FOR USE IN IRELAND

RoActemra® (tocilizumab)
Dosing Guide

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

- Rheumatoid Arthritis [Intravenous or subcutaneous]
- Giant Cell Arteritis [Subcutaneous]
- Polyarticular Juvenile Idiopathic Arthritis (also referred to as Juvenile Idiopathic Polyarthritis) [Intravenous or subcutaneous]
- Systemic Juvenile Idiopathic Arthritis [Intravenous or subcutaneous]
- RoActemra is indicated for the treatment of chimeric antigen receptor (CAR) T-cell induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients 2 years of age and older [Intravenous]
- RoActemra is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation [Intravenous]

This RoActemra Dosing Guide is additional risk minimisation material and is provided by Roche Products (Ireland) Limited as a condition of the RoActemra marketing authorisation. It contains important safety information that you need to be aware of when administering RoActemra.

This RoActemra Dosing Guide must be read together with the RoActemra Healthcare Professional and Patient Brochures (available online at www.hpra.ie), the RoActemra Summary of Product Characteristics and the Package Leaflet that comes with RoActemra (and is also available on www.medicines.ie) as it contains important information about RoActemra. Please read this information carefully before administering the product.

This material should be read in conjunction with the Summary of Product Characteristics (SmPC) which is available on www.medicines.ie before prescribing this medicine.

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Contents

RoActemra IV (RoActemra 20 mg/ml concentrate for solution for infusion)

RoActemra, in combination with methotrexate (MTX), is indicated for:

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

In these patients, RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.

RoActemra in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with MTX. RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra is indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and paediatric patients 2 years of age and older.

RoActemra is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation [Intravenous].

RoActemra SC (RoActemra 162 mg solution for injection in pre-filled syringe)

RoActemra in combination with methotrexate (MTX) is indicated for:

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

In these patients, RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra is indicated for the treatment of Giant Cell Arteritis (GCA) in adult patients.

RoActemra is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.

RoActemra in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with MTX. RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra SC (RoActemra 162 mg solution for injection in pre-filled pen (ACTPen))

RoActemra, in combination with methotrexate (MTX), is indicated for:

- the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- the treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

In these patients, RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra ACTPen is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 12 years of age and older, ant who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.

RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.

RoActemra ACTPen in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 12 years of age and older, who have responded inadequately to previous therapy with MTX.

RoActemra ACTPen can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra is indicated for the treatment of Giant Cell Arteritis (GCA) in adult patients.

Tocilizumab SC formulation is administered with a single-use pre-filled pen. Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of RA, sJIA, pJIA and/or GCA.

The RoActemra ACTPen should not be used to treat paediatric patients < 12 years of age since there is a potential risk of intramuscular injection due to thinner subcutaneous tissue layer.

The first injection should be performed under the supervision of a qualified health care professional. A patient or parent/guardian can inject RoActemra ACTPen only if the physician determines that it is appropriate and the patient or parent/guardian agrees to medical follow-up as necessary and has been trained in proper injection technique.

Patients who transition from tocilizumab IV therapy to SC administration should administer the first SC dose at the time of the next scheduled IV dose under the supervision of a qualified health care professional.

All patients treated with RoActemra should be given the Patient Alert Card.

Suitability of the patient or parent/guardian for subcutaneous home use should be assessed.

Prior to starting treatment with RoActemra

- It is important that you review the baseline checklist found under section “General Recommendations” in the Healthcare Professional (HCP) Brochure with your patient, the patient’s parents/guardians, or both.
- Allow ample time to discuss any questions your patient, the patient’s parents/guardians, or both may have.
- It is important that you review the information contained within the RoActemra Healthcare Professional (HCP) Brochure for RoActemra® (tocilizumab) intravenous (IV) and subcutaneous (SC) formulations and the RoActemra Patient Brochure with your patient, the patient’s parents/guardians, or both. These will help them understand what they may expect from the treatment of the patient’s condition with RoActemra.

For full information, see the Summary of Product Characteristics (SmPC) and the RoActemra Package Leaflet: Information for the user, which can be found on the European Medicines Agency website (www.ema.europa.eu) or www.medicines.ie.

RoActemra Patient Brochures and other information can be requested from Roche – please see relevant contact details at the end of this brochure. If you have questions or concerns, please call Roche Medical Information on (01) 4690700.

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

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

1. Weigh patient and calculate RoActemra dose based on indication

RoActemra dosing is calculated based on each patient's weight and the indication for which they are treated. The treatment frequency varies by indication. Verify the patient's weight and indication, then locate it on the charts (included on the following pages) 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 ensure that it has not changed from the time of the original calculation necessitating 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 relevant chart to check whether a dosing adjustment is necessary.

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.

RA: Dosing Preparation and Administration Guide with RoActemra IV

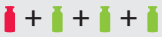
RoActemra IV dosing in RA patients is calculated based on each patient's weight as follows:

For the 8 mg/kg dose: Patient weight (kg) x 8 (mg/kg) = RoActemra dose.

For individuals whose body weight is more than 100 kg, doses exceeding 800 mg per infusion are not recommended.

Doses above 1.2 g have not been evaluated in clinical studies.

Dosing should take place at 4-week intervals.

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

pJIA: Dosing Preparation and Administration Guide with RoActemra IV

RoActemra IV dosing in pJIA patients is calculated based on each patient's weight as follows:

For patients weighing <30 kg: Patient's weight (kg) x 10 mg/kg = RoActemra dose.

For patients weighing ≥30 kg: Patient's weight (kg) x 8 mg/kg = RoActemra dose.

Dosing should take place at 4-week intervals.

The dose should be calculated based on the patient's body weight at each administration. A change in dose should only be based on a consistent change in the patient's body weight over time. 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.

	Weight (kg)	Weight (lbs)	Dose (mg)	Dose (ml)	Vial combinations
10 mg/kg	10	22.0	100	5.0	1 + 1
	12	26.4	120	6.0	1 + 1
	14	30.8	140	7.0	1 + 1
	16	35.2	160	8.0	1 + 1
	18	39.6	180	9.0	1
	20	44.0	200	10.0	1
	22	48.4	220	11.0	1 + 1 + 1
	24	52.8	240	12.0	1 + 1 + 1
	26	57.2	260	13.0	1 + 1
	28	61.6	280	14.0	1 + 1
8 mg/kg	30	66.0	240	12.0	1 + 1 + 1
	32	70.4	256	12.8	1 + 1
	34	74.8	272	13.6	1 + 1
	36	79.2	288	14.4	1 + 1 + 1 + 1
	38	83.6	304	15.2	1 + 1 + 1 + 1
	40	88.0	320	16.0	1 + 1 + 1 + 1
	42	92.4	336	16.8	1 + 1 + 1
	44	96.8	352	17.6	1 + 1 + 1
	46	101.2	368	18.4	1
	48	105.6	384	19.2	1
	50	110.0	400	20.0	1
	52	114.4	416	20.8	1 + 1 + 1 + 1
	54	118.8	432	21.6	1 + 1 + 1 + 1
	56	123.2	448	22.4	1 + 1
	58	127.6	464	23.2	1 + 1
	60	132.0	480	24.0	1 + 1
	62	136.4	496	24.8	1 + 1 + 1 + 1 + 1
	64	140.8	512	25.6	1 + 1 + 1 + 1 + 1
	66	145.2	528	26.4	1 + 1 + 1
	68	149.6	544	27.2	1 + 1 + 1
	70	154.0	560	28.0	1 + 1 + 1
	72	158.4	576	28.8	1 + 1
	74	162.8	592	29.6	1 + 1
	76	167.2	608	30.4	1 + 1 + 1 + 1
	78	171.6	624	31.2	1 + 1 + 1 + 1
	80	176.0	640	32.0	1 + 1 + 1 + 1
	82	180.4	656	32.8	1 + 1 + 1
	84	184.8	672	33.6	1 + 1 + 1
	86	189.2	688	34.4	1 + 1 + 1 + 1 + 1
	88	193.6	704	35.2	1 + 1 + 1 + 1 + 1
	90	198.0	720	36.0	1 + 1 + 1 + 1 + 1
	92	202.4	736	36.8	1 + 1 + 1 + 1
	94	206.8	752	37.6	1 + 1 + 1 + 1
	96	211.2	768	38.4	1 + 1
	98	215.6	784	39.2	1 + 1
	≥100	≥220.0	800	40.0	1 + 1

sJIA: Dosing Preparation and Administration Guide with RoActemra IV

RoActemra IV dosing in sJIA patients is calculated based on each patient's weight as follows:

For patients weighing <30 kg: Patient's weight (kg) x 12 mg/kg = RoActemra dose.

For patients weighing ≥30 kg: Patient's weight (kg) x 8 mg/kg = RoActemra dose.

Dosing should take place at 2-week intervals.

The dose should be calculated based on the patient's body weight at each administration. A change in dose should only be based on a consistent change in the patient's body weight over time. 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.

	Weight (kg)	Weight (lbs)	Dose (mg)	Dose (ml)	Vial combinations
12 mg/kg	10	22.0	120	6.0	🟢 + 🟢
	12	26.4	144	7.2	🟢 + 🟢
	14	30.8	168	8.4	🟡
	16	35.2	192	9.6	🟡
	18	39.6	216	10.8	🟢 + 🟢 + 🟢
	20	44.0	240	12.0	🟢 + 🟢 + 🟢
	22	48.4	264	13.2	🟡 + 🟢
	24	52.8	288	14.4	🟢 + 🟢 + 🟢 + 🟢
	26	57.2	312	15.6	🟢 + 🟢 + 🟢 + 🟢
	28	61.6	336	16.8	🟡 + 🟢 + 🟢
8 mg/kg	30	66.0	240	12.0	🟢 + 🟢 + 🟢
	32	70.4	256	12.8	🟡 + 🟢
	34	74.8	272	13.6	🟡 + 🟢
	36	79.2	288	14.4	🟢 + 🟢 + 🟢 + 🟢
	38	83.6	304	15.2	🟢 + 🟢 + 🟢 + 🟢
	40	88.0	320	16.0	🟢 + 🟢 + 🟢 + 🟢
	42	92.4	336	16.8	🟡 + 🟢 + 🟢
	44	96.8	352	17.6	🟡 + 🟢 + 🟢
	46	101.2	368	18.4	🔴
	48	105.6	384	19.2	🔴
	50	110.0	400	20.0	🔴
	52	114.4	416	20.8	🟡 + 🟢 + 🟢 + 🟢
	54	118.8	432	21.6	🟡 + 🟢 + 🟢 + 🟢
	56	123.2	448	22.4	🔴 + 🟢
	58	127.6	464	23.2	🔴 + 🟢
	60	132.0	480	24.0	🔴 + 🟢
	62	136.4	496	24.8	🟡 + 🟢 + 🟢 + 🟢 + 🟢
	64	140.8	512	25.6	🟡 + 🟢 + 🟢 + 🟢 + 🟢
	66	145.2	528	26.4	🔴 + 🟢 + 🟢
	68	149.6	544	27.2	🔴 + 🟢 + 🟢
	70	154.0	560	28.0	🔴 + 🟢 + 🟢
	72	158.4	576	28.8	🔴 + 🟡
	74	162.8	592	29.6	🔴 + 🟡
	76	167.2	608	30.4	🔴 + 🟢 + 🟢 + 🟢
	78	171.6	624	31.2	🔴 + 🟢 + 🟢 + 🟢
	80	176.0	640	32.0	🔴 + 🟢 + 🟢 + 🟢
	82	180.4	656	32.8	🔴 + 🟡 + 🟢
	84	184.8	672	33.6	🔴 + 🟡 + 🟢
	86	189.2	688	34.4	🔴 + 🟢 + 🟢 + 🟢 + 🟢
	88	193.6	704	35.2	🔴 + 🟢 + 🟢 + 🟢 + 🟢
	90	198.0	720	36.0	🔴 + 🟢 + 🟢 + 🟢 + 🟢
	92	202.4	736	36.8	🔴 + 🟡 + 🟢 + 🟢
	94	206.8	752	37.6	🔴 + 🟡 + 🟢 + 🟢
	96	211.2	768	38.4	🔴 + 🔴
	98	215.6	784	39.2	🔴 + 🔴
	≥100	≥220.0	800	40.0	🔴 + 🔴

CRS: Dosing Preparation and Administration Guide with RoActemra IV

RoActemra dosing in CRS patients is calculated based on each patient's weight as follows:

For patients weighing <30 kg: Patient's weight (kg) x 12 mg/kg = RoActemra dose.

For patients weighing ≥30 kg: Patient's weight (kg) x 8 mg/kg = RoActemra dose.

If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses of RoActemra may be administered. The interval between consecutive doses should be at least 8 hours.

Doses exceeding 800 mg per infusion are not recommended in CRS patients.

Subcutaneous administration is not approved for CRS.

COVID-19: Dosing Preparation and Administration Guide with RoActemra IV

The recommended posology for treatment of COVID-19 is a single 60-minute intravenous infusion of 8 mg/kg in patients who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation, see section 5.1 of the RoActemra 20 mg/mL concentrate for solution for infusion Summary of Product Characteristics (SmPC). If clinical signs or symptoms worsen or do not improve after the first dose, one additional infusion of RoActemra 8 mg/kg may be administered. The interval between the two infusions should be at least 8 hours.

For individuals whose body weight is more than 100 kg, doses exceeding 800 mg per infusion are not recommended (see section 5.2 of the SmPC).

Administration of RoActemra is not recommended in patients with COVID-19 who have any of the following laboratory abnormalities:

Laboratory test type	**Laboratory value**	**Action**
Liver enzyme	>10 x ULN	Administration of RoActemra is not recommended
Absolute neutrophil count	< 1 x 10^9/L	
Platelet count	< 50 x 10^3/μL	

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 for patients ≥30 kg or one 50 ml bag of 0.9% (9 mg/mL) sterile, non-pyrogenic sodium chloride solution for injection for patients <30 kg
- One intravenous (IV) catheter
- Gauze
- Tourniquet
- Gloves
- Alcohol/cleansing wipes
- Appropriate treatment to manage an anaphylactic reaction

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

Follow the recommended baseline patient questions as described in the RoActemra Healthcare Professional Brochure (Section 13 – General Recommendations) as well as the Summary of Product Characteristics (Section 4.4 – Warnings and Precautions).

4. Prepare the patient for the infusion

Review the RoActemra Patient Brochure with the patient. Answer any questions he or she might have.

RoActemra does not require premedication.

5. Prepare the RoActemra infusion

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 by a healthcare professional using aseptic technique.

- RoActemra should be refrigerated for storage. However, the diluted RoActemra solution should be allowed to reach room temperature before it is infused.
- The diluted RoActemra solution for infusion is physically and chemically stable in sodium chloride 9 mg/mL (0.9%) solution for injection 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 prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C–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 and should be disposed of in accordance with local requirements.
- **Weight-/indication-based dosing:**
  - **For RA, CRS (≥30 kg), sJIA (≥30 kg), COVID-19 (≥30 kg) and pJIA (≥30 kg):**
    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.

    Withdraw the required amount of RoActemra concentrate (**0.4 mL/kg**) from the vial and place 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.
  - **For sJIA, and CRS patients <30 kg:**
    From a 50 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.

    Withdraw the required amount of RoActemra concentrate (**0.6 mL/kg**) from the vial and place 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.
  - **For pJIA patients <30 kg:**
    From a 50 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.

    Withdraw the required amount of RoActemra concentrate (**0.5 mL/kg**) from the vial and place 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.
  - For COVID-19 patients

- 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.
- 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 accordance with local requirements when finished.

6. Begin the RoActemra infusion

The intravenous 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.

Monitor the patient for infusion related reactions.

Once the infusion is completed, remove the catheter and dispose of all supplies in accordance with local requirements, clean and bandage the infusion site and check the patient's vital signs.

Part II – Dosing administration guide with RoActemra SC using either the Pre-filled Syringe or Pre-filled Pen (RoActemra devices)

The pre-filled syringe is used in RA (162 mg once per week), GCA (162 mg once every week in combination with a tapering course of glucocorticoids), pJIA (162 mg once every 2 weeks in patients weighing ≥30 kg or once every 3 weeks in patients weighing <30 kg), and sJIA (162 mg once every week in patients weighing ≥30 kg or 162 mg once every 2 weeks in patients <30 kg) indications only.

The pre-filled pen (ACTPen) is used in the following indications only:

- RA (162 mg once per week)
- GCA (162 mg once every week in combination with a tapering course of glucocorticoids)
- In patients 12 years of age and older for the treatment of active systemic juvenile idiopathic arthritis (sJIA) (162 mg subcutaneously once every week in patients weighing greater than or equal to 30 kg or 162 mg subcutaneously once every 2 weeks in patients weighing less than 30 kg)
- In patients 12 years of age and older for the treatment of juvenile idiopathic polyarthritis (pJIA, rheumatoid factor positive or negative and extended oligoarthritis) (162 mg subcutaneously once every 2 weeks in patients weighing greater than or equal to 30 kg or 162 mg subcutaneously once every 3 weeks in patients weighing less than 30 kg).

Patients must have a minimum body weight of 10 kg when receiving RoActemra subcutaneously.

The pre-filled pen should not be used to treat paediatric patients < 12 years of age since there is a potential risk of intramuscular injection due to thinner subcutaneous tissue layer.

Instructions apply to both devices. Device-specific instructions are included in colour coded sections (pre-filled syringe = green; pre-filled pen (ACTPen) = orange).

Monitor the patient for injection related reactions.

This guide will walk you through the RoActemra SC injection process in 7 steps.

1. Gather all necessary supplies

You will need:

- One RoActemra pre-filled syringe OR pre-filled pen (ACTPen) (RoActemra devices) at room temperature
- A well-lit, clean, flat surface
- Puncture-resistant container/sharps container for disposal
- Alcohol/cleansing wipes
- Sterile cotton ball or gauze
- Clock or watch

RoActemra Pre-filled Syringe

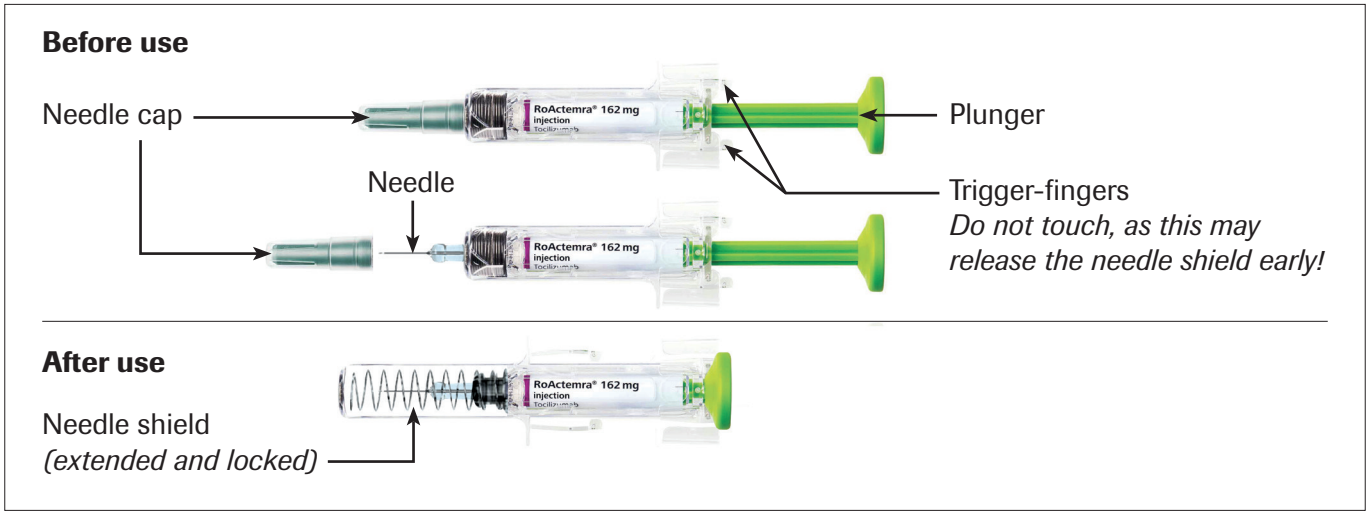


Figure A

RoActemra Pre-filled Pen (ACTPen)

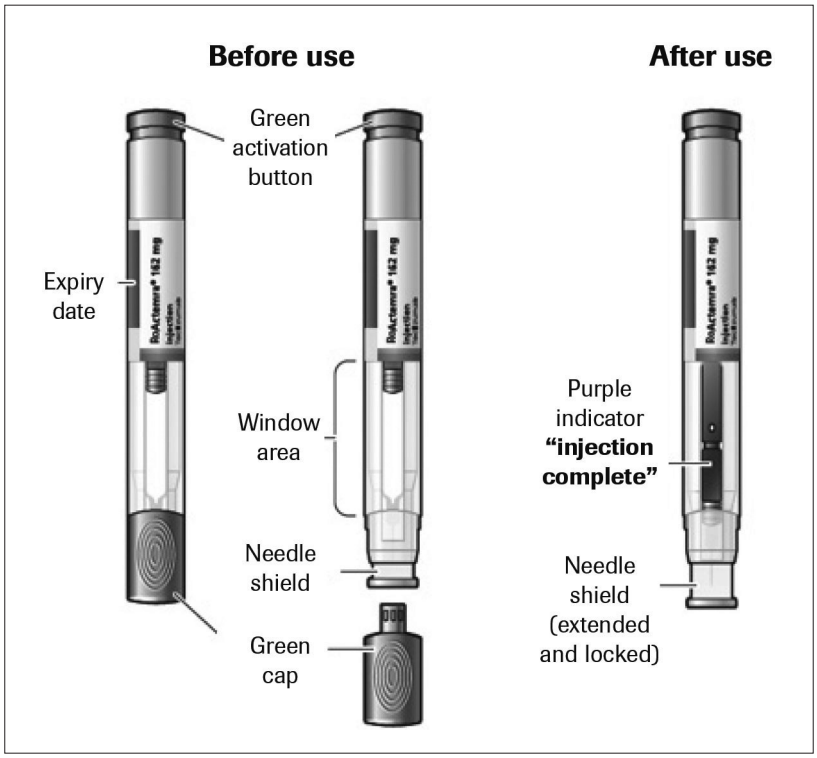


Figure B

2. Take baseline assessments

The first injection using the RoActemra device should be performed under the supervision of a qualified healthcare professional.

The healthcare professional should take baseline assessments to ensure the patient is healthy enough to receive the injection. Vital signs may include:

- Blood pressure
- Temperature
- Pulse

Follow the recommended baseline patient questions as described in the RoActemra Healthcare Professional Brochure (Section 13 – General Recommendations) as well as the Summary of Product Characteristics (Section 4.4 – Warnings and Precautions).

3. Preparation for injection

- Store the device in the refrigerator at 2°C-8°C in the original carton. Do not freeze.
- Allow the RoActemra device to reach room temperature (**18°C to 28°C**) after removing it from the refrigerator. Do not warm up the RoActemra device in any other way.
  - **Do not** speed up the warming process in any way, such as using the microwave or placing the RoActemra device in warm water.
  - **Do not** leave the RoActemra device to warm up in direct sunlight.
- Do not shake the RoActemra device.
- Do not reuse the RoActemra device.
- Do not try to take apart the RoActemra device at any time.
- Do not use the RoActemra device through clothing.
- **Before every use:**
  - **Check the RoActemra device to make sure it is not damaged**. Do not use the RoActemra device if it appears to be damaged or if you have accidentally dropped it.
  - If you are opening the box for the first time, check to make sure that it is properly sealed. **Do not** use the device if the box looks like it has already been opened.
  - Check that the device box is not damaged. **Do not** use device if the box looks damaged.
  - **Check the expiration date on device. Do not** use the RoActemra device if the expiration date has passed because it may not be safe to use. If the expiration date has passed, safely dispose of the RoActemra device in a sharps container and get a new one.
  - **Inspect the RoActemra device visually for particulate matter and discolouration** prior to administration. Do not use if the medicine is cloudy or contains particles, or is any colour besides colourless to slightly yellowish.
- Do not leave the RoActemra device unattended. Keep out of the reach of children.
- Stop administration of RoActemra immediately if an anaphylactic reaction or other serious hypersensitivity reaction occurs. Initiate appropriate therapy and permanently discontinue RoActemra.

Injection preparation: RoActemra 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, and multipacks containing 12 (3 packs of 4) pre-filled syringes. Not all pack sizes may be marketed.

- 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.
- Administer RoActemra 162 mg/0.9 ml within 8 hours once you remove it from the refrigerator and do not keep it above 30°C.
- Allow the pre-filled syringe to reach room temperature and wait for about 25 to 30 minutes before injecting RoActemra 162 mg/0.9 ml.
- Start the injection within 5 minutes after removing the cap, to prevent the medicine from drying out and blocking the needle.

Injection preparation: RoActemra Pre-filled Pen

- Do not remove the pre-filled pen cap until you are ready to inject RoActemra.
- Take the box containing the pre-filled pen out of the refrigerator.
- 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.
- 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 the injection to feel uncomfortable and it could take longer to inject.

4. Choose and prepare an injection site

- Wash your hands well with soap and water.
- Clean the chosen injection site area using the alcohol pad to reduce the risk of infection. 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. Let the skin dry for approximately 10 seconds. Do not touch the injection site again before giving the injection.
- Do not fan or blow on the clean area.
- **Injection site for the Pre-filled Syringe and Pre-filled Pen are as follows:**

  Pre-filled Syringe:

  – The recommended injection sites are the front and middle of your thighs and the lower part of the abdomen below the navel (belly button) except for the five centimetre area directly around the navel **(See Figure C)**.

  – If a caregiver is giving the injection, the outer area of the upper arms may also be used **(See Figure C)**.

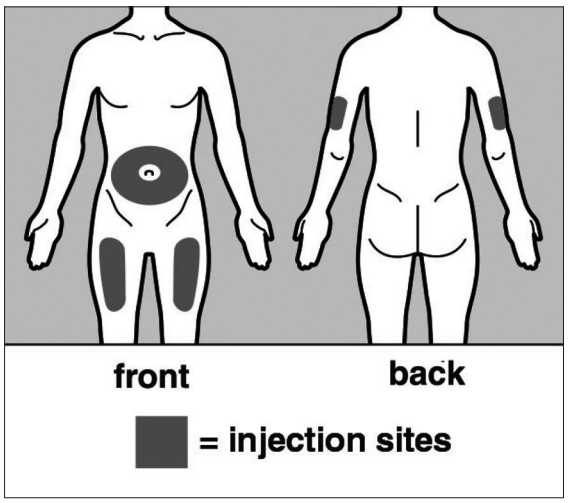


Figure C

Pre-filled Pen:

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

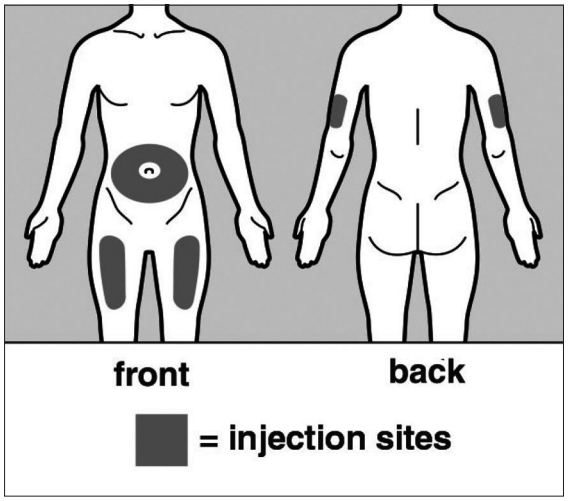


Figure D

- **Rotate injection site**

  Choose a different injection site for each new injection at least:

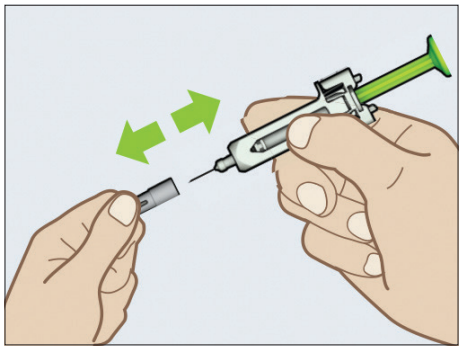
  - **Pre-filled Syringe: 1.5 inch (3 cm) from the area you used for your previous injection.**
  - **Pre-filled Pen: 1 inch (2.5 cm) from the last area you injected.**

- Do not inject into moles, scars, bruises, or areas where the skin is tender, red, hard or not intact. Do not inject into areas that could be bothered by a belt or waistband.

5. Administering the injection

Administration: RoActemra Pre-filled Syringe

1. Do not shake the pre-filled syringe. Hold the needle-shield of the syringe firmly with one hand and pull off the needle-cap with the other. Do not pull or press the plunger. Do not touch the needle or let it touch any surface. 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.



2. Pinch a fold of loose skin at the injection site to provide a firm surface for injection. Insert the needle with a quick, firm action. The needle may be inserted at an angle between 45° to 90°. Insert the needle all the way in. Then keep the syringe in position and let go of the pinched skin.

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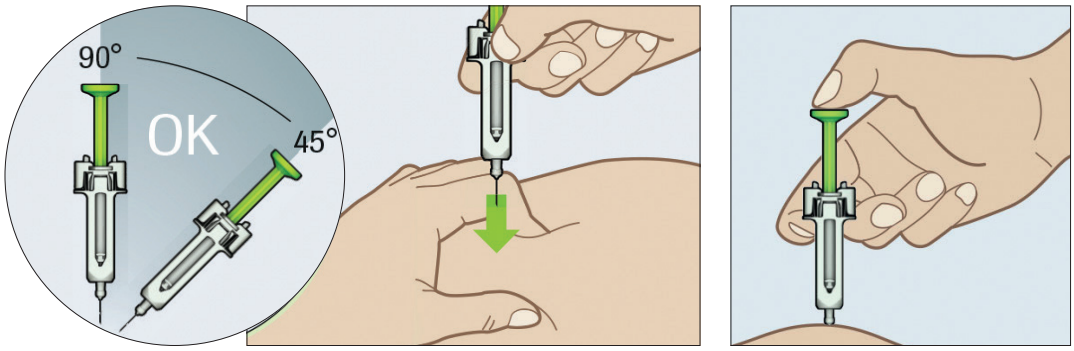
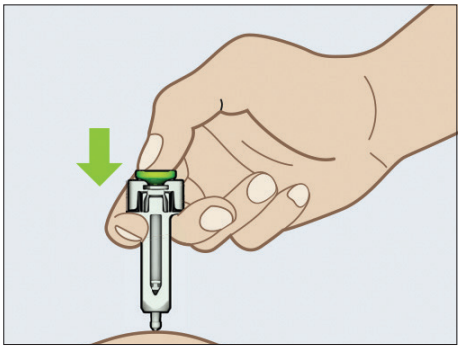
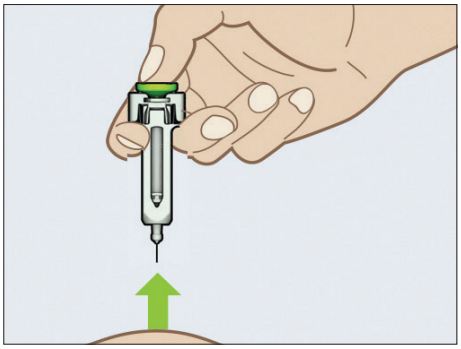


3. Slowly inject all the medicine by gently pushing the plunger all the way down. When the plunger is all the way down, keep pressing down to be sure all the medication has been injected.

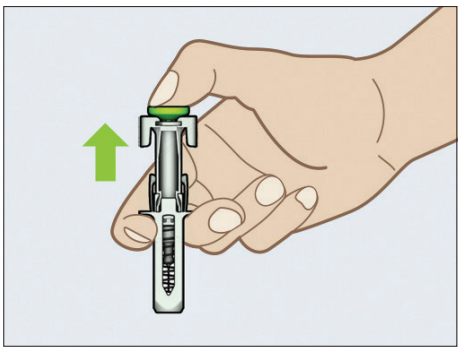
   If you cannot depress the plunger after you insert the needle, dispose of the pre-filled syringe in a puncture-resistant container and use a new pre-filled syringe.



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



5. Release the plunger, once the needle is completely removed from the skin, allowing the needle-shield to protect the needle. Throw away the used syringe in a puncture-resistant container or sharps container.



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.

Administration: RoActemra Pre-filled Pen

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

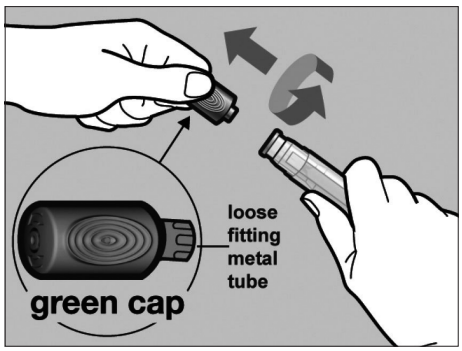


Figure E

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

- 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 F)**.

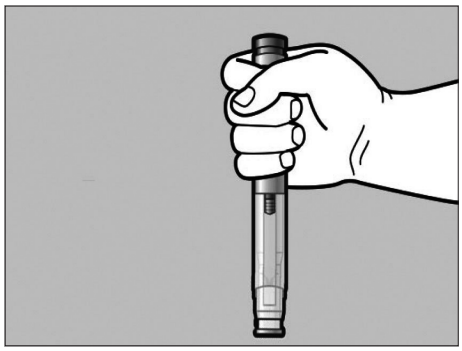


Figure F

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- Use your other hand to gently pinch the area of skin you cleaned, to prepare a firm injection site **(See Figure G)**. 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.

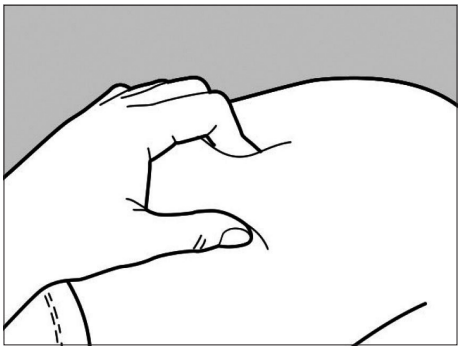

Figure G

- **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 H)**.
- 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.

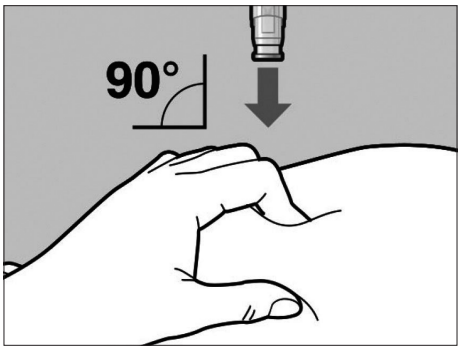

Figure H

- 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 I)**.

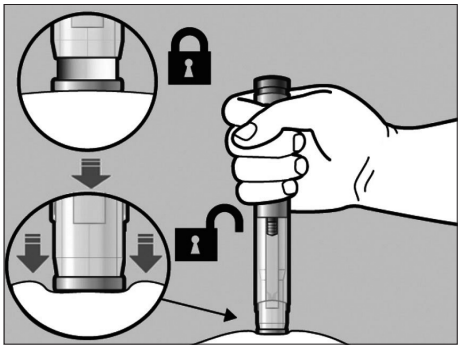

Figure I

- 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 J)**.

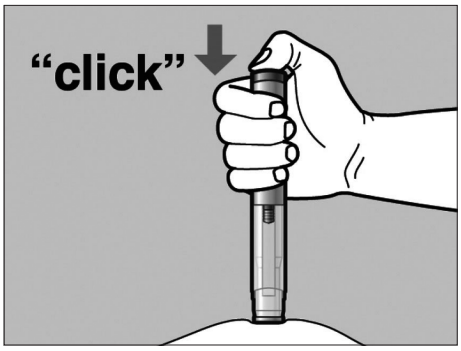

Figure J

- The purple indicator will move along the Window area during the injection **(See Figure K)**.
- Watch the purple indicator until it stops moving to be sure the full dose of medication is injected.

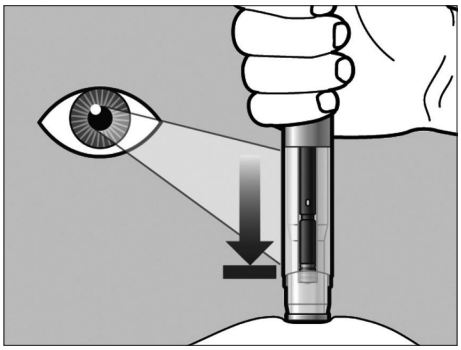

Figure K

- 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 the skin until the purple indicator stops moving.
- 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 L)**.

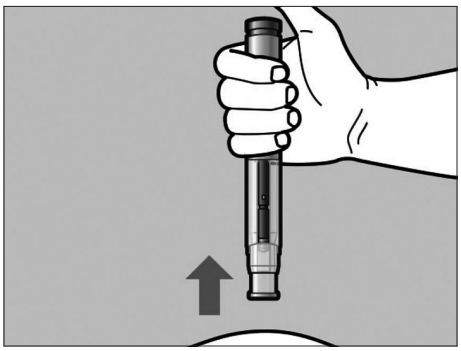

Figure L

- Check the Window area to see that it is filled with the purple indicator **(See Figure L)**.
- 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.
  - The full dose of RoActemra may not have been received by the patient. **Do not** try to reuse the pre-filled pen. Do not repeat the injection with another pre-filled pen. Contact the prescriber for advice.

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.

6. Dispose of the RoActemra device

- **Do not** put the cap back on the RoActemra device.
- Put the used uncapped RoActemra device directly into the sharps container.
  - **Do not throw away (dispose of) the device in the household trash and do not recycle it.**
  - Always keep the sharps container and RoActemra device out of the sight and reach of children.

7. Record your injection

Product traceability

In order to improve the traceability of biological medicinal products, the trade name and batch number of the administered product should be clearly recorded (or stated) in the patient file.

Call for reporting

For full information on all possible side effects please see the RoActemra Summary of Product Characteristics or Package Leaflet, which can be found at the EMA website (www.ema.europa.eu) or www.medicines.ie.

Reporting of suspected adverse events or reactions

Reporting suspected adverse events or reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions (see details below).

Where possible, healthcare professionals should report adverse events or reactions by brand name and batch number.

In the event of a suspected adverse event, please report it to:
Post: The Drug Surveillance Centre, Roche Products (Ireland) Limited,
3004 Lake Drive, Citywest, Naas Road, Dublin 24.
Telephone: (01) 4690700
Email: ireland.drug_surveillance_centre@roche.com

Alternatively, suspected adverse reactions should be reported to:
Website: www.hpra.ie

Further Information

For electronic copies of this risk minimisation material, refer to www.hpra.ie and download the required material (enter 'RoActemra' or 'tocilizumab' in the search box and click on 'EdM' next to any of the medicines that appear). **Alternatively if you would like hard copies**, please contact Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700) or email (ireland.drug_surveillance_centre@roche.com).

For further information about this medicine, please contact Medical Information at Roche Products (Ireland) Limited by telephone (01 4690700) or email (Ireland.druginfo@roche.com).

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