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RoActemra (*tocilizumab*)

An overview of RoActemra and why it is authorised in the EU

What is RoActemra and what is it used for?

RoActemra is a medicine used to treat:

- adults with severe rheumatoid arthritis that is getting worse in patients who have not been previously treated with a medicine called methotrexate;
- adults with moderate to severe active rheumatoid arthritis whose previous treatments with disease modifying antirheumatic drugs (DMARDs), such as methotrexate or medicines known as tumour necrosis factor (TNF) blockers, have not worked well or were not tolerated;
- children from 1 year of age with active systemic juvenile idiopathic arthritis in whom other treatments (with anti-inflammatory medicines called NSAIDs and corticosteroids) have not worked well enough;
- children from 2 years of age with juvenile idiopathic polyarthritis in whom treatment with methotrexate has not worked well enough.

RoActemra is used in combination with methotrexate for these conditions but it can be used on its own in patients for whom methotrexate is inappropriate.

RoActemra is also used to treat adults with giant cell arteritis, a disease in which arteries, usually of the head, are swollen.

RoActemra can also be used in adults and children from 2 years of age for the treatment of severe or life-threatening cytokine release syndrome (CRS, a condition that can cause nausea, vomiting, pain and low blood pressure). CRS is a side effect of certain cancer treatments and RoActemra is used for CRS caused by chimeric antigen receptors (CAR) T-cell medicines.

RoActemra contains the active substance tocilizumab.

How is RoActemra used?

RoActemra can only be obtained with a prescription and treatment should be started by a doctor who has experience in the diagnosis and treatment of the relevant condition.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

RoActemra 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. How RoActemra is given, its dose and how often it is given depends on the condition it is used to treat.

For more information about using RoActemra, see the package leaflet or contact your doctor or pharmacist.

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 (called an antigen) in the body. Tocilizumab attaches to the receptor for a messenger molecule or 'cytokine' called interleukin-6. This messenger is involved with inflammation and is found at high levels in patients with rheumatoid arthritis, systemic juvenile idiopathic arthritis, juvenile idiopathic polyarthritis, giant cell arteritis and CRS. By preventing interleukin-6 attaching to its receptors, tocilizumab reduces the inflammation and other symptoms of these diseases.

What benefits of RoActemra have been shown in studies?

Rheumatoid arthritis

In severe rheumatoid arthritis not previously treated with methotrexate, RoActemra given by infusion was investigated in one main study involving 1,162 patients. RoActemra, on its own or in combination with methotrexate, was compared with placebo (a dummy treatment) plus methotrexate. After 6 months of treatment, 45% of patients taking RoActemra in combination with methotrexate (130 out of 290) and 39% of patients taking RoActemra on its own (113 out of 292) achieved remission (did not show symptoms of the disease), compared with 15% of those taking placebo plus methotrexate (43 out of 287).

For the treatment of moderate to severe rheumatoid arthritis where other medicines were unsuccessful, RoActemra given by infusion was studied in five main studies involving a total of over 4,000 adults. In three of these studies, RoActemra was compared with placebo, as an add-on to failing treatment with conventional rheumatoid arthritis medicines in a total of over 3,000 patients. Results showed that patients adding RoActemra were around 4 times more likely to respond to treatment than those adding placebo. One of the studies, which involved 1,196 patients, also showed that the combination of RoActemra and methotrexate slowed down the damage to the joints and improved physical function after up to 2 years, when compared with the combination of placebo and methotrexate. In the fourth study, which included 498 patients who had an inadequate response to TNF blockers, patients receiving RoActemra with methotrexate were around 9 times more likely to respond than those receiving placebo with methotrexate. The fifth study involving 673 patients showed that patients receiving RoActemra on its own were more likely to respond than those taking methotrexate on its own. Almost 4,000 patients from these 5 studies went on to enter studies looking at the long-term effects of RoActemra treatment and results showed that response to RoActemra is maintained for at least 2 years.

RoActemra given by injection under the skin was investigated in two studies involving 1,918 patients with moderate to severe rheumatoid arthritis where previous treatment with DMARD had not worked well. In the first study, RoActemra was more effective than placebo in treating rheumatoid arthritis: after 6 months of treatment with RoActemra, 61% of patients responded to treatment compared with 32% on placebo. The other study, which compared RoActemra injected under the skin with RoActemra

given by infusion, showed that RoActemra injected under the skin was no less effective in achieving a response after 6 months.

Juvenile idiopathic arthritis

In systemic juvenile idiopathic arthritis, RoActemra given by infusion was compared with placebo in one main study involving 112 children in whom treatment with NSAID and corticosteroids did not work well enough. In this study 85% (64 out of 75) patients treated with RoActemra responded to treatment and no longer had fever after 3 months, compared with 24% (9 out of 37) patients receiving placebo.

Another study involving 51 children from 1 year of age showed that RoActemra given by injection under the skin had a similar distribution in the body and effect on the disease to that previously seen with RoActemra given by infusion.

Juvenile idiopathic polyarthritis

In juvenile idiopathic polyarthritis, RoActemra given by infusion was compared with placebo in one main study involving 166 children from 2 years of age who could not take methotrexate or it did not work well enough. Patients were allowed to continue treatment with methotrexate during the study. After 4 to 6 months of treatment, 26% of patients on RoActemra (21 out of 82) had a flare-up of symptoms during treatment, compared with 48% of patients taking placebo (39 out of 81).

Giant cell arteritis

In giant cell arteritis, RoActemra given by injection under the skin was found more effective than placebo in one main study involving 251 adults. All patients were also treated with a corticosteroid, which was stopped after reducing the dose gradually over 6 or 12 months. One year after starting treatment, 56% of patients treated with RoActemra once a week did not have symptoms compared with 14% patients receiving placebo.

Cytokine release syndrome (CRS)

RoActemra given by infusion was considered to be effective at treating severe CRS based on a review of data from 66 patients who experienced this condition after they were given CAR-T cell medicines to treat a blood cancer. The main measure of effectiveness was based on the number of patients whose CRS resolved within 14 days of the first dose of RoActemra, and who needed no more than two doses of the medicine, and no additional treatment other than corticosteroid medicines. Out of 51 patients who had CRS after being given the CAR-T cell medicine tisagenlecleucel, 39 responded to treatment with RoActemra (76.5%), while 8 out 15 patients (53.3%) who had CRS after being given axicabtagene ciloleucel responded.

What are the risks associated with RoActemra?

The most common side effects (occurring in up to 1 patient in 10) with RoActemra are upper respiratory tract infections (nose and throat infection), nasopharyngitis (inflammation of the nose and throat), headache, hypertension (high blood pressure) and abnormal liver function tests. The most serious side effects are serious infections, complications of diverticulitis (a disease affecting the gut) and hypersensitivity (allergic) reactions. For the full list of side effects of RoActemra, see the package leaflet.

RoActemra must not be used in patients who have an active, severe infection. Doctors should monitor patients carefully for signs of infection during treatment, and should prescribe RoActemra with caution in patients who have had recurring or long-term infections, or diseases that could increase the risk of infections, such as diverticulitis or diabetes. For the full list of restrictions, see the package leaflet.

Why is RoActemra authorised in the EU?

Studies show RoActemra is effective at reducing symptoms of several inflammatory conditions. The European Medicines Agency decided that RoActemra's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of RoActemra?

The company that markets RoActemra must supply all doctors expected to prescribe the medicine with an educational pack containing important information on the safety and correct use of RoActemra. The pack will also include a patient alert card with key safety information for patients.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of RoActemra have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of RoActemra are continuously monitored. Side effects reported with RoActemra are carefully evaluated and any necessary action taken to protect patients.

Other information about RoActemra:

RoActemra received a marketing authorisation valid throughout the EU on 16 January 2009.

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

This overview was last updated in 10-2018.