



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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

On 13 December 2017, Bristol-Myers Squibb Pharma EEIG officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application to extend the use of Opdivo to treat colorectal 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 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](http://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 metastatic colorectal cancer (bowel cancer that has spread to other parts of the body) where the cancer had certain genetic changes (called 'mismatch repair deficient' or 'microsatellite instability high'). It was to be used in adults who had previously been treated with fluoropyrimidines (a type of cancer medicines) together with other cancer medicines.

### 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 PD-1, a receptor (target) 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,



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 colorectal cancer, 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 provided results from a main study involving 74 adults with metastatic colorectal cancer, all of whom received Opdivo. Opdivo was not compared with any other treatment. The main measure of effectiveness was based on the proportion of patients whose cancer shrank and how long this improvement lasted.

### **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 metastatic colorectal cancer with specific genetic changes.

The CHMP was of the opinion that the results from the main study were insufficient to determine the benefit of Opdivo in these patients. The study did not compare Opdivo with other treatments and there were concerns about the design of the study and the criteria used to select and categorise study participants.

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 it was withdrawing because of the remaining uncertainties which 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 with 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 indications.