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Venclyxto (*venetoclax*)

An overview of Venclyxto and why it is authorised in the EU

What is Venclyxto and what is it used for?

Venclyxto is a cancer medicine used to treat adults with the following blood cancers:

- chronic lymphocytic leukaemia (CLL).
- acute myeloid leukaemia (AML).

For CLL, it is used either in combination with other cancer medicines or on its own.

Venclyxto can be used with obinutuzumab in patients who have not previously been treated for CLL or with rituximab in patients who have received at least one previous treatment. Obinutuzumab and rituximab are immunotherapy medicines (medicines that act through the body's defence system).

It can also be used on its own in:

- patients with particular genetic changes (17p deletion or *TP53* mutation) who cannot be treated with medicines known as B-cell receptor pathway inhibitors (ibrutinib and idelalisib) or if these medicines have stopped working.
- patients who do not have these genetic changes, after treatments with chemotherapy combined with immunotherapy as well as a B-cell receptor pathway inhibitor have both not worked.

For AML, Venclyxto is used in combination with either azacitidine or decitabine in adults who cannot have intensive chemotherapy.

Venclyxto contains the active substance venetoclax.

How is Venclyxto used?

Venclyxto should be started and supervised by a doctor with experience of cancer medicines and can only be obtained with a prescription. It is available as tablets (10, 50 and 100 mg) to be taken by mouth once a day with a meal.

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For CLL, the starting dose of Venclyxto is 20 mg daily and the dose is gradually increased over five weeks to 400 mg daily. It is then continued at a dose of 400 mg daily, and the length of treatment depends on which medicine it is given with. When given alone, Venclyxto is given for as long as treatment continues to work. For AML, the starting dose is 100 mg which is increased over three days to 400 mg daily. The dose may need to be reduced or treatment interrupted or stopped if certain side effects occur.

For more information about using Venclyxto, see the package leaflet or contact your doctor or pharmacist.

How does Venclyxto work?

The active substance in Venclyxto, venetoclax, attaches to a protein called Bcl-2. This protein is present in high amounts in leukaemia cancer cells, where it helps the cells survive for longer in the body and makes them resistant to cancer medicines. By attaching to Bcl-2 and blocking its actions, venetoclax causes the death of cancer cells and thereby slows down progression of the disease.

What benefits of Venclyxto have been shown in studies?

CLL

Studies have shown that a high proportion of patients have their cancer cells partially or completely cleared following treatment with Venclyxto on its own. In a main study of 107 previously treated patients with CLL and 17p deletion, 75% responded partially or completely to Venclyxto. In another study of 127 patients with or without 17p deletion or *TP53* mutation, the response rate was 70%. Patients in this second study had all previously taken B-cell receptor pathway inhibitors.

A third study in 389 patients with CLL who received at least one previous treatment showed that patients treated with Venclyxto plus rituximab lived longer without their disease getting worse (progression-free survival) than patients treated with rituximab and bendamustine (another cancer medicine).

Another study involving 432 patients with CLL who had not previously been treated for the disease found that patients treated with Venclyxto plus obinutuzumab lived longer without their disease getting worse compared with patients treated with chlorambucil (a chemotherapy medicine) plus obinutuzumab.

AML

A study involving 431 patients with AML who had not previously been treated for the disease found that 65% of patients treated with Venclyxto plus azacitidine had no sign of the disease (complete response), with or without recovery of blood cells compared with 25% of patients treated with azacitidine alone. Patients lived an average of 15 months with Venclyxto plus azacitidine compared with 10 months with azacitidine alone.

What are the risks associated with Venclyxto?

For CLL, the most common side effects with Venclyxto used with obinutuzumab or rituximab or on its own (seen in more than 1 in 10 people) are pneumonia (lung infection), nose and throat infection, low levels of neutrophils (a type of white blood cell), anaemia (low red blood cell counts), lymphopenia (low levels of lymphocytes, a type of white blood cell), hyperkalaemia (high blood potassium levels),

hyperphosphataemia (high blood phosphate levels), hypocalcaemia (low blood calcium levels), diarrhoea, nausea, vomiting, constipation and tiredness.

The most common serious side effects (seen in more than 1 in 10 people) were anaemia and reduced neutrophils. In AML, the most common side effects with Venclyxto used in combination with azacitidine (seen in more than 1 in 10 people) are pneumonia, sepsis (blood poisoning), urinary tract infection (infection of the structures that carry urine), neutropenia (low levels of neutrophils, a type of white blood cells) with or without fever, anaemia, thrombocytopenia (low levels of blood platelets), hypokalaemia (low levels of potassium), decreased appetite, dizziness, headache, nausea, diarrhoea, vomiting, stomatitis (inflammation of the lining of the mouth), abdominal pain, joint pain, weakness, tiredness, decreased weight and increased blood bilirubin levels (high blood levels of bilirubin, a breakdown product of red blood cells, which can cause yellowing of the skin and eyes).

The most common serious side effects (seen in more than 1 in 10 people) are pneumonia, sepsis, neutropenia with or without fever, anaemia, thrombocytopenia, hypokalaemia and bleeding. For the full list of side effects with Venclyxto, see the package leaflet.

Venclyxto must not be used with St. John's wort (a herbal remedy used to treat anxiety and depression). When used for CLL, Venclyxto must also not be used with medicines that are 'strong CYP3A inhibitors' during the early stages of treatment. For the full list of restrictions, see the package leaflet.

Why is Venclyxto authorised in the EU?

The European Medicines Agency decided that Venclyxto's benefits outweigh its risks and it can be authorised for use in the EU.

For CLL, a high proportion of patients respond to Venclyxto after other treatments have failed or are unsuitable. When used in combination with rituximab, Venclyxto prolonged the time patients lived without their disease getting worse.

The study in patients whose CLL had not been treated previously suggests that Venclyxto combined with obinutuzumab is a reasonable treatment option. The combination offers the possibility of avoiding side effects of chemotherapy medicines.

For AML, Venclyxto prolonged the time patients lived when given with azacitidine. Because decitabine is a medicine with similar characteristics to azacitidine EMA also considered that similar benefits are expected with decitabine.

Regarding safety, the side effects of Venclyxto are considered acceptable. Although there is a risk of tumour lysis syndrome, a complication that occurs when the cancer cells are being destroyed too quickly, this risk can be contained through preventive measures, such as increasing the dose gradually or reducing the dose, if needed.

What measures are being taken to ensure the safe and effective use of Venclyxto?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Venclyxto have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Venclyxto are continuously monitored. Side effects reported with Venclyxto are carefully evaluated and any necessary action taken to protect patients.

Other information about Venclyxto

Venclyxto received a conditional marketing authorisation valid throughout the EU on 5 December 2016. This was converted into a full marketing authorisation on 20 November 2018.

Further information on Venclyxto can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/Venclyxto.

This overview was last updated in 06-2021.