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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Opdivo (nivolumab)

On 20 July 2017, Bristol-Myers Squibb Pharma EEIG officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a new use of Opdivo in the treatment of liver cancer.

What is Opdivo?

Opdivo is a cancer medicine that contains the active substance nivolumab and is available as a concentrate that is made up into a solution for infusion (drip) into a vein.

Opdivo has been authorised since June 2015. It is already used for advanced melanoma (a skin cancer), non-small cell lung cancer, renal cell carcinoma (kidney cancer), Hodgkin's lymphoma (cancer affecting lymphocytes, a type of white blood cell), squamous cell cancer of the head and neck, and urothelial cancer (cancer of the bladder and urinary tract). Further information on Opdivo's current uses can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

What was Opdivo expected to be used for?

Opdivo was also expected to be used for the treatment of hepatocellular carcinoma (cancer that starts in the liver) in adults who had previously been treated with sorafenib (another cancer medicine).

How does Opdivo work?

The active substance in Opdivo, nivolumab, is a monoclonal antibody, a protein that has been designed to recognise and attach to a receptor (target) called PD-1 on 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,

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

nivolumab prevents PD-L1 and PD-L2 from switching off the T cells, thereby increasing the immune system's ability to kill cancer cells.

In hepatocellular carcinoma, Opdivo is expected to work in the same way as it does in its existing indications.

What did the company present to support its application?

The company mainly provided results from a study involving 145 adults with advanced hepatocellular carcinoma who received Opdivo and had previously been treated with sorafenib. Opdivo was not directly compared with any other medicine. The main measure of effectiveness was the proportion of patients whose cancer shrank in size ('overall response rate').

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the questions, there were still some unresolved issues.

What was the recommendation of the CHMP at that time?

Based on the review of the data and the company's response to the CHMP lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Opdivo could not have been approved for the treatment of hepatocellular carcinoma in adults who had previously been treated with sorafenib.

The CHMP was of the opinion that the study results provided by the company were insufficient to determine the benefit of Opdivo in patients with hepatocellular carcinoma. The study did not compare Opdivo directly with other treatments and there was insufficient information about patients in the study to be able to properly compare the results with those of other studies.

Therefore, the CHMP concluded that the medicine could not have been approved based on the data presented by the company.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that despite the promising data shown for Opdivo in the treatment of hepatocellular carcinoma, uncertainties about the design of the main study did not allow the CHMP to conclude that the benefit outweighed the risk at the present time.

The withdrawal letter is available here.

What consequences does this withdrawal have for patients in clinical trials?

The company informed the CHMP that the withdrawal does not have any consequences for patients currently included in clinical trials using Opdivo.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Opdivo for the treatment of other diseases?

There are no consequences on the use of Opdivo in its authorised uses.