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Withdrawal of application to change the marketing authorisation for RoActemra (tocilizumab)

Roche Registration GmbH withdrew its application for the use of RoActemra in the treatment of interstitial lung disease (disorders causing scarring in the lungs) associated with systemic sclerosis. Systemic sclerosis is a disease in which the immune system (the body's natural defences) is overactive, causing fibrosis (thickening) of the skin and damage to internal organs, including progressive scarring of the lungs.

The company withdrew the application on 13 September 2023.

What is RoActemra and what is it used for?

RoActemra is a medicine used to treat inflammatory conditions including rheumatoid arthritis in adults and systemic juvenile idiopathic arthritis in children. RoActemra can also be used in adults with COVID-19 who are receiving treatment with corticosteroid medicines by mouth or injection and require extra oxygen or mechanical ventilation.

RoActemra has been authorised in the EU since January 2009. It contains the active substance tocilizumab and is available as a solution to be injected under the skin and as a concentrate for making a solution for infusion (drip) into a vein.

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

What change had the company applied for?

The company applied for an extension of indication to add the treatment of adults with systemic sclerosis-associated interstitial lung disease where it was intended to be used to slow the rate of decline in lung function.

How does RoActemra work?

The active substance in RoActemra, tocilizumab, is a monoclonal antibody, a type of protein that has been designed to recognise and attach to a specific target in the body. Tocilizumab attaches to the receptor for a messenger molecule called interleukin-6, which is involved in inflammation and is found at high levels in patients with many inflammatory conditions. By preventing interleukin-6 from

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attaching to its receptors, tocilizumab reduces the inflammation and other symptoms of these diseases. In systemic sclerosis-associated interstitial lung disease, RoActemra is expected to work in the same way as it does in its existing uses.

What did the company present to support its application?

The company submitted results from two studies comparing RoActemra with placebo (a dummy treatment) in patients with systemic sclerosis. The main measure of effectiveness was the change in patients' skin thickness (as measured by the modified Rodnan Skin Score (mRSS)) after 48 weeks. The studies also looked at the decline in the functioning of the patients' lungs over 48 weeks, measured by their forced vital capacity (FVC). FVC is the maximum amount of air the patient can breathe out forcefully after taking in a deep breath, and this decreases as the condition gets worse.

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. 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 RoActemra could not have been authorised for the treatment of systemic sclerosis-associated interstitial lung disease.

The studies did not show an improvement in the patients' skin thickness, which was the main measure of effectiveness for the treatment of systemic sclerosis in the studies. Although further analyses suggested that RoActemra may slow the decline in FVC compared with placebo in a subgroup of patients who had interstitial lung disease associated with systemic sclerosis, there were several uncertainties around these results. This included uncertainties around the way the target population was defined and the possibility that the results were a chance finding.

Therefore, at the time of the withdrawal, the Agency's opinion was that the benefits of RoActemra in the treatment of systemic sclerosis-associated interstitial lung disease did not outweigh its 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 it is withdrawing the application because the efficacy data were not considered sufficient by the Agency to support the use of RoActemra in the treatment of systemic sclerosis-associated interstitial lung disease.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials using RoActemra.

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

What is happening with RoActemra for the treatment of other diseases?

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