Actemra
DOSING GUIDE

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

- Rheumatoid Arthritis [Intravenous]
- Polyarticular Juvenile Idiopathic Arthritis (also referred to as Juvenile Idiopathic Polyarthritis) [Intravenous]
- Systemic Juvenile Idiopathic Arthritis [Intravenous]

Contents

This Actemra Dosing Guide is a requirement of the Actemra product license and contains important safety information that you need to be aware of when administering Actemra. This Actemra Dosing Guide must be read together with the Actemra Healthcare Professional and Patient Brochures [available online at www.pharm.amand the Actemra Labeling/Summary of Product Characteristics that comes with Actemra (and is also available on www.pharm.am as it contains important information about Actemra.

Please read this information carefully before administering the product.

Actemra IV (Actemra 20 mg/ml concentrate for solution for infusion):

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

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying antirheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.
- In these patients, Actemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.
- Actemra 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 methotrexate.

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

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

Prior to starting treatment with Actemra:

- It is important that you review the pre-administration checklist found in the Patient Brochure: *What You Should Know About Actemra* with your patient, the patient's parents/guardians, or both.
- Allow sample time to discuss any questions your patient, the patient's parents/guardians, or both may have.

- It is important that you review the information contained within the *Important Efficacy and Safety Information for Healthcare Professionals* for Actemra® (tocilizumab) intravenous (IV) formulations and the Patient Brochure: *What You Should Know About Actemra* with your patient, the patient's parents/guardians, or both. These will help them understand what they may expect from the
treatment of the patient's condition with Actemra.

For full information, see the Summary of Product Characteristics (SmPC) and the Actemra Package Leaflet: Information for the user, which can be found on the site of "Scientific Centre of Drug and Medical Technology Expertise after academician E.Gabrielyan" CJSC website: www.pharm.am. There also available Patient Information Leaflet and Summary of Product Characteristics. In case of any question you may contact via the phone: (+374 10) 20 05 05 և (+374 96) 22 05 05.

Actemra Patient Brochures and other information can be requested from company representative. If you have questions or concerns, please call +374 91796688 to Gayane Ghazaryan or 37491721153, Nune Karapetyan.

1. PART I – INTRAVENOUS (IV) ADMINISTRATION OF ACTEMRA BY INFUSION

1 This guide will walk you through the Actemra infusion process in 6 steps

1 WEIGH PATIENT AND CALCULATE ACTEMRA DOSE BASED ON INDICATION

Actemra dosing is calculated based on each patient's weight and the indication for which they are treated. The treatment frequency varies by indication. Verify the patient's weight and indication, then locate it on the 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.

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

1.1.2 ⌇00 mg (20 ml) vials 2 mg (10 ml) vials 80 m 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.

1.1.2.1 RA: Dosing Preparation and Administration Guide with Actemra IV

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

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

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

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

1.1.2.4 pJIA: Dosing Preparation and Administration Guide with Actemra IV

Dosing should take place at 4-week intervals.

A change in dose of 8mg/kg or 10 mg/kg should only be based on a consistent change in the patient's body weight over time (e.g., within 3 weeks). 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.

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

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

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

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

1.1.2.5 sJIA: Dosing Preparation and Administration Guide with Actemra IV

Dosing should take place at 2-week intervals.

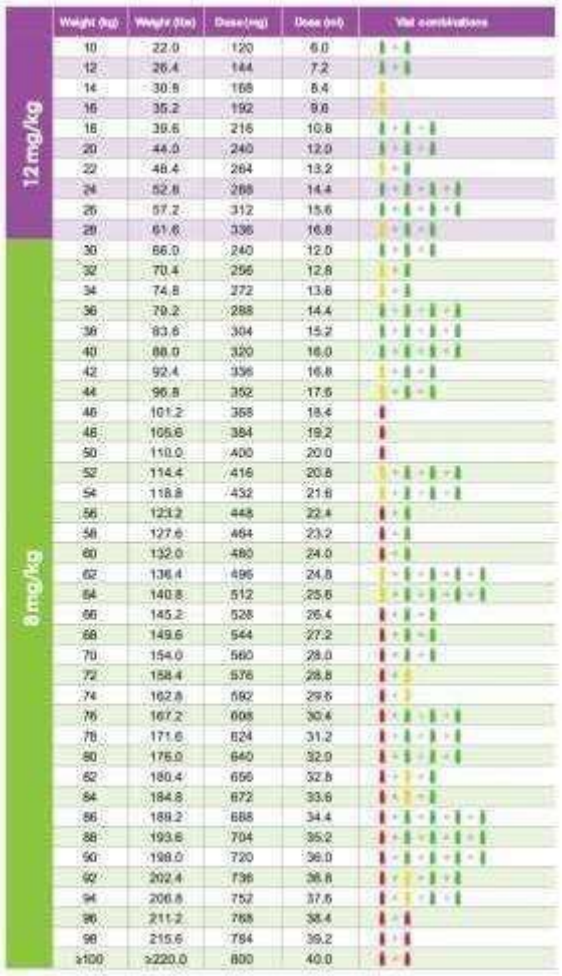
A change in dose of 8mg/kg or 12 mg/kg should only be based on a consistent change in the patient's body weight over time (e.g., within 3 weeks). If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.

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

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

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

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



	Weight (kg)	Weight (lbs)	Dose (mg)	Dose (ml)	Vial combinations
12 mg/kg	10	22.0	120	6.0	
	12	26.4	144	7.2	
	14	30.8	168	8.4	
	16	35.2	192	9.6	
	18	39.6	216	10.8	
	20	44.0	240	12.0	
	22	48.4	264	13.2	
	24	52.8	288	14.4	
	26	57.2	312	15.6	
	28	61.6	336	16.8	
8 mg/kg	30	66.0	240	12.0	
	32	70.4	256	12.8	
	34	74.8	272	13.6	
	36	79.2	288	14.4	
	38	83.6	304	15.2	
	40	88.0	320	16.0	
	42	92.4	336	16.8	
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	68	149.6	544	27.2	
	70	154.0	560	28.0	
	72	158.4	576	28.8	
	74	162.8	592	29.6	
	76	167.2	608	30.4	
	78	171.6	624	31.2	
	80	176.0	640	32.0	
	82	180.4	656	32.8	
	84	184.8	672	33.6	
	86	189.2	688	34.4	
	88	193.6	704	35.2	
	90	198.0	720	36.0	
	92	202.4	736	36.8	
	94	206.8	752	37.6	
	96	211.2	768	38.4	
	98	215.6	784	39.2	
	≥100	≥220.0	800	40.0	

2 GATHER ALL NECESSARY SUPPLIES

You will need:

- Actemra, at room temperature
- Syringes and large-bore needles
- One primary infusion set
- One 100 ml bag of 0.9% (9 mg/mL) sterile,non- pyrogenic sodium chloride solution for injection
- One intravenous (IV) catheter
- Gauze
- Tourniquet
- Gloves
- Alcohol/cleansing wipes

3 TAKE BASELINE ASSESSMENTS

Take baseline assessments to ensure the patient is healthy enough to

receive the infusion. Vital signs may include:

- Blood pressure
- Temperature
- Pulse

1.1.2.6 Follow the recommended baseline patient questions as described in the Actemra Healthcare Professional Brochure (Section 15 – General Recommendation) as well as the Summary of Product Characteristics (Section 4.4 – Warnings and Precautions).

4 PREPARE THE PATIENT FOR THE INFUSION

Review the Patient Brochure: *What You Should Know About Actemra* with the patient. Answer any questions he or she might have

Actemra does not require premedication

5 PREPARE THE ACTEMRA INFUSION

Actemra is a ready-mix solution and requires no reconstitution. The expiry date should always be checked before use. The Actemra concentrate for IV infusion should be diluted by a healthcare professional using aseptic technique.

- Actemra should be refrigerated for storage. However, the fully diluted Actemra solution should be allowed to reach room temperature before it is infused.
- The fully diluted Actemra solutions for infusion may be stored at 2°C–8°C or room temperature (if diluted under controlled and validated aseptic conditions) for up to 24 hours and should be protected from light.
- Actemra solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used.
- **Weight-/indication-based dosing:**
- **For RA, sJIA (>30 kg), and pJIA (>30 kg):** From a 100 ml infusion bag withdraw a volume of 0.9% (9 mg/ml) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of the Actemra solution
  required for the patient's dose.
- **For sJIA and pJIA patients < 30 kg:** Use a 50ml 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 Actemra solution required for the patient's dose.

- Actemra 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 Actemra with other medications.
- Slowly add Actemra 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 ACTEMRA INFUSION

1.1.2.7 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.

Monitor the patient for infusion related reactions.

1.1.3 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.

1.1.4

7 RECORD YOUR INJECTION

1.1.4.1 Product traceability

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

1.1.4.2 Call for reporting

1.1.4.3 If the patient experiences any side effects, talk to the doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

1.1.4.4 You can also report side effects directly via [the national reporting system]. By reporting side effects, you or the patient can help provide more information on the safety of this medicine.

Please report side-effects or if you If you need additional copies of the Patient or HCP Guides or have information on adverse event you may contact with the Scientific Centre of Drug and Medical Technology Expertise after academician Emil Gabrielyan via

contacts presented below: address: RA, Yerevan 0051, 49/5 Komitas avenue, tel.: (374 60) 830073, (+374 10) 230896, hot line: (+374 10) 200505; (+374 96) 220505; or email: vigilance@pharm.am; or via website: www.pharm.am.

1.2 COMPANY CONTACT POINT

Should you have any questions regarding to this, please contact to Gayane Ghazaryan, Local person for Pharmacovigilance for Hoffmann-La Roche products in Armenia Acti Group LLC., via mob.: +374 91 796688 or email address: gayaneh.ghazaryan@gmail.com; or Nune Karapetyan, Local backup for Pharmacovigilance of Roche Products in Armenia, via mob.: +374 91 721153 or email address: nune.karapetyan.roche@gmail.com.

Also you may contact to Local Safety Responsible, Roche Georgia LLC via tel: +995 322 506284, +995 322 507284 or emailing to georgia.safety@roche.com.

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