janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

IMPORTANT MEDICINE SAFETY INFORMATION

IMBRUVICA® (IBRUTINIB) – RISK OF FATAL CARDIAC EVENTS

14 April 2023

Dear Healthcare Professional

Janssen Pharmaceutica as directed by the South African Health Products Regulatory Authority (SAHPRA), wish to inform you about the risk of fatal cardiac events.

Background information 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, 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.
- in combination with rituximab for the treatment of adult patients with WM.

The risk of fatal cardiac events emanated from routine pharmacovigilance activities conducted by the Janssen Pharmaceutica International. The sudden death/cardiac death signal was triggered by findings from continuous monitoring and periodic evaluations of Janssen Pharmaceutica's global safety database, clinical data and literature. It was concluded from the findings that the use of ibrutinib (either as monotherapy or in combination with other anti-cancer treatments) was associated with an increased risk of fatal cardiac events, including events of sudden death. In randomised clinical trials, 20 of 2 257 (1,3 %) subjects treated with Imbruvica® had a fatal cardiac event compared to 16 of 2 228 (0,8 %) subjects in the comparator arm.

Furthermore, Janssen Pharmaceutica International reviewed clinical data for patients experiencing Grade 3+ cardiac events and assessed whether toxicities recurred for patients who dose-reduced Imbruvica®, after these toxicities versus patients who did not. Analyses indicate a lower incidence of recurrence of cardiac events for patients who dose-reduced Imbruvica®.

The Professional Information (PI) and Patient Information Leaflet (PIL) of Imbruvica are updated to appropriately reflect the below safety information.

Grade 4 haematological toxicities	Fourth	Discontinue Imbruvica®

Healthcare professionals are urged to report all suspected adverse events associated with the use of Imbruvica® to SAHPRA via Med Safety App that can be downloaded into a smart mobile phone through google Play or App store. Alternatively, reporting can be done via the eReporting link available on the SAHPRA website (www.sahpra.org.za) or by completing the ADR reporting form, accessible via the SAHPRA website and emailed to adr@sahpra.org.za.

For more information on ADR reporting, please contact the SAHPRA Vigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details below:

PRODUCT	ACTIVE	REGISTRATION NUMBER	CONTACT DETAILS Pharmacovigilance Unit	CONTACT DETAILS Medical Information
IMBRUVICA 140 mg capsules	Ibrutinib	50/26/0939 (South Africa) 20/26/0006 (Namibia)	**Tel:** +2711 518 7100 **Fax:** +2786 687 8942 or +2711 518 7108 Email: AdverseEventZA@its.jnj.com	**Tel:** 0860111117 **E-mail:** RA-medinfoemmarkets@its.jnj.com
IMBRUVICA film coated tablet range		55/26/0297-300 (South Africa)		

Yours sincerely

Moustafa KAMAL
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Moustafa Kamel
(Medical Affairs Director)

SARA COWIE
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Sara Cowie
(Responsible Pharmacist)