Step-by-Step Dosing and Administration Guide

RoActemra® (tocilizumab) intravenous (IV) and subcutaneous (SC) formulations

A guide to assist healthcare professionals with the dose, preparation and administration of RoActemra therapy in patients with rheumatoid arthritis (RA) and Giant Cell Arteritis (GCA)

This educational material is provided by Roche Products Limited and is mandatory as a condition of the Marketing Authorisation in order to further minimise important selected risks

Full prescribing information can be found in the RoActemra Summary of Product Characteristics (SmPC): www.medicines.org.uk

Contents

Part I – Intravenous (IV) administration of RoActemra by infusion

This section 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 Package Leaflet and the "What you should know about RoActemra" Patient Brochure with each patient. This dosing guide contains valuable information that will help your patients fully understand what they may expect from their treatment.

- RoActemra alert cards and other information can be requested from your sales representative or Medical Information. If you have questions or concerns, please email medinfo.uk@roche.com or call 0800 328 1629
- For full information, see the Summary of Product Characteristics (SmPC) and the Package Leaflet, which can be found on the Electronic Medicines Compendium (EMC) 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 again 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 × 200 mg + 3 × 80 mg
54	118.8	432	21.6	1 × 200 mg + 3 × 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 + 4 × 80 mg
64	140.8	512	25.6	1 × 200 mg + 4 × 80 mg
66	145.2	528	26.4	1 × 400 mg + 1 × 80 mg
68	149.6	544	27.2	1 × 400 mg + 1 × 80 mg
70	154.0	560	28.0	1 × 400 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 + 3 × 80 mg
78	171.6	624	31.2	1 × 400 mg + 3 × 80 mg
80	176.0	640	32.0	1 × 400 mg + 3 × 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 × 200 mg + 3 × 80 mg
88	193.6	704	35.2	1 × 400 mg + 1 × 200 mg + 3 × 80 mg
90	198.0	720	36.0	1 × 400 mg + 1 × 200 mg + 3 × 80 mg
92	202.4	736	36.8	1 × 400 mg + 1 × 200 mg + 2 × 80 mg
94	206.8	752	37.6	1 × 400 mg + 1 × 200 mg + 2 × 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 = RoActemra 8 mg/kg 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 should include:

- Blood pressure
- Temperature
- Pulse

Also ask the patient if they:

- Are taking other medicines. This includes prescription and non-prescription medications, vitamins and herbal supplements
- 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), or Simponi® (golimumab), Olumiant® (baricitinib), Xeljanz® (tofacitinib), Kevzara® (sarilumab)
- 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 gastrointestinal 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

RoActemra does not require premedication.

Review the Package Leaflet with the patient and answer any questions he or she might have.

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 a final volume of 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. After dilution, the prepared solution for infusion is physically and chemically stable in sodium chloride 9 mg/ml (0.9%) at 30°C for 24 hours. From a microbiological point of view, the prepared solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally be no longer than 24 hours at 2–8°C, unless dilution has taken place in controlled and validated aseptic conditions. 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 sterile, non-pyrogenic sodium chloride 0.9% (9 mg/ml) solution for injection equal to the volume of the RoActemra solution 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
- 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 the needle and syringe in a sharps container when finished

6. Begin the RoActemra infusion

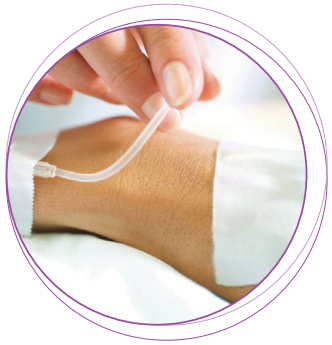
The infusion should be administered over one hour. It must be administered with an infusion set and should never be administered as an IV push or bolus.

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 even if they have received premedication with steroids and antihistamines. 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/serious infusion-related reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and RoActemra should be permanently discontinued. Fatal anaphylaxis has been reported after marketing authorisation during treatment with RoActemra IV.

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: RoActemra IV

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 IV 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.

- RoActemra should be refrigerated for storage and the fully diluted RoActemra solution should be allowed to reach room temperature before it is infused
- 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 the required amount of 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. The expiry date should always be checked before use
- Dispose of the needle and syringe in sharps container when finished

What is the infusion duration?

RoActemra is administered over one hour. 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?

After dilution, the prepared solution for infusion is physically and chemically stable in sodium chloride 9 mg/ml (0.9%) at 30°C for 24 hours. From a microbiological point of view, the prepared solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally be no longer than 24 hours at 2–8°C, unless dilution has taken place in controlled and validated aseptic conditions. 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/serious infusion-related reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and RoActemra should be permanently discontinued.

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

- 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 (common cold, sinus infections), nasopharyngitis, headache, temporary increases in blood pressure and increased alanine transaminase (ALT) levels.

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 8/4,009 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 56 out of 4,009 patients (1.4%) treated with RoActemra during the controlled and open label clinical studies. These reactions were generally observed during the second to fifth infusions of tocilizumab. Fatal anaphylaxis has been reported after marketing authorisation during treatment with intravenous RoActemra IV.

Frequently asked questions: RoActemra IV (continued)

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 Patient Information Leaflet and the "What you should know about RoActemra" Patient Brochure with each patient. This contains valuable information that will help your patients fully understand what they may expect from their treatment. All patients treated with RoActemra should be given the patient alert card.

If your patient would like more information about RoActemra, please direct them to the Patient Information Leaflet or contact medinfo.uk@roche.com or to call 0800 328 1629.

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

Part II – Subcutaneous (SC) administration of RoActemra by injection

Part IIa: Using a pre-filled syringe for RA and GCA

This section will walk you through the RoActemra injection process using a pre-filled syringe in 4 steps

Before therapy begins

Before beginning RoActemra therapy, it is important that you review the Patient Information Leaflet with each patient. This contains valuable information that will help your patients fully understand what they may expect from their treatment.

Prior to initiation, it is important that you review the 'What you need to know before you use RoActemra' section found in the Package Leaflet with your patient and allow ample time to discuss any questions he or she may have.

- RoActemra alert cards and other information can be requested from your sales representative. If you have questions or concerns, please email medinfo.uk@roche.com or call 0800 328 1629
- For full information, see the Summary of Product Characteristics (SmPC) and the Patient Information Leaflet, which can be found on the Electronic Medicines Compendium (EMC) website: www.medicines.org.uk/emc

1. Gather all necessary supplies

You will need:

- One RoActemra pre-filled syringe at room temperature
- A well-lit, clean, flat surface
- Sharps container
- Alcohol pad/cleansing wipes
- Sterile cotton ball or gauze
- Clock or watch

2. Take baseline assessments

Prior to initiation, it is important to take baseline assessments to ensure the patient is healthy enough to receive the injection.

Vital signs should include:

- Blood pressure
- Temperature
- Pulse

Also ask the patient if they:

- Are taking other medicines. This includes prescription and non-prescription medications, vitamins and herbal supplements
- Are taking any other medications to treat RA such as: Methotrexate (MTX), Enbrel® (etanercept), Humira® (adalimumab), Remicade® (infliximab), MabThera® (rituximab), Orencia® (abatacept), Kineret® (anakinra), Cimzia® (certolizumab pegol), or Simponi® (golimumab), Olumiant® (baricitinib), Xeljanz® (tofacitinib), Kevzara® (sarilumab)
- 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 gastrointestinal 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

3. Preparation for injection with the pre-filled syringe

- Prior to the injection, 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 even if they have received premedication with steroids and antihistamines. Most allergic reactions occur within 24 hours of RoActemra administration, although allergic reactions can occur at any time. Fatal anaphylaxis has been reported after marketing authorisation during treatment with RoActemra IV
- If an anaphylactic reaction or other serious hypersensitivity reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and RoActemra should be permanently discontinued

3. Preparation for injection with the pre-filled syringe

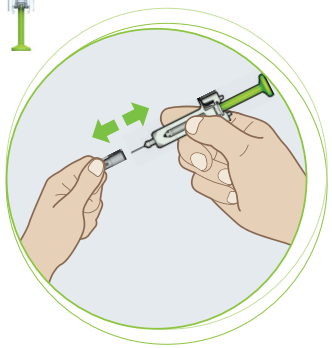
- RoActemra 162 mg is supplied in 0.9 ml of solution for injection as a pack of 4 single-use pre-filled syringes. The pre-filled syringes should be stored at 2– 8°C and should not be frozen. They should be kept in the outer carton to protect them from light and should be kept dry. The pre-filled syringes should be kept out of sight and reach of children. The expiry date should always be checked before use.
- Inspect the pre-filled syringe visually for particulate matter and discolouration prior to administration and check the expiration date. Do not use if the medicine has expired, is cloudy or contains particles, is any colour besides colourless to slightly yellowish, or if any part of the pre-filled syringe appears to be damaged
- Once removed from the refrigerator, RoActemra 162 mg/0.9 ml must be administered within 8 hours and should not be kept above 30°C
- After removing from the refrigerator, the pre-filled syringe should be allowed to reach room temperature (18–28ºC) by waiting for 25 to 30 minutes before injecting RoActemra 162 mg/0.9 ml. Do not warm up the pre-filled syringe in any other way
- The pre-filled syringe should not be shaken
- Wash your hands with soap and water
- Choose and prepare an injection site, preferably the front or middle of the thigh or lower part of the abdomen below the navel (except for the five centimetre area directly around the navel), and clean injection site with an alcohol pad. Let the skin dry for approximately 10 seconds. A different site should be used for subsequent injections
- Injections should never be given in moles, scars or areas where the skin is tender, bruised, red, hard, swollen or not intact. Do not inject into areas that could be bothered by a belt or waistband

- Patients should be assessed for their suitability to use RoActemra SC at home. Patients who are self-administering RoActemra should be advised to **seek immediate medical attention** if they experience any of the following signs or symptoms of systemic allergic reactions after receiving RoActemra:
  - 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

If your patient has experienced any allergic reaction symptoms after their last dose of RoActemra they must NOT administer the next dose until they have informed you (their doctor/HCP) and you have told them to take the next dose.

- Prior to the injection, inform the patient of potential injection site reactions. Most injection site reactions are mild-to-moderate in severity, do not necessitate drug discontinuation and usually resolve spontaneously. Injection site reaction symptoms include:
  - Erythema
  - Pruritus
  - Pain
  - Haematoma

4. Administering the injection with the pre-filled syringe



Step 1 – Remove needle cap

When ready to inject, firmly grip the syringe with one hand and pull the cap straight off with the other hand. Discard the cap. Do not pull or press the plunger, and do not shake the pre-filled syringe. After removing the needle cap, the injection must be started within **5 minutes** to prevent the medicine from drying out and blocking the needle. If the pre-filled syringe is not used within 5 minutes of removing the cap, you must dispose of it in a puncture resistant container and use a new pre-filled syringe. A small drop of liquid at the needle tip is normal.

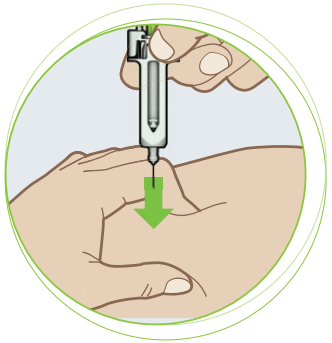
Never re-attach the needle cap after removal.

Step 2 – Pinch skin and insert needle, release skin

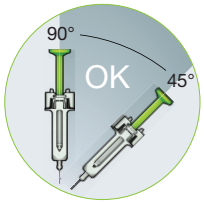
Pinch the skin at the injection site to provide a firm surface for injection.

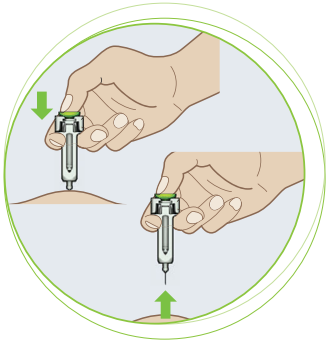
Insert the needle with a quick, firm action. The needle must be inserted all the way in at an angle between 45° and 90°.

Keep the syringe in position and release the pinched skin.



It is important to choose the correct angle (between 45° and 90°) to ensure the medication is delivered under the skin, otherwise the injection could be painful and the medication may not be administered correctly.





Step 3 – Slowly press down all the way then remove

Slowly inject all the medicine by gently pushing the plunger all the way down.

Keep an even pressure on the plunger and don't release the pressure once the injection has started.

Once the plunger is pushed all the way down, keep pressing down on the plunger to be sure all of the medicine is injected before taking the needle out of the skin.

Keep pressing down on the plunger while you take the needle out of the skin at the same angle as inserted.

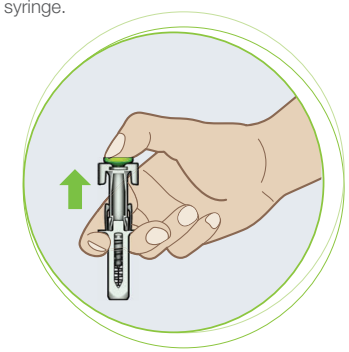
If, following insertion of the needle, you cannot depress the plunger, you must dispose of the pre-filled syringe in a puncture resistant container and use a new pre-filled syringe.

Step 4 – Release plunger and dispose

Once the needle is completely removed from the skin, release the plunger. This will automatically activate the needle shield.

Press gently on the injection area with a cotton wool ball or gauze swab.

Throw away the used syringe in a sharps container.



If the plunger is not fully depressed the needle shield will not extend to cover the needle when it is removed, and the patient may not have received the full dose of RoActemra:

- **Do not** touch the needle shield of the pre-filled syringe to avoid a needle-stick injury
- **Do not** try to re-use the pre-filled syringe
- **Do not** repeat the injection with another pre-filled syringe

Frequently asked questions

How is the RoActemra pre-filled syringe supplied?

RoActemra 162 mg is supplied in 0.9 ml of solution for injection as a pack of 4 single-use pre-filled syringes.

How do I store the RoActemra pre-filled syringe?

The pre-filled syringes should be stored at 2–8°C and should not be frozen. They should be kept in the outer carton to protect them from light and should be kept dry. The pre-filled syringes should be kept out of sight and reach of children.

How do I prepare the RoActemra pre-filled syringe for injection?

Do not shake the pre-filled syringe. Inspect the pre-filled syringe visually through the viewing window for particulate matter and discolouration prior to administration and check the expiration date. Do not use if the medicine is cloudy or contains particles, is any colour besides colourless to slightly yellowish, or if any part of the pre-filled syringe appears to be damaged. Once removed from the refrigerator, RoActemra 162 mg/0.9 ml must be administered within 8 hours and should not be kept above 30°C.

- After removing from the refrigerator, the pre-filled syringe must be allowed to reach room temperature (18–28ºC) by waiting at least 25–30 minutes before injecting RoActemra 162 mg/0.9 ml. Do not warm up the pre-filled syringe in any other way.

How do I prepare for injection and choose an appropriate injection site?

Wash your hands with soap and water. Choose an injection site, preferably the middle of the front thigh or lower part of the abdomen below the navel (except for the five centimetre area directly around the navel), and clean the injection site with an alcohol pad. Let the skin dry for approximately 10 seconds. A different site should be used for subsequent injections. Do not inject into moles, scars, or areas where the skin is tender, bruised, red, hard, swollen or not intact. Do not inject into areas that could be bothered by a belt or waistband.

What do I need to inform the patient of prior to injection?

Patients should be assessed for their suitability to use RoActemra SC at home. Prior to the injection, 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 even if they have received premedication with steroids and antihistamines. Most allergic reactions occur within 24 hours of RoActemra administration, although allergic reactions can occur at any time. Fatal anaphylaxis has been reported after marketing authorisation during treatment with RoActemra IV.

- Patients who are self-administering RoActemra should be advised to **seek immediate medical attention** if they experience any of the following signs or symptoms of systemic allergic reactions after receiving RoActemra:

- 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

If your patient has experienced any allergic reaction symptoms after their last dose of RoActemra they must NOT administer the next dose until they have informed you (their doctor/HCP) and you have told them to take the next dose.

- Prior to the injection, inform the patient of potential injection site reactions. Most injection site reactions are mild-to-moderate in severity, do not necessitate drug discontinuation and usually resolve spontaneously. Injection site reaction symptoms include:

- Erythema
- Pruritus
- Pain
- Haematoma

What should I look for during and after the injection?

If the injection is administered at the clinic, watch the patient closely for any immediate signs or symptoms of an allergic reaction. If an anaphylactic reaction or other serious hypersensitivity reaction occurs, administration of RoActemra should be stopped immediately, appropriate therapy initiated and RoActemra should be permanently discontinued.

Frequently asked questions (continued)

How do I open the pre-filled syringe?

Firmly grip the syringe with one hand and pull the cap straight off with the other hand. After removing the needle cap, the injection must be started within 5 minutes to prevent the medicine from drying out and blocking the needle. If the pre-filled syringe is not used within 5 minutes of removing the cap, you must dispose of it in a puncture resistant container and use a new pre-filled syringe. Never re-attach the needle cap after removal.

How do I start the injection with the pre-filled syringe?

Pinch the skin at the injection site to provide a firm surface for injection. Insert the needle with a quick, firm action. The needle must be inserted all the way in at an angle between 45° and 90°. Keep the syringe in position and release the pinched skin.

How should I inject the medicine?

Slowly inject all the medicine by gently pushing the plunger all the way down. When the plunger is all the way down, keep pressing down to be sure all the medication has been injected.

If, following insertion of the needle, you cannot depress the plunger, you must dispose of the pre-filled syringe in a puncture resistant container and use a new pre-filled syringe.

How should I remove the needle from the skin?

Keep the plunger pushed down while you take the needle out of the skin at the same angle it was inserted.

What should I do when the needle is completely removed from the skin?

Once the needle is completely removed from the skin, release the plunger, allowing the needle-shield to protect the needle. Throw away the used syringe in a sharps container.

If your patient would like more information about RoActemra, please direct them to the Patient Information Leaflet or contact medinfo.uk@roche.com or to call 0800 328 1629.

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

Part IIb – Subcutaneous (SC) administration of RoActemra by Pre-filled Pen for RA and GCA

This guide will walk you through the RoActemra injection process using an autoinjector ACTpen.

Before therapy begins

Before beginning RoActemra therapy, it is important that you review the Package Leaflet, the What You Should Know About RoActemra Patient Brochure, and the pre-administration checklist with each patient.

This dosing guide contains valuable information that will help your patients fully understand what they may expect from their treatment.

- RoActemra alert cards and other information can be requested from your sales representative or Medical Information. If you have questions or concerns, please email medinfo.uk@roche.com or call 0800 328 1629
- For full information, see the Summary of Product Characteristics (SmPC) and the Package Leaflet, which can be found on the Electronic Medicines Compendium (EMC) website: www.medicines.org.uk/emc

What you need to know to use your RoActemra pre-filled pen (ACTPen) safely

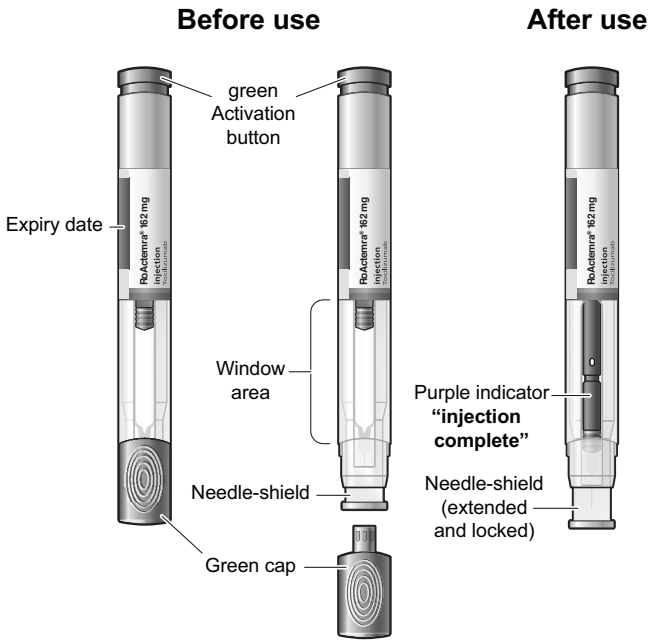
Read and follow the Instructions for Use that come with your RoActemra pre-filled pen before you start using it and each time you get a prescription refill. Before you use the RoActemra pre-filled pen for the first time, make sure your healthcare provider shows you the right way to use it.

Important: Keep your unused pre-filled pens in the original carton and keep in the refrigerator at 2°C to 8°C (36°F to 46°F). **Do not freeze.**

- **Do not remove the pre-filled pen cap until you are ready to inject RoActemra.**
- **Do not try to take apart the pre-filled pen at any time.**
- **Do not reuse the same pre-filled pen.**
- **Do not use the pre-filled pen through clothing.**
- **Do not leave the pre-filled pen unattended.**
- **Keep out of the reach of children.**

Parts of your RoActemra pre-filled pen **(See Figure A).**

Figure A



1. Gather all necessary supplies

You will need:

- One RoActemra pre-filled pen
- Alcohol pad / Cleansing wipes
- Sterile cotton ball or gauze
- Puncture-resistant container or sharps container for safe disposal of pre-filled pen cap and used pre-filled pen (see **Step 5 "Dispose of the pre-filled pen"**)

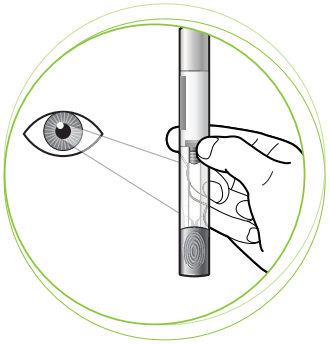
2. Preparing for a RoActemra Injection

Find a comfortable space with a clean, flat, working surface.

- Take the box containing the pre-filled pen out of the refrigerator.
- If you are opening the box for the first time, check to make sure that it is properly sealed. **Do not** use the pre-filled pen if the box looks like it has already been opened.
- Check that the pre-filled pen box is not damaged. **Do not** use RoActemra pre-filled pen if the box looks damaged.
- **Check the expiration date on the pre-filled pen box. Do not** use the pre-filled pen if the expiration date has passed because it may not be safe to use.
- Open the box, and remove 1 single-use RoActemra pre-filled pen from the box.
- Return any remaining pre-filled pens in the box to the refrigerator.
- **Check the expiration date on the RoActemra pre-filled pen (See Figure A). Do not** use it if the expiration date has passed because it may not be safe to use. If the expiration date has passed, safely dispose of the pre-filled pen in a sharps container and get a new one.
- **Check the pre-filled pen to make sure it is not damaged.** Do not use the pre-filled pen if it appears to be damaged or if you have accidentally dropped the pre-filled pen.
- Place the pre-filled pen on a clean, flat surface and let the pre-filled pen warm up for 45 minutes to allow it to reach room temperature. If the pre-filled pen does not reach room temperature, this could cause your injection to feel uncomfortable and it could take longer to inject.
- **Do not** speed up the warming process in any way, such as using the microwave or placing the pre-filled pen in warm water.
- **Do not** leave the pre-filled pen to warm up in direct sunlight.

Do not remove the green cap while allowing your RoActemra pre-filled pen to reach room temperature.

- Hold your RoActemra pre-filled pen with the green cap pointing down **(See Figure B)**.



- Look in the clear Window area. Check the liquid in the RoActemra pre-filled pen **(See Figure B)**. It should be clear and colorless to pale yellow. **Do not** inject RoActemra if the liquid is cloudy, discolored, or has lumps or particles in it because it may not be safe to use. Safely dispose of the pre-filled pen in a sharps container and get a new one.
- Wash your hands well with soap and water.

Figure B

3. Choose and Prepare an Injection Site

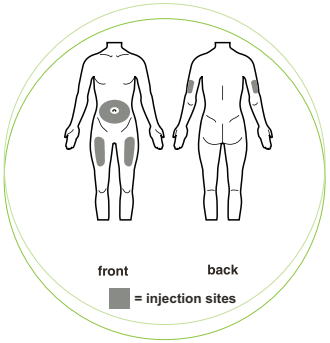


Figure C

Choose an Injection Site

The front of your thigh or your abdomen except for the 2-inch (5cm) area around your navel are the recommended injection sites **(See Figure C)**.

The outer area of the upper arms may also be used only if the injection is being given by a caregiver. Do not attempt to use the upper arm area by yourself **(See Figure C)**.

Rotate Injection Site

Choose a different injection site for each new injection at least 1 inch (2.5cm) from the last area you injected.

Do not inject into moles, scars, bruises, or areas where the skin is tender, red, hard or not intact.

Prepare the Injection Site

Wipe the injection site with an alcohol pad in a circular motion and let it air dry to reduce the chance of getting an infection. **Do not** touch the injection site again before giving the injection. **Do not** fan or blow on the clean area.

4. Inject RoActemra

Hold the RoActemra pre-filled pen firmly with one hand. Twist and pull off the green cap with the other hand **(See Figure D)**. The green cap contains a loose fitting metal tube.

If you cannot remove the green cap you should ask a caregiver for help or contact your healthcare provider.

Important: Do not touch the needle shield which is located at the tip of the pre-filled pen below the Window area (see Figure A), to avoid accidental needle stick injury.

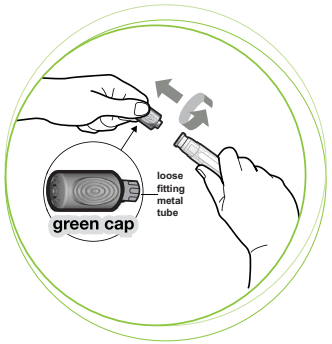


Figure D

Figure E

Throw away the green cap in a sharps container.

After you remove the green cap, the pre-filled pen is ready for use. If the pre-filled pen is not used within 3 minutes of the cap removal, the pre-filled pen should be disposed of in the sharps container and a new pre-filled pen should be used.

Never reattach the green cap after removal.

Hold the pre-filled pen comfortably in 1 hand by the upper part, so that you can see the Window area of the pre-filled pen **(See Figure E)**.

Use your other hand to gently pinch the area of skin you cleaned, to prepare a firm injection site **(See Figure F)**. The pre-filled pen requires a firm injection site to properly activate.

Pinching the skin is important to make sure that you inject under the skin (into fatty tissue) but not any deeper (into muscle). Injection into muscle could cause the injection to feel uncomfortable.

Figure F

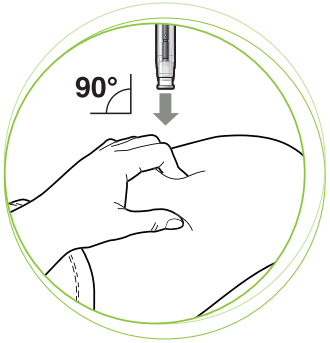


Figure G

Do not press the green activation button yet.

Place the needle-shield of the pre-filled pen against your pinched skin at a 90° angle **(See Figure G)**.

It is important to use the correct angle to make sure the medicine is delivered under the skin (into fatty tissue), or the injection could be painful and the medicine may not work.

Figure H

To use the pre-filled pen, you first have to unlock the green Activation button.

To unlock it, press the pre-filled pen firmly against your pinched skin until the needle-shield is completely pushed in **(See Figure H)**.

Continue to keep the needle-shield pushed in.

If you don't keep the needle-shield completely pushed against the skin, the green Activation button will not work.

Continue to pinch the skin while you keep the pre-filled pen in place.

Press the green Activation button to start the injection. A "click" sound indicates the start of the injection. Keep the green button pressed in and continue holding the pre-filled pen pressed firmly against your skin **(See Figure I)**. If you cannot start the injection you should ask for help from a caregiver or contact your healthcare provider.

Figure I

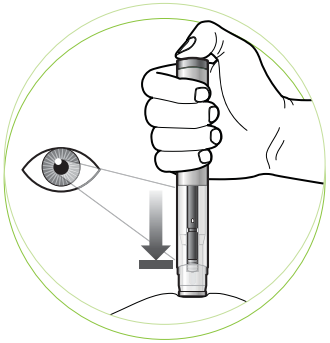


Figure J

The purple indicator will move along the Window area during the injection **(See Figure J)**.

Watch the purple indicator until it stops moving to be sure the full dose of medication is injected.

The injection may take up to **10 seconds**.

You may hear a second "click" during the injection but you should continue to hold the pre-filled pen firmly against your skin until the purple indicator stops moving.

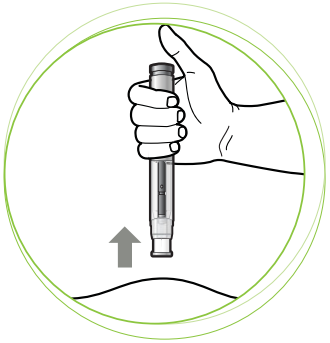


Figure K

When the purple indicator has stopped moving, release the green button. Lift the pre-filled pen straight off of the injection site at a 90° angle to remove the needle from the skin. The needle-shield will then move out and lock into place covering the needle **(See Figure K**).

Check the Window area to see that it is filled with the purple indicator **(See Figure K)**.

If the Window area is not filled by the purple indicator then the needle-shield may not have locked. **Do not** touch the needle-shield of the pre-filled pen, because you may stick yourself with the needle. If the needle is not covered, carefully place the pre-filled pen into the sharps container to avoid any injury with the needle.

You may not have received your full dose of RoActemra. Do not try to re-use the pre-filled pen. **Do not** repeat the injection with another pre-filled pen. Call your healthcare provider for help.

After the Injection

There may be a little bleeding at the injection site. You can press a cotton ball or gauze over the injection site.

Do not rub the injection site.

If needed, you may cover the injection site with a small bandage.

5. Dispose of the pre-filled pen

The RoActemra pre-filled pen should not be reused. Put the used pre-filled pen into your sharps container (see **"How do I dispose of used pre-filled pens?"**) **Do not** put the cap back on the pre-filled pen.

If your injection is given by another person, this person must also be careful when removing the pre-filled pen and disposing of it to prevent accidental needle stick injury and passing infection.

How do I dispose of used pre-filled pens?

Put your used RoActemra pre-filled pen and green cap in a sharps disposal container right away after use **(See Figure L)**.

Do not throw away (dispose of) the pre-filled pen and the green cap in your household trash and do not recycle them.

Dispose of the full container as instructed by your healthcare provider or pharmacist.

Always keep the puncture-resistant container out of the sight and reach of children.

Keep the RoActemra pre-filled pen and disposal container out of the reach of children.

Record your Injection

Write the date, time, and specific part of your body where you injected yourself. It may also be helpful to write any questions or concerns about the injection so you can ask your healthcare provider.

If you have any questions or concerns about your RoActemra pre-filled pen, talk to your healthcare provider familiar with RoActemra.

Figure L

If your patient would like more information about RoActemra, please direct them to the Patient Information Leaflet or contact medinfo.uk@roche.com or to call 0800 328 1629.

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Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Reporting forms and information can be found at www.medicinesauthority.gov.mt/adrportal. Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44(0)1707 367554.

As RoActemra is a biological medicine, healthcare professionals should report adverse reactions by brand name and batch number.

Date of preparation: April 2018 RXUKACTE00065b Ver1.0