



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EPAR summary for the public

Opdivo

nivolumab

This is a summary of the European public assessment report (EPAR) for Opdivo. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Opdivo.

For practical information about using Opdivo, patients should read the package leaflet or contact their doctor or pharmacist.

What is Opdivo and what is it used for?

Opdivo is a cancer medicine used on its own or with another cancer medicine, ipilimumab, to treat adults with advanced melanoma, a type of skin cancer that has spread to other parts of the body or cannot be surgically removed.

Opdivo is also used on its own to treat adults with:

- a lung cancer called non-small cell lung cancer (NSCLC) that has spread locally or to other parts of the body in patients who have previously been treated with other cancer medicines (chemotherapy);
- advanced renal cell carcinoma, a kidney cancer, in patients who have been previously treated with other cancer medicines;
- classical Hodgkin lymphoma, a cancer of the lymphocytes (a type of white blood cell), that has not improved or has returned after an autologous stem cell transplant (a procedure where the bone marrow is replaced with the patient's own stem cells to form new bone marrow that produces healthy blood cells) and treatment with brentuximab vedotin (another cancer medicine);
- squamous cell cancer of the head and neck (SCCHN) in patients whose cancer is progressing despite treatment with platinum-based cancer medicines;

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- urothelial cancer, a cancer of the bladder and urinary tract, that has spread locally and cannot be surgically removed or has spread to other parts of the body. It is used when treatment with platinum-based cancer medicines has not worked.

Opdivo contains the active substance nivolumab.

How is Opdivo used?

Treatment with Opdivo must be started and supervised by a doctor experienced treating cancer. The medicine can only be obtained with a prescription.

Opdivo is available as a concentrate that is made up into a solution for infusion (drip) into a vein. The dose and frequency to be given depends on whether it is used alone or in combination with ipilimumab. Treatment is given for as long as the patient benefits from it. The doctor may need to delay doses if certain side effects occur, or stop treatment altogether if side effects are severe. For further information, see the package leaflet.

How does Opdivo work?

The active substance in Opdivo, nivolumab, is a monoclonal antibody, a type of protein that has been designed to recognise and attach to a receptor (target) called PD-1 found on certain cells of the immune system called T cells. Cancer cells can produce proteins (PD-L1 and PD-L2) that attach to this receptor and switch off the activity of the T cells, preventing them from attacking the cancer. By attaching to the receptor, nivolumab prevents PD-L1 and PD-L2 from switching off the T cells, thereby increasing the ability of the immune system to kill cancer cells.

What benefits of Opdivo have been shown in studies?

Advanced melanoma

Opdivo used on its own was studied in two main studies in patients with advanced melanoma. The first study, involving 418 previously untreated advanced melanoma patients, found that patients treated with Opdivo survived longer than patients who received the cancer medicine dacarbazine: 73% of patients treated with Opdivo were alive at 12 months compared with 42% of patients given dacarbazine. The second study looked at 405 advanced melanoma patients whose disease had got worse despite previous treatment with a cancer medicine. In this study, where patients were followed up for at least 6 months, around 32% (38 out of 120) of patients given Opdivo responded to treatment and had a reduction in their tumours compared with about 11% (5 out of 47) of patients given investigator's choice of treatment (dacarbazine or a combination of carboplatin and paclitaxel).

An additional study in 945 previously untreated advanced melanoma patients investigated Opdivo in combination with ipilimumab, Opdivo used alone or ipilimumab used alone. Patients who were given Opdivo plus ipilimumab lived for another 11.5 months without their disease getting worse and patients given only Opdivo lived for another 6.9 months without their disease getting worse. Patients given only ipilimumab lived for 2.9 months without their disease getting worse.

More patients were alive after 2 years with Opdivo and ipilimumab treatment (64%) than with Opdivo alone (59%) or ipilimumab alone (45%).

The study included patients whose cancer cells produced high levels of PD-L1 as well as patients whose cancer cells produced low levels of PD-L1. Improvements in the time patients lived without their disease getting worse when treated with Opdivo plus ipilimumab relative to Opdivo used on its own were only seen for patients whose cancer cells produced low levels of PD-L1.

NSCLC

In NSCLC that had spread locally or to other parts of the body, Opdivo improved the average time patients survived compared with docetaxel (another cancer medicine). Studies have shown benefit in two forms of NSCLC, known as non-squamous and squamous.

For non-squamous NSCLC, one main study involved 582 patients whose disease had progressed despite previous treatments. The average survival with Opdivo was 12.2 months, compared with 9.4 months with docetaxel. For squamous NSCLC, a study involving 272 patients showed that patients given Opdivo survived for 9.2 months, compared with 6.0 months in patients given docetaxel. Supportive information was also provided from another study indicating that Opdivo could produce a response in patients with squamous NSCLC whose disease had progressed despite several previous treatments.

Advanced renal cell carcinoma

Opdivo was compared with everolimus in one main study involving 821 patients with advanced renal cell carcinoma whose disease advanced despite previous treatment. Patients given Opdivo survived for 25.0 months, compared with 19.6 months in patients given everolimus.

Classical Hodgkin lymphoma

Opdivo was studied in one main study and a supportive study involving a total of 95 patients with classical Hodgkin lymphoma whose disease had not responded or had returned after autologous stem cell transplantation and treatment with brentuximab vedotin. Opdivo was used on its own and not compared with any other medicine. After treatment, cancer cells were partially or completely cleared in around 66% of patients (63 out of 95).

SCCHN

Opdivo was investigated in one main study involving 361 patients with SCCHN whose cancer progressed despite previous treatment with platinum medicines. Opdivo was used on its own and was compared with another cancer medicine (cetuximab, methotrexate or docetaxel) chosen by the treating doctor. Patients given Opdivo survived on average for 7.5 months, compared with 5.1 months in patients given other treatments.

Urothelial cancer

Opdivo was investigated in one main study involving 270 patients with urothelial cancer whose cancer got worse or returned despite previous treatment with platinum medicines. Opdivo was used on its own and not compared with any other medicine. In the study, 20% of patients (54 out of 270) responded to treatment and had a tumour size reduction.

What are the risks associated with Opdivo?

The most common side effects with Opdivo (which may affect more than 1 in 10 people) are tiredness, diarrhoea, nausea (feeling sick), rash and pruritus (itching), most of which are mild to moderate in severity. These side effects were also among the most common side effects when Opdivo was used together with ipilimumab. The other common side effects of the combination, which are also mostly mild or moderate, are pyrexia (fever), decreased appetite, hypothyroidism (an underactive thyroid gland), vomiting, colitis (inflammation of the gut), abdominal pain, arthralgia (joint pain), headache and breathing difficulty.

Opdivo is also commonly associated with side effects related to the activity of the immune system on body organs. Most will go away with appropriate treatment or on stopping Opdivo.

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

Why is Opdivo approved?

The European Medicines Agency considered that Opdivo has been convincingly shown to benefit patients with certain advanced cancers (melanoma, NSCLC, renal cell carcinoma or SCCHN) by either increasing patients' survival or the time they could live without their disease getting worse. In studies of urothelial cancer where other treatments had failed, patients responded to treatment with Opdivo. Studies of classical Hodgkin lymphoma involved only a small number of patients. However, high response rates were seen in these patients, in whom other treatments had failed and who had few other treatment options. Side effects from Opdivo were considered manageable with appropriate measures and were outweighed by the benefits. The Agency therefore decided that Opdivo's benefits are greater than its risks and recommended that it be approved for use in the EU.

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

The company that markets Opdivo will provide educational packs for doctors who are expected to prescribe Opdivo containing information on how the medicine should be used, how to manage side effects, particularly those related to the activity of the immune system, and possible risks for classical Hodgkin lymphoma patients if they go on to have an allogeneic stem cell transplant (a transplant of stem cells from a donor). The company will also provide an alert card for patients with information on the risks of the medicine, as well as instructions on when to contact their doctor if they experience symptoms. The company will also provide further data on the long-term benefits of Opdivo and carry out studies to try to identify which patients are most likely to benefit from treatment with the medicine.

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

Other information about Opdivo

The European Commission granted a marketing authorisation valid throughout the European Union for Opdivo on 19 June 2015.

The full EPAR for Opdivo can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_public_assessment_reports. For more information about treatment with Opdivo, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2017.