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**Questions and answers**

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

On 11 October 2017, Merck Sharp & Dohme officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application to extend the use of Keytruda in non-small cell lung cancer (NSCLC) to include metastatic non-squamous NSCLC in combination with chemotherapy.

## What is Keytruda?

Keytruda is a cancer medicine already authorised for use on its own to treat NSCLC. Keytruda is used specifically when the tumour produces a protein known as PD-L1 and is advanced or has spread to other parts of the body (metastatic).

Keytruda is also authorised to treat melanoma (a skin cancer), classical Hodgkin lymphoma (a blood cancer) and urothelial cancer (a cancer of the bladder and urinary tract).

Keytruda has been authorised in the EU since July 2015. It contains the active substance pembrolizumab.

Further information on Keytruda's current uses can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

## What was Keytruda expected to be used for?

Keytruda was also expected to be used in combination with the chemotherapy medicines pemetrexed and carboplatin in NSCLC patients with metastatic 'non-squamous' NSCLC, irrespective of whether their tumour produced the PD-L1 protein.

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## How does Keytruda work?

The active substance in Keytruda, pembrolizumab, is a monoclonal antibody (a type of protein) that has been designed to recognise and block a receptor 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, pembrolizumab stops the cancer switching off these immune cells, thereby increasing the ability of the immune system to kill the cancer cells.

## What did the company present to support its application?

The applicant presented data from a study involving 123 patients with locally advanced or metastatic NSCLC, which compared Keytruda taken together with pemetrexed and carboplatin chemotherapy with chemotherapy alone. The measures of effectiveness were the number of patients whose cancer shrank in size (overall response rate) and the time patients lived without their disease getting worse (progression free survival).

## 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. The CHMP was assessing the company's responses to the questions at the time of the withdrawal.

## 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 Keytruda could not have been approved for the treatment of metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin.

The CHMP's main concern was that the available data did not allow firm conclusions on the effectiveness and safety of Keytruda in these patients and further data from ongoing studies were needed in order to assess its benefits and risks.

## 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 its decision was based on the CHMP's consideration that uncertainties remain due to the limited number of patients included in the main study, despite the data provided for Keytruda in the applied use.

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 with Keytruda.

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 Keytruda in its authorised uses?

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