RoActemra® (tocilizumab) for Rheumatoid Arthritis

STEP-BY-STEP DOSING AND ADMINISTRATION GUIDE

A guide to assist healthcare professionals with the dose preparation and administration of RoActemra therapy in patients with rheumatoid arthritis

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Intravenous (IV) administration of RoActemra by infusion

This guide will walk you through the RoActemra infusion process in 6 steps

Before therapy begins

Before beginning RoActemra therapy, it is important that you review the *What You Should Know About RoActemra patient brochure* with each patient. This educational tool contains valuable information that will help your patients fully understand what they may expect from their treatment.

Prior to each infusion, it is important that you review the pre-administration checklist found in the *What You Should Know About RoActemra patient brochure* with your patient and allow ample time to discuss any questions he or she may have.

- RoActemra patient brochures and other information can be requested from your sales representative. If you have questions or concerns, please email medinfo.uk@roche.com or call +44 8003281629.
- For full information, see the Summary of Product Characteristics (SmPC) and the Package Leaflet, which can be found on the Electronic Medicines Compendium website (www.medicines.org.uk/emc)

1 Weigh patient and calculate RoActemra dose

RoActemra dosing is calculated based on each patient's weight. Verify the patient's weight, then locate it on the chart to find the corresponding dose and recommended vial combination.

If the patient's dose has been calculated prior to the infusion date, take his or her weight to make sure that it has not changed from the time of the original calculation to require a change in dose. If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.

8 mg/kg				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (ml)	Vial combinations
50	110.0	400	20.0	1 × 400 mg
52	114.4	416	20.8	1 × 400 mg + 1 × 80 mg
54	118.8	432	21.6	1 × 400 mg + 1 × 80 mg
56	123.2	448	22.4	1 × 400 mg + 1 × 80 mg
58	127.6	464	23.2	1 × 400 mg + 1 × 80 mg
60	132.0	480	24.0	1 × 400 mg + 1 × 80 mg
62	136.4	496	24.8	1 × 200 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
64	140.8	512	25.6	1 × 200 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
66	145.2	528	26.4	1 × 400 mg + 1 × 80 mg + 1 × 80 mg
68	149.6	544	27.2	1 × 400 mg + 1 × 80 mg + 1 × 80 mg
70	154.0	560	28.0	1 × 400 mg + 1 × 80 mg + 1 × 80 mg
72	158.4	576	28.8	1 × 400 mg + 1 × 200 mg
74	162.8	592	29.6	1 × 400 mg + 1 × 200 mg
76	167.2	608	30.4	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
78	171.6	624	31.2	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
80	176.0	640	32.0	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
82	180.4	656	32.8	1 × 400 mg + 1 × 200 mg + 1 × 80 mg
84	184.8	672	33.6	1 × 400 mg + 1 × 200 mg + 1 × 80 mg
86	189.2	688	34.4	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
88	193.6	704	35.2	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
90	198.0	720	36.0	1 × 400 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
92	202.4	736	36.8	1 × 400 mg + 1 × 200 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
94	206.8	752	37.6	1 × 400 mg + 1 × 200 mg + 1 × 80 mg + 1 × 80 mg + 1 × 80 mg
96	211.2	768	38.4	2 × 400 mg
98	215.6	784	39.2	2 × 400 mg
≥100	≥220.0	800	40.0	2 × 400 mg

RoActemra dosing is calculated based on each patient's weight as follows:
For the 8 mg/kg dose: Patient weight (kg) x 8 (mg/kg) = RoActemra 8 mg dose.
For individuals whose body weight is more than 100 kg, doses exceeding 800 mg per infusion are not recommended.

Once the dose is calculated, choose the vial combination of RoActemra that best matches the patient's needs. RoActemra is available in three different dosing vials:

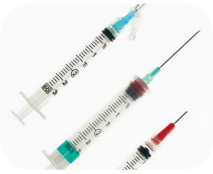
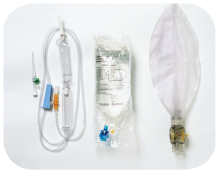
400 mg (20 ml) vials 200 mg (10 ml) vials 80 mg (4 ml) vials

Inspect the vials for particulate matter and discolouration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be used.

2 Gather all necessary supplies

You will need:

- RoActemra, at room temperature
- Syringes and large-bore needles
- One primary infusion set
- One 100 mL bag of 0.9% (9 mg/ml) sterile,non-pyrogenic sodium chloride solution for injection
- One intravenous (IV) catheter
- Gauze
- Tourniquet
- Gloves
- Alcohol/cleansing wipes


3 Take baseline assessments

Take baseline assessments to ensure the patient is healthy enough to receive the infusion.
Vital signs may include:

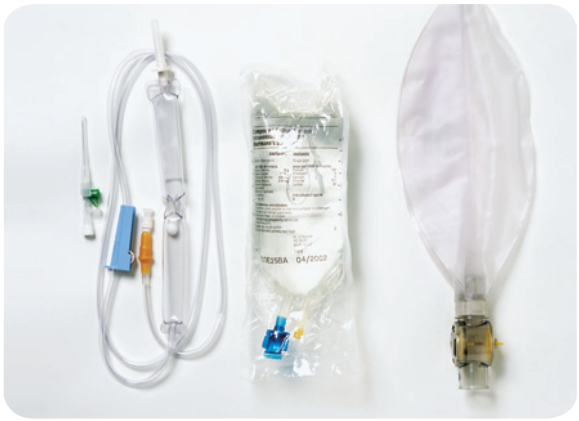
- Blood pressure
- Temperature
- Pulse

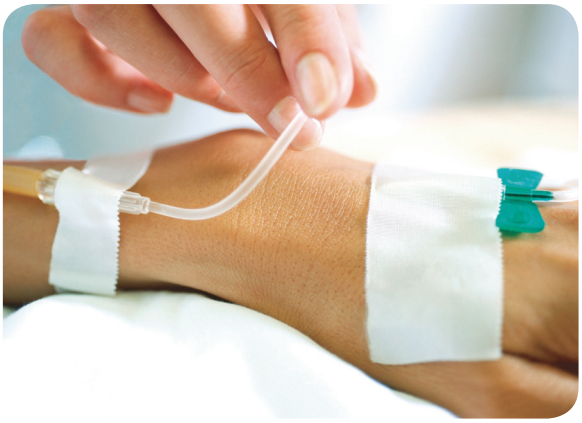
Also ask the patient if they:

- Are taking other medicines. This includes prescription and non-prescription medications, vitamins and herbals
- Are taking any other medications to treat rheumatoid arthritis (RA) such as methotrexate (MTX), Enbrel® (etanercept), Humira® (adalimumab), Remicade® (infliximab), MabThera® (rituximab), Orencia® (abatacept), Kineret® (anakinra), Cimzia® (certolizumab pegol) and Simponi® (golimumab)
- Have had any allergic reactions to previous medications, including RoActemra
- Are pregnant, might be pregnant, intend to become pregnant or are breast-feeding
- Have an infection or are being treated for an infection; have had or now have hepatitis or any disease of the liver; have a history of stomach ulcers or diverticulitis; have had or now have impaired lung function (e.g. interstitial lung disease)
- Have diabetes or other underlying conditions that may predispose them to infections
- Are planning or are scheduled to have surgery; have had a recent vaccination (such as a flu shot) or are scheduled to have one
- Have cancer, cardiovascular risk factors, such as raised blood pressure and raised cholesterol levels, or moderate to severe kidney function problems

4 Prepare the patient for the infusion

- Review the *What You Should Know About RoActemra patient brochure* with the patient and answer any questions he or she might have
- RoActemra does not require premedication





5 Prepare the RoActemra infusion

RoActemra should not be infused concomitantly in the same IV line with other medications. No physical or biochemical compatibility studies have been conducted to evaluate the co-administration of RoActemra with other medications.

RoActemra is a ready-mix solution and requires no reconstitution. The expiry date should always be checked before use. The RoActemra concentrate for IV infusion should be diluted to 100 ml by a healthcare professional using aseptic technique.

- RoActemra should be refrigerated for storage and the fully diluted RoActemra solution should be allowed to reach room temperature before it is infused. The fully diluted RoActemra solutions for infusion should be used immediately. If not used immediately it may be stored at 2–8°C or room temperature (if diluted under controlled and validated aseptic conditions) for up to 24 hours and should be protected from light. RoActemra solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used
- From a 100 ml infusion bag, withdraw a volume of 0.9% (9 mg/ml) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of the RoActemra solution required for the patient's dose
- Slowly add RoActemra concentrate for IV infusion from each vial into the infusion bag. To mix the solution, gently invert the bag to avoid foaming

- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted
- Dispose of needle and syringe in sharps containers when finished

6 Begin the RoActemra infusion

The infusion should be administered over 60 minutes. **It must be administered with an infusion set and should never be administered as an IV push or bolus.**

- Prior to the infusion, inform the patient that serious allergic reactions including anaphylaxis have been reported in association with RoActemra. Such reactions may be more severe, and potentially fatal, in patients who have experienced allergic reactions during previous treatment with RoActemra. Most allergic reactions occur during infusion or within 24 hours of RoActemra administration, although allergic reactions can occur at any time. If an anaphylactic reaction or other serious hypersensitivity reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and permanently discontinued. Fatal anaphylaxis has been reported after marketing authorisation during treatment with RoActemra.
- Instruct the patient to **seek immediate medical attention** if they notice any of the following signs or symptoms of systemic allergic reactions:
  - Rash, itching or hives
  - Shortness of breath or trouble breathing
  - Swelling of the lips, tongue or face
  - Chest pain
  - Feeling dizzy or faint
  - Severe stomach pain or vomiting
  - Hypotension

Once the infusion is completed, remove the catheter and dispose of all supplies properly, clean and bandage the infusion site and check the patient's vital signs.

FREQUENTLY ASKED QUESTIONS

How do I store RoActemra vials?

RoActemra must be refrigerated at 2–8°C. Do not freeze. Protect the vials from light by storing in the original package until time of use.

What vial sizes are available, and which should we stock?

RoActemra is available in three different dosing vials: 400 mg (20 ml), 200 mg (10 ml) and 80 mg (4 ml). As the dosing of RoActemra is calculated based upon patient weight, you may need a supply of all three dosing vials on hand in order to select the correct vial combination for each patient.

Do I need to administer premedication?

No premedication is required before administering RoActemra. However, an IV of medication-free 0.9% (9 mg/ml) sterile, non-pyrogenic sodium chloride solution should be administered to open and prepare the patient's vein for the infusion.

How do I prepare RoActemra for infusion? What diluents can I use?

RoActemra concentrate for IV infusion should be diluted to 100 ml using aseptic technique.

- From a 100 ml infusion bag, withdraw a volume of 0.9% (9 mg/ml) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of the RoActemra concentrate required for the patient's dose, under aseptic conditions
- Slowly add RoActemra concentrate for IV infusion from each vial into the infusion bag. To mix the solution, gently invert the bag to avoid foaming
- RoActemra should be refrigerated for storage and the fully diluted RoActemra solution should be allowed to reach room temperature before it is infused
- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted. The expiry date should always be checked before use
- Dispose of needle and syringe in sharps containers when finished

What is the infusion duration?

RoActemra is administered over 60 minutes. It must be administered with an infusion set and should never be administered as an IV push or bolus.

How do I store the diluted infusion? What is the stability of RoActemra?

The fully diluted RoActemra solutions for infusion may be stored at 2–8°C or room temperature (if diluted under controlled and validated aseptic conditions) for up to 24 hours, and should be protected from light. RoActemra solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used.

What should I look for during the infusion?

Watch the patient closely for any signs and symptoms of hypersensitivity, including anaphylaxis. Most allergic reactions occur during infusion or within 24 hours of RoActemra administration, although allergic reactions can occur at any time. If an anaphylactic reaction or other serious hypersensitivity reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and permanently discontinued.

Instruct the patient to **seek immediate medical attention** if they notice any of the following signs or symptoms of systemic allergic reactions:

- Rash, itching or hives
- Shortness of breath or trouble breathing
- Swelling of the lips, tongue or face
- Chest pain
- Feeling dizzy or faint
- Severe stomach pain or vomiting
- Hypotension

What kinds of side effects and reactions can occur during or after the infusion, and how common are they?

The most common side effects with RoActemra are upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT.

Adverse events associated with infusion (selected events occurring during or within 24 hours of infusion) were reported by 6.9% of patients in the RoActemra 8 mg/kg plus DMARD group and 5.1% of patients in the placebo plus DMARD group. Events reported during the infusion were primarily episodes of hypertension; events reported within 24 hours of finishing an infusion were headache and skin reactions (rash, urticaria). These events were not treatment-limiting.

The rate of anaphylactic reactions, occurring in a total of six out of 3,778 patients (0.2%), was several-fold higher with the 4 mg/kg dose, compared to the 8 mg/kg dose. Clinically significant hypersensitivity reactions associated with RoActemra and requiring treatment discontinuation were reported in a total of 13 out of 3,778 patients (0.3%) treated with RoActemra during the controlled and open-label clinical studies. These reactions were generally observed during the second to fifth infusions of RoActemra. Fatal anaphylaxis has been reported during treatment with RoActemra.

How frequently should I monitor the patient's vital signs?

Take the patient's vital signs before and after each infusion.

What if patients cannot schedule their infusion in exactly 4 weeks?

RoActemra should be administered once every 4 weeks. Contact the prescriber for any deviations from that schedule.

What information do I need to provide the patient about RoActemra?

Before beginning RoActemra therapy, it is important that you review the *What You Should Know About RoActemra* brochure with each patient. This educational tool contains valuable information that will help your patients fully understand what they may expect from their treatment.

Prior to each infusion, it is important that you review the preadministration checklist found in the *What You Should Know About RoActemra patient brochure*. The patient should be allowed ample time to review and discuss any questions he or she may have.

If the patient would like more information about RoActemra, please direct him or her to email medinfo.uk@roche.com or to call +44 8003281629.

For full information, see the Summary of Product Characteristics (SmPC) and the Patient Leaflet, which can be found on the Electronic Medicines Compendium website (www.medicines.org.uk/emc).

If you have any further questions relating to RoActemra please contact Roche Medical Information on +44 (0)800 3281629 or email: medinfo.uk@roche.com.

Suspected adverse reactions associated with the use of RoActemra should be reported to: Medicines Authority Post-licensing Directorate 203. Level 3. Rue D'Argens, Gzira GZR 1368, or at: http://www.medicinesauthority.gov.mt/adrportal. Suspected adverse events should also be reported to Roche by phone on +44 (0)1707 367554, fax on +44 (0)1707 367582 or e-mail at welwyn.uk_dsc@roche.com.

RXUKACTE00016 July 2013