Important Efficacy and Safety Information for Healthcare Professionals

RoActemra® (tocilizumab) for Rheumatoid Arthritis (RA) and Giant Cell Arteritis (GCA)

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

Contents

Indications and usage

RoActemra IV

- RoActemra IV, in combination with methotrexate (MTX), is indicated for:
  - the treatment of severe, active and progressive 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 has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with MTX
- The efficacy and safety of intravenously (IV) administered RoActemra in alleviating the signs and symptoms of RA and radiographic response were assessed in the Phase III development programme in five randomised, double-blind, controlled, multi-centre studies. Studies I–V enrolled patients ≥18 years of age with active RA diagnosed according to the American College of Rheumatology (ACR) criteria and who had at least eight tender and six swollen joints at baseline. Study II examined the efficacy of RoActemra on the rate of progression of joint damage and improvement of physical function in RA patients

RoActemra SC

- RoActemra SC, in combination with methotrexate (MTX), is indicated for:
  - the treatment of severe, active and progressive 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 has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with MTX.
- RoActemra initially in combination with glucocorticoids, is indicated for the treatment of GCA in adult patients.
- The efficacy and safety of subcutaneously (SC) administered RoActemra in alleviating the signs and symptoms of RA and radiographic response were assessed in the Phase III development programme in two randomised, double-blind, controlled, multi-centre studies, SC-I and SC-II. Both studies required patient to be ≥18 years of age with moderate-to-severe active RA diagnosed according to ACR criteria. In SC-I, patients had at least four tender and four swollen joints at baseline; in SC-II, patients had at least eight tender and six swollen joints at baseline. SC-II study examined the efficacy of RoActemra in the prevention of progression of structural joint damage and improvement of physical function in RA patients. All patients recieved background non-biologic DMARD(s) throughout the studies.
- The efficacy and safety of RoActemra 162 mg SC once every week has been studied in one Phase III study (WA28119) with 251 Giant Cell Arteritis (GCA) patients. The total patient years duration in the RoActemra all exposure population was 138.5 patient years in the 12 month double blind placebo controlled phase of the study. The overall safety profile observed in the RoActemra treatment groups was consistent with the known safety profile of RoActemra.

Patient counselling information and laboratory monitoring

Patients should be advised of the potential risks and benefits of RoActemra

Infections

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents including RoActemra. Inform patients that RoActemra may lower their resistance to infections.

RoActemra treatment must not be initiated in patients with active infections. Healthcare professionals should exercise caution when considering the use of RoActemra in patients with a history of recurring or chronic infections or with underlying conditions, e.g. diverticulitis, diabetes and interstitial lung disease which may predispose patients to infections. Administration of RoActemra should be interrupted if a patient develops a serious infection until the infection is controlled.

Instruct the patient to **seek immediate medical attention** if signs or symptoms suggesting infection appear in order to ensure rapid evaluation and appropriate treatment. Signs or symptoms of infection may include:

- Fever
- Persistent cough
- Weight loss
- Throat pain or soreness
- Wheezing
- Red or swollen skin blisters, skin tears or wounds
- Severe weakness or tiredness

Hypersensitivity reactions

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/injection or 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.

Instruct the patient to **seek immediate medical attention** if signs or symptoms suggesting a systemic allergic reaction appear in order to ensure rapid evaluation and appropriate treatment. Possible signs or symptoms of a systemic allergic reaction include:

- 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

RoActemra IV

During the infusion, watch the patient closely for any signs and symptoms of hypersensitivity, including anaphylaxis. 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.

RoActemra SC

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.

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 symptoms suggestive of an allergic reaction. They should not take the next dose until they have informed you (their doctor/HCP) and you have told them to take the next dose.

Gastrointestinal side effects

Inform patients that some patients who have been treated with RoActemra have had serious side effects in the stomach and intestines including diverticulitis. Instruct the patient to **seek immediate medical attention** if signs or symptoms of severe, persistent abdominal pain, haemorrhage and/or unexplained change in bowel habits with fever appear, to ensure rapid evaluation and appropriate treatment.

Before you prescribe RoActemra, ask the patient if they:

- Have an infection, are being treated for an infection or have a history of recurring infections
- Have signs of an infection, such as a fever, cough or headache, or are feeling unwell
- Have herpes zoster or any other skin infection with open sores
- Have had any allergic reactions to previous medications, including RoActemra
- Are pregnant, might be pregnant, intend to become pregnant, or are breast-feeding
- Have diabetes or other underlying conditions that may predispose him or her to infection
- Have tuberculosis (TB), or have been in close contact with someone who has had TB
  - As recommended for other biologic therapies in rheumatoid arthritis, patients should be screened for latent TB infection prior to starting RoActemra therapy. Patients with latent TB should be treated with standard anti-mycobacterial therapy before initiating RoActemra
- Are taking other biological drugs to treat RA, or are receiving atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin or benzodiazepines
- Have had or currently have viral hepatitis or any another hepatic disease
- Have a history of gastrointestinal ulcers or diverticulitis
- Have recently received a vaccination or are scheduled for any vaccination
- Have cancer, cardiovascular risk factors, such as raised blood pressure and raised cholesterol levels, or moderate to severe kidney function problems
- Have persistent headaches

Laboratory monitoring

Neutrophils and platelets should be monitored 4 to 8 weeks after start of therapy and thereafter according to standard clinical practice. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored every 4 to 8 weeks for the first 6 months of treatment, followed by every 12 weeks thereafter. Lipids should be monitored 4 to 8 weeks following initiation of RoActemra therapy. Patients should be managed according to local clinical guidelines for management of hyperlipidaemia.

Clinical response

The potential benefits associated with RoActemra treatment

RoActemra IV

The percentages of patients achieving ACR20, ACR50 and ACR70 are shown below. In all studies, patients treated with 8 mg/kg RoActemra had significantly higher ACR20, ACR50 and ACR70 response rates versus MTX- or placebo-treated patients at Week 24. Some patients experienced ACR20 responses as early as 2 weeks for the RoActemra doses studied.

ACR responses in placebo-/MTX-/DMARD-controlled studies (percent of patients)

	Study I AMBITION		Study II LITHE		Study III OPTION		Study IV TOWARD		Study V RADIATE	
Week	RoActemra 8 mg/kg	MTX	RoActemra 8 mg/kg + MTX	Placebo + MTX	RoActemra 8 mg/kg + MTX	Placebo + MTX	RoActemra 8 mg/kg + DMARD	Placebo +DMARD	RoActemra 8 mg/kg + MTX	Placebo + MTX
	n=286	n=284	n=398	n=393	n=205	n=204	n=803	n=413	n=170	n=158
ACR20										
24	70%*	52%	56%*	27%	59%*	26%	61%*	24%	50%*	10%
52			56%*	25%						
ACR50										
24	44%†	33%	32%*	10%	44%*	11%	38%*	9%	29%*	4%
52			36%*	10%						
ACR70										
24	28%†	15%	13%*	2%	22%*	2%	21%*	3%	12%†	1%
52			20%*	4%						

MTX: Methotrexate; DMARD: Disease-modifying anti-rheumatic drug
*p<0.0001, TCZ vs. Placebo + MTX/DMARD
†p<0.01, TCZ vs. Placebo + MTX/DMARD

Patients in Studies I to V had a mean Disease Activity Score (DAS28) of 6.5 to 6.8 at baseline. Significant reductions in DAS28 from baseline (mean improvement) of 3.1 to 3.4 were observed in RoActemra-treated patients compared with control patients (1.3–2.1). The proportion of patients achieving DAS28 clinical remission (DAS28 <2.6) was significantly higher in patients receiving RoActemra (28% to 34%) compared with 1% to 12% of control patients at 24 weeks. In Study II, 65% of patients achieved DAS28 <2.6 at 104 weeks compared with 48% at 52 weeks and 33% at Week 24.

RoActemra IV versus adalimumab in monotherapy

A 24-week double-blinded study that compared RoActemra monotherapy with adalimumab monotherapy, evaluated 326 patients with RA who were intolerant of MTX or where continued treatment with MTX was considered inappropriate (including MTX inadequate responders). Patients in the RoActemra arm received an intravenous (IV) infusion of tocilizumab (8 mg/kg) every 4 weeks (q4w) and a subcutaneous (SC) placebo injection every 2 weeks (q2w). Patients in the adalimumab arm received an adalimumab SC injection (40 mg) q2w plus an IV placebo infusion q4w. A statistically significant superior treatment effect was seen in favour of RoActemra over adalimumab in control of disease activity from baseline to week 24 for the primary endpoint of change in DAS28 and for all secondary endpoints (Table below).

Efficacy results favouring RoActemra monotherapy versus adalimumab monotherapy

	ADA + Placebo (IV) n=162	RoActemra + Placebo (SC) n=163	p value*
Primary Endpoint - Mean Change from baseline at Week 24			
DAS28 (adjusted mean)	-1.8	-3.3	
Difference in adjusted mean (95% CI)	-1.5 (-1.8, -1.1)		<0.0001
Secondary Endpoints - Percentage of Responders at Week 24†			
DAS28 <2.6, n (%)	17 (10.5)	65 (39.9)	<0.0001
DAS28 ≤3.2, n (%)	32 (19.8)	84 (51.5)	<0.0001
ACR20 response, n (%)	80 (49.4)	106 (65.0)	0.0038
ACR50 response, n (%)	45 (27.8)	77 (47.2)	0.0002
ACR70 response, n (%)	29 (17.9)	53 (32.5)	0.0023

*p value is adjusted for region and duration of RA for all endpoints and additionally baseline value for all continuous endpoints.
†Non-responder imputation used for missing data. Multiplicity controlled using Bonferroni-Holm Procedure
ADA: adalimumab

RoActemra SC in RA

The percentages of patients achieving ACR20, ACR50 and ACR70 are shown below. In Study SC-I, 1,262 patients were randomised 1:1 to receive RoActemra SC 162 mg every week or RoActemra IV 8 mg/kg every 4 weeks, in combination with non-biologic DMARD(s). Study SC-I met its primary endpoint, demonstrating non-inferiority of RoActemra SC versus RoActemra IV in the proportion of patients achieving ACR20 responses at Week 24.

ACR responses in Study SC-I (% patients) at Week 24

	Study SC-I*	
	RoActemra SC 162 mg every week + DMARD n=558	RoActemra IV 8mg/kg every 4 weeks + DMARD n=537
ACR20 Week 24	69.4%	73.4%
Weighted difference (95% CI)	-4.0 (-9.2, 1.2)	
ACR50 Week 24	47.0%	48.6%
Weighted difference (95% CI)	-1.8 (-7.5, 4.0)	
ACR70 Week 24	24.0%	27.9%
Weighted difference (95% CI)	-3.8 (-9.0, 1.3)	

*Per protocol population

Patients in Study SC-I had a mean DAS28 at baseline of 6.6 and 6.7 on the SC and IV arms, respectively. At Week 24, a significant reduction in DAS28 from baseline (mean improvement) of 3.5 was observed on both treatment arms, and a comparable proportion of patients had achieved DAS28 clinical remission (DAS28 <2.6) in the SC (38.4%) and IV (36.9%) arms.

RoActemra SC in Patients with Giant Cell Arteritis:

A statistically significant superior treatment effect was seen in favour of RoActemra over placebo in achieving steroid-free sustained remission at Week 52 on RoActemra + 26 weeks prednisone taper compared with placebo + 26 weeks prednisone taper and with placebo + 52 weeks prednisone taper.

The percentage of patients achieving sustained remission at week 52 is shown in the table below.

Efficacy results from Study WA28119

	Placebo + 26 week prednisone taper N=50	Placebo + 52 week prednisone taper N=51	RoActemra 162mg SC weekly + 26 week prednisone taper N=100	RoActemra 162 mg SC every other week + 26 week prednisone taper N=49
Primary Endpoint				
Sustained remission (TCZ groups vs PBO+26)				
Responders at Week 52, n (%)	7 (14%)	9 (17.6%)	56 (56%)	26 (53.1%)
Unadjusted difference in proportions (99.5% CI)	N/A	N/A	42%* (18.00, 66.00)	39.06%* (12.46, 65.66)
Key Secondary Endpoint				
Sustained remission (TCZ groups vs PBO+52)				
Responders at Week 52, n (%)	7 (14%)	9 (17.6%)	56 (56%)	26 (53.1%)
Unadjusted difference in proportions (99.5% CI)	N/A	N/A	38.35%* (17.89 , 58.81)	35.41%** (10.41 ,60.41)
Other Secondary Endpoints				
Time to first GCA flare[1] (TCZ groups vs PBO+26) HR (99% CI)	N/A	N/A	0.23* (0.11, 0.46)	0.28** (0.12, 0.66)
Time to first GCA flare[1] (TCZ groups vs PBO+52) HR (99% CI)	N/A	N/A	0.39** (0.18, 0.82)	0.48 (0.20, 1.16)
Time to first GCA flare[1] (Relapsing patients; TCZ groups vs PBO +26) HR (99% CI)	N/A	N/A	0.23*** (0.09,0.61)	0.42 (0.14, 1.28)
Time to first GCA flare[1] (Relapsing patients; TCZ groups vs PBO + 52) HR (99% CI)	N/A	N/A	0.36 (0.13, 1.00)	0.67 (0.21,2.10)
Time to first GCA flare[1] (New-onset patients; TCZ groups vs PBO +26) HR (99% CI)	N/A	N/A	0.25*** (0.09, 0.70)	0.20*** (0.05, 0.76)
Time to first GCA flare[1] (New-onset patients; TCZ groups vs PBO + 52) HR (99% CI)	N/A	N/A	0.44 (0.14, 1.32)	0.35 (0.09, 1.42)
Cumulative glucocorticoid dose (mg)				
median at Week 52 (TCZ groups vs PBO+26)	3296.00	N/A	1862.00*	1862.00*
median at Week 52 (TCZ groups vs PBO +52)	N/A	3817.50	1862.00*	1862.00*
Exploratory Endpoints				
Annualized relapse rate, Week 52§				
Mean (SD)	1.74 (2.18)	1.30 (1.84)	0.41 (0.78)	0.67 (1.10)

Warnings and precautions

Infections

Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents including RoActemra. RoActemra treatment should not be initiated in patients with active infections. Administration of RoActemra should be interrupted if a patient develops a serious infection until the infection is controlled. Healthcare professionals should exercise caution when considering the use of RoActemra in patients with a history of recurring or chronic infections or with underlying conditions (e.g. diverticulitis, diabetes or interstitial lung disease) which may predispose patients to infections.

Vigilance for the timely detection of serious infection is recommended for patients receiving immunosuppressive agents such as RoActemra for moderate-to-severe RA or GCA as signs and symptoms of acute inflammation may be lessened, associated with suppression of the acute phase reaction. The effects of RoActemra on C-reactive protein (CRP), neutrophils and signs and symptoms of infection should be considered when evaluating a patient for a potential infection. **Patients should be instructed to contact their healthcare professional immediately if any symptoms suggesting infection appear, in order to ensure rapid evaluation and appropriate treatment.**

Tuberculosis

As recommended for other biologic treatments, all patients should be screened for latent TB infection prior to starting RoActemra therapy. Patients with latent TB should be treated with standard anti-mycobacterial therapy before initiating RoActemra. Prescribers are reminded of the risk of false negative tuberculin skin and interferon-gamma TB blood test results, especially in patients who are severely ill or immunocompromised.

Patients should be instructed to seek medical advice if signs/symptoms (e.g. persistent cough, wasting/weight loss, low grade fever) suggestive of a TB infection occur during or after therapy with RoActemra.

Viral reactivation

Viral reactivation (e.g. hepatitis B virus) has been reported with biologic therapies for RA. In clinical studies with RoActemra, patients who screened positive for hepatitis were excluded.

Complications of diverticulitis

Events of diverticular perforations as complications of diverticulitis have been reported uncommonly with RoActemra. RoActemra should be used with caution in patients with previous history of intestinal ulceration or diverticulitis. Patients presenting with symptoms potentially indicative of complicated diverticulitis, such as abdominal pain, haemorrhage and/or unexplained change in bowel habits with fever should be evaluated promptly for early identification of diverticulitis, which can be associated with gastrointestinal perforation.

Hypersensitivity reactions

Serious hypersensitivity reactions, including anaphylaxis, have been reported in association with RoActemra. Such reactions may be more severe, and potentially fatal in patients who have experienced hypersensitivity reactions during previous treatment with RoActemra, even if they have received premedication with steroids and antihistamines. 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. Fatal anaphylaxis has been reported after marketing authorisation during treatment with intravenous RoActemra IV.

Instruct the patient to **seek immediate medical attention** if signs or symptoms suggesting a systemic allergic reaction appear in order to ensure rapid evaluation and appropriate treatment. Possible signs or symptoms of a systemic allergic reaction include:

- 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

RoActemra IV

During the infusion, watch the patient closely for any signs and symptoms of hypersensitivity, including anaphylaxis. 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.

RoActemra SC

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.

Patients should be assessed for their suitability to use RoActemra SC at home. Instruct the **patients who are self-administering RoActemra to seek immediate medical attention** if they experience any symptoms suggestive of an allergic reaction and not take the next dose until they have informed their doctor **AND** their doctor has told them to take the next dose if they have experienced any allergic reaction symptoms after receiving RoActemra.

Active hepatic disease and hepatic impairment

Treatment with RoActemra, particularly when administered concomitantly with MTX, may be associated with elevations in hepatic transaminases, therefore caution should be exercised when considering treatment of patients with active hepatic disease or hepatic impairment.

Laboratory parameters

Neutrophils

Decreases in neutrophil counts have occurred following treatment with RoActemra 8 mg/kg IV once every 4 weeks and RoActemra 162 mg SC once a week in combination with DMARDs. There may be an increased risk of neutropenia in patients who have previously been treated with a TNF antagonist.

In patients not previously treated with RoActemra, initiation is not recommended in patients with an absolute neutrophil count (ANC) below 2 x 10^9/L. In patients who develop an ANC <0.5 x 10^9/L, continued treatment is not recommended.

Severe neutropenia may be associated with an increased risk of serious infections, although there has been no clear association established in clinical trials with RoActemra to date.

Neutrophils should be monitored 4 to 8 weeks after start of therapy and thereafter according to standard clinical practice.

Low absolute neutrophil count (ANC)

Laboratory value (cells x 10^9/L)	Action	
	RoActemra IV	**RoActemra SC**
ANC >1	Maintain RoActemra dose	Maintain RoActemra dose
ANC 0.5 to 1	Interrupt RoActemra dosing When ANC increases >1 x 10^9/L resume RoActemra at 4 mg/kg and increase to 8 mg/kg as clinically appropriate	Interrupt RoActemra dosing When ANC increases >1 x 10^9/L resume RoActemra dosing every other week and increase to every week injection, as clinically appropriate
ANC <0.5	Discontinue RoActemra	Discontinue RoActemra

Platelets

Decreases in platelet counts have occurred following treatment with RoActemra 8 mg/kg IV and RoActemra 162 mg SC in combination with MTX.

Caution should be exercised when considering initiation of RoActemra treatment in patients with a low platelet count (i.e. platelet count below 100 x 10^3/µL). In patients who develop a platelet count <50 x 10^3/µL, continued treatment is not recommended.

Platelets should be monitored 4 to 8 weeks after start of therapy and thereafter according to standard clinical practice.

Low platelet count

Laboratory value (cells x 10^3/µL)	Action	
	RoActemra IV	**RoActemra SC**
50 to 100	Interrupt RoActemra dosing When platelet count >100 x 10^3/µL resume RoActemra at 4 mg/kg and increase to 8 mg/kg as clinically appropriate	Interrupt RoActemra dosing When platelet count increases above 100 x 10^3/µL resume RoActemra dosing every other week and increase to every week injection as clinically appropriate
<50	Discontinue RoActemra	Discontinue RoActemra

Hepatic transaminases

In clinical trials, transient or intermittent mild and moderate elevations of hepatic transaminases have been reported commonly with RoActemra treatment, without progression to hepatic injury. An increased frequency of these elevations was observed when potential hepatotoxic drugs (e.g. MTX) were used in combination with RoActemra. When clinically indicated, other liver function tests including bilirubin should be considered.

Caution should be exercised when considering initiation of RoActemra treatment in patients with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >1.5 x upper limit of normal (ULN). In patients with baseline ALT or AST >5 x ULN, treatment is not recommended.

ALT and AST levels should be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter. For ALT or AST elevations >3 to 5 x ULN, RoActemra treatment should be interrupted.

Liver enzyme abnormalities

Laboratory value	Action	
	RoActemra IV	**RoActemra SC**
>1 to 3 x ULN	Modify the dose of the concomitant MTX if appropriate For persistent increases in this range, reduce RoActemra dose to 4 mg/kg or interrupt RoActemra until ALT or AST have normalised Restart with 4 mg/kg or 8 mg/kg, as clinically appropriate	Dose-modify concomitant DMARDs if appropriate For persistent increases in this range, reduce RoActemra dose frequency to every other week injection or interrupt RoActemra until ALT or AST have normalised Restart with weekly or every other week injection, as clinically appropriate
>3 to 5 x ULN	Interrupt RoActemra dosing until <3 x ULN and follow recommendations above for >1 to 3 x ULN For persistent increases >3 x ULN (confirmed by repeat testing), discontinue RoActemra	Interrupt RoActemra dosing until <3 x ULN and follow recommendations above for >1 to 3 x ULN For persistent increases >3 x ULN, discontinue RoActemra
>5 x ULN	Discontinue RoActemra	Discontinue RoActemra

Lipids

Elevations in lipid parameters including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides were observed in patients treated with RoActemra. In the majority of patients, there was no increase in atherogenic indices, and elevations in total cholesterol responded to treatment with lipid-lowering agents.

Assessment of lipid parameters should be performed 4 to 8 weeks following initiation of RoActemra therapy. Patients should be managed according to local clinical guidelines for management of hyperlipidaemia.

Neurological disorders

Physicians should be vigilant for symptoms potentially indicative of new-onset central demyelinating disorders. The potential for central demyelination with RoActemra is currently unknown.

Malignancy

The risk of malignancy is increased in patients with RA. Immunomodulatory medicinal products may increase the risk of malignancy.

Vaccinations

Live and live-attenuated vaccines should not be given concurrently with RoActemra as clinical safety has not been established. It is recommended that all patients, particularly the elderly be brought up to date with all immunisations in agreement with current immunisation guidelines prior to initiating RoActemra therapy. The interval between live vaccinations and initiation of RoActemra therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents.

Cardiovascular risk

RA patients have an increased risk for cardiovascular disorders and should have risk factors (e.g. hypertension, hyperlipidaemia) managed as part of usual standard of care.

Renal impairment

No dose adjustment is required in patients with mild renal impairment. RoActemra has not been studied in patients with moderate to severe renal impairment. Renal function should be monitored closely in these patients.

Product traceability

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

Undesirable effects

Summary of the safety profile

The most commonly reported adverse drug reactions (ADRs) occuring in ≥ 5% of patients treated with RoActemra monotherapy or in combination with DMARDs were upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT. The most serious ADRs were serious infections, complications of diverticulitis, and hypersensitivity reactions.

RoActemra IV

Infections

In the 6-month controlled studies, the rate of all infections reported with RoActemra 8 mg/kg plus DMARD treatment was 127 events per 100 patient-years compared with 112 events per 100 patient-years in the placebo plus DMARD group. In the long-term exposure population, the overall rate of infections with RoActemra was 108 events per 100 patient-years exposure.

In 6-month controlled clinical studies, the rate of serious infections with RoActemra 8 mg/kg plus DMARDs was 5.3 events per 100 patient-years exposure compared with 3.9 events per 100 patient-years exposure in the placebo plus DMARD group. In the monotherapy study the rate of serious infections was 3.6 events per 100 patient-years of exposure in the RoActemra group and 1.5 events per 100 patient-years of exposure in the MTX group.

In the long-term exposure population, the overall rate of serious infections (bacterial, viral and fungal) was 4.7 events per 100 patient-years. Reported serious infections, some with fatal outcome, included active tuberculosis, which may present with intrapulmonary or extrapulmonary disease, invasive pulmonary infections, including candidiasis, aspergillosis, coccidioidomycosis and pneumocystis jirovecii, pneumonia, cellulitis, herpes zoster, gastroenteritis, diverticulitis, sepsis and bacterial arthritis. Cases of opportunistic infections have been reported.

Other adverse reactions

RoActemra IV

Summary of ADRs occurring in patients with RA receiving RoActemra treatment as monotherapy or in combination with MTX or other DMARDs in the double-blind controlled period

System organ class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)
Infections and infestations	Upper respiratory tract infections	Cellulitis, Pneumonia, Oral herpes simplex, Herpes zoster	Diverticulitis
Gastrointestinal disorders		Abdominal pain, Mouth ulceration, Gastritis	Stomatitis, Gastric ulcer
Skin and subcutaneous tissue disorders		Rash, Pruritus, Urticaria	
Nervous system disorders		Headache, Dizziness	
Investigations		Hepatic transaminases increased, Weight increased, Total bilirubin increased*	
Vascular disorders		Hypertension	
Blood and lymphatic system disorders		Leukopaenia, Neutropaenia	
Metabolism and nutrition disorders	Hypercholesterolaemia*		Hypertriglyceridaemia
General disorders and administration site conditions		Peripheral oedema, Hypersensitivity reactions	
Eye disorders		Conjunctivitis	
Respiratory, thoracic and mediastinal disorders		Cough, Dyspnoea	
Renal disorders			Nephrolithiasis
Endocrine disorders			Hypothyroidism

* Includes elevations collected as part of routine laboratory monitoring

Infusion reactions

In the 6-month controlled trials, 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 tocilizumab and requiring treatment discontinuation were reported in a total of 56 out of 4,009 patients (1.4%) treated with tocilizumab during the controlled and open label clinical studies. These reactions were generally observed during the second to fifth infusions of tocilizumab (for further information, see section 4.4 of the SmPC). Fatal anaphylaxis has been reported after marketing authorisation during treatment with intravenous tocilizumab (see section 4.4 of the SmPC).

Interstitial lung disease

Impaired lung function may increase the risk for developing infections. There have been post-marketing reports of interstitial lung disease (including pneumonitis and pulmonary fibrosis), some of which had fatal outcomes.

Immunogenicity

A total of 2,876 patients have been tested for anti-RoActemra antibodies in the 6-month controlled clinical trials. Of the 46 patients (1.6%) who developed anti-RoActemra antibodies, 6 had an associated medically significant hypersensitivity reaction, of which 5 led to permanent discontinuation of treatment. 30 patients (1.1%) developed neutralising antibodies.

Gastrointestinal perforation

During the 6-month controlled clinical trials, the overall rate of gastrointestinal perforation was 0.26 events per 100 patient years with RoActemra therapy. In the long-term exposure population the overall rate of gastrointestinal perforation was 0.28 events per 100 patient years. Reports of gastrointestinal perforation on RoActemra were primarily reported as complications of diverticulitis including generalised purulent peritonitis, lower gastrointestinal perforation, fistulae and abscess.

Haematological abnormalities:

Neutrophils

In the 6-month controlled trials decreases in neutrophil counts below 1 x 10^9/ L occurred in 3.4% of patients on RoActemra 8 mg/kg plus DMARDs compared to < 0.1% of patients on placebo plus DMARDs. Approximately half of the patients who developed an ANC < 1 x 10^9/ L did so within 8 weeks after starting therapy. Decreases below 0.5 x 10^9/ L were reported in 0.3% patients receiving RoActemra 8 mg/kg plus DMARDs. Infections with neutropenia have been reported.

During the double-blind controlled period and with long-term exposure, the pattern and incidence of decreases in neutrophil counts remained consistent with what was seen in the 6-month controlled clinical trials.

Platelets

In the 6-month controlled trials decreases in platelet counts below 100 x 10^3/ µL occurred in 1.7% of patients on RoActemra 8 mg/kg plus DMARDs compared to < 1% on placebo plus DMARDs. These decreases occurred without associated bleeding events.

During the double-blind controlled period and with long-term exposure, the pattern and incidence of decreases in platelet counts remained consistent with what was seen in the 6-month controlled clinical trials.

Very rare reports of pancytopenia have occurred in the post marketing setting.

During the 6-month controlled trials transient elevations in ALT/AST > 3 x ULN were observed in 2.1% of patients on RoActemra 8 mg/kg compared to 4.9% of patients on MTX and in 6.5% of patients who received 8 mg/kg RoActemra plus DMARDs compared to 1.5% of patients on placebo plus DMARDs.

The addition of potentially hepatotoxic drugs (e.g. MTX) to tocilizumab monotherapy resulted in increased frequency of these elevations. Elevations of ALT/AST > 5 x ULN were observed in 0.7% of RoActemra monotherapy patients and 1.4% of tocilizumab plus DMARD patients, the majority of whom were discontinued permanently from tocilizumab treatment. These elevations were not associated with clinically relevant increase in direct bilirubin, nor were they associated with clinical evidence of hepatitis or hepatic impairment. During the double-blind controlled period, the incidence of indirect bilirubin greater than the upper limit of normal, collected as a routine laboratory parameter, is 6.2% in patients treated with 8 mg/kg RoActemra + DMARD. A total of 5.8% of patients experienced an elevation of indirect bilirubin of > 1 to 2 x ULN and 0.4% had an elevation of > 2 x ULN.

During the double-blind controlled period and with long-term exposure, the pattern and incidence of elevation in ALT/AST remained consistent with what was seen in the 6-month controlled clinical trials.

Lipid parameters

During the 6-month controlled trials, increases of lipid parameters such as total cholesterol, triglycerides, LDL cholesterol, and/or HDL cholesterol have been reported commonly. With routine laboratory monitoring it was seen that approximately 24% of patients receiving RoActemra in clinical trials experienced sustained elevations in total cholesterol ≥ 6.2 mmol/ L, with 15% experiencing a sustained increase in LDL to ≥ 4.1 mmol/ L. Elevations in lipid parameters responded to treatment with lipid-lowering agents.

During the double-blind controlled period and with long-term exposure, the pattern and incidence of elevations in lipid parameters remained consistent with what was seen in the 6-month controlled trials.

Malignancies

The risk of malignancy is increased in patients with RA. Immunomodulatory medicinal products may increase the risk of malignancy. The clinical data are insufficient to assess the potential incidence of malignancy following exposure to tocilizumab. Long-term safety assessments are ongoing.

Skin reactions

Very rare reports of Stevens-Johnson Syndrome have ocurred in the post marketing setting.

RoActemra SC in RA

The safety of RoActemra SC in RA includes one double-blind, controlled, multicentre study, SC-I. The safety and immunogenicity observed for RoActemra SC was consistent with the known safety profile of RoActemra IV, with a higher frequency of injection site reactions observed with RoActemra SC.

Injection site reactions

Injection site reactions (including erythema, pruritus, pain and haematoma) were mild to moderate in severity. The majority were resolved without any treatment and none necessitated drug discontinuation.

Immunogenicity

No correlation of antibody development to clinical response or adverse events was observed.

Haematological abnormalities:

Neutrophils

During routine laboratory monitoring in the RoActemra 6 month controlled clinical trial SC-I, a decrease in neutrophil count below 1 × 10^9/L occurred in 2.9% of patients on the subcutaneous weekly dose.

There was no clear relationship between decreases in neutrophils below 1 x 10^9/L and the occurrence of serious infections.

Platelets

During routine laboratory monitoring in the RoActemra 6 month clinical trial SC-I, none of the patients on the SC weekly dose had a decrease in platelet count to ≤50 × 10^3 / µL.

Hepatic transaminase elevations

During routine laboratory monitoring in the RoActemra 6-month controlled clinical trial SC-I, elevation in ALT or AST ≥3 x ULN occurred in 6.5% and 1.4% of patients, respectively on the subcutaneous weekly dose.

Lipid parameters

During routine laboratory monitoring in the RoActemra 6 month controlled clinical trial SC-I, 19% of patients experienced sustained elevations in total cholesterol > 6.2 mmol/L (240 mg/dL), with 9% experiencing a sustained increase in LDL to ≥ 4.1 mmol/L (160 mg/dL) on the subcutaneous weekly dose.

RoActemra SC in GCA

The safety of subcutaneous RoActemra has been studied in one Phase III study (WA28119) with 251 GCA patients. The total patient years duration in the RoActemra all exposure population was 138.5 patient years in the 12 month double blind placebo controlled phase of the study. The overall safety profile observed in the RoActemra treatment groups was consistent with the known safety profile of RoActemra

Injection site reactions

In the RoActemra subcutaneous weekly group, a total of 6% (6/100) of patients reported an adverse reaction occurring at the site of a subcutaneous injection. No injection site reaction was reported as a serious adverse event or required treatment discontinuation.

Infections

The rate of infection/serious infection events was balanced between the RoActemra weekly group (200.2/9.7 events per 100 patient years) vs. placebo plus 26 weeks prednisone taper (156.0/4.2 events per 100 patient years) and placebo plus 52 weeks taper (210.2/12.5 events per 100 patient years) groups.

Immunogenicity

In the RoActemra subcutaneous weekly group, one patient (1%, 1/100) developed positive neutralizing anti-RoActemra antibodies, though not of the IgE isotype. This patient did not develop a hypersensitivity reaction.

Haematological abnormalities:

Neutrophils

During routine laboratory monitoring in the Roactemra 12 month controlled clinical trial, a decrease in neutrophil count below 1×10^9/L occurred in 4% of patients in the RoActemra subcutaneous weekly group. This was not observed in either of the placebo plus prednisone taper groups.

Platelets

During routine laboratory monitoring in the RoActemra 12 month controlled clinical trial, one patient (1%, 1 / 100) in the RoActemra subcutaneous weekly group had a single transient occurence of decrease in platelet count to $<100 \times 10^3$ / µL without associated bleeding events. A decrease in platelet counts below 100×10^3 / µL was not observed in either of the placebo and prednisone taper groups.

Hepatic transaminase elevations

During routine laboratory monitoring in the RoActemra 12 month controlled clinical trial, elevation in ALT ≥3 x ULN occurred in 3% of patients in the RoActemra subcutaneous weekly group compared to 2% in the placebo + 52 week prednisone taper group and none in the placebo + 26 week prednisone taper group. An elevation in AST > 3 ULN occurred in 1% of patients in the RoActemra subcutaneous weekly group, compared to no patients in either of the placebo + prednisone taper groups.

Lipid parameters

During routine laboratory monitoring in the RoActemra 12 month controlled clinical trial, 34% of patients experienced sustained elevations in total cholesterol > 6.2 mmol/l (240 mg/dl), with 15% experiencing a sustained increase in LDL to ≥ 4.1 mmol/l (160 mg/dl) in the RoActemra subcutaneous weekly group.

Drug-drug interactions

Interaction studies have only been performed in adults.

Concomitant administration of a single dose of 10 mg/kg RoActemra with 10 to 25 mg MTX once weekly had no clinically significant effect on MTX exposure.

There is no experience of the use of RoActemra with TNF antagonists or other biological treatments for RA. RoActemra is not recommended for use with other biological agents.

Interactions with CYP450 substrates

The expression of hepatic CYP450 enzymes is suppressed by cytokines, such as IL-6, that stimulate chronic inflammation. Thus, CYP450 expression may be reversed when potent cytokine inhibitory therapy, such as RoActemra, is introduced.

In vitro studies with cultured human hepatocytes demonstrated that IL-6 caused a reduction in CYP1A2, CYP2C9, CYP2C19 and CYP3A4 enzyme expression. RoActemra normalises expression of these enzymes.

In a study in RA patients, levels of simvastatin (CYP3A4) were decreased by 57% one week following a single dose of RoActemra, to the level similar to, or slightly higher than, those observed in healthy subjects.

When starting or stopping therapy with RoActemra, patients taking medicinal products which are individually adjusted and are metabolised via CYP450, CYP3A4, CYP1A2 or CYP2C9 (e.g. methylprednisolone, dexamethasone, (with the possibility for oral glucocorticoid withdrawal syndrome), atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin or benzodiazepines) should be monitored as doses may need to be increased to maintain therapeutic effect. Given its long elimination half-life, the effect of RoActemra on CYP450 enzyme activity may persist for several weeks after stopping therapy.

Use in specific populations

Pregnancy

There are no adequate data from the use of RoActemra in pregnant women. A study in animals has shown an increased risk of spontaneous abortion/embryo-foetal death at a high dose. The potential risk for humans is unknown.

RoActemra should not be used during pregnancy unless clearly necessary.

Women of childbearing potential

Women of childbearing potential must use effective contraception during and up to 3 months after treatment.

Breast-feeding

It is unknown whether RoActemra is excreted in human breast milk. The excretion of RoActemra in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with RoActemra should be made taking into account the benefit of breast-feeding to the child and the benefit of RoActemra therapy to the woman.

Fertility

Available non-clinical RoActemra data do not suggest an effect on fertility.

Elderly

No dose adjustment is required in patients aged 65 years and older.

Renal impairment

No dose adjustment is required in patients with mild or moderate renal impairment. RoActemra has not been studied in patients with moderate to severe renal impairment. Renal function should be closely monitored in these patients.

Hepatic impairment

RoActemra has not been studied in patients with hepatic impairment. Therefore, no dose recommendations can be made.

Paediatric patients

The safety and efficacy of RoActemra SC fixed-dose formulation in children from birth to less than 18 years have not been established. No data are available.

Dosage and administration

RoActemra IV

The recommended dose of RoActemra for adult patients with RA is 8 mg/kg body weight, but no higher than 800 mg, given every 4 weeks as a 1-hour, single-drip IV infusion.

- RoActemra can be used concomitantly with MTX or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate
- RoActemra has not been studied in combination with TNF antagonists or other biologic treatments for RA. RoActemra is not recommended for use with other biologic agents
- It is not recommended to initiate RoActemra treatment in patients with a low neutrophil count, i.e. absolute neutrophil count (ANC) less than 2×10^9/L. In patients who develop an ANC $< 0.5 \times 10^9$/L, continued treatment is not recommended
- Caution should be exercised when considering initiation of RoActemra treatment in patients with a low platelet count (i.e. platelet count below 100×10^3/µL). In patients who develop a platelet count $< 50 \times 10^3$/µL, continued treatment is not recommended
- Caution should be exercised when considering initiation of RoActemra treatment in patients with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 1.5 x upper limit of normal (ULN). In patients with baseline ALT or AST > 5 x ULN, treatment is not recommended. For ALT or AST elevations > 3 to 5 x ULN confirmed by repeat testing, RoActemra treatment should be interrupted until < 3 x ULN
- Reduction of dose from 8 mg/kg to 4 mg/kg is recommended for management of certain dose-related laboratory changes including elevated liver enzymes, neutropenia and thrombocytopenia

General considerations for IV administration

RoActemra concentrate for intravenous infusion should be **diluted to 100 mL by a healthcare professional using aseptic technique.**

- From a 100 mL infusion bag, withdraw a volume of 0.9% (9 mg/mL) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of 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 100 mL infusion bag. This should be a final volume of 100 mL. 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
- 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 2–8ºC, 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
- Allow the fully diluted RoActemra solution to reach room temperature (18º–28ºC) prior to infusion
- The infusion should be administered over one hour, and must be administered with an infusion set. Do not administer as an IV push or bolus
- 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

For further information, please consult the Step-by-Step Dosing and Administration Guide for RoActemra

RoActemra SC (Pre-filled syringe or Pre-filled pen)

In patients with Rheumatoid Arthritis

The recommended dose of RoActemra for adult patients with RA is 162 mg given once every week as a single, fixed subcutaneous injection with a pre-filled syringe or a pre-filled pen.

- RoActemra can be used concomitantly with MTX or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate
- RoActemra has not been studied in combination with TNF antagonists or other biologic treatments for RA. RoActemra is not recommended for use with other biological agents

In patients with Giant Cell Arteritis

The recommended posology is subcutaneous 162 mg once every week in combination with a tapering course of glucocorticoids. RoActemra can be used alone following discontinuation of glucocorticoids.

Remission does not need to be achieved by glucocorticoids prior to initiating RoActemra treatment.

In the event of patients experiencing a relapse of GCA during the course of RoActemra therapy, the prescribing healthcare professional should consider re-introducing RoActemra if it had been discontinued and/or escalating the dose of concomitant glucocorticoids (or restarting glucocorticoid therapy if it has been discontinued) according to best medical judgement/treatment guidelines.

RoActemra monotherapy should not be used for the treatment of acute relapses as efficacy in this setting has not been established.

Based upon the chronic nature of GCA, treatment beyond 52 weeks should be guided by disease activity, physician discretion, and patient choice.

General dose advice (Pre-filled syringe or pre-filled pen)

- It is not recommended to initiate RoActemra treatment in patients with a low neutrophil count, i.e. absolute neutrophil count (ANC) less than 2 x 10^9/L. In patients who develop an ANC <0.5 x 10^9/L, continued treatment is not recommended
- Caution should be exercised when considering initiation of RoActemra treatment in patients with a low platelet count (i.e. platelet count below 100 x 10^3/µL). In patients who develop a platelet count <50 x 10^3/µL, continued treatment is not recommended
- Caution should be exercised when considering initiation of RoActemra treatment in patients with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >1.5 x upper limit of normal (ULN). In patients with baseline ALT or AST >5 x ULN, treatment is not recommended. For ALT or AST elevations >3 to 5 x ULN, RoActemra treatment should be interrupted

- RoActemra dosing interruption or reduction in frequency of administration of SC dose from every week to every other week dosing is recommended for management of certain dose-related laboratory changes including elevated liver enzymes, neutropenia, and thrombocytopenia

General considerations for SC administration

RoActemra 162 mg is supplied in 0.9 mL of solution for injection as a pack of 4 single use pre-filled syringes or pre-filled pens. The following should be considered before administration:

- The pre-filled syringes or pre-filled pens should be stored at 2–8°C and should not be frozen
- The pre-filled syringes or pre-filled pens should be kept in the outer carton to protect them from light and should be kept dry. The pre-filled syringes or pre-filled pens should be kept out of sight and reach of children
- Inspect the pre-filled syringe or pre-filled pen visually for particulate matter and decolouration prior to administration. 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 or pre-filled pen appears to be damaged
- Once removed from the refrigerator, RoActemra SC must be administered within 8 hours and should not be kept above 30°C
- After removing the **pre-filled syringe** from the refrigerator:
  - The pre-filled syringe should be allowed to reach room temperature (18–28°C) 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
  - After removing the needle cap, the syringe must be used 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.
  - 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.
- After removing the **pre-filled pen** from the refrigerator:
  - The pre-filled pen should be allowed to reach room temperature (18–28°C) by waiting for 45 minutes before injecting RoActemra 162 mg/0.9 mL. Do not warm up the pre-filled pen in any other way
  - After removing the needle cap, the syringe must be used within 3 minutes to prevent the medicine from drying out and blocking the needle. If the pre-filled pen is not used within 3 minutes of removing the cap, you must dispose of it in a puncture resistant container and use a new pre-filled pen. Never re-attach the needle cap after removal.

- The pre-filled syringe and pre-filled pen should not be shaken
- After proper training in injection technique, patients may self-inject with RoActemra if you determine that it is appropriate

For further information, please consult the Step-by-Step Dosing and Administration Guide for RoActemra

Switching from RoActemra IV to RoActemra SC

- Limited information is available regarding switching patients from RoActemra IV formulation to RoActemra SC fixed-dose formulation. The once-every-week dosing interval of RoActemra SC should be followed
- Patients transitioning from IV to SC formulation should administer their first SC dose instead of the next scheduled IV dose under the supervision of a qualified healthcare professional

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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