Early Access to Medicines Scheme – Treatment protocol – Information for patients

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation) to UK patients that have a high unmet clinical need. The medicines included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life threatening conditions where there are no adequate treatment options. More information about the scheme can be found here: http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The information below is intended for you, the patient, and is provided by the pharmaceutical company that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation). More information about medicines licensing can be found here: http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Informed consent should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine outweigh any potential risks.

Information for the patient:

Information for the patient

Venetoclax 10 mg, 50 mg, and 100 mg film-coated tablets
venetoclax

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What venetoclax is and what it is used for

What venetoclax is
Venetoclax belongs to a group of medicines called "BCL-2 inhibitors".

What Venetoclax is used for
Venetoclax is used to treat patients with Chronic Lymphocytic Leukaemia (CLL) whose cancer cells have certain changes called "17p deletion" or "TP53 mutation" in their genes, or have been treated with other medicines to treat CLL in the past.

CLL is a type of cancer affecting white blood cells called lymphocytes and the lymph nodes. In CLL, the lymphocytes multiply too quickly and live for too long, so that there are too many of them in the blood.

How Venetoclax works
Venetoclax works by blocking a protein in the body called "BCL-2". This is a protein that helps cancer cells survive. Blocking this protein helps to kill and lower the number of cancer cells. It also slows down the worsening of the disease.

2. What you need to know before you take Venetoclax

Do not take Venetoclax if:
- you are allergic to venetoclax or any of the other ingredients of this medicine (listed in section 6).

- you are taking any of the medicines listed below when you start your treatment and during the time when your dose is gradually being increased (usually over 5 weeks). This is because serious or life-threatening effects can occur when venetoclax is taken with these medicines:
    - ketoconazole, voriconazole, posaconazole, or itraconazole for fungal infections
    - clarithromycin for bacterial infections
    - ritonavir for HIV infection.

  When your venetoclax dose has been increased to the full standard dose, check with your doctor if you can now take these medicines again.

- if you are taking a herbal medicine called St. John's wort, used for depression. If you are not sure about this, talk to your doctor, pharmacist or nurse before taking this medicine.

Tell your doctor, pharmacist, or nurse about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Your doctor may need to stop certain medicines when you first start taking venetoclax and during the first five weeks when your dose is gradually increased to the full standard dose.

Warnings and precautions
Talk to your doctor, pharmacist, or nurse before taking venetoclax if:

- you have any kidney problems as your risk for side effect called tumour lysis syndrome may increase
- you have liver problems as your risk for side effects may increase
- you think you may have an infection or have had a long lasting or repeated infection
- you are due to have a vaccine.

If any of the above apply to you, or you are not sure, talk to your doctor, pharmacist, or nurse before taking venetoclax.

Tumour Lysis Syndrome
Some people may develop unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells during treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. This is called TLS (Tumour Lysis Syndrome). The risk for TLS is in the first 5 weeks of treatment with venetoclax.

Your doctor pharmacist or nurse will do blood tests to check for TLS.

Your doctor may give you also medicines to help prevent the build up of uric acid in your body before you start treatment with venetoclax.

Drinking plenty of water helps to remove cancer cell products from your body through urine, and may decrease the chances of you getting TLS (see section 3).

Tell your doctor, pharmacist or nurse immediately if you get any of the symptoms of TLS listed in section 4.

If you are at risk of TLS you may be treated in hospital so that you can be given fluids into the vein if needed, have blood tests done more often and to check for side effects. This is to see if you can continue to take venetoclax safely.

Children and adolescents
Venetoclax should not be used in children and adolescents. This is because it has not been studied in these age groups.

Other medicines and Venetoclax
Tell your doctor if you take any of the following medicines as these can increase or decrease the amount of venetoclax in your blood:

- medicines for fungal infections – ketoconazole, itraconazole, fluconazole, posaconazole, or voriconazole
- medicines called antibiotics to treat bacterial infections – clarithromycin, ciprofloxacin, erythromycin, nafcillin, or rifampicin
- medicines to prevent seizures or to treat epilepsy – carbamazepine, phenytoin
- medicines for HIV infection – efavirenz, etravirine, ritonavir
- medicines to treat raised blood pressure or angina – bosentan, verapamil, diltiazem
- a herbal medicine known as St. John's wort
- a medicine to treat sleep disorder (narcolepsy) known as modafinil

Tell your doctor if you take any of the following medicines as venetoclax may affect how they work:

- blood thinners warfarin, dabigatran
- a medicine used to treat heart problems known as digoxin
- a medicine for cancer known as everolimus
- a medicine used to prevent organ rejection known as sirolimus

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, herbal medicines and supplements. This is because venetoclax may affect the way some other medicines work. Also some other medicines can affect the way venetoclax works. Your doctor may change your dose of venetoclax.

Venetoclax with food and drink
Do not eat grapefruit products, Seville oranges (bitter oranges), or starfruit (carambola) while you are taking venetoclax – this includes eating them, drinking the juice or taking a supplement that might contain them. This is because they can increase the amount of venetoclax in your blood.

Pregnancy
- Do not get pregnant while you are taking this medicine. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist, or nurse for advice before taking this medicine.
- Venetoclax should not be used during pregnancy. There is no information about the safety of venetoclax in pregnant women.

Contraception
- Women of childbearing age must use a highly effective method of birth control during treatment and for at least one month after receiving venetoclax to avoid becoming pregnant. If you are using hormonal contraceptive pills or devices, you must also use a barrier method of contraception (such as condoms) as the effect of hormonal contraceptive pills or devices may be affected by venetoclax.
- Tell your doctor immediately if you become pregnant while you are taking this medicine.

Breast-feeding
Do not breast-feed while you are taking this medicine. It is not known whether the active substance in

venetoclax passes into breast milk.

Fertility
Based on findings in animals, venetoclax may cause male infertility (low or no sperm count). This may affect your ability to father a child. Ask your doctor for advice before starting treatment with venetoclax.

Driving and using machines
You may feel tired after taking venetoclax, which may affect your ability to drive or use any tools or machines.

3. How to take Venetoclax

Always take this medicine exactly as your doctor, pharmacist, or nurse has told you. Check with your doctor, pharmacist, or nurse if you are not sure.

How much to take
You will begin treatment with venetoclax at a low dose for 1 week. Your doctor will gradually increase the dose over the next four weeks to the full standard dose. For the first 4 weeks you will get a new pack each week.

- the starting dose is 20 mg (two 10 mg tablets) once a day for 7 days.
- the dose will be increased to 50 mg (one 50 mg tablet) once a day for 7 days.
- the dose will be increased to 100 mg (one 100 mg tablet) once a day for 7 days.
- the dose will be increased to 200 mg (two 100 mg tablets) once a day for 7 days.
- the dose will be increased to 400 mg (four 100 mg tablets) once a day. You will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.

How to take Venetoclax
- Take the tablets with a meal at approximately the same time each day
- Swallow the tablets with a glass of water
- Do not chew, crush, or break the tablets
- During the first 5 weeks of treatment, you should take the tablets in the morning to help with your appointments for blood tests, if needed.

If you vomit after taking venetoclax, do not take any additional dose that day. Take the next dose at the usual time the next day. If you have problems taking venetoclax, talk to your doctor.

Drink plenty of water
It is very important that you drink plenty of water when taking venetoclax during the first 5 weeks of treatment. This will help to continuously remove cancer cell breakdown products from your blood through your urine.

You should start drinking at least 1.5 to 2 litres of water daily two days before starting venetoclax. You may include non-alcoholic and non-caffeinated drinks in this amount, but exclude grapefruit, Seville orange, or starfruit (carambola) juices. You should continue to drink at least 1.5 to 2 litres of water on the day you start venetoclax. Drink the same amount of water (at least 1.5 to 2 litres daily) two days before and on the day that your venetoclax dose is increased.

If your doctor thinks that you are at risk of TLS, you may be treated in the hospital so that you can be given

extra fluids into the vein if needed, have your blood tests done more often and be checked for side effects. This is to see if you can continue to take venetoclax safely.

If you take more Venetoclax than you should
If you take more venetoclax than you should, talk to your doctor, pharmacist, or nurse or go to hospital immediately. Take the tablets and this leaflet with you.

If you forget to take Venetoclax
- If it is less than 8 hours since the time you usually take your dose, take it as soon as possible.
- If it is more than 8 hours since the time you usually take your dose, do not take the dose that day. Return to your normal dose schedule the next day.
- Do not take a double dose to make up for a forgotten dose.
- If you are not sure talk to your doctor, pharmacist or nurse.

Do not stop taking Venetoclax
Do not stop taking this medicine unless your doctor tells you to. If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Tumour lysis syndrome (TLS) (common – may affect up to 1 in 10 people)
Seek medical attention immediately if you notice any of the symptoms of TLS:
- fever or chills
- feeling or being sick (nausea or vomiting)
- feeling confused
- feeling short of breath
- irregular heart beat
- dark or cloudy urine
- feeling unusually tired
- muscle pain or uncomfortable joints
- fits or seizures
- presence of abdominal pain and distension

Venetoclax can cause other serious side effects, including:

Low white blood cell count (neutropenia) (very common – may affect more than 1 in 10 people)
Your doctor will check your blood count during treatment with venetoclax. Low white blood cell count can increase your risk for infection. Signs may include fever, chills, feeling weak or confused, cough, pain or burning feeling when passing urine. Some infections can be serious and may lead to death. Tell your doctor immediately if you have signs of an infection while taking venetoclax.

Tell your doctor if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people)
upper respiratory tract infection – signs include runny nose, sore throat or cough

diarrhoea
feeling or being sick (nausea or vomiting)
constipation
feeling tired

Blood tests may also show
lower number of red blood cells
higher level of a body salt (electrolyte) called phosphorous

Common (may affect up to 1 in 10 people)
- pneumonia
- urinary tract infection
- low white blood cell counts with fever (febrile neutropenia)

Blood tests may also show:
higher level of creatinine
higher level of urea
higher level of potassium
lower level of calcium

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, or nurse This includes any possible side effects not listed in this leaflet.

5. How to store Venetoclax

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after EXP.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Venetoclax contains
The active substance is venetoclax. Each film-coated tablet contains 10 mg, 50 mg or 100 mg venetoclax.
The other ingredients are copovidone, polysorbate 80 (E433), colloidal anhydrous silica (E551), anydrous calcium hydrogen phosphate (E341 (ii)), sodium stearyl fumarate.
The 10 mg tablet pale yellow film coating contains: iron oxide yellow (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol (E1521), talc (E553b).
The 50 mg tablet beige film coating contains: iron oxide yellow (E172), iron oxide red (E172), iron oxide black (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol (E1521), talc (E553b)
The 100 mg tablet pale yellow film coating contains:iron oxide yellow (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol (E1521), talc (E553b).

What Venetoclax looks like and contents of the pack
Venetoclax 10 mg film-coated tablet is pale yellow, round 6 mm diameter.
Venetoclax 50 mg film-coated tablet is beige, oblong 14 mm long.
Venetoclax 100 mg film-coated tablet is pale yellow, oblong 17.2 mm long.

Venetoclax tablets are packed into foil blister cards for one weeks treatment or bottles as follows:

1. Weekly blister card of 10 mg tablets (14 tablets)
2. Weekly blister card of 50 mg tablets (7 tablets)
3. Weekly blister card of 100 mg tablets (7 tablets)
4. Weekly blister card of 100 mg tablets (14 tablets)
5. Bottle containing 120 x 100 mg tablets

Scientific Opinion Holder

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Additional information:

Informed Consent Form – This document will be explained to the patient thoroughly before their treatment commences. The patient will be requested to sign the form and a copy will be given to them to keep.

Contact information:

AbbVie Medical Information: ukmedinfo@abbvie.com or telephone: 01628 561092 (option 3)