

17<sup>th</sup> July 2017

## Direct Healthcare Professional Communication

### **IMBRUVICA® ▼ (ibrutinib) and risk of hepatitis B reactivation: Hepatitis B virus status to be established before initiating treatment with IMBRUVICA**

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA), Janssen-Cilag Limited would like to inform you of:

#### ***Summary***

**Cases of hepatitis B virus (HBV) reactivation have been reported in patients receiving IMBRUVICA® (ibrutinib), therefore:**

- **Patients should be tested for HBV infection before starting treatment with Imbruvica.**
- **If patients have positive hepatitis B serology, consultation with a liver disease expert is recommended before starting treatment with Imbruvica.**
- **Patients with positive hepatitis B serology who require Imbruvica should be monitored and managed, according to local medical standards of care, to prevent hepatitis B virus (HBV) reactivation.**

#### ***Further Information on the safety concern and recommendations***

A cumulative review of data from clinical trials and postmarketing cases has identified reports of hepatitis B reactivation in ibrutinib-treated patients. To date, there have been no reports of fulminant liver failure leading to liver transplantation. However, one fatal case has been reported which was due to hepatitis B reactivation and concurrent metastatic melanoma of the liver, lung and spleen. The time-to-onset of hepatitis B reactivation was variable with no clear pattern. Ibrutinib was discontinued or interrupted, in the majority of cases. In general patients were managed with HBV antiviral medication, according to their local standard of care, and as a result there was a reduction in HBV viral load. In some cases, the role of ibrutinib therapy in the onset of the event was confounded by prior or concomitant chemoimmunotherapy associated with viral reactivation. Some of the patients had a documented history of hepatitis B and in other cases baseline hepatitis B serology status was not reported.

Among patients in company sponsored clinical trials, the frequency of hepatitis B reactivation is uncommon (0.2%). Patients with active hepatitis B were excluded from these sponsored trials.

The Summary of Product Characteristics (SmPC) and the package leaflet for Imbruvica will be updated to reflect the new safety information, as recommended by the European Medicines Agency and the MHRA.

The IMBRUVICA Summary of Product Characteristics is available from <http://www.medicines.org.uk/emc/>

### ***Call for reporting***

**▼ *This medicinal product is subject to additional monitoring to support risk management and it is therefore important to report any suspected adverse events.***

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system.

Suspected adverse reactions should be reported to the MHRA through the Yellow Card Scheme: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD" (no other address details necessary)
- by emailing [yellowcard@mhra.gov.uk](mailto:yellowcard@mhra.gov.uk)
- at the back of the British National Formulary (BNF)
- by telephoning the MHRA Yellow Card free phone reporting line: 0800-731-6789
- or by electronic download through the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset dates, treatment dates, product brand name and batch numbers.

Suspected adverse reactions should also be reported to Janssen-Cilag Limited on tel: 01494 567447, fax: 01494 567799 or by email at [dsafety@its.jnj.com](mailto:dsafety@its.jnj.com)

### ***Company contact points***

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

Janssen-Cilag Ltd. Medical Information Department:

Email: [medinfo@its.jnj.com](mailto:medinfo@its.jnj.com)

Telephone: 0800 731 8450 or 01494 567 444

Yours faithfully,



Dr Rozlyn Bekker  
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Janssen-Cilag Ltd.