Package Leaflet: Information for the user

RoActemra 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 RoActemra.

What is in this leaflet:

1. What RoActemra is and what it is used for

RoActemra 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. RoActemra helps to reduce symptoms such as pain and swelling in your joints and can also improve your performance of daily tasks. RoActemra 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.

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

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

- **RoActemra is used to treat children with sJIA**. RoActemra 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. RoActemra is used to improve the symptoms of sJIA and can be given in combination with methotrexate or alone.

- **RoActemra is used to treat children with pJIA**. RoActemra 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. RoActemra is used to improve the symptoms of pJIA and can be given in combination with methotrexate or alone.

- **RoActemra is used to treat adults and children** aged 2 years and over with severe or life-threatening **cytokine release syndrome (CRS)**, a side-effect in patients treated with chimeric antigen receptor (CAR) T-cell therapies used to treat certain types of cancer.

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

You are not to be given RoActemra
- 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 RoActemra.

- 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. RoActemra 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 RoActemra. 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 RoActemra, 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 RoActemra. Certain types of vaccines should not be used while receiving RoActemra.

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

- 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 RoActemra.

- 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 RoActemra, 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
RoActemra 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 RoActemra.

Other medicines and RoActemra
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. RoActemra 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, RoActemra is not recommended for use with other biological medicines for the treatment of RA, sJIA or pJIA.

Pregnancy, breast-feeding and fertility
RoActemra 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 RoActemra, 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 RoActemra 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.

RoActemra 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 RoActemra is given

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

RoActemra 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 RoActemra 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 RoActemra 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 RoActemra 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 RoActemra 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 RoActemra 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 RoActemra once every 4 weeks through a drip in the vein (intravenous infusion) over one hour.

Patients with CRS
The usual dose of RoActemra is **8 mg for every kg of body weight if you weigh 30 kg or more**.
The dose is **12 mg for every kg of body weight if you weigh less than 30 kg**.
RoActemra can be given alone or in combination with corticosteroids.

If you are given more RoActemra than you should
Since RoActemra 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 RoActemra
Since RoActemra 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 RoActemra
You should not stop using RoActemra 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, RoActemra can cause side effects, although not everybody gets them. Side effects could occur at least up to 3 months after your last dose of RoActemra.

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

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

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.

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.

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.
- stevens-johnson syndrome (skin rash, which may lead to severe blistering and peeling of the skin)

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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 RoActemra

Keep RoActemra 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 RoActemra 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 RoActemra looks like and contents of the pack
RoActemra is a concentrate for solution for infusion. The concentrate is a clear to opalescent, colourless to pale yellow liquid.
RoActemra 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.

Marketing Authorisation Holder
Roche Registration GmbH
Emil-Barell-Strasse 1
79639 Grenzach-Wyhlen
Germany

Manufacturer
Roche Pharma AG
Emil-Barell-Str. 1
D-79639 Grenzach-Wyhlen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
N.V. Roche S.A.
Tél/Tel: +32 (0) 2 525 82 11

България
Рош България ЕООД
Тел: +359 2 818 44 44

Česká republika
Roche s. r. o.
Tel: +420 - 2 20382111

Danmark
Roche a/s
Tlf: +45 - 36 39 99 99

Deutschland
Roche Pharma AG
Tel: +49 (0) 7624 140
oder
Chugai Pharma Europe
Zweigniederlassung Deutschland
Tel: +49 (0) 69 663000 0

Eesti
Roche Eesti OÜ
Tel: + 372 - 6 177 380

Ελλάδα
Roche (Hellas) A.E.
Τηλ: +30 210 61 66 100

España
Roche Farma S.A.
Tel: +34 - 91 324 81 00

France
Roche
Tél: +33 (0) 1 47 61 40 00
ou
Chugai Pharma France
Tél: +33 (0) 1 56 37 05 20

Hrvatska
Roche d.o.o
Tel: +385 1 47 22 333

Luxembourg/Luxemburg
(Voir/siehe Belgique/Belgien)

Magyarország
Roche (Magyarország) Kft.
Tel: +36 - 23 446 800

Malta
(See Ireland)

Nederland
Roche Nederland B.V.
Tel: +31 (0) 348 438050

Norge
Roche Norge AS
Tlf: +47 - 22 78 90 00

Österreich
Roche Austria GmbH
Tel: +43 (0) 1 27739

Polska
Roche Polska Sp.z o.o.
Tel: +48 - 22 345 18 88

Portugal
Roche Farmacêutica Química, Lda
Tel: +351 - 21 425 70 00

România
Roche România S.R.L.
Tel: +40 21 206 47 01

Ireland
Roche Products (Ireland) Ltd.
Tel: +353 (0) 1 469 0700

Ísland
Roche a/s
c/o Icepharma hf
Sími: +354 540 8000

Italia
Roche S.p.A.
Tel: +39 - 039 2471

Κύπρος
Γ.Α.Σταμάτης & Σια Λτδ.
Τηλ: +357 - 22 76 62 76

Latvija
Roche Latvija SIA
Tel: +371 - 6 7039831

Lietuva
UAB "Roche Lietuva"
Tel: +370 5 2546799

Slovenija
Roche farmacevtska družba d.o.o.
Tel: +386 - 1 360 26 00

Slovenská republika
Roche Slovensko, s.r.o.
Tel: +421 - 2 52638201

Suomi/Finland
Roche Oy
Puh/Tel: +358 (0) 10 554 500

Sverige
Roche AB
Tel: +46 (0) 8 726 1200

United Kingdom
Roche Products Ltd.
Tel: +44 (0) 1707 366000
or
Chugai Pharma UK Ltd.
Tel: +44 (0) 208 987 5600

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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu/. There are also links to other websites about rare diseases and treatments.

The following information is intended for healthcare professionals only:

Instructions for dilution prior to administration
Parenteral medicinal products should be inspected visually for particulate matter or discoloration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted.

RA and CRS adult patients (≥ 30 kg)
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) solution for injection from a 100 mL infusion bag, equal to the volume of RoActemra concentrate required for the patients dose, under aseptic conditions. The required amount of RoActemra concentrate (0.4 mL/kg) should be withdrawn from the vial and placed in the 100 mL infusion bag. This should be a final volume of 100 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

Use in the paediatric population

sJIA, pJIA and CRS patients ≥ 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) solution for injection from a 100 mL infusion bag, equal to the volume of RoActemra concentrate required for the patients dose, under aseptic conditions. The required amount of RoActemra concentrate (**0.4 mL/kg**) should be withdrawn from the vial and placed in the 100 mL infusion bag. This should be a final volume of 100 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

sJIA and CRS patients < 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) solution for injection from a 50 mL infusion bag, equal to the volume of RoActemra concentrate required for the patients dose, under aseptic conditions. The required amount of RoActemra concentrate (**0.6 mL/kg**) should be withdrawn from the vial and placed in the 50 mL infusion bag. This should be a final volume of 50 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

pJIA patients < 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) solution for injection from a 50 mL infusion bag, equal to the volume of RoActemra concentrate required for the patients dose, under aseptic conditions. The required amount of RoActemra concentrate (**0.5 mL/kg**) should be withdrawn from the vial and placed in the 50 mL infusion bag. This should be a final volume of 50 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

RoActemra is for single-use only.

Any unused product or waste material should be disposed of in accordance with local requirements.