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Questions and answers

Withdrawal of the marketing authorisation application for Plivensia (sirukumab)

On 26 October 2017, Janssen-Cilag International NV officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Plivensia, for the treatment of rheumatoid arthritis.

What is Plivensia?

Plivensia is a medicine that contains the active substance sirukumab. It was to be available as a solution for injection in pre-filled pens and syringes (50 mg).

What was Plivensia expected to be used for?

Plivensia was expected to be used in adults with moderate to severe rheumatoid arthritis, a disease that causes inflammation of the joints.

The medicine was to be used in patients when treatment with one or more medicines known as disease-modifying anti-rheumatic drugs (DMARDs) had not worked well enough or had led to troublesome side effects. Plivensia was to be used with methotrexate (a DMARD) or alone if the patient could not take methotrexate.

How does Plivensia work?

The active substance in Plivensia, sirukumab, is a monoclonal antibody, a type of protein which has been designed to block a molecule called interleukin-6. Interleukin-6 is involved in causing inflammation and is found at high levels in the joints of patients with rheumatoid arthritis. By blocking interleukin-6, sirukumab reduces inflammation and other symptoms associated with rheumatoid arthritis.

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What did the company present to support its application?

The company presented data from three main studies involving over 3,000 patients. Two studies compared Plivensia with placebo (a dummy treatment) in patients with moderate to severe rheumatoid arthritis for whom treatment with a DMARD or with an anti-TNF agent (another type of medicine for rheumatoid arthritis) had not worked well enough or had led to troublesome side effects. The main measure of effectiveness was a reduction in symptoms of 20% or more, based on a standard rating score (ACR-20), after 16 weeks of treatment.

The third study compared Plivensia with adalimumab (a monoclonal antibody targeting a chemical messenger called tumour necrosis factor - TNF) in patients who could not take methotrexate or whose condition had not responded adequately to methotrexate; the study looked at the improvement in how patients' joints worked (based on a standard rating score called DAS28-ESR) after 24 weeks of treatment.

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 last round of 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 Plivensia could not have been approved for the treatment of moderate to severe rheumatoid arthritis.

The CHMP's main concern was that the long-term safety of Plivensia had not been well characterised due to limitations in the design of the main studies.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that, because of lack of proven long-term safety, the benefits of Plivensia did not outweigh its risks, and that further studies were needed.

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

In its letter notifying the Agency of the withdrawal of the application, the company stated that, given the need for additional clinical data and the fact that other treatments blocking the action of interleukin-6 are available, it wishes to prioritise other programs in its portfolio.

The withdrawal letter is available here.

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

The company informed the CHMP that it will discontinue the ongoing long-term extension study with Plivensia in patients with rheumatoid arthritis.

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