Venetoclax (Venclexta®)

What is Venetoclax?

Venetoclax (also known as Venclexta®) is a new type of drug that has been proven effective in another blood cancer called chronic lymohocytic lymphoma (CLL) and is being actively investigated for the treatment of myeloma. It belongs to a class of drugs known as BCL-2 inhibitors which work by accelerating cell death.

How does Venetoclax work?

Normal cells in the body are programmed to die after a certain amount of time or when they are damaged. BCL-2 is a protein that prevents this programmed death of some cells and can be found in higher amounts in myeloma cells.

Venetoclax inhibits the action of BCL-2, causing the myeloma cells to die.

In some cases, a diagnosis of myeloma includes certain genetic abnormalities. One of these is a translocation or rearranging of chromosomes 11 and 14, t(11;14). Patients with this genetic abnormality are known to have higher amounts of BCL-2 within the myeloma cells, therefore venetoclax works especially well for these people.

This genetic abnormality is discovered in the cytogenetic testing performed as part the bone marrow biopsy. The doctor will explain the results of these tests and if each patient has any genetic abnormalities.

How is Venetoclax given?

Venetoclax is an oral drug, given as a tablet usually once per day.

Though venetoclax has been shown to work on its own (as a monotherapy), its effects have been shown to be enhanced when given in combination with other anti-myeloma treatments such as dexamethasone and bortezomib (Velcade®).

When is Venetoclax available for use in Australia on the Pharmaceutical Benefits Scheme (PBS)?

The Australian Therapeutic Goods Administration (TGA) have approved venetoclax as a safe and effective treatment. However, it has not yet been listed to be subsidised by the Pharmaceutical Benefits Scheme (PBS).

What are the possible side effects?

Low blood counts

Venetoclax can cause a decrease in the number of red blood cells, white blood cells and platelets in the blood. A low red blood cell count may cause anaemia and fatigue. If anaemic, a blood transfusion may be necessary.

A low white blood cell count will increase the risk of infection. People having venetoclax treatment are especially susceptible to upper respiratory tract infections. To avoid infections, extra precautions will be required such as diligent hand washing and avoidance of people with infections. A sign of infection is a fever or temperature of 38°C or above.

If a patient's temperature is 38°C or above, medical attention must be sought immediately

If the white cell count is consistently low, it may be necessary to have an injection of granulocyte-colony stimulating factor (G-CSF), to increase the white blood cell count. The doctor will also prescribe medication to help prevent infections.

A low platelet count (thrombocytopenia) increases the risk of bruising and bleeding. If the platelet count is too low a platelet transfusion may be required.

The blood counts will be measured regularly to monitor for changes. In some cases, treatment may be delayed until blood counts have improved.

Nausea and vomiting

About a quarter of people having venetoclax therapy will experience nausea and vomiting. Anti nausea medication can be prescribed to prevent and treat these symptoms.

Diarrhoea

Whilst usually mild and easily manageable, diarrhoea can become problematic in some cases but easily managed with simple treatments. It is important to alert the doctor as soon as symptoms commence as there is a risk of dehydration when experiencing diarrhoea.

Constipation

A decrease in the normal frequency of bowel movements may occur whilst taking venetoclax. It may be accompanied by gas, pain, or pressure in the stomach. Constipation is usually easier to prevent than to treat.

To relieve the symptoms of constipation, patients can eat a healthy diet which is high in fibre. Fibre absorbs water making stools softer, bulkier and easier to eliminate. Drinking plenty of fluids (aim for

about 8 glasses of water a day) helps the fibre work. Pear or prune juice may also help. Regular gentle exercise keeps the bowels more active to help move things along. Gentle laxatives (consult a nurse or pharmacist) may be needed but if constipation continues to be a problem, talk with the doctor.

Fatigue

Many patients on venetoclax experience fatigue. It can be difficult to distinguish between fatigue that is directly related to venetoclax treatment and fatigue that is caused by the myeloma itself. A balanced diet, adequate fluid intake, regular exercise and adequate sleep can help minimise the effects of fatigue.

Precautions

Grapefruit products, Seville oranges (often found in marmalade) and starfruit have been known to interact with venetoclax and should be avoided while taking this treatment.

Published by Myeloma Australia May 2018. Thank you to Myeloma UK whose fact sheet formed the basis of this publication.