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

On 27 June 2018, 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 for the treatment of stomach cancer.

What is Opdivo?

Opdivo is a cancer medicine currently authorised to treat the following cancers: melanoma (skin cancer), non-small cell lung cancer, renal cell carcinoma (kidney cancer), classical Hodgkin lymphoma (a blood cancer), squamous cell cancer of the head and neck, and urothelial (bladder) cancer.

Opdivo has been authorised since June 2015 and contains the active substance nivolumab.

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 expected to be used to treat stomach cancer, including cancers that occur at the junction of the stomach and oesophagus (the tube that leads from the mouth to the stomach).

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 specific structure.

Nivolumab attaches to a receptor called PD-1 which is 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.

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What did the company present to support its application?

The company presented data from a main study comparing Opdivo with placebo (a dummy treatment) in 493 patients with cancer of the stomach or at the junction of the stomach and oesophagus. All patients were Japanese, Korean or Taiwanese and had recurring cancer that could not be surgically removed or treated with standard therapy. The study looked at how long the patients lived while taking Opdivo.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the documentation provided by the company and formulated lists of questions.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 stomach cancer.

The CHMP noted that in the main study Opdivo treatment led to a limited improvement in survival (around 1 month). Furthermore, it was not clear that even this benefit would be seen in European patients, as the patients in the study were from populations who are known to be affected differently by stomach cancer. In the absence of further data, it was not possible to establish that the benefits of Opdivo outweighed its risks for European patients.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that a benefit of Opdivo in the treatment of stomach cancer had not been demonstrated.

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 would not allow the CHMP to conclude that the benefits outweighed the risks 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 there are no 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 cancers?

There are no consequences for Opdivo in its authorised uses.