

APPROVAL WITH CONDITIONS OF ^{Pr}GLEEVEC* (imatinib mesylate) 100 MG AND 400 MG TABLETS FOR THE TREATMENT OF PEDIATRIC PATIENTS WITH NEWLY DIAGNOSED, PHILADELPHIA CHROMOSOME-POSITIVE, CHRONIC MYELOID LEUKEMIA (CML) IN CHRONIC PHASE

FACT SHEET

What is GLEEVEC*?

GLEEVEC* is a drug containing an active ingredient called imatinib mesylate and is supplied as 100 mg and 400 mg tablets. GLEEVEC* belongs to a class of anti-cancer agents called Tyrosine Kinase Inhibitors.

Health Canada has approved GLEEVEC* with conditions, under the Notice of Compliance with Conditions (NOC/c) policy for the treatment of pediatric patients with newly diagnosed, Philadelphia chromosome-positive, chronic myeloid leukemia (CML) in chronic phase. This authorization reflects the promising nature of the clinical evidence and safety which must be verified and/or extended with further studies. Products, approved under Health Canada's NOC/c policy, have demonstrated promising benefit, are of high quality, and possess an acceptable safety profile based on a benefit/risk assessment.

What is GLEEVEC* used for?

This current conditional approval for GLEEVEC* is for pediatric patients with newly diagnosed, Philadelphia chromosome-positive, CML in chronic phase.

Previous Conditional approvals for GLEEVEC* are for adult patients with:

- a. Newly diagnosed, Philadelphia chromosome-positive, CML in chronic phase.
- b. Unresectable and/or metastatic gastrointestinal stromal tumors (GIST).

Previous approvals for GLEEVEC* are for adult patients with:

- a. CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.
- b. Newly diagnosed, Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL, as a single agent, for induction phase only).
- c. Relapsed (return of signs and symptoms of the disease) or refractory (cancer cells do not decrease even though treatment is given) Ph+ALL.

What is Chronic Myeloid Leukemia (CML)?

Leukemia is a type of cancer in which cancer cells are found in the blood and the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called "blasts" that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets.

Chronic Myeloid Leukemia is a type of leukemia where the bone marrow produces an excessive number of abnormal white blood cells named myeloid cells. These abnormal cells suppress the production of normal white blood cells, which act to protect the body against infection.

What are the symptoms of CML?

In the early stage, most of patients may have no symptoms of cancer and may only be diagnosed through routine blood tests that show an increase in white blood cells. In later stages, patients experience infections, bleeding, fever, chills, sweats, weakness, fatigue and headaches.

What are the phases of CML?

The disease is called chronic myeloid leukemia as it can progress very slowly through 3 different phases. These different phases are the stages used to plan treatment.

The three phases of CML are:

- Chronic phase: This phase may last for about 4 to 5 years. Initially, patients in this phase usually have minor symptoms and their cancer is usually detected by routine blood tests. Traditionally, most patients have received interferon therapy alone or with other drugs. Patients can also be treated with bone marrow transplants.
- Accelerated phase: This phase may last from 6 to 18 months. The white blood cell count increases and the disease is harder to control with conventional treatments.
- Blast crisis: This is the final phase of the disease and may last about 3 to 6 months.

How does GLEEVEC* work?

GLEEVEC* works by inhibiting the growth of abnormal white blood cells by blocking the activity of a protein involved in the development of CML. GLEEVEC* specifically targets the activity of certain enzymes called tyrosine kinases that play an important role within certain cancer cells.

What are the advantages of GLEEVEC* over other therapies?

Treatment options for pediatric patients with newly diagnosed, Philadelphia chromosome-positive CML in chronic phase are limited. The available treatments generally include chemotherapy (using drugs to kill cancer cells) and immunotherapy (using drugs that stimulate the body's own immune system to kill cancer cells). Sometimes a combination of immunotherapy and chemotherapy may be used. The only known cure for CML is bone marrow transplantation, but is a treatment associated with many risks and is not an option for all patients. GLEEVEC* represents a potential benefit for the treatment of pediatric patients with chronic myeloid leukemia, a serious, life-threatening condition with few treatment options. The clinical results from pediatric patients treated with GLEEVEC* showed hematological and cytogenetic responses with a favorable benefit/risk ratio.

What do patients need to know about using GLEEVEC*?

GLEEVEC* should only be prescribed by a doctor who is experienced in the use of anti-cancer drugs. Possible serious side effects with GLEEVEC* include:

- Serious heart failure and decrease in the amount of blood pumped by the heart;
- Serious bleeding;
- Fluid retention.

Before taking GLEEVEC*, patients should tell their doctor or pharmacist if the following applies to them:

- have or ever have had a liver problem.

There is no experience with the use of GLEEVEC* in children under 2 years of age.

Can GLEEVEC* be taken with other drugs?

GLEEVEC* may interact with other medications, including over-the-counter medications (medications that can be purchased without a prescription, e.g. acetaminophen) or herbal products (e.g. St-John's Wort). Patients should inform their doctor or pharmacist about all drugs that they are taking. GLEEVEC* may increase or decrease blood levels of certain drugs, which may increase side effects or decrease the effectiveness of treatment.

During treatment with GLEEVEC*, patients should not start taking a new medicine before talking with their doctor or pharmacist.

What are the side effects and how serious are they?

Most patients taking GLEEVEC* can have some side effects which are usually mild to moderate. Most side effects can be managed through additional medications, dose adjustment, or other measures.

Nausea, vomiting were the most commonly reported individual adverse events with an incidence similar to that seen in adult patients. Although most patients experienced side effects at some time during the studies, the incidence of Grade 3/4 adverse events was low. Higher frequencies of hypocalcemia (low blood calcium), hyperglycemia (high blood sugar), hypoglycemia (low blood sugar), hypophosphatemia (less than normal blood level of phosphates), hypoalbuminemia (less than normal blood level of albumin protein) and hyponatremia (abnormally low concentration of sodium in blood) were observed in pediatric patients compared to adult patients.

Who should not be treated with GLEEVEC*?

GLEEVEC* should not be taken by patients with a known allergy (hypersensitivity) to the active ingredient (imatinib mesylate) or to any of the other ingredients of GLEEVEC*.

How is GLEEVEC* taken?

GLEEVEC* should only be prescribed by a doctor who is experienced in the use of anti-cancer drugs.

GLEEVEC* should be taken by mouth during a meal and with a large glass of water. Avoid grapefruit juice while being treated with GLEEVEC*. The tablets should be swallowed whole. The 400 mg tablet can be broken in half.

For pediatric patients that cannot swallow the tablet(s), the tablets can be placed in water or apple juice, use 200 mL for 400 mg tablet or 50 mL for 100 mg tablet. Stir with a spoon to completely disintegrate the tablet(s), then drink the whole content immediately. Rinse the container with water or apple juice and drink it to make sure no trace of disintegrated tablet(s) is left.

What else should patients know about taking GLEEVEC*?

Store GLEEVEC* at room temperature (15- 30°C). Protect tablets from moisture.

Where can I learn more about GLEEVEC*?

If you have any questions concerning GLEEVEC*, kindly contact our Medical Information Department at 1-800-363-8883.

Please consult your doctor or pharmacist with any questions or concerns you may have regarding your individual condition.

This document including the GLEEVEC* Prescribing Information and Patient Information can be found on Novartis' Website (<http://www.novartis.ca>).

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