Step-by-Step Dosing and Administration Guide

RoActemra® (tocilizumab) intravenous (IV) for Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Systemic Juvenile Idiopathic Arthritis (sJIA)

A guide to assist healthcare professionals with the dose preparation and administration of RoActemra therapy in patients with active polyarticular juvenile idiopathic arthritis or systemic juvenile idiopathic arthritis

Contents

Part I – RoActemra for Polyarticular Juvenile Idiopathic Arthritis (pJIA)

Indication for patients with pJIA

RoActemra in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (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.

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 discuss the information contained within the ***Important Efficacy and Safety Information sJIA and pJIA Healthcare Professional Brochure*** and the Package Leaflet with the patient and the patient's parents/guardians. These brochures contain valuable information that will help your patients and their parents/guardians understand what they may expect from treatment with RoActemra.

Prior to each infusion, it is important that you review the ***Important Efficacy and Safety Information sJIA and pJIA Healthcare Professional Brochure*** and discuss with the patient and their parents/guardians the information highlighted within the ***Patient Counselling Information and Laboratory Monitoring*** section. Allow ample time to discuss any questions they or their parents/guardians 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 contact +44(0)1707 361010.
- 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.

RoActemra dosing in pJIA patients is based on the following formulae:

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

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

Dosing is every 4 weeks

Please refer to the sJIA & pJIA Dosing Card for more details

	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 + 1
	80	176.0	640	32.0	1 + 1 + 1 + 1 + 1
	82	180.4	656	32.8	1 + 1 + 1 + 1
	84	184.8	672	33.6	1 + 1 + 1 + 1
	86	189.2	688	34.4	1 + 1 + 1 + 1 + 1 + 1
	88	193.6	704	35.2	1 + 1 + 1 + 1 + 1 + 1
	90	198.0	720	36.0	1 + 1 + 1 + 1 + 1 + 1
	92	202.4	736	36.8	1 + 1 + 1 + 1 + 1
	94	206.8	752	37.6	1 + 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

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 50 ml (patients <30 kg) or 100 ml (patients ≥30 kg) 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/patient's parents/guardians if the patient:

- Is taking other biological drugs to treat pJIA, or receiving atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin or benzodiazepines
- Is taking any other medication. This includes prescription and non-prescription medications, vitamins and herbals
- Has had any allergic reactions to previous medications, including RoActemra
- Is sexually active (if the patient is of childbearing age) and may be pregnant, intends to become pregnant or is breastfeeding
- Has an infection or is being treated for an infection; has had or now has hepatitis or any disease of the liver; has a history of stomach ulcers or diverticulitis; has had or now has impaired lung function (e.g. interstitial lung disease)
- Has diabetes or other underlying conditions that may predispose them to infections
- Is planning or are scheduled to have surgery; has had a recent vaccination (e.g. MMR) or is scheduled to have one
- Has 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 Package Leaflet with the patient and their parents/guardians. Answer any questions they may 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.

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 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 30ºC 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 2ºC–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

For 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 RoActemra concentrate required for the patient's dose
- The required amount of RoActemra concentrate (0.5 ml/kg) should be withdrawn from the vial and placed in the 50 ml infusion bag. This should be a final volume of 50 ml

For patients ≥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 RoActemra concentrate required for the patient's dose
- The required amount of RoActemra concentrate (0.4 ml/kg) should be withdrawn from the vial and placed in the 100 ml infusion bag. This should be a final volume of 100 ml

- 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 and their parents/guardians 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 and their parents/guardians 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 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 50 ml (for patients <30 kg) or 100 ml (for patients ≥30 kg) using aseptic technique.

- From a 50 or 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
- 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 the needle and syringe in sharps containers 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 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 and their parents/guardians to 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 alanine transamine (ALT) levels.

Infusion-related reactions are defined as all events occurring during or within 24 hours of an infusion. Following 184.4 patient-years of exposure with RoActemra in pJIA patients, 11 patients (5.9%) experienced infusion reactions during the infusion and 38 patients (20.2%) experienced an event within 24 hours of an infusion.

The most common events occuring during infusion were headache, nausea and hypotension, and those within 24 hours of infusion were dizziness and hypotension. In general, the adverse drug reactions observed during or within 24 hours of an infusion were similar in nature to those seen in rheumatoid arthritis (RA) and systemic juvenile idiopathic arthritis (sJIA) patients.

No clinically significant hypersensitivity reactions requiring treatment discontinuation were reported during the clinical programme.

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 discuss the information contained within the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and the Package Leaflet with the patient and the patient's parents/guardians. These brochures contain valuable information that will help your patients and their parents/guardians understand what they may expect from their treatment with RoActemra. All patients treated with RoActemra should be given the patient alert card.

Prior to each infusion, it is important that you review the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and particularly discuss with the patient and their parents/guardians the information highlighted within the ***Patient Counselling Information and Laboratory Monitoring*** section. Allow ample time to discuss any questions he or she or their parents/guardians may have.

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 the patient would like more information about RoActemra, please direct him or her to email medinfo.uk@roche.com or to call +44(0)1707 361010.

Part II – RoActemra for Systemic Juvenile Idiopathic Arthritis (sJIA)

Indication for patients with sJIA

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 non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to methotrexate [MTX] or where treatment with MTX is inappropriate) or in combination with MTX.

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 discuss the information contained within the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and the Package Leaflet with the patient and the patient's parents/guardians. These brochures contain valuable information that will help your patients and their parents/guardians understand what they may expect from treatment with RoActemra.

Prior to each infusion, it is important that you review the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and discuss with the patient and their parents/guardians the information highlighted within the ***Patient Counselling Information and Laboratory Monitoring*** section. Allow ample time to discuss any questions they or their parents/guardians 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 contact +44(0)1707 361010.
- 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.

RoActemra dosing in sJIA patients is based on the following formulae:

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

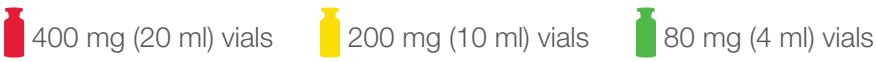
For patients weighing ≥30 kg
Patient's weight (kg) x 8 = RoActemra dose (mg)

Dosing is every 2 weeks

Please refer to the sJIA & pJIA Dosing Card for more details

	Weight (kg)	Weight (lbs)	Dose (mg)	Dose (ml)	Vial combinations
12 mg/kg	10	22.0	120	6.0	1 + 1
	12	26.4	144	7.2	1 + 1
	14	30.8	168	8.4	1
	16	35.2	192	9.6	1
	18	39.6	216	10.8	1 + 1 + 1
	20	44.0	240	12.0	1 + 1 + 1
	22	48.4	264	13.2	1 + 1
	24	52.8	288	14.4	1 + 1 + 1 + 1
	26	57.2	312	15.6	1 + 1 + 1 + 1
	28	61.6	336	16.8	1 + 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	2
	48	105.6	384	19.2	2
	50	110.0	400	20.0	2
	52	114.4	416	20.8	1 + 1 + 1 + 1 + 1
	54	118.8	432	21.6	1 + 1 + 1 + 1 + 1
	56	123.2	448	22.4	2 + 1
	58	127.6	464	23.2	2 + 1
	60	132.0	480	24.0	2 + 1
	62	136.4	496	24.8	1 + 1 + 1 + 1 + 1 + 1
	64	140.8	512	25.6	1 + 1 + 1 + 1 + 1 + 1
	66	145.2	528	26.4	2 + 1 + 1
	68	149.6	544	27.2	2 + 1 + 1
	70	154.0	560	28.0	2 + 1 + 1
	72	158.4	576	28.8	2 + 1
	74	162.8	592	29.6	2 + 1
	76	167.2	608	30.4	2 + 1 + 1 + 1
	78	171.6	624	31.2	2 + 1 + 1 + 1
	80	176.0	640	32.0	2 + 1 + 1 + 1
	82	180.4	656	32.8	2 + 1 + 1
	84	184.8	672	33.6	2 + 1 + 1
	86	189.2	688	34.4	2 + 1 + 1 + 1 + 1
	88	193.6	704	35.2	2 + 1 + 1 + 1 + 1
	90	198.0	720	36.0	2 + 1 + 1 + 1 + 1
	92	202.4	736	36.8	2 + 1 + 1 + 1
	94	206.8	752	37.6	2 + 1 + 1 + 1
	96	211.2	768	38.4	2 + 1
	98	215.6	784	39.2	2 + 1
	≥100	≥220.0	800	40.0	2 + 1

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:



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 50 ml (patients <30 kg) or 100 ml (patients ≥30 kg) 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/patient's parents/guardians if the patient:

- Is taking other biological drugs to treat sJIA, or receiving atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin or benzodiazepines
- Is taking any other medication. This includes prescription and non-prescription medications, vitamins and herbals
- Has had any allergic reactions to previous medications, including RoActemra
- Is sexually active (if the patient is of childbearing age) and may be pregnant, intends to become pregnant or is breastfeeding
- Has an infection or is being treated for an infection; has had or now has hepatitis or any disease of the liver; has a history of stomach ulcers or diverticulitis; has had or now has impaired lung function (e.g. interstitial lung disease)
- Has diabetes or other underlying conditions that may predispose them to infections
- Is planning or are scheduled to have surgery; has had a recent vaccination (e.g. MMR) or is scheduled to have one
- Has cancer, cardiovascular risk factors such as raised blood pressure and raised cholesterol levels, or moderate to severe kidney function problems
- Has a history of macrophage activation syndrome (MAS)

4. Prepare the patient for the infusion

Review the Package Leaflet with the patient and their parents/guardians. Answer any questions they may 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 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 30ºC 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

For 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 RoActemra concentrate required for the patient's dose
- The required amount of RoActemra concentrate (0.6 ml/kg) should be withdrawn from the vial and placed in the 50 ml infusion bag. This should be a final volume of 50 ml

For patients ≥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 RoActemra concentrate required for the patient's dose
- The required amount of RoActemra concentrate (0.4 ml/kg) should be withdrawn from the vial and placed in the 100 ml infusion bag. This should be a final volume of 100 ml

- 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 and their parents/guardians 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 and their parents/guardians 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 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 50 ml (for patients <30 kg) or 100 ml (for patients ≥30 kg) using aseptic technique.

- From a 50 or 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
- 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 the needle and syringe in sharps containers 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 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 and their parents/guardians 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
- Feeling dizzy or faint
- Severe stomach pain or vomiting

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 alanine transamine (ALT) levels.

Infusion-related reactions are defined as all events occurring during or within 24 hours of an infusion. In the 12-week controlled clinical study, 4% of patients from the RoActemra group experienced events occurring during infusion. One event (angioedema) was considered serious and life-threatening, and the patient was discontinued from study treatment.

In the RoActemra group, 16% of patients experienced an event within 24 hours of infusion compared to 5.4% of patients in the placebo group during the 12-week clinical study. In the RoActemra group, the events included, but were not limited to, rash, urticaria, diarrhea, epigastric discomfort, arthralgia and headache. One of these events, urticaria, was considered serious.

Clinically significant hypersensitivity reactions associated with RoActemra and requiring treatment discontinuation were reported in <1% (one out of 112) patients treated with RoActemra during the controlled and open-label clinical study.

What should I do if the patient develops macrophage activation syndrome (MAS)?

MAS is a serious life-threatening disorder that may develop in sJIA patients. This syndrome is thought to be triggered by infections or changes in medications, but can occur without clear reasons or aetiology. In clinical trials, RoActemra has not been studied in patients during an episode of active MAS. If your patient has a history of MAS, it is necessary to assess the risk and benefit to the patient before initiating RoActemra therapy.

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 2 weeks?

RoActemra should be administered once every 2 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 discuss the information contained within the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and the Package Leaflet with the patient and the patient's parents or guardians. These brochures contain valuable information that will help your patients and their parents/guardians understand what they may expect from their treatment with RoActemra. All patients treated with RoActemra should be given the patient alert card.

Prior to each infusion, it is important that you review the ***Important Efficacy and Safety Information pJIA and sJIA Healthcare Professional Brochure*** and particularly discuss with the patient and their parents/guardians the information highlighted within the ***Patient Counselling Information and Laboratory Monitoring*** section. Allow ample time to discuss any questions he or she or their parents/guardians may have.

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 the patient would like more information about RoActemra, please direct him or her to email medinfo.uk@roche.com or to call +44(0)1707 361010.

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

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

If you have any further questions relating to RoActemra please contact Roche Medical Information on +44(0)1707 361010 or email: medinfo.uk@roche.com.

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.

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