Direct Healthcare Professional Communication

20 May 2021

Venclyxto ▼ (venetoclax) film coated tablets(EU/1/16/1138/001-007): Updated recommendations on tumour lysis syndrome (TLS) in CLL patients

Dear Healthcare Professional,

AbbVie Deutschland GmbH & Co. KG in agreement with the European Medicines Agency (EMA) and the Malta Medicines Authority(MMA) would like to inform you of the following:

Summary

- **Fatal cases of TLS have been observed even in patients receiving the lowest venetoclax dose used in dose-titration schedule.**
- **TLS is a known risk of venetoclax.**
- **Strict adherence to dose titration and TLS risk minimisation measures as outlined in the SmPC is required for all patients.**
- **A patient card will be provided to prescribing haematologists to be given to each patient.**

Background on the safety concern

Venetoclax is a selective inhibitor of the B cell lymphoma-2 (BCL-2) protein which restores programmed cell death in cancer cells. It is indicated for the treatment of adult patients with previously treated chronic lymphocytic leukaemia (CLL) as monotherapy or in combination with rituximab and in previously untreated CLL in combination with obinutuzumab.

The administration of venetoclax can cause rapid reduction in tumour burden, and thus poses a risk for TLS at initiation and during the dose-titration phase in all CLL patients.

Rapid reduction of tumour volume can lead to metabolic abnormalities which can sometimes progress to clinically toxic effects, including renal insufficiency, cardiac arrhythmias, seizures, and death (i.e., clinical TLS). Fatal cases of TLS were reported in the postmarketing setting in CLL patients treated with venetoclax. Some of these events have occurred in patients receiving a single dose of venetoclax 20 mg (the lowest dose used at initiation and during the dose-titration phase) and in patients with low-to-medium TLS risk.

The SmPC is revised to reflect the updated recommendations and emphasize the importance of strict adherence to the TLS risk minimization measures for **all** CLL patients, regardless of the tumour burden and other known risk factors for TLS.

To minimize the risk of TLS in CLL patients, prescribers should:

- Assess patient-specific factors for level of TLS risk including comorbidities, particularly reduced renal function, tumor burden, and splenomegaly prior to first dose of venetoclax
- Provide prophylactic hydration and anti-hyperuricaemics to all patients prior to first dose of venetoclax
- Perform blood chemistry monitoring and tumour burden category assessment
- Follow recommended dose modifications and actions in case of blood chemistry changes or symptoms suggestive of TLS related to venetoclax
- Provide each patient with the Patient card (which will be distributed to prescribing haematologists). This card will include the importance of hydration and a list of symptoms of TLS which should prompt the patient to seek immediate medical attention in case of their occurrence.

Call for reporting

For any side effects please report to the Medicines Authority Post-Licensing Directorate, ADR Reporting Website: www. medicinesauthority.gov.mt/adrportal or to the local representative of AbbVie: V.J. Salomone Pharma Ltd., Pharmacovigilance line on +356 99644126. By reporting side effects, you can help provide more information on the safety of this medicine.

▼ Venclyxto is subject to additional monitoring. This will allow quick identification of new safety information.

Company contact points

You may contact our Medical Information department at V.J. Salomone Pharma Ltd., Pharmacovigilance line on +356 99644126 if you have any questions about the information contained in this letter.

Annexes

The revised product information will be available on the EMA website in July.

Yours Faithfully,

Ali Amer
Medical Director
Levant-E

Signature: 

Electronically signed by: Ali Amer
Reason: Management Approval
Date: May 25, 2021 16:04 GMT+2

Email: ali.amer@abbvie.com