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Yervoy (*ipilimumab*)

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

What is Yervoy and what is it used for?

Yervoy is a cancer medicine used in adults and adolescents from 12 years of age with advanced melanoma (a type of skin cancer) and in adults with advanced renal cell carcinoma (a kidney cancer).

Yervoy is usually used in combination with another medicine, nivolumab, but can also be used on its own for melanoma.

For renal cell carcinoma, Yervoy is given to patients who have not been treated before and are at moderate or high risk of their cancer getting worse.

Yervoy contains the active substance ipilimumab.

How is Yervoy used?

Yervoy is given by infusion (drip) into a vein over 90 minutes and the dose depends on the patient's body weight.

When Yervoy is used alone, the patient receives a dose every 3 weeks for a total of 4 doses. When used with nivolumab, the patient receives a dose of Yervoy and of nivolumab every 3 weeks for 4 doses followed by treatment with nivolumab alone.

The doctor may delay doses if certain side effects occur, and stop treatment altogether if side effects are severe.

Yervoy can only be obtained with a prescription and treatment should be started and supervised by a specialist doctor experienced in treating cancer. For more information about using Yervoy, see the package leaflet or contact a doctor or pharmacist.

How does Yervoy work?

The active substance in Yervoy, ipilimumab, is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognise and attach to a specific target in the body.

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Ipilimumab increases the number and the activity of a type of white blood cells called T cells which form part of the immune system and which can kill cancer cells. It acts on T cells by attaching to and blocking the activity of CTLA-4, a protein that controls the activity of T cells.

What benefits of Yervoy have been shown in studies?

Advanced melanoma

Several studies have shown that Yervoy is effective in prolonging the lives of patients with advanced melanoma.

In a study involving 676 adults in whom previous treatment for advanced melanoma had not worked or had stopped working, overall survival with Yervoy combined with an experimental medicine called 'gp100' was 10 months, compared with 6 months in patients receiving gp100 alone.

In a study involving 502 adults whose advanced melanoma had not been treated previously, patients treated with high-dose Yervoy and dacarbazine lived for 11 months on average, compared with 9 months for those given placebo (a dummy treatment) plus dacarbazine. However, about one-third of the patients could not complete Yervoy treatment due to side effects.

In a study involving 727 adults with advanced melanoma, patients treated with Yervoy 3 mg per kg lived for around 12 months on average compared with 16 months for those treated with 10 mg per kg. However, patients treated with the higher dose had more side effects and were less likely to complete treatment as a result. Several other studies involving previously untreated adults found that patients treated with Yervoy at 3 mg per kg lived for 13.5 months on average.

In two small studies involving a total of 30 adolescents aged 12 to 18 years with advanced melanoma, treatment with Yervoy produced similar levels of medicine in blood as in adults. The effects of Yervoy in adolescents are expected to be similar to those in adults. Because the medicine has been studied in very few adolescents, there is uncertainty about the medicine's side effects. Therefore, all adolescents treated with Yervoy will be monitored closely.

Finally, two studies found the combination of Yervoy and nivolumab effective for treating advanced melanoma in adults who had not been treated previously, and whose cancer produced a protein called PD-L1. In the first of these studies involving 945 adults, patients treated with Yervoy and nivolumab lived for 11.7 months on average without their disease getting worse compared with 6.9 months for those treated with nivolumab alone and 2.9 months for those treated with Yervoy alone. In the second study involving 142 adults, the disease was controlled in 56% of patients receiving Yervoy and nivolumab compared with 9% of patients receiving Yervoy alone.

Advanced renal cell carcinoma

One main study involving 1,096 adults with previously untreated advanced renal cell carcinoma compared treatment with Yervoy and nivolumab versus treatment with another cancer medicine for renal cell carcinoma, sunitinib. The results showed that in patients at moderate or high risk of their cancer getting worse, patients given the combination lived overall longer than those given sunitinib. After 24 months, 66.5% of patients given the combination were alive compared with 52.9% in the sunitinib group. In addition, 41.6% of patients (177 out of 423) responded to the treatment with the combination compared with 26.5% (112 out of 416) of those receiving sunitinib. The time patients lived before their disease got worse was 11.6 months with the combination compared with 8.4 with sunitinib.

What are the risks associated with Yervoy?

Yervoy is commonly associated with side effects resulting from excessive activity of the immune system, including severe reactions and inflammation. Most will improve with appropriate treatment or on stopping Yervoy. The most common side effects (which may affect more than 1 in 10 people) are diarrhoea, rash, itching, tiredness, nausea (feeling sick), vomiting, decreased appetite and abdominal pain (belly ache). Additional common side effects when Yervoy is used with nivolumab include fever, reduced or increased levels of thyroid hormones, colitis (inflammation of the lower gut), joint pain, headache and breathing difficulty.

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

Why is Yervoy authorised in the EU?

The European Medicines Agency noted that Yervoy improves survival in melanoma, a condition where overall survival rates are low. The most frequent side effects of the medicine are mild to moderate in severity. Because studies with Yervoy have included very few adolescents, the company has committed to collecting information on side effects, including any effects on growth and sexual maturation. In the treatment of advanced renal cell carcinoma, Yervoy in combination with nivolumab also increases patients' survival, and side effects are considered acceptable.

The Agency decided that Yervoy's benefits are greater than its risks and it can be authorised for use in the EU. In the treatment of melanoma, despite longer survival with a dose of 10 mg per kg, the Agency recommended using Yervoy at a dose of 3 mg per kg because the higher dose caused more side effects and worsened patients' quality of life after the start of treatment.

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

The company that markets Yervoy must ensure that all healthcare professionals expected to prescribe the medicine as well as patients are given a brochure with safety information on the medicine including the side effects resulting from excessive activity of the immune system. Patients will also receive from their doctor an alert card summarising key safety information on the medicine.

As it is not clear how much Yervoy contributes to the benefits when given in combination with nivolumab in patients with advanced renal cell carcinoma, the company must conduct a study to determine the precise contribution of Yervoy and if the risks associated with Yervoy can be further minimised.

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

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

Other information about Yervoy

Yervoy received a marketing authorisation valid throughout the EU on 13 July 2011.

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

This overview was last updated in 12-2018.