03-03-2016

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 *Malta Medicines Authority*, the undersigned Marketing Authorisation Holders 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 or unsuspected adverse reactions associated with these products in accordance with the national spontaneous reporting system. Report forms can be downloaded from http://www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gzira GZR 1368, Malta or sent by email to postlicensing.medicinesauthority@gov.mt.

Healthcare professionals may also report any adverse events suspected to be associated with the use of:

- *Tasigna® to Novartis Pharma Services Inc. Representative Office Malta by phone on +35621222872, by fax on +35622487219 or e-mail at* drug_safety.malta@novartis.com.
- *Sprycel®to AM Mangion Ltd by phone on +35623976333 or by e-mail on pv@ammangion.com.mt.*

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

The medicines that are currently available to the local market are Tasigna® and Sprycel®. If you have further questions or require additional information regarding:

Tasigna® please contact *Novartis Pharma Services Inc. Representative Office Malta by phone on +35621222872, by fax on +35622487219 or e-mail at novartis.malta@novartis.com.*

Sprycel® please contact *AM Mangion Ltd by phone on +35679373456 or e-mail on raquilina@ammangion.com.mt.*

Yours sincerely,

Signature	Signature	Signature	Signature
Graziella Vella	Roger Aquilina	Nikos Baibas	Nils Eckardt
Name	Name	Name	Name
DRA Head/ QP	Hospital Medical Rep	Medical Director of Pfizer Hellas S.A.	Head Medical Affairs Europe
Function	Function	Function	Function
Novartis Pharma	*Bristol-Myers-Squibb local representative*	*Pfizer*	*Arlad Pharma*