Direct Healthcare Professional Communication

03 June 2021

Venetoclax▼ (Venclyxto): Updated recommendations on tumour lysis syndrome (TLS) in CLL patients

Dear Healthcare Professional,

AbbVie Ltd in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) 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 Summary of Product Characteristics (SmPC) is required for all patients.**
- **A patient alert 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.

Venetoclax in combination with obinutuzumab is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

Venetoclax in combination with rituximab is indicated for the treatment of adult patients with CLL who have received at least one prior therapy.

Venetoclax monotherapy is indicated for the treatment of CLL:

- in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor, or
- in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor.

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.

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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 being revised to reflect the updated recommendations and emphasise the importance of strict adherence to the TLS risk minimisation measures for **all** CLL patients, regardless of the tumour burden and other known risk factors for TLS.

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

- Assess patient-specific factors for level of TLS risk including comorbidities, particularly reduced renal function (e.g. creatinine clearance <80ml/min), 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 alert 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

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

Healthcare professionals are asked to report any suspected adverse drug reactions to the MHRA via the Yellow Card scheme. Reports can be made via:

- the Yellow Card website https://yellowcard.mhra.gov.uk/
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS, SystmOne, Vision, MiDatabank) for healthcare professionals.

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

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

Adverse events should also be reported to AbbVie at GBPV@abbvie.com or by telephoning 01628 561092 (option 1).

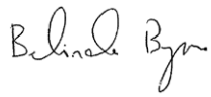
Company contact points

You may contact our Medical Information department at 01628 561092 (option 3) or ukmedinfo@abbvie.com if you have any questions about the information contained in this letter.

Annexes

The revised Summary of Product Characteristics and Patient Information Leaflet will be updated on the eMC https://www.medicines.org.uk/emc.

Yours faithfully,



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