

## Direct Healthcare Professional Communication

<Date>

### **Venclyxto ▼ (venetoclax) film coated tablets: Updated recommendations on tumour lysis syndrome (TLS) in CLL patients**

Dear Healthcare Professional,

<Marketing Authorisation Holder> in agreement with the European Medicines Agency (EMA) and the <National Competent Authority> 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***

<A reminder of the need and how to report adverse reactions in accordance with the national spontaneous reporting system, including the details (e.g., name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

▼ 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 <insert phone number and e-mail, if available> if you have any questions about the information contained in this letter.

**Annexes**

<Link to the revised product information such as information on the website of a competent authority, **if applicable**>

## Communication Plan for Direct Healthcare Professional Communication

| DHPC COMMUNICATION PLAN                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Medicinal product(s)/active substance(s)</b>                                 | Venclyxto (venetoclax)                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Marketing authorisation holder(s)</b>                                        | AbbVie Deutschland GmbH & Co. KG                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Safety concern and purpose of the communication</b>                          | <p>Inform about important revised information on Tumor Lysis Syndrome (TLS) minimization measures in the summary of product characteristics (SmPC).</p> <p>The SmPC is being amended to further specify factors for TLS risk assessment, clarify TLS prophylaxis and patient monitoring and to emphasize that adherence to TLS mitigation measures as outlined in the SmPC is essential for all CLL patients to minimize TLS risk.</p> |
| <b>DHPC recipients</b>                                                          | <p>Haematologists</p> <p>The target group should be further defined at national level, in agreement with the respective National Competent Authority.</p> <p>Distribution channels and mechanism (mailing, emails, etc.) to be agreed with National Competent Authorities.</p>                                                                                                                                                         |
| <b>Member States where the DHPC will be distributed</b>                         | All Member states where Venclyxto is authorised in the EU/EEA.                                                                                                                                                                                                                                                                                                                                                                         |
| Timetable                                                                       | Date                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| DHPC and communication plan (in English) agreed by PRAC                         | 18 March 2021                                                                                                                                                                                                                                                                                                                                                                                                                          |
| DHPC and communication plan (in English) agreed by CHMP                         | 20 May 2021                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Submission of translated DHPCs to the national competent authorities for review | 27 May 2021                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Agreement of translations by national competent authorities                     | 03 June 2021                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Dissemination of DHPC                                                           | 10 June 2021                                                                                                                                                                                                                                                                                                                                                                                                                           |