

11-04-2016

**BCR-ABL tyrosine kinase inhibitors (imatinib▼, dasatinib, nilotinib, bosutinib▼, ponatinib▼) and risk of hepatitis B reactivation: screen patients for hepatitis B virus before treatment**

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency, 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 death.**

**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 starting treatment in patients with positive HBV serology (including those with active disease) 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 resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or death.

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 TKIs, 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***

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report

- all suspected ADRs that are serious or result in harm. (Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.)
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

▼Imatinib, bosutinib and ponatinib are subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

It is easiest and quickest to report ADRs online via the Yellow Cards website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing [yellowcard@mhra.gsi.gov.uk](mailto:yellowcard@mhra.gsi.gov.uk)
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

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

Any suspected ADRs should also be reported to the company responsible for the product. Please refer to contact details below.

### ***Company contact point***

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

<b>Company</b>	<b>Product Name</b>	<b>Email</b>	<b>Phone</b>	<b>Fax</b>
Novartis Europharm Ltd.	Glivec® (imatinib)	medinfo.uk@novartis.com	01276 698370	01276 698449
Bristol-Myers Squibb	Sprycel® (dasatinib)	medical.information@bms.com	0800 731 1736	01895 523677
Novartis Europharm Ltd.	Tasigna® (nilotinib)	medinfo.uk@novartis.com	01276 698370	01276 698449
Pfizer Ltd.	Bosulif® (bosutinib)	medical.information@pfizer.com	01304 616161	
ARIAD Pharma Ltd.	Iclusig® (ponatinib)	eumedinfo@ariad.com	0080 000 02743	

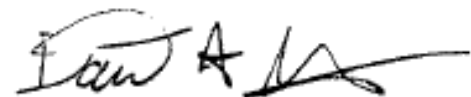
Yours sincerely,



Dr Dimitrios Georgiopoulos  
Medical Director  
Novartis Pharmaceuticals UK Ltd



Dr Jane Tiller  
Head of Medical, Europe Markets, Canada and Australia  
Bristol-Myers Squibb Pharmaceuticals Ltd



David Montgomery  
Medical Director,  
Pfizer Ltd.



Dr Michael Thompson  
Medical Director  
ARIAD Pharma Ltd.