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Withdrawal of application to change the marketing authorisation for Keytruda (*pembrolizumab*)

Merck Sharp & Dohme B.V. withdrew its application for the use of Keytruda in the treatment of cancer of the oesophagus (food pipe).

The company withdrew its application on 10 December 2019.

What is Keytruda and what is it used for?

Keytruda is a medicine already used to treat several cancers: melanoma (a skin cancer); non-small cell lung cancer, a type of lung cancer; classical Hodgkin lymphoma (a cancer of the white blood cells); urothelial cancer (a cancer of the bladder and urinary tract); a cancer affecting the head and neck known as head and neck squamous cell carcinoma and renal cell carcinoma (a kidney cancer).

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

What change had the company applied for?

The company applied to add to the medicine's authorised uses the treatment of cancer of the oesophagus that has come back and is locally advanced or metastatic. The medicine was to be used in patients whose tumours produce high levels of a protein known as PD-L1 and who had previously been treated with other cancer medicines.

How does Keytruda work?

In the treatment of oesophageal cancer, Keytruda is expected to work in the same way as it does in its existing uses.

The active substance in Keytruda, pembrolizumab, is a monoclonal antibody (a type of protein) that has been designed to block a receptor (target) called PD-1. Some cancers can make proteins called PD-L1 and PD-L2 that combine with PD-1 to switch off the activity of certain cells of the immune system (the body's natural defences) preventing them from attacking the cancer. By blocking PD-1,

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pembrolizumab stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells.

What did the company present to support its application?

Keytruda was investigated in a main study involving 628 patients with advanced or metastatic cancer of the oesophagus. Keytruda was compared with other cancer treatments (paclitaxel, docetaxel, or irinotecan). The main measure of effectiveness was patients' overall survival (how long patients lived).

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and had prepared questions for the company. After the Agency had assessed the company's responses to the questions, there were still some unresolved issues.

What did the Agency recommend at that time?

Based on the review of the information and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Keytruda could not have been authorised for cancer of the oesophagus.

The Agency considered that the results from the study did not show that Keytruda was effective at prolonging the lives of patients with cancer of the oesophagus.

Therefore, at the time of the withdrawal, the Agency's opinion was that the balance of benefits and risks of Keytruda in the treatment of cancer of the oesophagus could not be established.

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 is withdrawing the application because the results of the study were not considered sufficient to support an extension of indication at this time.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients who are receiving Keytruda for the treatment of cancer of the oesophagus in clinical trials.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.

What is happening with Keytruda in other uses?

There are no consequences for Keytruda in its authorised uses.