

Important Safety Information on GLEEVEC*(imatinib mesylate)



September 21, 2006

SUBJECT: Recent safety information regarding reports of heart problems in patients using GLEEVEC* (imatinib mesylate)

After discussions with Health Canada, Novartis is advising Canadians about the risk for decreased heart function in patients using GLEEVEC* (imatinib mesylate).

GLEEVEC* (imatinib mesylate) is used to treat adult patients who have a specific type of blood cancer called Chronic Myeloid Leukemia (CML) and a specific type of cancer of the stomach and bowels known as gastrointestinal stromal tumour (GIST).

A recently published article in Nature Medicine¹ reported that ten patients who received treatment with GLEEVEC* later developed decreased heart function and congestive heart failure. Congestive heart failure occurs when the pumping ability of the heart becomes weaker than normal. Several of the patients who were affected also had other medical conditions, including high blood pressure, diabetes, previous history of heart disease, or had received other drugs which might have contributed to their increased risk for congestive heart failure.

Information from animal studies has also suggested that there may be a possible relationship between GLEEVEC* and decreased heart function. This requires further investigation.

While Novartis is further investigating this possible relationship, we recommend that:

- **If you are using GLEEVEC*, and have high blood pressure, diabetes or a past history of heart disease, you should discuss the risks for heart failure with your physician, who will want to monitor your heart function more closely.**
- **If you are using GLEEVEC* and have symptoms suggestive of heart failure, such as leg swelling, chest pain, or shortness of breath, you should see your doctor immediately.**
- **You should not stop taking GLEEVEC* without prior discussion with your doctor.**
- **Your doctor may want to consider assessing your heart function before starting GLEEVEC*.**

Although, “cardiac failure” is already listed in the Canadian GLEEVEC* prescribing information as an ‘infrequent’ event (0.1-1% chance), Novartis will be working with Health Canada to include any new safety information in the Canadian GLEEVEC* prescribing information.

Novartis Pharmaceuticals Canada Inc. has also issued a letter to health professionals informing them of the above-mentioned updated safety information. A copy of the Health Care Professional letter and this communication are available on the Health Canada website (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/index_e.html).

If you have questions about your current treatment, please contact your doctor or pharmacist.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health products. If you have had a serious or unexpected reaction to GLEEVEC* you may notify either Novartis Pharmaceuticals Canada Inc. or Health Canada as follows:

Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, (QC) H9S 1A9
Phone: 1-800-363-8883

Any suspected adverse reaction can also be reported to:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or
Fax: (613) 957-0335
To report an Adverse Reaction (AR), consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789
cadrmpp@hc-sc.gc.ca

The AR Reporting Form (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.html) and the AR Guidelines (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html) can be found on the Therapeutic Products Directorate web site or in The Canadian Compendium of Pharmaceuticals and Specialties.

For media inquiries please contact Jason Jacobs at (514) 633-7872.

Reference:

1. Cardiotoxicity of the cancer therapeutic agent imatinib mesylate. Kerkela R, Grazette L, Yacobi R et al. *Nature Medicine*; advance online publication July 23rd, 2006.

^{Pr}GLEEVEC* is a registered trademark.