EMA/4229/2025
EMEA/H/C/005636

Welireg (*belzutifan*)

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

What is Welireg and what is it used for?

Welireg is a cancer medicine used to treat:

- adults with advanced clear cell renal cell carcinoma (a type of kidney cancer) that has worsened despite two or more previous treatments, including a PD-(L)1 inhibitor and at least two types of VEGF-targeted medicines. 'Advanced' means that the cancer has started to spread;
- adults with von Hippel-Lindau (VHL) disease who need treatment for associated, localised (confined to one area of the body) renal cell carcinoma, central nervous system haemangioblastomas (a type of brain cancer) or pancreatic neuroendocrine tumours (a type of pancreatic cancer), and who cannot have surgery or other local treatments. VHL disease is a genetic condition that causes tumours and cysts to grow in certain parts of the body.

Welireg contains the active substance belzutifan.

How is Welireg used?

Welireg can only be obtained with a prescription and treatment should only be started and supervised by a doctor who has experience in treating patients with cancer.

Welireg is available as tablets to be taken once daily by mouth. Treatment is given for as long as the patient benefits from it or until side effects become unacceptable.

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

How does Welireg work?

The active substance in Welireg, belzutifan, works by blocking the action of a protein called hypoxia-inducible factor 2 alpha (HIF-2α), which is involved in the growth of cells, the formation of new blood vessels and cancer growth. By blocking the action of this protein, belzutifan can prevent the formation of new blood vessels, cutting off the blood supply that keeps cancer cells growing, and reduce the growth of the cancer.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What benefits of Welireg have been shown in studies?

Advanced clear cell renal cell carcinoma (RCC)

A main study showed that Welireg was at least as effective as another approved cancer medicine, everolimus, in treating advanced clear cell renal cell carcinoma.

The study found that among the 369 patients whose condition had worsened despite previous treatments, those receiving Welireg lived for around 22 months, while those who received everolimus lived for around 18 months. In addition, people receiving Welireg lived for an average of 4.6 months without the cancer getting worse, compared with 5.4 months for those who received everolimus.

von Hippel-Lindau (VHL) disease-associated tumours

A main study showed that Welireg was effective in treating people with certain VHL disease-associated tumours.

The main measure of effectiveness was the proportion of patients with renal cell carcinoma who either had no signs of cancer or whose cancer shrank following treatment with Welireg. 41 out of 61 patients with this cancer (67%) achieved this response, which was maintained for at least 18 months in 29 patients. Reponses were also seen in patients with central nervous system haemangioblastomas and pancreatic neuroendocrine tumours. This study did not compare Welireg with any other treatment or with placebo (a dummy treatment).

What are the risks associated with Welireg?

For the full list of side effects and restrictions with Welireg, see the package leaflet.

The most common side effects with Welireg (which may affect more than 1 in 10 people) include anaemia (low levels of red blood cells), tiredness, nausea (feeling sick), dyspnoea (difficulty breathing), dizziness and hypoxia (lack of oxygen in body tissues). Some side effects with Welireg can be serious. The most common are hypoxia, anaemia and dyspnoea and may affect up to 1 in 10 people.

Using Welireg during pregnancy can cause miscarriage and serious harm to a developing baby. Therefore, Welireg must not be used by pregnant women with VHL disease-associated tumours and should only be used by pregnant women with advanced clear cell renal cell carcinoma if the doctor considers it absolutely necessary. Women able to have children must take a pregnancy test before starting treatment with Welireg to confirm that they are not pregnant. Women should use an effective form of contraception before and during treatment with Welireg and for at least 1 week after stopping treatment. Welireg can reduce the effectiveness of hormonal contraception. Therefore, women taking Welireg must also use a non-hormonal contraception method such as having their partner use a condom.

Why is Welireg authorised in the EU?

At the time of approval there were limited treatment options for adults with advanced clear cell renal cell carcinoma whose cancer had worsened despite two or more previous treatments, including a type of cancer medicine called PD-(L)1 inhibitor and at least two types of VEGF-targeted cancer medicines. A main study showed that Welireg is at least as effective as a comparator medicine in prolonging survival and delaying worsening of the disease in these patients.

At the time of approval there was no authorised treatment for adults with VHL disease who required treatment for associated tumours. Although the main study in these patients did not compare Welireg

with another cancer treatment or with placebo, and only included a small number of patients, it showed that Welireg was effective in reducing the cancer size or eliminating signs of cancer.

With respect to safety, the side effects of Welireg in the studies were manageable. The European Medicines Agency therefore decided that Welireg's benefits are greater than its risks and that it can be authorised for use in the EU.

Welireg has been given conditional authorisation. This means that it has been authorised on the basis of less comprehensive data than are normally required because it fulfils an unmet medical need. The Agency considers that the benefit of having the medicine available earlier outweighs any risks associated with using it while awaiting further evidence.

The company must provide further data on Welireg. It must submit the results from two ongoing studies to confirm the effectiveness and safety of Welireg in adults with certain VHL disease-associated tumours. Every year, the Agency will review any new information that becomes available.

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

The company that markets Welireg will provide a guide for healthcare professionals and a card for patients, explaining the risks of serious harm to a developing baby, the precautions to be taken to avoid pregnancy during treatment and the course of action if a woman becomes pregnant during treatment.

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

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

Other information about Welireg

Welireg received a conditional marketing authorisation valid throughout the EU on 12 February 2025.

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

This overview was last updated in 02-2025.