

Early Access to Medicines Scientific Opinion - Public Assessment Report	
<b>Product</b>	<b>Venetoclax 10mg film-coated tablets Venetoclax 50mg film-coated tablets Venetoclax 100mg film-coated tablets</b>
<b>Condition</b>	<b>Venetoclax is a medicine used in the Early Access to Medicines Scheme to treat a type of blood cancer in adults known as chronic lymphocytic leukaemia.</b>
<b>Full indication</b>	<b>Venetoclax is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) in the presence of 17p deletion or <i>TP53</i> mutation, and who are unsuitable for or have failed a B-cell receptor pathway inhibitor.</b>  <b>Venetoclax is indicated for the treatment of adult patients with CLL in the absence of 17p deletion or <i>TP53</i> mutation, and who are unsuitable for or have failed both chemo-immunotherapy and a B-cell receptor pathway inhibitor.</b>
<b>Company</b>	<b>AbbVie Ltd</b>
<b>EAMS number</b>	<b>41042/0001</b>

## Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to doctors who may wish to prescribe the unlicensed medicine under their own responsibility. More information about the scheme can be found here: <http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The scientific opinion is based on the information supplied to the MHRA on the benefits and risks of a promising new medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to licence such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here: <http://www.gmc-uk.org/mobile/news/14327>

**Venetoclax 10mg film-coated tablets**  
**Venetoclax 50mg film-coated tablets**  
**Venetoclax 100mg film-coated tablets**

## What is Venetoclax?

Venetoclax is the active substance of an anticancer medicine, which is available as tablets; 10 milligrams (mg), 50 milligrams (mg) and 100 milligrams (mg).

**What is Venetoclax used to treat?**

Venetoclax is used to treat adults with chronic lymphocytic leukaemia (CLL), a type of blood cancer. If a laboratory test shows that the cancer cells have a change in the chromosome called 17p deletion, or a change in the gene called *TP53* mutation, Venetoclax is used after treatment with type of anticancer treatment known as a B-cell receptor pathway inhibitor (e.g. ibrutinib or idelalisib). If the cancer cells do not have 17p deletion or *TP53* mutation, Venetoclax is used after an anticancer treatment known as chemo-immunotherapy, in addition to a B-cell receptor pathway inhibitor.

**How is Venetoclax used?**

Treatment must be started and supervised by a doctor experienced in the use of anticancer therapies.

Before treatment, it is necessary that the cancer is investigated for a specific chromosome change called 17p deletion, or a specific gene change called *TP53* mutation. The 17p deletion or *TP53* mutation should be determined by a clinical laboratory using a valid test method.

The starting dose is 20 mg (two 10 mg tablets) once a day. The dose is increased slowly over a 5 week period to the standard dose of 400 mg (four 100 mg tablets) once a day for as long as necessary. This gradual increase is necessary to prevent a serious side effect known as tumour lysis syndrome which is caused by cancer cell breakdown products.

**How does Venetoclax work?**

Venetoclax is a B-cell lymphoma (Bcl-2) family inhibitor. The cancer cells rely on the Bcl-2 protein for survival. Blocking this protein can cause the cancer cells to die. Treatment with Venetoclax can reduced the number of cancer cells in the blood and body organs. In some cases the cancer cells become undetectable.

**How has Venetoclax been studied?**

Venetoclax 400 mg daily as monotherapy (not in combination with other anticancer medicines) has been investigated in three clinical studies (called M12-175, M13-982 and M14-032). So far 289 patients with CLL, whose disease did not respond to other therapies or came back after other therapies, have been studied. Previous therapies included chemo-immunotherapy and B-cell receptor pathway inhibitors. The studies included patients with CLL with and without the 17p deletion or *TP53* mutation. The main measure of anticancer activity was the response of the cancer to Venetoclax treatment. Response included a reduction in the number of cancer cells in the body, an increase in the numbers of healthy blood cells, and an improvement in symptoms.

**What are the benefits and risks of Venetoclax?*****Benefits***

The proportion of patients with a response to Venetoclax 400 mg daily averaged 73% across the three studies. In some patients, the cancer cells became undetectable. For the majority of responders, the benefit was maintained for more than one year. There was also some improvement in quality of life measures. Benefits were seen irrespective of the type of previous therapy, or the presence of the 17p deletion or *TP53* mutation.

***Risks***

The commonest side effects of Venetoclax seen in the clinical studies were neutropenia (reduced numbers of white blood cells) [50% of patients], anaemia (reduced number of red blood cells) [29%], diarrhoea [39%], nausea [36%] and fatigue [26%]. Serious side effects such as pneumonia can occur in up to 1 in 10 patients. Tumour lysis syndrome is an important risk of Venetoclax treatment (see: How is Venetoclax used?). However the risk can be reduced to around 3% by following the dosing guide, keeping hydrated, using preventative medicines and having regular tests. Some high risk patients may need to be hospitalized during the early stages of treatment.

**Why has Venetoclax been given a positive Early Access to Medicine Scientific opinion?**

CLL is a life threatening disease. Patients whose cancer has the 17p deletion or *TP53* mutation respond better to B-cell receptor inhibitors than chemo-immunotherapy. If they do not respond to a B-cell receptor inhibitor, or if the cancer comes back, their treatment options are limited. Patients whose cancer does not have the 17p deletion or *TP53* mutation may respond to B-cell receptor inhibitors and chemo-immunotherapy. If they do not respond to these treatments, or if the cancer comes back, their treatment options are also limited.

In clinical studies, Venetoclax was able to reduce the levels of blood cancer cells in these patients, allowing normal blood cells to recover. The MHRA has considered the benefits of Venetoclax in this difficult to treat condition and concluded that the benefits are greater than the risks.

**What are the uncertainties?**

Results regarding the duration of response (how long Venetoclax works for) and the overall survival of patients treated with Venetoclax are still preliminary. The safety profile of Venetoclax has only been studied in a relatively moderate number of patients and some side effects may not yet be known.

**Are there on-going clinical studies?**

Two of the clinical studies discussed above (M13-982 and M14-032) are on-going. In addition, two studies (M13-365 and MURANO) to investigate the combination of Venetoclax and rituximab (another anti-cancer medicine) in CLL are underway.

**What measures are in place to monitor and manage risks?**

A risk management plan has been developed to ensure that Venetoclax is used as safely as possible. Based on this plan, the company that makes Venetoclax must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including the side effects of treatment and recommendations for preventing or minimising these side effects.

Information will be collected about patients before they enter the scheme. The company will ask the healthcare professionals to report adverse effects experienced by patients receiving venetoclax through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the Company.

**Other information about Venetoclax – see EAMS Treatment Protocol**