

AUTHORIZATION WITH CONDITIONS OF ^{Pr}GLEEVEC* (imatinib mesylate) 100 MG AND 400 MG TABLETS FOR THE ADJUVANT TREATMENT OF ADULT PATIENTS WHO ARE AT INTERMEDIATE TO HIGH RISK OF RELAPSE FOLLOWING COMPLETE RESECTION OF KIT (CD117) POSITIVE GIST

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 authorized GLEEVEC* with conditions, under the Notice of Compliance with Conditions (NOC/c) Policy for the adjuvant treatment of adult patients who are at intermediate to high risk of relapse following complete resection of Kit (CD117) positive gastrointestinal stromal tumors (GIST). This authorization reflects the promising nature of the clinical evidence and safety which must be verified and/or extended with further studies. Products authorized 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 the adjuvant treatment of adult patients who are at intermediate to high risk of relapse following complete resection (completely removed) of Kit (CD117) positive gastrointestinal stromal tumors (GIST).

Previous Conditional approvals for GLEEVEC* are for patients with:

- Newly diagnosed, Philadelphia chromosome-positive, chronic myeloid leukemia (CML) in chronic phase in adult and pediatric patients.
- Kit (CD117) positive unresectable (non operable) and/or metastatic (has spread to other parts of the body) malignant gastrointestinal stromal tumors (GIST) in adult patients.

Previous non-conditional approvals for GLEEVEC* are for adult patients with:

- CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.
- Newly diagnosed, Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL, as a single agent, for induction phase only).
- Relapsed (return of signs and symptoms of the disease) or refractory (cancer cells do not decrease even though treatment is given) Ph+ALL.
- Myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements (group of blood diseases in which some blood cells start growing out of control).
- Aggressive sub-types of systemic mastocytosis (ASM¹ and SM-AHNMD¹) without the D816V c-Kit mutation. If c-Kit mutational status in patients with ASM or SM-AHNMD¹ is not known or unavailable, treatment with GLEEVEC* may be considered if there is no satisfactory response to other therapies (ASM is a cancer in which certain blood cells (named "mast" cells) start growing out of control).

¹ ASM: Aggressive systemic mastocytosis; SM-AHNMD: Systemic mastocytosis with an associated clonal hematological non-mast-cell disorder.

- Advanced hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) with FIP1L1-PDGFR α rearrangement (HES/CEL are blood diseases in which some blood cells (named “eosinophils”) start growing out of control).
- Unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP: cancer of the tissue beneath the skin in which some cells start growing out of control).

What is Gastrointestinal Stromal Tumors (GIST)?

GIST is a type of cancer of the Gastrointestinal (GI) system (stomach and the bowels) that arises from uncontrolled cell growth of the supporting tissue of these organs. A GIST may occur anywhere along the GI system.

What are the symptoms of GIST?

GISTs are rare tumors that arise in the wall of the gastrointestinal tract. These tumors may not cause any symptoms unless they are in a certain location or grow to a certain size. Because of the nonspecific symptoms, a delayed diagnosis is generally associated with GISTs, with an average duration of symptoms of 6 months. The most frequent symptoms of GISTs are abdominal discomfort or pain and bleeding into the intestinal tract, a palpable mass and mild abdominal pain.

How does GLEEVEC* work?

GLEEVEC* is a small molecule that specifically targets the activity of several tumor proteins (enzymes) called tyrosine kinases that play an important role within certain cancer cells. In GISTs, an abnormal Kit protein sends out a constant signal that tells the cells to keep growing resulting in tumor formation; GLEEVEC* works by blocking, or turning off, the signal from the Kit protein, so the cancerous cells stop growing out of control.

What is adjuvant therapy? And how does GLEEVEC* work as adjuvant therapy in GIST?

Adjuvant therapy refers to additional treatment given after a main mode of therapy. Adjuvant therapy with GLEEVEC* in GIST refers to treatment following complete removal of GIST through surgery (the primary or initial treatment) in order to reduce the risk of recurrence (the risk of the tumor coming back again). Even when an operation has gone well and the tumor has been removed completely, there is still a risk that the GIST will come back.

What are the advantages of GLEEVEC* over other therapy?

The most common treatment used for GIST is surgery, however when surgery successfully removes a GIST, some clinical studies showed that the tumor was still found to come back in one out of every two patients. The results of a recent Phase III clinical study (ACOSOG-Z9001) compared GLEEVEC* with placebo (a dummy treatment) in 713 patients whose cancer had been removed with surgery. This study measured how long the patients lived without their cancer coming back. In these patients with GIST whose tumor had been removed with surgery, the patients taking GLEEVEC* lived for longer without their cancer coming back than those patients taking placebo.

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; Rhabdomyolysis has been rarely observed; serious bleeding; fluid retention; liver failure (in some cases, fatal); gastrointestinal perforation (a hole through the wall of the stomach, or small intestine, or large bowel) in some cases, fatal.

Before you (or your child) take GLEEVEC talk to your doctor or pharmacist:*

- if you have or ever have had a liver, kidney or heart problem,
- if you are or plan to get pregnant. Women who might get pregnant are advised to use an effective method of birth control while taking GLEEVEC*,
- if you are a male patient and are concerned about your fertility (ability to father a child),
- if you are breast-feeding, GLEEVEC* can get to the breast milk and may cause harm to your child,
- if you had your thyroid removed and are receiving treatment with a thyroid hormone such as levothyroxine.

While taking GLEEVEC*, if you feel dizzy or if you have blurred vision, do not drive a vehicle or operate any tools or machinery.

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.

GLEEVEC* therapy was generally well tolerated by most GIST patients during the GIST adjuvant setting study (ACOSO-Z9001).

The most frequently reported adverse reactions were similar to those reported in other clinical studies in other patient populations and include diarrhea, fatigue, nausea, edema (fluid retention), decreased hemoglobin (low levels of the red blood cells), rash, vomiting and abdominal pain. No new adverse reactions were reported in the adjuvant GIST treatment setting that had not been previously reported in other patient populations including patients with unresectable (non-operable) and/or malignant metastatic (has spread to other parts of the body) GIST.

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.

The recommended dose of GLEEVEC* for the adjuvant treatment of adult patients following complete resection of GIST is 400 mg/day. In the adjuvant setting, the optimal treatment duration with GLEEVEC* is not known.

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.

Treatment should be continued as long as you continue to benefit from it.

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*, 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>).

GIST ALLIANCE Program:

Novartis has created the GIST ALLIANCE Program, which is a patient support program (PSP) designed to provide patient health information and reimbursement assistance to patients who have been prescribed GLEEVEC* as indicated in the Product Monograph. This specialized PSP represents a service offered at no cost to the patient and is fully confidential. For more information please call toll free 1-866-996-GIST (1-866-996-4478).

*GLEEVEC is a registered trademark.