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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 a blood cancer known as chronic lymphocytic leukaemia (CLL).

Venclyxto can be used in combination with rituximab (another cancer medicine) in patients who have received at least one previous treatment.

It can also be used on its own in:

- patients with particular genetic changes (17p deletion or TP53 mutation) that make them unsuitable for chemo-immunotherapy (a type of cancer treatment). In these patients, Venclyxto is used when medicines known as B-cell receptor pathway inhibitors (ibrutinib and idelalisib) are not suitable or have failed.
- patients who do not have these genetic changes after treatments with chemo-immunotherapy and a B-cell receptor pathway inhibitor have both failed.

Venclyxto contains that active substance venetoclax.

How is Venclyxto used?

Venclyxto is available as tablets (10, 50 and 100 mg) to be taken by mouth once a day with a meal. The starting dose is 20 mg daily and the dose is gradually increased over 5 weeks to 400 mg.

When Venclyxto is used in combination with rituximab, the recommended dose of Venclyxto is 400 mg once a day. Patients should have taken Venclyxto at the daily dose of 400 mg for 7 days before starting therapy with rituximab. Venclyxto should be taken for 24 months from day 1 of the first cycle of rituximab.

When Venclyxto is used on its own, treatment should continue for as long as the patient improves or remains stable and the side effects are tolerable. If the patient experiences certain side effects, treatment may be stopped temporarily or the dose reduced.

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Venclyxto should be started and supervised by a doctor with experience of cancer medicines and can only be obtained with a prescription.

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 CLL 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 the progression of the disease.

What benefits of Venclyxto have been shown in studies?

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.

Another 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).

What are the risks associated with Venclyxto?

The most common side effects with Venclyxto used on its own (seen in more than 1 in 5 people) are low levels of neutrophils (a type of white blood cell), diarrhoea, nausea, anaemia (low red blood cell counts), nose and throat infection and tiredness. The most common side effects when Venclyxto is used with rituximab are low level of neutrophils, diarrhoea and nose and throat infection.

The most common serious side effects (seen in more than 2 in 100 people) in patients receiving Venclyxto in combination with rituximab or on its own are pneumonia (lung infection), fever associated with reduced neutrophils and tumour lysis syndrome (a complication caused by breakdown of cancer cells). For the full list of side effects with Venclyxto, see the package leaflet.

Venclyxto must not be used with medicines known as ‘strong CYP3A inhibitors’ during the early stages of treatment and must also not be used with St. John’s wort (a herbal preparation used to treat anxiety and depression). 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.

A high proportion of patients respond to Venclyxto after other treatments have failed or are unsuitable. Studies showed patients with particular genetic mutations (17p deletion or *TP53* mutations) that make them unsuitable for chemo-immunotherapy responding well to Venclyxto used on its own. A high response rate was also seen in patients whose previous treatment with ibrutinib or idelalisib failed. When used in combination with rituximab, Venclyxto was shown to prolong the time patients lived without their disease getting worse.

Regarding safety, the medicine's side effects 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.

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