Package Leaflet: Information for the user

Actemra 20 mg/mL concentrate for solution for infusion
Tocilizumab

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

In addition to this leaflet, you will be given a **Patient Alert Card**, which contains important safety information that you need to be aware of before and during treatment with Actemra.

What is in this leaflet:

1. What Actemra is and what it is used for

Actemra contains the active substance tocilizumab, which is a protein made from specific immune cells (monoclonal antibody), that blocks the action of a specific protein (cytokine) called interleukin-6. This protein is involved in inflammatory processes of the body, and blocking it can reduce the inflammation in your body. Actemra helps to reduce symptoms such as pain and swelling in your joints and can also improve your performance of daily tasks. Actemra has been shown to slow the damage to the cartilage and bone of the joints caused by the disease and to improve your ability to do normal daily activities.

- **Actemra is used to treat adults** with moderate to severe active rheumatoid arthritis (RA), an autoimmune disease, if previous therapies did not work well enough. Actemra is usually given in combination with methotrexate. However, Actemra can be given alone if your doctor determines that methotrexate is inappropriate.

- Actemra can also be used to treat adults who have not had previous methotrexate treatment if they have severe, active and progressive rheumatoid arthritis.

- **Actemra is used to treat children with sJIA**. Actemra is used for children aged 2 years and over who have ***active systemic juvenile idiopathic arthritis*** (***sJIA***), an inflammatory disease that causes pain and swelling in one or more joints as well as fever and rash. Actemra is used to improve the symptoms of sJIA and can be given in combination with methotrexate or alone.

- **Actemra is used to treat children with pJIA**. Actemra is used for children aged 2 years and over with active ***polyarticular juvenile idiopathic arthritis*** (***pJIA***), an inflammatory disease that

causes pain and swelling in one or more joints. Actemra is used to improve the symptoms of pJIA and can be given in combination with methotrexate or alone.

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2. What you need to know before you are given Actemra

You are not to be given Actemra

- if you are **allergic** to tocilizumab or any of the other ingredients of this medicine (listed in Section 6).
- if you have an active, severe infection.

If any of these applies to you, tell the doctor or nurse giving you the infusion.

Warnings and precautions

Talk to your doctor or nurse before you are given Actemra.

- If you experience **allergic reactions** such as chest tightness, wheezing, severe dizziness or light-headedness, swelling of the lips or skin rash during or after the infusion, then **tell your doctor immediately.**

- If you have any kind of **infection**, short- or long-term, or if you often get infections. **Tell your doctor immediately** if you feel unwell. Actemra can reduce your body's ability to respond to infections and may make an existing infection worse or increase the chance of getting a new infection.

- If you have had **tuberculosis**, tell your doctor. Your doctor will check for signs and symptoms of tuberculosis before starting Actemra. If symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever), or any other infection appear during or after therapy tell your doctor immediately.

- If you have had **intestinal ulcers** or **diverticulitis**, tell your doctor. Symptoms would include abdominal pain and unexplained changes in bowel habits with a fever.

- If you have **liver disease**, tell your doctor. Before you use Actemra, your doctor may do a blood test to measure your liver function.

- **If any patient has recently been vaccinated** (either adult or child), or is planning a vaccination, tell your doctor. All patients, especially children, should be up-to-date with all their vaccinations before they start treatment with Actemra. Certain types of vaccines should not be used while receiving Actemra.

- If you have **cancer**, tell your doctor. Your doctor will have to decide if you can still be given Actemra.

- If you have **cardiovascular risk factors** such as raised blood pressure and raised cholesterol levels, tell your doctor. These factors need to be monitored while receiving Actemra.

- If you have moderate to severe **kidney function problems**, your doctor will monitor you.

- If you have **persistent headaches**.

Your doctor will perform blood tests before you are given Actemra, and during your treatment, to determine if you have a low white blood cell count, low platelet count or high liver enzymes.

Children and adolescents
Actemra is not recommended for use in children under 2 years of age.

If a child has a history of ***macrophage activation syndrome***, (activation and uncontrolled proliferation of specific blood cells), tell your doctor. Your doctor will have to decide if they can still be given Actemra.

Other medicines and Actemra
Tell your doctor if you are taking any other medicines (or your child is, if they are the patient), or have recently taken any. This includes medicines obtained without a prescription. Actemra can affect the way some medicines work, and the dose of these may require adjustment. If you are using medicines containing any of the following active substances, **tell your doctor**:

- methylprednisolone, dexamethasone, used to reduce inflammation
- simvastatin or atorvastatin, used to reduce **cholesterol levels**
- calcium channel blockers (e.g. amlodipine), used to treat **raised blood pressure**
- theophylline, used to treat **asthma**
- warfarin or phenprocoumon, used as a **blood thinning agents**
- phenytoin, used to treat **convulsions**
- ciclosporin, used to **suppress your immune system** during organ transplants
- benzodiazepines (e.g. temazepam), used to **relieve anxiety.**

Due to lack of clinical experience, Actemra is not recommended for use with other biological medicines for the treatment of RA, sJIA or pJIA.

Pregnancy, breast-feeding and fertility
Actemra is not to be used in pregnancy unless clearly necessary. Talk to your doctor if you are pregnant, may be pregnant, or intend to become pregnant.

Women of childbearing potential must use effective contraception during and up to 3 months after treatment.

Stop breast-feeding if you are to be given Actemra, and talk to your doctor. Leave a gap of at least 3 months after your last treatment before you start breast-feeding. It is not known whether Actemra is passed into breast milk.

The data available so far does not suggest any effect on fertility from this treatment.

Driving and using machines
This medicine can cause dizziness. If you feel dizzy, do not drive or use machines.

Actemra contains sodium
This medicine contains 26.55 mg sodium per maximum dose of 1200 mg. Take this into account if you are on a low-sodium diet. However, doses below 1025 mg of this medicine contain less than 23 mg sodium, so they are virtually sodium free.

3. How Actemra is given

This medicine is subject to restricted medical prescription by your doctor.

Actemra will be given to **you as a drip into a vein, by a doctor or a nurse.** They will dilute the solution, set up the intravenous infusion and monitor you during and after the treatment.

Adult patients with RA
The usual dose of Actemra is 8 mg per kg of body weight. Depending on your response, your doctor may decrease your dose to 4 mg/kg then increase back to 8 mg/kg when appropriate.

Adults will be given Actemra once every 4 weeks through a drip in the vein (intravenous infusion) over one hour.

Children with sJIA (aged 2 and over)
The usual dose of Actemra depends on your weight.
- If you weigh less than 30 kg: the dose is **12 mg for every kilogram of body weight**
- If you weigh 30 kg or more, the dose is **8 mg for every kilogram of body weight**

The dose is calculated based on your body weight at each administration.

Children with sJIA will be given Actemra once every 2 weeks through a drip in the vein (intravenous infusion) over one hour.

Children with pJIA (aged 2 and over)
The usual dose of Actemra depends on your weight.
- If you weigh less than 30 kg: the dose is **10mg for every kilogram of body weight**
- If you weigh 30 kg or more: the dose is **8 mg for every kilogram of body weight**

The dose is calculated based on your body weight at each administration.

Children with pJIA will be given Actemra once every 4 weeks through a drip in the vein (intravenous infusion) over one hour.

If you are given more Actemra than you should
Since Actemra is given by a doctor or nurse, it is unlikely that you will be given too much. However, if you are worried, talk to your doctor.

If you miss a dose of Actemra
Since Actemra is given by a doctor or nurse, it is unlikely that you will miss a dose. However, if you are worried, talk to your doctor or nurse.

If you stop being given Actemra
You should not stop using Actemra without discussing with your doctor first.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, Actemra can cause side effects, although not everybody gets them. Side effects could occur at least up to 3 months after your last dose of Actemra.

Possible serious side effects: tell a doctor straight away.
These are common: they may affect up to 1 in every 10 users

Allergic reactions during or after infusion:
- difficulty with breathing, chest tightness or light-headedness
- rash, itching, hives, swelling of the lips, tongue or face

If you notice any of these, tell your doctor **immediately**.

Signs of serious infections
- fever and chills
- mouth or skin blisters
- stomach ache

Signs and symptoms of liver toxicity
These may affect up to 1 in every 1000 users
- tiredness,
- abdominal pain,
- jaundice (yellow discoloration of skin or eyes)

If you notice any of these, tell your doctor **as soon as possible.**

Very common side effects:
These may affect more than 1 in every 10 users
- upper respiratory tract infections with typical symptoms such as cough, blocked nose, runny nose, sore throat and headache
- high blood fat (cholesterol) levels.

Common side effects:
These may affect up to 1 in every 10 users
- lung infection (pneumonia)
- shingles (herpes zoster)
- cold sores (oral herpes simplex), blisters
- skin infection (cellulitis) sometimes with fever and chills
- rash and itching, hives
- allergic (hypersensitivity) reactions
- eye infection (conjunctivitis)
- headache, dizziness, high blood pressure
- mouth ulcers, stomach pain
- fluid retention (oedema) in the lower legs, weight increase
- cough, shortness of breath
- low white blood cell counts shown by blood tests (neutropenia, leucopenia)
- abnormal liver function tests (increased transaminases)
- increased bilirubin shown by blood tests
- low fibrinogen levels in the blood (a protein involved in blood clotting).

Uncommon side effects:
These may affect up to 1 in every 100 users
- diverticulitis (fever, nausea, diarrhoea, constipation, stomach pain)
- red swollen areas in the mouth
- high blood fat (triglycerides)
- stomach ulcer
- kidney stones
- underactive thyroid.

Rare side effects:
These may affect up to 1 in every 1,000 users
- Stevens-Johnson syndrome (skin rash, which may lead to severe blistering and peeling of the skin)
- Fatal Allergic Reactions (Anaphylaxis [fatal])
- inflammation of the liver (hepatitis), jaundice

Very rare side effects:
These may affect up to 1 in every 10,000 users
- low counts for white blood cells, red blood cells and platelets in blood tests.
- liver failure

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Children with sJIA
In general, side effects in sJIA patients were of a similar type to those in adults with RA. Some side effects were seen more often: inflamed nose and throat, diarrhoea, lower white blood cell counts and higher liver enzymes.

Children with pJIA
In general, side effects in pJIA patients were of a similar type to those in adults with RA. Some side effects were seen more often: inflamed nose and throat, headache, feeling sick (nausea) and lower white blood cell counts.

5. How to store Actemra

Keep Actemra out of the sight and reach of children.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Do not use this medicine after the expiry date which is stated on the carton.

6. Contents of the pack and other information

What Actemra contains

- The active substance is tocilizumab.
  Each 4 mL vial contains 80 mg tocilizumab (20 mg/mL).
  Each 10 mL vial contains 200 mg tocilizumab (20 mg/mL).
  Each 20 mL vial contains 400 mg tocilizumab (20 mg/mL).

- The other ingredients are sucrose, polysorbate 80, disodium phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate and water for injections.

What Actemra looks like and contents of the pack

Actemra is a concentrate for solution for infusion. The concentrate is a clear to opalescent, colourless to pale yellow liquid.
Actemra is supplied as vials containing 4 mL, 10 mL and 20 mL concentrate for solution for infusion.
Pack size of 1 and 4 vials. Not all pack sizes may be marketed.

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