Dear Healthcare Professional Communication for Ibrutinib Patient Information Leaflet (Version Aug 2022)

Monday, May 20, 2024

Dear Healthcare professional,

As Janssen Cliag International N.V, we would like to inform the health community about an IMBRUVICA PIL new version that was missed from distribution. The IMBRUVICA PIL version "August 2022" was not implemented/distributed with Imbruvica packs, while the distribution of version "December 2021" has continued.

Summary of the situation:

- Janssen Cliag International N.V decided to distribute DHPC Letter to communicate some of IMBRUVICA PIL version August 2022 key information. This DHPC Letter started to be distributed across Gulf countries in November 2022
- This PIL version "August 2022" was not distributed with Imbruvica packs from Aug 2022 till date. Therefore, the new information highlighted in the DHPC Letter was not implemented in the PIL.
- So, we decided to send new DHPC letter to ensure well receiving of this important information to patients and health community. An updated PIL will be implemented as soon as possible.

Summary of the updates:

- Ibrutinib may affect the heart, especially if patients already have heart diseases such as rhythm problems, heart failure, high blood pressure, have diabetes or are of advanced age.
- Patients with advanced age, Eastern Cooperative Oncology Group (ECOG) performance status ≥2, or cardiac co-morbidities may be at greater risk of cardiac events including sudden fatal cardiac events, however, abnormal fast heat beats and cardiac arrest (heart stops beating) are considered uncommon cardiac side effects.
- Prior to initiating ibrutinib, clinical evaluation of cardiac history and function should be performed.
- In patients with risk factors for cardiac events, benefits and risks should be assessed before initiating treatment with Imbruvica; alternative treatment may be considered.
- Patients should be carefully monitored during treatment for signs of deterioration of cardiac function and if this occurs, clinically managed.
- Patients should inform you immediately if they feel breathless have difficulty breathing when lying down, swelling of the feet, ankles or legs and weakness/tiredness during treatment with Ibrutinib – these may be signs of heart failure.
- Ibrutinib should be withheld for any new onset or worsening grade 2 cardiac failure or grade 3 cardiac arrhythmias. Treatment may be resumed as per new dose modification recommendations, section 4.2 of the EU SmPC.

Background on the safety concern

Ibrutinib is indicated:

- as a single agent for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).
- as a single agent or in combination with rituximab or Obinutuzumab or Venetoclax for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).
- as a single agent or in combination with bendamustine and rituximab (BR) for the treatment of adult patients with CLL who have received at least one prior therapy.
- as a single agent for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. Ibrutinib in combination with rituximab is indicated for the treatment of adult patients with WM.

Assessment of data from the randomized clinical trials (RCT) pool of ibrutinib showed a nearly 5-fold higher crude incidence of sudden cardiac death, sudden death, or cardiac death in the ibrutinib arm (11 cases; 0.48%) versus the comparator arm (2 cases; 0.10%). When adjusted for exposure, a 2- fold increase in the incidence rate (EAIR, expressed as number of subjects with events divided by patient-months at risk) of events of sudden cardiac death, sudden death or cardiac death was observed in the ibrutinib arm (0.0002) versus the comparator arm (0.0001).

Based on an assessment of available data on the cardiotoxicity of ibrutinib, further measures to minimize the cardiac risk will be implemented in the product information. Patients with advanced age, Eastern Cooperative Oncology Group (ECOG) performance status ≥2, or cardiac co-morbidities may be at greater risk of events including sudden fatal cardiac events.

Appropriate clinical evaluation of cardiac history and function should be performed prior to initiating Imbruvica. Patients should be carefully monitored during treatment for signs of clinical deterioration of cardiac function and if this occurs, clinically managed. Consider further evaluation (e.g., ECG, echocardiogram), as indicated for patients in whom there are cardiovascular concerns.

For patients with relevant risk factors for cardiac events, carefully assess benefit/risk before initiating treatment with Imbruvica; alternative treatments may be considered.

Patients should tell their HCP immediately if they feel breathless have difficulty breathing when lying down, swelling of the feet, ankles or legs and weakness/tiredness during treatment with Ibrtuinib – these may be signs of heart failure.

In addition, the MAH reviewed clinical data for patients experiencing Grade 3+ cardiac events and assessed whether toxicities recurred for patients who dose-reduced IMBRUVICA versus patients who did not dose reduce subsequent to these toxicities. Analyses indicate a lower incidence of recurrence of cardiac events for patients who dose-reduced IMBRUVICA compared to those who did not reduce the dose of IMBRUVICA.

On this basis, section 4.2 of the EU SmPC is being updated with new dose recommendations.

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of Imbruvica in accordance with the national spontaneous reporting system.

Ministry of Health and Prevention/Drug Department/Pharmacovigilance and Medical Device section
Telephone 80011111
Email: pv@mohap.gov.ae
P.O. Box 1853 Dubai

Company contact point

For full prescribing information, please refer to the data sheet or contact Johnson & Johnson Middle East FZ LLC, Mohamed Bin Rashid Academic Medical Centre –Building 14, Level 7 – Dubai Healthcare City – Dubai 505080, United Arab Emirates
Tel: +97144297200
Fax: +97144297150
To report Adverse Events/Product Complaint, please contact us at Email: GCC-PV2@its.jnj.com
Hotline: +971559816775

Yours Faithfully,

Bulent Ozturk

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