Health Canada Endorsed Important Safety Information on
PrTASIGNA* (nilotinib)

NOVARTIS

April 9, 2013

Dear Healthcare Professional:

Subject: **Updated information regarding the possible risk of developing atherosclerosis-related diseases with the use of TASIGNA* (nilotinib)**

Novartis Pharmaceuticals Canada Inc. ("Novartis"), in collaboration with Health Canada, would like to inform you of important information regarding reports of atherosclerosis-related diseases in patients treated with TASIGNA* (nilotinib).

TASIGNA* belongs to the pharmacological class of protein-tyrosine kinase inhibitors. It has received conditional marketing authorization for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML) in chronic phase. TASIGNA* has also received non-conditional marketing authorization for the treatment of adult patients with Ph+ chronic and accelerated phase CML who are resistant to or intolerant of at least one prior therapy, including imatinib.

- Cases of atherosclerosis-related diseases have been reported during clinical trials and post marketing experience with the use of TASIGNA*.
- Patients should be monitored for signs of atherosclerosis-related diseases during treatment with TASIGNA*. Monitoring of lipid and glucose profiles should also be performed before and frequently during treatment with TASIGNA* and as clinically indicated.
- Updated information regarding Tasigna safety profile has been added to the product monograph under the Warnings and Precautions, common clinical adverse drug reactions and post-marketing adverse reactions sections.

In a Phase III study (A2303) in newly diagnosed Ph+ CML patients, atherosclerosis-related diseases such as peripheral arterial occlusive disease, femoral artery stenosis, coronary artery stenosis, carotid artery stenosis, and cerebrovascular accident were reported in patients taking TASIGNA* (5.0% for TASIGNA* 300 mg BID and 6.1% for TASIGNA* 400 mg BID). A review of the Novartis global safety database search (between January 1st, 2005 and January 31, 2013) identified a total of 277 cases of atherosclerosis, of which 14 were Canadian cases. The cumulative patient exposure since the first launch of TASIGNA* in 2007 is estimated to be approximately 39,299 patient-years.

The Canadian Product Monograph for TASIGNA* (nilotinib) has recently been revised to include these new recommendations. A copy of most up-to-date TASIGNA* (nilotinib) Product Monograph can be found at: http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp. It is recommended that health care professionals follow current clinical guidelines for the diagnosis and management of patients with signs and symptoms of events due to atherosclerosis.

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 product treatments. Any case of serious atherosclerosis or other serious or unexpected adverse reactions in patients receiving TASIGNA* should be reported to Novartis or Health Canada. Novartis will continue to monitor atherosclerosis-related events and appreciates your collaboration in ensuring the monitoring of patients and continued reporting of any potential adverse drug reactions.

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

To correct your mailing address or fax number, contact Novartis Pharmaceuticals Canada Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

For other health product inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Should you have any questions or require additional information regarding the use of TASIGNA*, please contact Novartis Pharmaceuticals Canada Inc., Medical Information Department at 1-800-363-8883.

Sincerely,

Jean Godin, M.D.
Chief Scientific Officer and Vice-President Clinical and Regulatory Affairs

*TASIGNA is a registered trademark.