RoACTEMRA for Systemic Juvenile Idiopathic Arthritis (sJIA)

STEP-BY-STEP INFUSION INSTRUCTIONS

A guide to assist healthcare professionals with the dose preparation and administration of RoACTEMRA therapy in patients with active Systemic Juvenile Idiopathic Arthritis

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Prescribing information can be found on the back cover

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Quick Reference Guide

1. Go through the pre-administration checklist with your patient and their parents/guardian, determine his or her infection risk and history
2. Take baseline assessments to ensure the patient is healthy enough to receive the infusion
3. Weigh the patient and calculate the RoACTEMRA dose required using the dose calculation table
4. Gather all supplies necessary for RoACTEMRA infusion
5. Prepare the patient for the infusion of RoACTEMRA by answering any questions they or their parents/guardians might have and preparing the infusion set and intravenous site
6. Prepare the RoACTEMRA infusion using aseptic technique
7. Begin the RoACTEMRA infusion, administered over 1 hour using an infusion set

Dosing Preparation and Administration Guide

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.

This booklet will guide you through the RoACTEMRA infusion process in 7 steps.

Before therapy begins

Before beginning RoACTEMRA therapy, and prior to each infusion, it is important that you discuss the information contained within the *Healthcare Professional Brochure - Important Efficacy and Safety Information* (highlighting the information in the *Patient Counselling Information and Laboratory Monitoring* section) and the *Patient Brochure - What you should know* with the patient and the patient's parents/guardians. These brochures contain valuable information that will help your patients and their parents/guardians fully understand what to expect from treatment with RoACTEMRA. Allow ample time to discuss any questions they may have.

RoACTEMRA patient brochures and other information can be requested from your sales representative. If you have questions, please contact Roche Medical Information at **medinfo.uk@roche.com** or **+44 800 328 1629**.

Prior to each infusion, it is important that you review step 1 (Pre-administration Checklist) in this booklet with your patient and their parent/guardian and allow ample time to discuss any questions they may have.

Blood tests will need to be carried out according to the following schedule:

Blood tests required prior to starting therapy:

- 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. 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 an ANC < 0.5 x 10^9/ l or 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 ALT or AST > 1.5 x ULN. In patients with baseline ALT or AST > 5 x ULN, treatment is not recommended.

Blood tests required during treatment:

- Neutrophils and platelets should be monitored at the time of 2nd infusion and thereafter according to standard clinical practice.
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored at the time of the second infusion and thereafter according to good clinical practice. When clinically indicated, other liver function tests including bilirubin should be considered.
- Lipid parameters should be assessed 4 – 8 weeks after start of therapy and manage according to local guidelines.

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1 Pre-administration checklist

To determine the patient's risk of infection and history, ask the patient's parents/guardians if the patient:

- Has an infection or is being treated for an infection
- Is taking any other medication. This includes prescription or non-prescription drugs, statins, vitamins and herbals
- Has recently had a live or live-attenuated vaccine, including any travel vaccines, or is scheduled to have one
- Is sexually active (if the patient is of childbearing age) and is planning a pregnancy or is breastfeeding
- Has cancer or a history of cancer
- Is allergic (hypersensitive) to any of the ingredients of RoACTEMRA
- Has diabetes, hypertension and/or hyperlipidaemia
- Has tuberculosis (TB), or has been in close contact with someone who has had TB. The patient should be tested for TB before beginning RoACTEMRA therapy
- Has symptoms that may be due to complicated diverticulitis, such as abdominal pain, haemorrhage and/or unexplained change in bowel habits with fever
- Has had or now has any disease of the liver including active hepatic disease or hepatic impairment
- Has haematological abnormalities – low neutrophils or platelet count, elevated liver enzymes and lipids
- Has symptoms that may be due to a central demyelinating disorder
- Is on a controlled sodium diet
- Has a history of macrophage activation syndrome (MAS)

For further information and treatment recommendations in case of abnormal laboratory parameters, see the Healthcare Professional brochure entitled *'Healthcare Professional Brochure – Important Efficacy and Safety Information.'*

Discuss with the patient and their parents/guardians any questions that they may have about this information.

2 Take baseline assessments

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

- Blood pressure
- Temperature
- Pulse

3 Weigh patient and calculate RoACTEMRA dose

RoACTEMRA dosing is calculated based on each patient's weight. Use the calculation provided on this page, or locate the patient's weight on the chart to find the corresponding dose.

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, then refer to the chart to check whether a dosing adjustment is necessary.

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

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

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

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

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

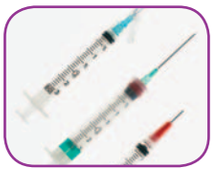
Please refer to the RoACTEMRA Pocket Dosing Guide for sJIA for more details

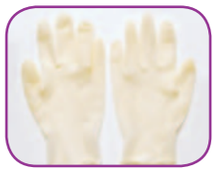
	Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial combinations
12 mg/kg	10	22.0	120	6.0	1 × 80 mg
	11	24.2	132	6.6	1 × 80 mg + 1 × 20 mg
	12	26.4	144	7.2	1 × 80 mg + 1 × 20 mg + 1 × 4 mg
	13	28.6	156	7.8	1 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	14	30.8	168	8.4	1 × 200 mg
	15	33.0	180	9.0	1 × 200 mg + 1 × 20 mg
	16	35.2	192	9.6	1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	17	37.4	204	10.2	1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	18	39.6	216	10.8	1 × 200 mg + 1 × 80 mg
	19	41.8	228	11.4	1 × 200 mg + 1 × 80 mg + 1 × 20 mg
	20	44.0	240	12.0	1 × 200 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg
	21	46.2	252	12.6	1 × 200 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	22	48.4	264	13.2	1 × 200 mg + 2 × 80 mg
	23	50.6	276	13.8	1 × 200 mg + 2 × 80 mg + 1 × 20 mg
	24	52.8	288	14.4	1 × 200 mg + 2 × 80 mg + 1 × 20 mg + 1 × 4 mg
	25	55.0	300	15.0	1 × 200 mg + 2 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	26	57.2	312	15.6	2 × 200 mg + 1 × 80 mg
	27	59.4	324	16.2	2 × 200 mg + 1 × 80 mg + 1 × 20 mg
	28	61.6	336	16.8	2 × 200 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg
	29	63.8	348	17.4	2 × 200 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	30	66.0	240	12.0	3 × 80 mg
	31	68.2	248	12.4	3 × 80 mg + 1 × 20 mg
	32	70.4	256	12.8	3 × 80 mg + 1 × 20 mg + 1 × 4 mg
	33	72.6	264	13.2	3 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	34	74.8	272	13.6	3 × 80 mg + 1 × 200 mg
	35	77.0	280	14.0	3 × 80 mg + 1 × 200 mg + 1 × 20 mg
	36	79.2	288	14.4	3 × 80 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	37	81.4	296	14.8	3 × 80 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	38	83.6	304	15.2	3 × 80 mg + 2 × 200 mg
	39	85.8	312	15.6	3 × 80 mg + 2 × 200 mg + 1 × 20 mg
	40	88.0	320	16.0	3 × 80 mg + 2 × 200 mg + 1 × 20 mg + 1 × 4 mg
	41	90.2	328	16.4	3 × 80 mg + 2 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	42	92.4	336	16.8	4 × 80 mg + 1 × 200 mg
	43	94.6	344	17.2	4 × 80 mg + 1 × 200 mg + 1 × 20 mg
	44	96.8	352	17.6	4 × 80 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	45	99.0	360	18.0	4 × 80 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	46	101.2	368	18.4	1 × 400 mg
	47	103.4	376	18.8	1 × 400 mg + 1 × 20 mg
	48	105.6	384	19.2	1 × 400 mg + 1 × 20 mg + 1 × 4 mg
	49	107.8	392	19.6	1 × 400 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	50	110	400	20.0	1 × 400 mg + 1 × 200 mg
	51	112.2	408	20.4	1 × 400 mg + 1 × 200 mg + 1 × 20 mg
	52	114.4	416	20.8	1 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	53	116.6	424	21.2	1 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	54	118.8	432	21.6	1 × 400 mg + 2 × 200 mg
	55	121	440	22.0	1 × 400 mg + 2 × 200 mg + 1 × 20 mg
8 mg/kg	56	123.2	448	22.4	1 × 400 mg + 1 × 80 mg
	57	125.4	456	22.8	1 × 400 mg + 1 × 80 mg + 1 × 20 mg
	58	127.6	464	23.2	1 × 400 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg
	59	129.8	472	23.6	1 × 400 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	60	132	480	24.0	1 × 400 mg + 2 × 80 mg
	61	134.2	488	24.4	1 × 400 mg + 2 × 80 mg + 1 × 20 mg
	62	136.4	496	24.8	1 × 400 mg + 2 × 80 mg + 1 × 20 mg + 1 × 4 mg
	63	138.6	504	25.2	1 × 400 mg + 2 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	64	140.8	512	25.6	1 × 400 mg + 3 × 80 mg
	65	143	520	26.0	1 × 400 mg + 3 × 80 mg + 1 × 20 mg
	66	145.2	528	26.4	1 × 400 mg + 3 × 80 mg + 1 × 20 mg + 1 × 4 mg
	67	147.4	536	26.8	1 × 400 mg + 3 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	68	149.6	544	27.2	1 × 400 mg + 4 × 80 mg
	69	151.8	552	27.6	1 × 400 mg + 4 × 80 mg + 1 × 20 mg
	70	154	560	28.0	1 × 400 mg + 4 × 80 mg + 1 × 20 mg + 1 × 4 mg
	71	156.2	568	28.4	1 × 400 mg + 1 × 200 mg
	72	158.4	576	28.8	1 × 400 mg + 1 × 200 mg + 1 × 20 mg
	73	160.6	584	29.2	1 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	74	162.8	592	29.6	1 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	75	165	600	30.0	1 × 400 mg + 2 × 200 mg
	76	167.2	608	30.4	1 × 400 mg + 2 × 200 mg + 1 × 20 mg
	77	169.4	616	30.8	1 × 400 mg + 2 × 200 mg + 1 × 20 mg + 1 × 4 mg
	78	171.6	624	31.2	1 × 400 mg + 2 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	79	173.8	632	31.6	1 × 400 mg + 3 × 200 mg
	80	176	640	32.0	1 × 400 mg + 3 × 200 mg + 1 × 20 mg
	81	178.2	648	32.4	1 × 400 mg + 3 × 200 mg + 1 × 20 mg + 1 × 4 mg
	82	180.4	656	32.8	1 × 400 mg + 3 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	83	182.6	664	33.2	1 × 400 mg + 4 × 200 mg
	84	184.8	672	33.6	1 × 400 mg + 4 × 200 mg + 1 × 20 mg
	85	187	680	34.0	1 × 400 mg + 4 × 200 mg + 1 × 20 mg + 1 × 4 mg
	86	189.2	688	34.4	1 × 400 mg + 4 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	87	191.4	696	34.8	2 × 400 mg + 1 × 80 mg
	88	193.6	704	35.2	2 × 400 mg + 1 × 80 mg + 1 × 20 mg
	89	195.8	712	35.6	2 × 400 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg
	90	198	720	36.0	2 × 400 mg + 1 × 80 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	91	200.2	728	36.4	2 × 400 mg + 1 × 200 mg
	92	202.4	736	36.8	2 × 400 mg + 1 × 200 mg + 1 × 20 mg
	93	204.6	744	37.2	2 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg
	94	206.8	752	37.6	2 × 400 mg + 1 × 200 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	95	209	760	38.0	2 × 400 mg + 2 × 200 mg
	96	211.2	768	38.4	2 × 400 mg + 1 × 400 mg
	97	213.4	776	38.8	2 × 400 mg + 1 × 400 mg + 1 × 20 mg
	98	215.6	784	39.2	2 × 400 mg + 1 × 400 mg + 1 × 20 mg + 1 × 4 mg
	99	217.8	792	39.6	2 × 400 mg + 1 × 400 mg + 1 × 20 mg + 1 × 4 mg + 1 × 2 mg
	≥100	≥220	800	40.0	2 × 400 mg + 1 × 400 mg + 1 × 200 mg

4 Gather all necessary supplies

You will need:

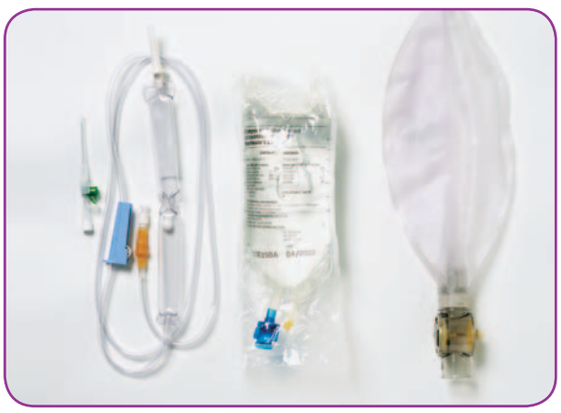
- RoACTEMRA, at room temperature
- Syringes and large-bore needles
- One primary infusion set with Y site
- One 50 ml (patients <30 kg) or 100 ml (patients ≥30 kg) bag of 0.9% (9 mg/ml) sodium chloride
- One intravenous (IV) catheter
- Gauze
- Tourniquet
- Gloves
- Alcohol/cleansing wipes
- Appropriate treatment to manage an infusion-related anaphylactic reaction




5 Prepare the patient for the infusion

- Review the *Patient Brochure – What You Should Know* with the patient and their parents/guardians. Answer any questions they may have
- RoACTEMRA does not require premedication. Start infusion of 0.9% (9mg/mL) sodium chloride




6 Prepare the RoACTEMRA infusion

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

RoACTEMRA is a ready-mix solution and requires no reconstitution. RoACTEMRA concentrate for IV infusion should be diluted by a healthcare professional using aseptic technique as follows:

- Parenteral drug products should be inspected visually for particulate matter or discolouration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted
- Although RoACTEMRA should be refrigerated for storage, the fully diluted RoACTEMRA solution should be allowed to reach room temperature before it is infused. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°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 sterile, non-pyrogenic 0.9% (9 mg/ml) sodium chloride solution for injection equal to the volume of RoACTEMRA concentrate required for the patient's dose under aseptic conditions

For Patients ≥30 kg

- From a 100 ml infusion bag, withdraw a volume of sterile, non-pyrogenic 0.9% (9 mg/ml) 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 infusion bag. To mix the solution, gently invert the bag to avoid foaming
- Dispose of needle and syringe in sharps containers when finished

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7 Begin the RoACTEMRA infusion

The infusion should be administered over 1 hour. **It must be administered with an infusion set and should never be administered as an IV push or bolus.**

Prior to the infusion, inform the patient and their parent/guardian of potential hypersensitivity reactions. Most reactions happen during infusion or within 24 hours after infusion. Such reactions may be more severe, and potentially fatal in patients who have experienced hypersensitivity reactions during previous infusions even if they have received premedication with steroids and antihistamines.

In the 12 week controlled phase of the trial one event (angioedema) occurred during infusion which was considered serious and life threatening which led to study treatment discontinuation. Events which may occur within 24 hours of infusion may include (but are not limited to):

- Rash
- Urticaria
- Diarrhoea
- Epigastric discomfort
- Arthralgia
- Headache

One of these events, urticaria, was considered serious.

During the infusion, watch the patient closely for any hypersensitivity or anaphylactic reaction. Appropriate treatment should be available for immediate use in the event of an anaphylactic reaction or other serious hypersensitivity / serious infusion related reaction. Administration of RoACTEMRA should be stopped immediately and permanently discontinued.

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

Adverse events should be reported to Roche Products Limited. Please contact the Drug Safety Centre, Roche Products Limted, 6 Falcon Way, Shire Park, Welwyn Garden City, Hertfordshire, England. Telephone number +44 1707 367554. Adverse events may otherwise be reported via the national Adverse Drug Reactions (ADRs) reporting system. Reporting forms and information can be found at: http://medicinesauthority.gov.mt/phvigilance.htm

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 storage in the original package until time of use.

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

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

Do I need to administer premedication?

No premedication is required before administering RoACTEMRA.

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) with sterile, non-pyrogenic 0.9% (9 mg/ml) sodium chloride solution for injection using aseptic technique as follows:

- Parenteral drug products should be inspected visually for particulate matter or discolouration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted
- From a 50 or 100 ml infusion bag, withdraw a volume of sterile non-pyrogenic sodium chloride 9 mg/ml (0.9%) solution for injection equal to the volume of the RoACTEMRA concentrate required for the patient's dose under aseptic conditions
- Slowly add RoACTEMRA concentrate for IV infusion from each vial into the infusion bag. To mix the solution, gently invert the bag to avoid foaming
- Although RoACTEMRA should be refrigerated for storage, the fully diluted RoACTEMRA solution should be allowed to reach room temperature before it is infused
- Dispose of needle and syringe in sharps containers when finished

What is the infusion duration?

RoACTEMRA is administered over a 1-hour period. It must be administered with an infusion set and should never be administered as an IV push or bolus.

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

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

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After dilution, the prepared solution for infusion is physically and chemically stable at 30°C for 24 hours. The prepared solution for infusion should be used immediately. If not, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C–8°C, unless dilution has taken place in controlled and validated aseptic conditions.

What should I look for during the infusion?

Watch the patient closely for any hypersensitivity, including anaphylaxis. Most reactions happen during infusion or within 24 hours after infusion. Such reactions may be more severe, and potentially fatal in patients who have experienced hypersensitivity reactions during previous infusions even if they have received premedication with steroids and antihistamines.

Reactions that may occur within 24 hours of an infusion may include (but are not limited to):

- Rash
- Urticaria
- Diarrhoea
- Epigastric discomfort
- Arthralgia
- Headache

During the infusion, watch the patient closely for any hypersensitivity reaction. If an anaphylactic reaction or other serious hypersensitivity / serious infusion related reaction occurs, administration of RoACTEMRA should be stopped immediately, a physician is called immediately and RoACTEMRA should be permanently discontinued.

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

In general the adverse drug reactions (ADRs) in sJIA patients were similar in type to those seen in patients with rheumatoid arthritis (RA).

The most commonly reported ADRs in RA patients were upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT. Reported serious infections were similar to those seen in RA patients with the addition of varicella and otitis media.

One event (angioedema) was reported during an infusion and was considered to be serious and life threatening and the patient discontinued study treatment. Events within 24 hours of infusion included but were not limited to rash, urticaria, diarrhoea, 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 out of 112 patients (<1%) treated with RoACTEMRA.

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 review the *Patient Brochure - What you should know* with the patient and the patient's parents or guardians. This brochure contains valuable information that will help your patients and their parents/guardians fully understand what they may expect from their treatment.

Prior to each infusion, it is important that you review the *Healthcare Professional Brochure - Important Efficacy and Safety Information* 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 that they may have.

To request further information about RoACTEMRA, please call Medical Information on +44 800 328 1629 or email medinfo.uk@roche.com.

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PRESCRIBING INFORMATION:

Please refer to RoActemra SPC for full prescribing information.

Indications: Rheumatoid Arthritis (RA): RoActemra, in combination with methotrexate (MTX), is indicated for the treatment of moderate to severe active rheumatoid arthritis (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. **Systemic juvenile idiopathic arthritis (sJIA):** Indicated for the treatment of active sJIA in patients ≥ 2 years of age, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.

Dosage and Administration: Patients should be given the Patient Alert Card. **RA:** 8 mg/kg iv infusion given once every 4 weeks. Doses exceeding 800 mg per infusion are not recommended. **sJIA:** 8 mg/kg for patients weighing ≥ 30 kg or 12 mg/kg for patients weighing < 30 kg, given as iv infusion every 2 weeks.

Dose adjustments: RA: Dose reduction to 4 mg/kg, or interruptions, are recommended in the event of raised liver enzymes, low absolute neutrophil count (ANC) or low platelet count. RoActemra should not be initiated in patients with ANC count below 2 x 10^9/l. **sJIA:** Interrupt treatment in the event of raised liver enzymes, low ANC or low platelet count; dose reductions have not been studied in these patients.

Contraindications: Hypersensitivity to any component of the product; active, severe infections.

Precautions: Both indications: *Infections:* Cases of serious and sometimes fatal infections have been reported; interrupt therapy until controlled. Caution in patients with recurring/chronic infections, or other conditions which may predispose to infection. *Tuberculosis:* Screen for and treat latent TB prior to starting therapy. *Hypersensitivity reactions:* Serious hypersensitivity reactions have been reported and may be more severe and potentially fatal in patients who have experienced hypersensitivity reactions with previous infusions even if they have received premedication with steroids and antihistamines. Appropriate treatment should be available for immediate use if anaphylaxis occurs. If an anaphylactic reaction or other serious hypersensitivity/serious infusion related reaction occurs, permanently discontinue RoActemra. *Hepatic disease/ impairment:* Use with caution in patients with active hepatic disease/impairment. *Transaminase elevations:* Not recommended in patients with ALT or AST > 5 x ULN; caution in patients with ALT or AST > 1.5 x ULN. *Haematological abnormalities:* Caution in patients with platelet count < 100 x 10^3/µl. Continued treatment not recommended in patients with ANC < 0.5 x 10^9/l or platelet count < 50 x 10^3/µl. *Lipid parameters:* If elevated, follow local guidelines for managing hyperlipidaemia. *Vaccinations:* Live and live attenuated vaccines should not be given concurrently. *Combined with other biologic treatments:* Not recommended. **RA only:** *Viral reactivation:* Has been reported with biologics. *Diverticulitis:* Caution in patients with a history of intestinal ulceration or diverticulitis. Patients with symptoms of complicated diverticulitis should be evaluated promptly. **sJIA only:** Macrophage activation syndrome (MAS) is a serious life-threatening disorder which may develop in sJIA patients. Tocilizumab treatment has not been studied during active MAS.

Interactions: Patients taking other medicines which are metabolised via CYP450 3A4, 1A2, or 2C9 should be monitored as doses may need to be adjusted.

Pregnancy and Lactation: Women should use contraception during and for 3 months after treatment. A decision on whether to continue/discontinue breastfeeding on RoActemra therapy should take into account relative benefits to mother and child.

Undesirable effects: RA: *Very common ADRs (≥ 1/10):* URTI, hypercholesterolaemia. *Common ADRs (≥ 1/100 to < 1/10):* cellulitis, pneumonia, oral herpes simplex, herpes zoster, abdominal pain, mouth ulceration, gastritis, rash, pruritus, urticaria, headache, dizziness, increased hepatic transaminases, increased weight and increased total bilirubin, hypertension, leukopenia, neutropenia, peripheral oedema, hypersensitivity reactions, conjunctivitis, cough, dyspnoea. *Medically significant events: Infections:* Opportunistic and serious infections have been reported, some serious infections had a fatal outcome. Impaired lung function may increase the risk of developing infections. There have been post-marketing reports of interstitial lung disease, some of which had a fatal outcome. *GI perforations:* Primarily reported as complications of diverticulitis. *Infusion reactions:* Clinically significant hypersensitivity reactions requiring treatment discontinuation were reported and were generally observed during the 2nd–5th infusions. Fatal anaphylaxis has been reported. *Other:* Decreased neutrophil count, decreased platelet count, hepatic transaminase elevations, lipid parameter increases, very rare cases of pancytopenia. **sJIA:** In general ADRs similar in type to those in RA. *Medically significant events: Infections:* Serious infections were similar to those seen in RA, with additions of varicella and otitis media. *Infusion reactions:* A hypersensitivity reaction that resulted in treatment discontinuation occurred in one out of 112 patients (< 1%). *Other:* decreased neutrophil count, decreased platelet count, decreased IgG, hepatic transaminase elevations, lipid parameter increases. Consult SPC for other ADRs.

Legal category: POM.

Presentations and Basic NHS Costs: 80 mg of tocilizumab in 4 ml (20 mg/ml) 1 vial: £102.40, 20 mg of tocilizumab in 10 ml (20 mg/ml) 1 vial: £256.00, 400 mg of tocilizumab in 20 ml (20 mg/ml) 1 vial: £512.00.

Marketing Authorisation Numbers: EU/1/08/492/01 (80 mg), EU/1/08/492/03 (200 mg), EU/1/08/492/05 (400 mg).

Marketing Authorisation Holder: Roche Registration Limited, 6 Falcon Way, Welwyn Garden City, Herts AL7 1TW. RoActemra is a registered trade mark.

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Adverse events should be reported to Roche Products Limited. Please contact the Drug Safety Centre, Roche Products Limted, 6 Falcon Way, Shire Park, Welwyn Garden City, Hertfordshire, England. Telephone number +44 1707 367554. Adverse events may otherwise be reported via the national Adverse Drug Reactions (ADRs) reporting system. Reporting forms and information can be found at: http://medicinesauthority.gov.mt/phvigilance.htm

RoACTEMRA®
tocilizumab