

STEP-BY-STEP INFUSION
INSTRUCTIONS FOR
RoACTEMRA



 **RoACTEMRA**[®]
tocilizumab

This guide will walk you through the RoACTEMRA infusion process in **6** steps.

Before therapy begins

Before beginning RoACTEMRA therapy, it is important that you review the *What You Should Know About RoACTEMRA* flipchart with each patient. This educational tool contains valuable information that will help your patients fully understand what they may expect from their treatment.

Prior to each infusion, it is important that you review the preadministration checklist found in the *What You Should Know About RoACTEMRA* flipchart with your patient and allow ample time to discuss any questions he or she may have.

RoACTEMRA patient brochures and other information can be requested from your sales representative. If you have questions or concerns, please visit [\[insert local Web site\]](#) or call [\[insert affiliate contact number\]](#).

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Weigh patient and calculate RoACTEMRA dose

RoACTEMRA dosing is calculated based on each patient's weight. 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 it has not changed from the time of the original calculation to require a change in dose. If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.


















































































RoACTEMRA dosing is calculated based on each patient's weight as follows:

For the 8 mg/kg dose: Patient weight (kg) X 8 (mg/kg) = RoACTEMRA 8 mg dose.

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

Once the dose is calculated, choose the vial combination of RoACTEMRA that best matches the patient's needs. RoACTEMRA is available in 3 different dosing vials:

 400 mg (20 mL) vials  200 mg (10 mL) vials  80 mg (4 mL) vials

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	 + 

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Gather all necessary supplies

You will need:

- RoACTEMRA, at room temperature
- Syringes and large-bore needles
- One primary infusion set
- One 100-mL bag of 0.9% (9 mg/mL) sodium chloride
- 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

Also ask the patient if they:

- Are taking other medicines. This includes prescription and non-prescription drugs, vitamins and herbals
- Are taking any other drugs to treat rheumatoid arthritis (RA) such as methotrexate (MTX), Enbrel® (etanercept), Humira® (adalimumab), Remicade® (infliximab), MabThera® (rituximab), Orencia® (abatacept) and Kineret® (anakinra)
- Are pregnant, might be pregnant, intend to become pregnant, or are breast-feeding
- Have an infection or are being treated for an infection; have had or now have hepatitis or any disease of the liver; have a history of stomach ulcers or diverticulitis
- Are planning or are scheduled to have surgery; just got a vaccine (such as a flu shot) or are scheduled to get one; are being treated for high cholesterol
- Have cancer, cardiovascular risk factors such as raised blood pressure and raised cholesterol levels or moderate-to-severe kidney function problems

Enbrel® is a registered trademark of Amgen Inc. and Wyeth Pharmaceuticals; Humira® is a registered trademark of Abbott Laboratories; Remicade® is a registered trademark of Schering-Plough Corporation; MabThera® is a registered trademark of F. Hoffmann-La Roche Ltd; Orencia® is a registered trademark of Bristol-Myers Squibb Company; Kineret® is a registered trademark of Amgen Inc.

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Prepare the patient for the infusion

- Review the *What You Should Know About RoACTEMRA* flipchart with the patient and answer any questions he or she might have
- RoACTEMRA does not require premedication



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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 to 100 mL by a healthcare professional using aseptic technique as follows:

- Although RoACTEMRA should be refrigerated for storage, the fully diluted RoACTEMRA solution should be allowed to reach room temperature before it is infused. The fully diluted RoACTEMRA 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. RoACTEMRA solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used
- From a 100-mL infusion bag, withdraw a volume of 0.9% (9 mg/mL) sodium chloride injection equal to the volume of the RoACTEMRA solution required for the patient's dose
- Slowly add RoACTEMRA concentrate for IV infusion from each vial into the infusion bag. To mix the solution, gently invert the bag to avoid foaming
- Parenteral drug products should be inspected visually for particulate matter and discoloration 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

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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 of potential hypersensitivity reactions. Most reactions happen during infusion or within 24 hours after infusion. They can range from mild to severe.

- Mild to moderate reactions include:
 - Hypertension
 - Headache
 - Skin reactions, such as rash, pruritus and urticaria
- Severe reactions include:
 - Anaphylaxis
- During the infusion, watch the patient closely for any hypersensitivity reaction. If you believe the patient is experiencing a reaction to the infusion, immediately stop the infusion and call their physician



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

FREQUENTLY ASKED QUESTIONS

How do I store RoACTEMRA vials?

RoACTEMRA must be refrigerated at 2°C–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 3 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 3 dosing vials on hand in order to select the correct vial combination for each patient.

Do I need to administer premedication?

No premedication is required before administering RoACTEMRA. However, an IV of medication-free 0.9% (9 mg/mL) sodium chloride should be administered to open and prepare the patient's vein for the infusion.

How do I prepare RoACTEMRA for infusion? What diluents can I use?

RoACTEMRA concentrate for IV infusion should be diluted to 100 mL using aseptic technique as follows:

- From a 100-mL infusion bag, withdraw a volume of 0.9% (9 mg/mL) sodium chloride injection equal to the volume of the RoACTEMRA solution required for the patient's dose
- 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
- Parenteral drug products should be inspected visually for particulate matter and discoloration 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

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°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.

RoACTEMRA solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used.

What should I look for during the infusion?

Watch the patient closely for any hypersensitivity, including anaphylaxis. Most reactions happen during infusion or within 24 hours after infusion. They can range from mild to severe.

- Mild to moderate reactions include:
 - Hypertension
 - Headache
 - Skin reactions, such as rash, pruritus and urticaria
- Severe reactions include:
 - Anaphylaxis

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

The most common side effects with RoACTEMRA are upper respiratory tract infections (common cold, sinus infection), headache, temporary increases in blood pressure, rash and dizziness.

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.

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

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

What if patients cannot schedule their infusion in exactly 4 weeks?

RoACTEMRA should be administered once every 4 weeks. Contact the prescriber for any deviations from that schedule.

What information do I need to provide the patient about RoACTEMRA?

Before beginning RoACTEMRA therapy, it is important that you review the *What You Should Know About RoACTEMRA* flipchart with each patient. This educational tool contains valuable information that will help your patients fully understand what they may expect from their treatment.

Prior to each infusion, it is important that you review the preadministration checklist found in the *What You Should Know About RoACTEMRA* flipchart. The patient should be allowed ample time to review and discuss any questions they may have.

If the patient would like more information about RoACTEMRA, please direct him or her to visit [\[insert local Web site\]](#) or to call [\[insert affiliate contact number\]](#).

RoACTEMRA® (tocilizumab) Important Safety Information

Therapeutic indications

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 methotrexate.

Contraindications

Hypersensitivity to the active substance or to any of the excipients. Active, severe infections.

Infections

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 (eg, diverticulitis, diabetes) which may predispose patients to infections.

Vigilance for the timely detection of serious infection is recommended for patients receiving biological treatments for moderate to severe RA 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 when any symptoms suggesting infection appear, in order to assure rapid evaluation and appropriate treatment.

Tuberculosis

As recommended for other biological treatments in RA, patients should be screened for latent tuberculosis (TB) infection prior to starting RoACTEMRA therapy. Patients with latent TB should be treated with standard anti-mycobacterial therapy before initiating RoACTEMRA.

Viral reactivation

Viral reactivation (eg, hepatitis B virus) has been reported with biologic therapies for rheumatoid arthritis. In clinical studies with tocilizumab, 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 have been reported in association with infusion of RoACTEMRA in approximately 0.3% of patients. Appropriate treatment should be available for immediate use in the event of an anaphylactic reaction during administration of 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.

Hepatic transaminase elevations

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 potentially hepatotoxic drugs (eg, MTX) were used in combination with RoACTEMRA.

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 >3-5 x ULN, confirmed by repeat testing, RoACTEMRA treatment should be interrupted.

Haematological abnormalities

Decreases in neutrophil and platelet counts have occurred following treatment with RoACTEMRA 8 mg/kg in combination with MTX. There may be an increased risk of neutropaenia in patients who have previously been treated with a TNF antagonist.

Caution should be exercised when considering initiation of RoACTEMRA treatment in patients with a low neutrophil or platelet count (ie, absolute neutrophil count (ANC) <2 x 10⁹/L or platelet count below 100 x 10⁹/μL). In patients with an ANC <0.5 x 10⁹/L or a platelet count <50 x 10⁹/μL treatment is not recommended.

Severe neutropenia may be associated with an increased risk of serious infections, although there has been no clear association between decreases in neutrophils and the occurrence of serious infections in clinical trials with RoACTEMRA to date.

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

Lipid parameters

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.

Cardiovascular risk

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

Combination with TNF antagonists

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

Sodium

This medicinal product contains 1.17 mmol (or 26.55 mg) sodium per maximum dose of 1200 mg. To be taken into consideration by patients on a controlled sodium diet. Doses below 1025 mg of this medicinal product contain less than 1 mmol sodium (23 mg), ie, essentially 'sodium free'.

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

RoACTEMRA should not be used during pregnancy unless clearly necessary.

Lactation

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.

Undesirable effects

The most commonly reported adverse drug reactions (occurring in ≥5% of patients treated with RoACTEMRA monotherapy or in combination with DMARDs) were upper respiratory tract infections, nasopharyngitis, headache, hypertension and increased ALT.

 **RoACTEMRA**[®]
tocilizumab

