potential harm to the fetus. Be sure to inform your doctor if you are or think you may be pregnant. You should not breast-feed while taking Gleevec.

The following serious side effects have been reported in patients taking Gleevec:

- Severe fluid retention, which can cause swelling around the eyes or swelling of the lower legs, lungs, and heart: fatal in rare cases
- Increased pressure in the heart or brain; fatal in rare cases
- Low levels of certain blood cells
- Heart failure/cardiogenic shock
- Liver problems
- Skin blistering
- Hemorrhage (abnormal bleeding)

- Low levels of thyroid hormone

Your doctor will check you closely for any side effects to stop more serious complications from occurring. Patients with heart disease or risk factors for heart failure should also be monitored carefully.

- Gleevec is sometimes associated with stomach or intestinal irritation. Gleevec should be taken with food and a large glass of water to minimize this problem. There have been rare reports, including deaths, of stomach or intestinal perforation (a small hole or tear).

Common side effects of Gleevec

Almost all patients treated with Gleevec experience side effects at some time. Most side effects are mild to moderate in severity. Some common side effects you may experience include:

- Fluid retention
- Muscle cramps or pain and bone pain
- Abdominal pain
- Vomiting
- Diarrhea
- Decreased hemoglobin
- Nausea
- Fatigue
- Rash
- Anorexia (loss of appetite)

If you are experiencing any of the above mentioned side effects please be sure to speak with your doctor immediately.

Some side effects can be managed with the help of other medicines and advice from your doctor, while others may require stopping Gleevec therapy for a while or changing the dose. However, in some cases, Gleevec therapy may need to be discontinued.

- Take Gleevec exactly as prescribed. Do not change your dose or stop taking Gleevec unless you are told to do so by your doctor. If you miss a dose, take your dose as soon as possible, unless it is almost time for your next dose. In this case, your missed dose should not be taken. A double dose should not be taken to make up for any missed dose. You should take Gleevec with a meal and a large glass of water.
- Do not take any other medications without talking to your doctor or pharmacist first, including over-the-counter medications such as Tylenol[®] (acetaminophen); herbal products (St. John's wort, Hypericum perforatum); Coumadin[®] (warfarin sodium); rifampin; erythromycin; metoprolol; ketoconazole, and Dilantin[®] (phenytoin). Taking these with Gleevec may affect how they work, or affect how Gleevec works.

- You should also tell your doctor if you are taking or plan to take iron supplements. Patients should also avoid grapefruit juice and other foods that may affect how Gleevec works.
- Tell your doctor if you experience side effects during therapy with Gleevec, including fever, shortness of breath, blood in your stools, jaundice (yellowing of the skin and/or eyes), sudden weight gain, symptoms of heart failure, or if you have a history of heart disease or risk factors for heart disease.
- After the approval of Gleevec, the following adverse events have been reported in patients treated with Gleevec: compression of the heart due to increased fluid, swelling of the brain, GI perforation (holes in the stomach or intestine), and sudden lung failure. These events, including some fatalities, may or may not have been drug related.

Tylenol (acetaminophen) is a registered trademark of McNeil Consumer & Specialty Pharmaceuticals a division of McNeil PPC, Inc. Coumadin (warfarin sodium) is a registered trademark of Bristol-Myers Squibb Company. Dilantin (phenytoin) is a registered trademark of Parke-Davis, a division of Pfizer Inc.

Please see enclosed full prescribing information for Gleevec (imatinib mesylate) Tablets.

Sincerely,



John Hohneker, MD
Senior Vice President, US Clinical Development & Medical Affairs – Oncology