



**DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION ON
THE ASSOCIATION OF SPRYCEL[®] (DASATINIB) WITH
PULMONARY ARTERIAL HYPERTENSION (PAH)**

Date: 27/01/2013

Dear Healthcare Professional:

Bristol-Myers Squibb (BMS), in agreement with Saudi Food and Drug Authority (SFDA) would like to provide you with important safety information about the potential risk of pre-capillary pulmonary arterial hypertension (PAH) associated with dasatinib (Sprycel[®]).

Considerations for health care professionals

A review of the BMS pharmacovigilance database has identified cases of PAH in association with Sprycel treatment. Please follow the advice below to monitor patients for the development of PAH:

- Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease before starting dasatinib.
- An echocardiography should be performed at treatment initiation in every patient presenting symptoms of cardiac disease and considered in patients with risk factor for cardiac or pulmonary disease.
- Patients who develop dyspnea and fatigue after initiation of dasatinib should be evaluated for common etiologies (e.g. pleural effusion, pulmonary edema, anemia, lung infiltration).
- During this evaluation, guidelines for non-hematologic adverse reactions should be followed. If the adverse reaction is severe, treatment must be withheld until the event has resolved or improved.
- If no alternative diagnosis is found, a diagnosis of PAH should be considered. The diagnostic approach for PAH should follow standard practice guidelines.^{1,2}

- ° If PAH is confirmed, dasatinib should be permanently discontinued. Follow-up of patients diagnosed with PAH should follow standard practice guidelines.^{1,2}

Further information on the safety concern

While a recent review of the BMS pharmacovigilance database between June 2006 and June 2011 retrieved 60 cases of pulmonary hypertension (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. PAH was reported after initiation of dasatinib therapy, including after more than 1 year of treatment. Patients with PAH reported during dasatinib treatment were commonly taking concomitant medications or had co-morbidities in addition to the underlying malignancy.

Improvements in hemodynamic and clinical parameters have been observed in some patients with PAH after stopping dasatinib therapy.

In consideration of the above, the Package Insert for Sprycel® (dasatinib) film-coated tablets has been updated in section 5 **【Warning and Precautions】** and section 6 **【Adverse Reactions】**.³

Further information on recommendations to healthcare professionals

Healthcare professionals are recommended to follow current standard published clinical consensus guidelines for the diagnosis and management of patients with signs and symptoms suggestive of PAH.¹⁻⁴

For management of PAH in patients receiving dasatinib therapy, please follow the information provided in section 5 **【Warning and Precautions】** of the Package Insert.⁵

Communication information

Bristol-Myers Squibb will Continue to monitor the safety of Sprycel® and notify SFDA of any serious adverse events for evaluation.

You can assist us in monitoring the safety of Sprycel® by reporting adverse reaction to us
Fax: (+966-1-4169085) or by email BMS safety mail (Khaled.khaled@bms.com)

Or to the National Pharmacovigilance and Drug Safety Center at fax: +966-1-2057662 or by E-mail to: npc.drug@sfd.gov.sa

Should you have any questions regarding the use of Sprycel[®], please contact Bristol-Myers Squibb Medical Information at 01 460 1534 (9:00 -17:00, Sunday to Thursday).

Yours sincerely,



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Please send correspondence to:
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REFERENCES

- 1 Galiè N, et al. *Eur Heart J.* 2009;30(20):2493-537.
- 2 Galiè N, et al. *Eur Respir J.* 2009;34(6):1219-63.
- 3McLaughlin VV, et al. *J Am Coll Cardiol.* 2009;53(17):1573-619.
- 4 McLaughlin VV, et al. *Circulation.* 2009;119(16):2250-94.
- 5 SPRYCEL (dasatinib) Dasatinib Tablets Package Insert 1284903A0 Rev. October 2011- Approved by SFDA on DD/MM/2012. "Awaiting Saudi FDA Approval, date of approval will be provided"