23rd March 2016

Direct Healthcare Professional Communication

BCR-ABL tyrosine kinase inhibitors (imatinib, dasatinib, nilotinib, bosutinib, ponatinib) –Need to screen patients for hepatitis B virus before treatment due to risk of hepatitis B reactivation

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and Health Products Regulatory Authority (HPRA), Novartis, Pfizer, BMS and Ariad would like to inform you of the following:

Summary:

Cases of Reactivation of hepatitis B virus (HBV) have occurred in patients who are chronic carriers of HBV after they received BCR-ABL tyrosine kinase inhibitors (TKIs). Some cases of HBV reactivation resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome.

Recommendations:

- **Patients should be tested for HBV infection before initiating treatment with BCR-ABL TKIs.**
- **Consult experts in liver disease and in the treatment of HBV before treatment in patients with positive HBV serology (including those with active disease) is initiated and for patients who test positive for HBV infection during treatment.**
- **Closely monitor patients who are carriers of HBV requiring treatment with BCR-ABL TKIs for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.**

Background on the safety concern and recommendations

A recent cumulative review of data from clinical trials and postmarketing 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 hepatitis B,

for other cases, the serologic status at baseline was not known. An increase in viral load or positive serology was diagnosed upon HBV reactivation.

HBV reactivation is considered a class-effect of BCR-ABL TKI, although the mechanism and the frequency of HBV reactivation during exposure is not known at this time.

As recommended by the European Medicines Agency (EMA) and National Competent Authorities, the summary of product characteristics (SmPC) and the package leaflet of all BCR-ABL TKIs will be updated to reflect the new safety information.

Call for reporting of adverse reactions

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with these products in accordance with the national spontaneous reporting system.
Please report any suspected adverse reactions associated with the use of these products in accordance with the national requirements via the national spontaneous reporting system **to HPRA Pharmacovigilance, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland. Tel: 01 676 4971. Fax 01 676 2517. Website** www.hpra.ie. **E-mail:** medsafety@hpra.ie

When reporting please provide as much information as possible, including information about medical history, test results, any concomitant medication, onset and treatment dates.

Company contact point

If you have further questions or require additional information please contact:

Company	**Product Name**	**Email**	**Phone**
Novartis Ireland Limited	Glivec® (imatinib)	medinfo.dublin@novartis.com	01-2601255
Bristol Myers Squibb	Sprycel® (dasatinib)	Medical.information@bms.com	1 800 749 749
Novartis Ireland Limited	Tasigna® (nilotinib)	medinfo.dublin@novartis.com	01-2601255
Pfizer Ltd.	Bosulif® (bosutinib)	EUMEDINFO@Pfizer.com	1 800 633 363
ARIAD Pharma Ltd.	Iclusig® (ponatinib)	eumedinfo@ariad.com	0080000027423

Yours sincerely,

Betts Vicki

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