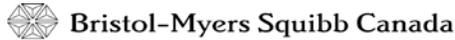


**Health Canada Endorsed Important Safety Information on  
SPRYCEL\* (dasatinib) and Pulmonary Arterial Hypertension (PAH)**



26 August 2011

**Subject: Pulmonary Arterial Hypertension (PAH) reported with SPRYCEL\* (dasatinib)**

Dear Healthcare Professional:

Bristol-Myers Squibb Canada (BMS), in collaboration with Health Canada, would like to inform you of important new safety information regarding reports of serious pulmonary arterial hypertension (PAH) in patients treated with SPRYCEL\* (dasatinib).

SPRYCEL\* (dasatinib) belongs to the pharmacological class of protein-tyrosine kinase inhibitors. It has received marketing authorization (with conditions) for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase. SPRYCEL\* (dasatinib) has also received marketing authorization for the treatment of adult patients with Ph+ chronic, accelerated, or blast phase CML and adult patients with Ph+ acute lymphoblastic leukemia (ALL) who are resistant or intolerant to previous therapies.

- A total of 60 serious pulmonary hypertension (PH) cases have been reported worldwide, between June 2006 and June 2011, including 12 cases of pulmonary arterial hypertension (PAH) confirmed by right heart catheterization, in association with SPRYCEL\* treatment. No Canadian cases of PH or PAH have been reported during this time period.
- Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease before initiating SPRYCEL\* therapy.
- Patients who develop symptoms suggestive of PAH such as dyspnea and fatigue after initiation of treatment with SPRYCEL\* should be evaluated for more common etiologies and treatment should be withheld during evaluation, if symptoms are severe.
- The diagnosis of PAH should be considered if no alternative diagnosis can be found.
- Improvements in hemodynamic and clinical parameters have been observed in patients with PAH following cessation of SPRYCEL\* therapy.
- SPRYCEL\* should be permanently discontinued if the diagnosis of PAH is confirmed.

Pulmonary Arterial Hypertension (PAH), a subtype of PH, is a rare, severe and progressive disease with no apparent cause, characterized by vascular proliferation and remodelling of the small pulmonary arteries, leading to increased pulmonary artery

pressure and vascular resistance. PAH is diagnosed by right heart catheterization and defined by haemodynamic criteria including a mean pulmonary arterial pressure of 25 mmHg or higher and pulmonary capillary wedge pressure of 15 mmHg or lower (pre-capillary PH in the absence of post-capillary PH).

A review of the reports submitted between June 2006 and June 2011 to the Bristol-Myers Squibb global pharmacovigilance database identified a total of 60 cases of PH reported by healthcare professionals. Of these 60 cases, 36 cases were reported as pulmonary hypertension and 24 cases as pulmonary arterial hypertension (PAH) including a subset of 12 cases of PAH confirmed by right-heart catheterization. None of these cases were from Canada. Based on the total sales volume for the same period, the cumulative worldwide exposure to SPRYCEL\* (dasatinib) is estimated to be 32, 882 patients.

Some patients diagnosed with PAH during SPRYCEL\* (dasatinib) therapy were taking concomitant medications or had co-morbidities in addition to the underlying malignancy.

The Canadian Product Monograph for SPRYCEL\* (dasatinib) has recently been revised to include this important new safety finding. A copy of most up-to-date Product Monograph can be found at: <http://webprod3.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>

It is recommended that healthcare professionals follow current clinical guidelines for the diagnosis and management of patients with signs and symptoms suggestive of PAH.

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 PH or PAH and other serious or unexpected adverse reactions in patients receiving SPRYCEL\* (dasatinib) should be reported to BMS Canada or Health Canada at the following addresses:

Any suspected adverse drug reactions can be reported to:

Bristol-Myers Squibb Canada  
2344 Alfred-Nobel, suite 300  
Montréal, Canada  
H4S 0A4  
Tel: 866-463-6267

Any suspected adverse reaction can also be reported to:

Canada Vigilance Program  
Marketed Health Products Directorate  
HEALTH CANADA  
Address Locator: 0701D  
Ottawa, Ontario, K1A 0K9  
Tel: 613-957-0337 or Fax: 613-957-0335

To report an Adverse Reaction, consumers and health professionals may call toll free:  
Tel: 866-234-2345, Fax: 866-678-6789,  
CanadaVigilance@hc-sc.gc.ca

You can also report any suspected adverse reactions associated with the use of health products to the Health Canada Vigilance Program by one of the following ways:

- Report online at: [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)
- Call toll-free at: 1-866-234-2345 or call 613-957-0337
- Complete a Reporting Form and Fax toll-free to: 1-866-678-6789,
- Email: [CanadaVigilance@hc-sc.gc.ca](mailto:CanadaVigilance@hc-sc.gc.ca)
- Mail to:  
Canada Vigilance Program  
Health Canada  
Postal Locator 0701E  
Ottawa, Ontario K1A 0K9  
Tel: 613-957-0337 or Fax: 613-957-0335

The Canada Vigilance Adverse Reaction Reporting Form, postage paid labels, and the Adverse Reaction Guidelines can be found on the MedEffect™ Health Canada Web site or in the *Canadian Compendium of Pharmaceuticals and Specialties*:

[http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei\\_form-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_form-eng.php)

[http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/\\_fs-if/2009-ar-ei-guide-prof/index-eng.php](http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-prof/index-eng.php)

**For other health product inquiries related to this communication, please contact Health Canada at:**

Marketed Health Products Directorate (MHPD)  
E-mail: [mhpd\\_dpdc@hc-sc.gc.ca](mailto:mhpd_dpdc@hc-sc.gc.ca)  
Telephone: 613-954-6522  
Fax: 613-952-7738

Should you have any medical enquiries regarding SPRYCEL\* (dasatinib), please contact our Medical Information Department at 866-463-6267.

Sincerely,

***original signed by***

H. Mitchell Shulman, MDCM, FRCPC, CSPQ  
Vice-President, Medical

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