



11 Dec 2016

**Direct Healthcare Professional Communication
on the association of BCR-ABL targeting Tyrosine Kinase inhibitors (TKIs)
including SPRYCEL® (dasatinib) with the risk of hepatitis B virus
reactivation**

Dear Healthcare Professional,

Bristol Myers Squibb in agreement with Saudi Food and Drug Authority (SFDA) would like to inform you about important new safety information for dasatinib.

Summary:

BCR-ABL TKIs have been associated with hepatitis B virus (HBV) reactivation, including individual case reports for Sprycel®. In some instances, HBV reactivation occurring in conjunction with other BCR-ABL TKIs resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome.

Recommendations:

- **Screening for HBV should be considered in accordance with published guidelines before starting therapy with Sprycel®. Consultation with a physician with expertise in the treatment of HBV is recommended for patients who test positive for HBV serology.**
- **Patients who are carriers of HBV and require treatment with BCR-ABL TKIs should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months following termination of therapy. In patients who develop reactivation of HBV while receiving Sprycel, prompt consultation with a physician with expertise in the treatment of HBV is recommended.**

Background on the safety concern and recommendations

A recent cumulative review of data from clinical trials and post-marketing experience has shown that HBV reactivation can occur in chronic HBV carriers, after they received BCR-ABL TKIs. Some of these cases included acute hepatic failure or fulminant hepatitis leading to liver transplantation or fatal outcome. These case reports indicate that HBV reactivation may occur at any time during TKI treatment. Some of these patients had a documented history of HBV, for other cases, the serologic status at baseline was not known. HBV reactivation is considered a class-effect of BCR-ABL TKIs, although the mechanism and the frequency of HBV reactivation during exposure is not known at this time.

Further information on recommendations to healthcare professionals

SPRYCEL (dasatinib) is an oral tyrosine kinase inhibitor indicated for the treatment of adult patients with:

- newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in the chronic phase.

- chronic, accelerated or myeloid or lymphoid blast Ph+ CML with resistance or intolerance to prior therapy including imatinib.
- Ph+ acute lymphoblastic leukaemia (ALL) with resistance or intolerance to prior therapy.

Reporting suspected adverse events

Please report suspected adverse reactions associated with any medicinal products to the:

National Pharmacovigilance and Drug Safety Center (NPC):

- Toll free number: 8002490000
- Fax: +966-11-2057662
- E-mail: npc.drug@sFDA.gov.sa

Bristol Myers Squibb Please contact:

- Pharmacovigilance Department in Bristol-Myers Squibb, Saudi Arabia:
At: Safety_saudiArabia@bms.com or call +00966 11 219 9780

Company contact Information

Should you have any questions or require additional information regarding the use of SPRYCEL® (dasatinib), please contact: Bristol-Myers Squibb Medical Information at 800 844 7710 or email Medinfo.saudiArabia@bms.com

Yours sincerely,



Dr. Kamel Ismail
Medical Director-Saudi Arabia

