Package leaflet: Information for the user

RoActemra 162 mg solution for injection in pre-filled syringe
tocilizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it onto others. It may harm them even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

In addition to this leaflet, you will be given a **Patient Alert Card**, which contains important safety information that you need to be aware of before and during treatment with RoActemra.

What is in this leaflet:

1. What RoActemra is and what it is used for

RoActemra contains the active substance tocilizumab, which is a protein made from specific immune cells (monoclonal antibody), that blocks the action of a specific protein (cytokine) called interleukin-6. This protein is involved in inflammatory processes of the body, and blocking it can reduce the inflammation in your body. RoActemra is used to treat:

- **adults with moderate to severe active rheumatoid arthritis (RA)**, an autoimmune disease, if previous therapies did not work well enough.

- **adults with severe, active and progressive rheumatoid arthritis (RA),** who have not had previous treatment with methotrexate.

  RoActemra helps to reduce RA symptoms such as pain and swelling in your joints, and can also improve your performance of daily tasks. RoActemra has been shown to slow the damage to the cartilage and bone of the joints caused by the disease and to improve your ability to do normal daily activities.

  RoActemra is usually given in combination with another medicine for RA called methotrexate. However, RoActemra can be given alone if your doctor determines that methotrexate is inappropriate.

- **adults with a disease of the arteries called giant cell arteritis** (**GCA**), caused by inflammation of the body's largest arteries, especially those that supply blood to the head and neck. Symptoms include headache, fatigue and jaw pain. Effects can include strokes and blindness.

RoActemra can reduce pain and swelling in the arteries and veins in your head, neck and arms.

GCA is often treated with medicines called steroids. They are usually effective, but can have side effects if used at high doses for a long time. Reducing the steroid dose can also lead to a flare-up of the GCA. Adding RoActemra to the treatment means that steroids can be used for a shorter time, while still controlling GCA.

- **children and adolescents, aged 1 year and over, with active *systemic juvenile idiopathic arthritis (sJIA)*,** an inflammatory disease that causes pain and swelling in one or more joints as well as fever and rash.

  RoActemra is used to improve the symptoms of sJIA. It can be given in combination with methotrexate or alone.

- **children and adolescents, aged 2 years and over, with active *polyarticular juvenile idiopathic arthritis* (*pJIA*).** This is an inflammatory disease that causes pain and swelling in one or more joints.

  RoActemra is used to improve the symptoms of pJIA. It can be given in combination with methotrexate or alone**.**

2. What you need to know before you use RoActemra

Do not use RoActemra
- if you or a child patient you look after are allergic to tocilizumab or any of the other ingredients of this medicine (listed in section 6).
- if you or a child patient you look after have an active, severe infection.

If either of these applies to you, tell a doctor. Do not use RoActemra.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using RoActemra.

- If you experience **allergic reactions** such as chest tightness, wheezing, severe dizziness or light-headedness, swelling of the lips, tongue, face or skin itching, hives or rash during or after the injection, then **tell your doctor immediately.**

- Do not take the next dose until you have informed your doctor AND your doctor has told you to take the next dose if you have experienced any allergic reaction symptoms after RoActemra administration.
- If you have any kind of **infection**, short- or long-term, or if you often get infections. **Tell your doctor immediately** if you feel unwell. RoActemra can reduce your body's ability to respond to infections and may make an existing infection worse or increase the chance of getting a new infection.

- If you have had **tuberculosis**, tell your doctor. Your doctor will check for signs and symptoms of tuberculosis before starting RoActemra. If symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever) or any other infection appear during or after therapy tell your doctor immediately.

- If you have had **intestinal ulcers** or **diverticulitis**, tell your doctor. Symptoms would include abdominal pain and unexplained changes in bowel habits with a fever.

- If you have **liver disease**, tell your doctor. Before you use RoActemra, your doctor may do a blood test to measure your liver function.

- **If any patient has recently been vaccinated,** or is planning a vaccination**,** tell your doctor. All patients should be up-to-date with all their vaccinations before they start treatment with RoActemra. Certain types of vaccines should not be given while receiving RoActemra.

- If you have **cancer**, tell your doctor. Your doctor will have to decide if you can still be given RoActemra.

- If you have **cardiovascular risk factors** such as raised blood pressure and raised cholesterol levels, tell your doctor. These factors need to be monitored while receiving RoActemra.

- If you have moderate to severe **kidney function problems**, your doctor will monitor you.

- If you have **persistent headaches**.

Your doctor will perform a blood test before you receive RoActemra, to determine if you have a low white blood cell count, low platelet count or high liver enzymes.

Children and adolescents
RoActemra subcutaneous injection is not recommended for use in children under 1 year of age. RoActemra must not be given to children with sJIA weighing less than 10 kg.

If a child has a history of ***macrophage activation syndrome*** (activation and uncontrolled proliferation of specific blood cells), tell your doctor. Your doctor will have to decide if they can still be given RoActemra.

Other medicines and RoActemra
Tell your doctor if you are taking any other medicines, or have recently taken any. RoActemra can affect the way some medicines work, and the dose of these may require adjustment. If you are using medicines containing any of the following active substances, **tell your doctor:**
- methylprednisolone, dexamethasone, used to reduce inflammation
- simvastatin or atorvastatin, used to reduce cholesterol levels
- calcium channel blockers (e.g. amlodipine), used to treat raised blood pressure
- theophylline, used to treat asthma
- warfarin or phenprocoumon, used as a blood thinning agents
- phenytoin, used to treat convulsions
- ciclosporin, used to suppress your immune system during organ transplants
- benzodiazepines (e.g. temazepam), used to relieve anxiety

Due to lack of clinical experience, RoActemra is not recommended for use with other biological medicines for the treatment of RA, sJIA, pJIA or GCA.

Pregnancy, breast-feeding and fertility

RoActemra is not to be used in pregnancy unless clearly necessary. Talk to your doctor if you are pregnant, may be pregnant, or intend to become pregnant.

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

Stop breast-feeding if you are to be given RoActemra, and talk to your doctor. Leave a gap of at least 3 months after your last treatment before you start breast-feeding. It is not known whether RoActemra is passed into breast milk.

Driving and using machines
This medicine can cause dizziness. If you feel dizzy, do not drive or use machines.

3. How to use RoActemra

Always use this medicine exactly as your doctor, pharmacist or nurse has told you. You should check with your doctor, pharmacist or nurse if you are not sure.

The treatment will be prescribed and started by healthcare professionals experienced in the diagnosis and treatment of RA, sJIA, pJIA or GCA.

The recommended dose
The dose for RA and GCA adults is 162 mg (the content of 1 pre-filled syringe) given once a week.

Children and adolescents with sJIA (aged 1 year and over)
The usual dose of RoActemra depends on the patient's weight.
- If the patient weighs **less than 30 kg**: the dose is 162 mg (the content of 1 pre-filled syringe) once every 2 weeks
- If the patient weighs **30 kg or more**: the dose is 162 mg (the content of 1 pre-filled syringe) once every week

Children and adolescents with pJIA (aged 2 and over)
The usual dose of RoActemra depends on the patient's weight.
- If the patient weighs **less than 30 kg**: the dose is 162 mg (the content of 1 pre-filled syringe), **once every 3 weeks**
- If the patient weighs **30 kg or more**: the dose is 162 mg (the content of 1 pre-filled syringe), **once every 2 weeks.**

RoActemra is given by injection under the skin (*subcutaneously*). At the start, your doctor or nurse may inject RoActemra. However, your doctor may decide that you may inject RoActemra yourself. In this case you will get training on how to inject RoActemra yourself. Parents and carers will get training on how to inject RoActemra for patients who cannot inject themselves, such as children.

Talk to your doctor if you have any questions about giving yourself or a child patient you look after an injection. You will find detailed "Instructions for administration" at the end of this leaflet.

If you use more RoActemra than you should
Because RoActemra is given in one pre-filled syringe, it is unlikely that you will receive too much. However, if you are worried, talk to your doctor, pharmacist or nurse.

If an adult with RA or GCA or a child or adolescent with sJIA misses or forgets a dose
It is very important to use RoActemra exactly as prescribed by your doctor. Keep track of your next dose.
- If you miss your weekly dose within 7 days, take your dose on the next scheduled day.
- If you miss your once every 2 weeks dose within 7 days, inject a dose as soon as you remember and take your next dose at your regular scheduled time.
- If you miss your dose by more than 7 days, or you are not sure when to inject RoActemra, call your doctor or pharmacist.

If a child or adolescent with pJIA misses or forgets a dose
It is very important to use RoActemra exactly as prescribed by the doctor. Keep track of the next dose.
- If a dose is missed within 7 days, inject a dose as soon as you remember and give the next dose at the regular scheduled time.

- If a dose is missed by more than 7 days, or you are not sure when to inject RoActemra, call the doctor or pharmacist.

If you stop using RoActemra
You should not stop using RoActemra without discussing with your doctor first.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, RoActemra can cause side effects, although not everybody gets them.
Side effects could occur 3 months or more after your last dose of RoActemra.

Possible serious side effects: tell a doctor straight away.
These are common: they may affect up to 1 in every 10 users

Allergic reactions during or after injection:
- difficulty with breathing, chest tightness or light-headedness
- rash, itching, hives, swelling of the lips, tongue or face.

If you notice any of these, tell your doctor **immediately**.

Signs of serious infections:
- fever and chills
- mouth or skin blisters
- stomach ache.

Signs and symptoms of liver toxicity
These may affect up to 1 in every 1000 users
- tiredness,
- abdominal pain,
- jaundice (yellow discolouration of skin or eyes).

If you notice any of these, tell your doctor **as soon as possible**.

Very common side effects:
These may affect 1 in 10 patients or more
- upper respiratory tract infections with typical symptoms such as cough, blocked nose, runny nose, sore throat and headache,
- high blood fat (*cholesterol*) levels
- injection site reactions.

Common side effects:
These may affect up to 1 in 10 patients
- lung infection (pneumonia)
- shingles (herpes zoster)
- cold sores (oral herpes simplex), blisters
- skin infection (cellulitis) sometimes with fever and chills
- rash and itching, hives
- allergic (hypersensitivity) reactions
- eye infection (conjunctivitis)
- headache, dizziness, high blood pressure
- mouth ulceration, stomach pain
- fluid retention (oedema) in the lower legs, weight increase
- cough, shortness of breath

- low white blood cell counts shown by blood tests (neutropenia, leucopenia)
- abnormal liver function tests (increased transaminases)
- increased bilirubin shown by blood tests
- low fibrinogen levels in the blood (a protein involved in blood clotting).

Uncommon side effects:
These may affect up to 1 in every 100 patients
- diverticulitis (fever, nausea, diarrhoea, constipation, stomach pain)
- red swollen areas in the mouth
- high blood fat (triglycerides)
- stomach ulcer
- kidney stones
- underactive thyroid.

Rare side effects:
These may affect up to 1 in every 1,000 patients
- Stevens-Johnson syndrome (skin rash, which may lead to severe blistering and peeling of the skin)
- Fatal Allergic Reactions (Anaphylaxis [fatal])
- inflammation of the liver (hepatitis), jaundice.

Very rare side effects:
These may affect up to 1 in every 10,000 patients
- low counts for white blood cells, red blood cells and platelets in blood tests
- liver failure.

Side effects in children and adolescents with sJIA or pJIA
Side effects in children and adolescents with sJIA or pJIA are generally similar to those in adults. Some side effects are seen more often in children and adolescents: inflamed nose and throat, headache, feeling sick (nausea) and lower white blood cell counts.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store RoActemra

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the pre-filled syringe label and carton (EXP). The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Once removed from the refrigerator, the pre-filled syringe can be stored up to 2 weeks at or below 30°C.

Keep the pre-filled syringes in the outer carton in order to protect from light and moisture.

Do not use if the medicine is cloudy or contains particles, is any colour besides colourless to yellowish, or any part of the pre-filled syringe appears to be damaged.

The syringe should not be shaken. After removing the cap the injection must be started 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 cap removal, you must dispose of it in a puncture resistant container and use a new pre-filled syringe.

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.

6. Contents of the pack and other information

What RoActemra contains

- The active substance is tocilizumab.
  Each pre-filled syringe contains 162 mg tocilizumab in 0.9 mL.

- The other ingredients are L-Histidine, L-Histidine monohydrochloride monohydrate, L-Arginine hydrochloride, L-Methionine, Polysorbate 80 and Water for injections. May contain L-Arginine.

What RoActemra looks like and contents of the pack
RoActemra is a solution for injection. The solution is colourless to slightly yellowish.

RoActemra is supplied as a 0.9 mL pre-filled syringe containing 162 mg tocilizumab solution for injection.

Each pack contains 4 pre-filled syringes **with multipacks containing 12 (3 packs of 4) pre-filled syringes. Not all pack sizes may be marketed.**

Marketing Authorisation Holder and Manufacturer
Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Roche Products Ltd.
Tel: +44 (0) 1707 366000
or
Chugai Pharma UK Ltd.
Tel: +44 (0) 208 987 5600

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What do I need to know to use my RoActemra pre-filled syringe safely?

It is important to read, understand and follow these instructions so that you or your caregiver uses the RoActemra syringe correctly. These instructions do not replace training from your healthcare provider. Your healthcare provider should show you how to prepare and inject properly before you use the RoActemra syringe for the first time. Ask your healthcare provider any questions you may have. Do not attempt to administer an injection until you are sure that you understand how to use the RoActemra syringe.

Please also read the Patient Leaflet that comes with the RoActemra syringe for the most important information you need to know about the medicine. It is important to remain under your healthcare provider's care while using RoActemra.

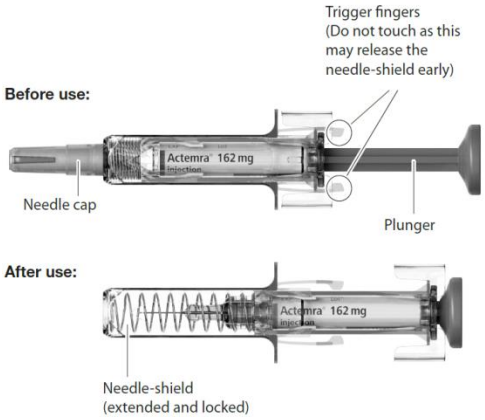
Important Information:

- Do not use the syringe if it appears to be damaged
- Do not use if medicine is cloudy, hazy, discoloured or contains particles
- Do not try to take apart the syringe at any time
- Do not remove the needle-cap until you are ready to inject
- Do not inject through clothing covering the skin
- Never re-use the same syringe
- Do not touch the syringe trigger fingers as this may damage the syringe

Storage

Keep the RoActemra syringe and all medicines out of the sight and reach of children. Always store the syringe in a refrigerator at a temperature of 2°C - 8°C. Once removed from the refrigerator, the pre-filled syringe can be stored up to 2 weeks at or below 30°C. The prefilled syringe must always be kept in the carton. Protect the syringe from freezing and from light. Keep the syringes dry.

Pre-filled Syringe parts



You will need the following to give your injection:
Included in the box:

- Pre-filled Syringe

Not included in the box:

- Alcohol pad
- Sterile cotton ball or gauze
- Puncture-resistant container or sharps container for safe disposal of needle-cap and used syringe

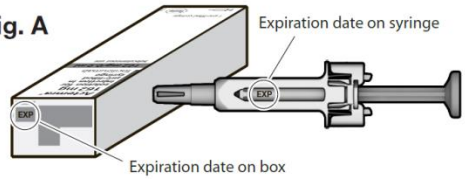
A place to prepare your supplies:

- **Find a well-lit, clean, flat surface such as a table**

Step 1. Visually check the syringe

- Take the box containing the syringe out of the refrigerator and open the box. Do not touch the trigger fingers on the syringe as this may damage the syringe.
- Remove the syringe from the box and visually examine the syringe, as well as the medicine in the syringe. This is important to ensure that the syringe and medicine are safe to use.
- Check the expiration date on the box and syringe (See Fig. A) to make sure that it has not passed (expired). Do not use the syringe if the expiration date has passed. This is important to ensure that the syringe and medicine are safe to use.

Fig. A



Dispose of the syringe and do not use if:

- the medicine is cloudy
- the medicine contains particles
- the medicine is any colour besides colourless to yellowish
- any part of the syringe appears to be damaged

Step 2. Allow the syringe to adjust to room temperature

- Do not remove the needle-cap on your syringe until Step 5. Early removal of the needle-cap can cause the medication to dry out and block the needle.

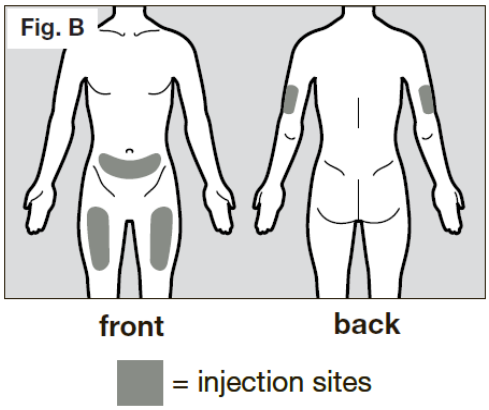
- Place the syringe on a clean flat surface and allow the syringe to come to room temperature (18°C – 28°C) for about 25-30 minutes to warm up. Not allowing the syringe to come to room temperature could result in an uncomfortable injection and it may be difficult to depress the plunger.
- Do not warm up the syringe in any other way.

Step 3. Clean your hands

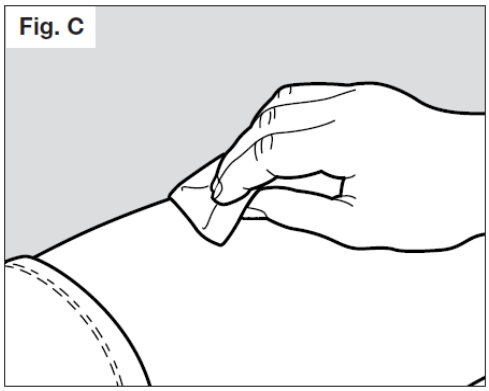
- Wash your hands with soap and water.

Step 4. Choose and prepare an injection site

- The recommended injection sites are the front and middle of your thighs and the lower part of the abdomen below the navel (belly button) except for the five centimetre area directly around the navel. (See Fig. B)
- If a caregiver is giving the injection, the outer area of the upper arms may also be used. (See Fig. B)



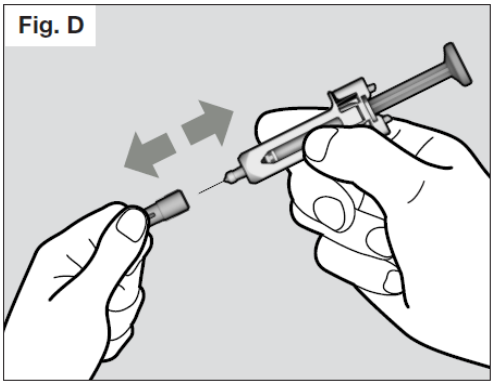
- You should use a different place each time you give yourself an injection, at least three centimetres from the area you used for your previous injection.
- Do not inject into areas that could be bothered by a belt or waistband. Do not inject into moles, scars, bruises, or areas where the skin is tender, red, hard or not intact.
- Clean the chosen injection site area using the alcohol pad (See Fig. C), to reduce the risk of infection.



- Let the skin dry for approximately 10 seconds.
- Be sure not to touch the cleaned area prior to the injection. Do not fan or blow on the clean area.

Step 5. Remove needle-cap

- Do not hold the syringe by the plunger while removing the needle-cap.
- Hold the needle-shield of the syringe firmly with one hand and pull off the needle-cap with the other hand. (See Fig. D) If you cannot remove the needle cap you should request the help of a caregiver or contact your healthcare provider.



- Do not touch the needle or let it touch any surface.
- You may see a drop of liquid at the end of the needle. This is normal.
- Throw away the needle-cap in the puncture resistant container or sharps container.

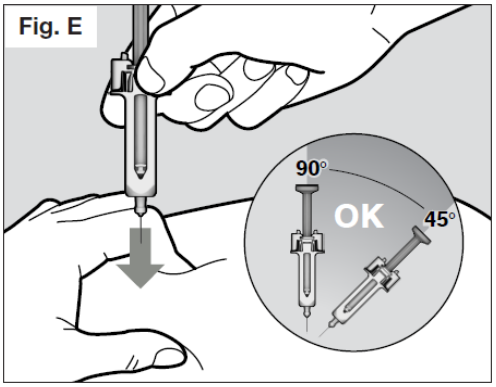
NOTE: Once the needle-cap is removed, the syringe must be used immediately.

- If it is not used within 5 minutes of cap removal, the syringe must be disposed of in the puncture resistant container or sharps container and a new syringe must be used. If the needle cap is removed for more than 5 minutes, it may be more difficult to perform an injection as the medicine can dry out and block the needle.

- Never reattach the needle-cap after removal.

Step 6. Give the injection

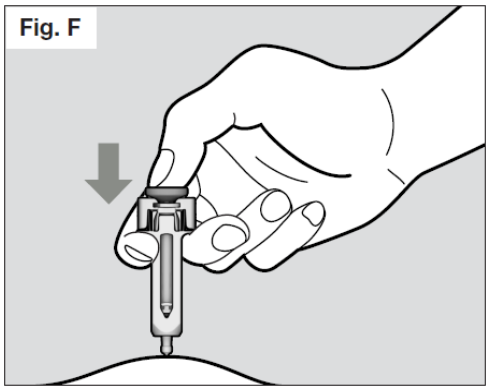
- Hold the syringe comfortably in your hand.
- To be sure the needle can be inserted correctly under the skin, pinch a fold of loose skin at the clean injection site with your free hand. Pinching the skin is important to ensure that you inject under the skin (into fatty tissue) but not any deeper (into muscle). Injection into muscle could result in an uncomfortable injection.
- Do not hold or push on the plunger while inserting the needle into the skin.
- Insert the needle all the way into the pinched skin at an angle between 45° to 90° with a quick, firm action. (See Fig. E).



It is important to choose the correct angle to ensure the medication is delivered under the skin (into fatty tissue), otherwise the injection could be painful and the medication may not work.

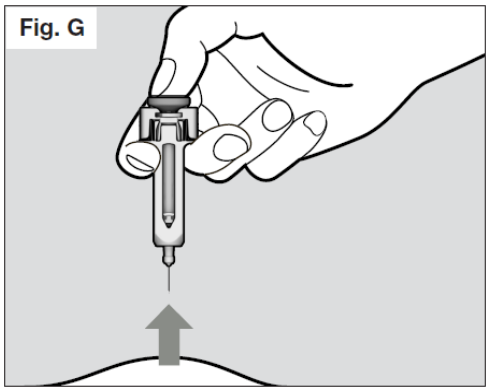
- Then keep the syringe in position and let go of the pinch of skin.
- Slowly inject all of the medicine by gently pushing the plunger all the way down. (See Fig. F). You must press the plunger all the way down to ensure that you get the full dose of medication and to ensure the trigger fingers are completely pushed to the side. If the plunger is not fully depressed the needle shield will not extend to cover the needle when it is removed. If the needle is not covered proceed carefully, and place the syringe into the puncture resistant container to avoid injury with the needle.

Fig. F



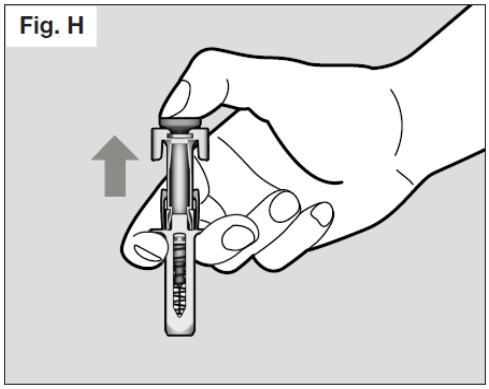
- Once the plunger is pushed all the way down, keep pressing down on the plunger to be sure all of the medicine is injected before taking the needle out of the skin.
- Keep pressing down on the plunger while you take the needle out of the skin at the same angle as inserted. (See Fig. G)
- If following insertion of the needle, you cannot press down the plunger, you must dispose of the pre-filled syringe in a puncture resistant container and use a new pre-filled syringe (starting again at Step 2). If you still experience difficulty, you should consult your healthcare provider.

Fig. G



- Once the needle is removed completely from the skin, you can release the plunger, allowing the needle-shield to protect the needle. (See Fig. H)

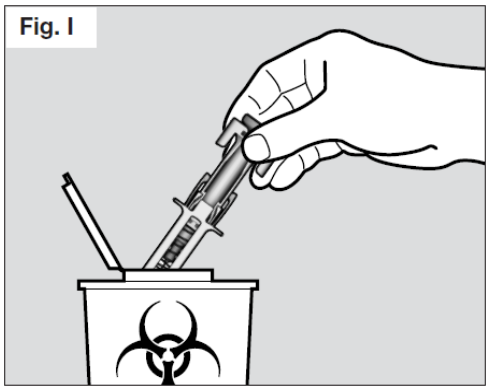
Fig. H



- If you see drops of blood at the injection site, you can press a sterile cotton ball or gauze over the injection site for approximately 10 seconds.
- Do not rub the injection site.

Step 7. Dispose of the syringe

- Do not try to re-cap your syringe.
- Throw away used syringes in a puncture-resistant container or sharps container. Ask your healthcare provider or pharmacist for information about where you can get a "sharps" container or what other types of puncture-resistant containers you can use to safely dispose of your used syringes, if you do not have one. (See Fig. I)



Check with your healthcare provider for instructions about the right way to throw away used syringes. There may be local or state laws about how to throw away used syringes.

Do not throw away used syringes or the puncture resistant container in household trash and do not recycle them.

- Dispose of the full container as instructed by your healthcare provider or pharmacist.
- Always keep the puncture-resistant container out of the sight and reach of children.

Patient advice regarding hypersensitivity reactions (also known as anaphylaxis, if severe)

If you develop symptoms such as, but not limited to skin rash, itching, chills, swelling of face, lips, tongue or throat, chest pain, wheezing, difficulty breathing or swallowing or feeling dizzy or faint at any time while not at the clinic during or following an RoACTEMRA injection you should seek emergency care immediately.

Patient advice regarding early recognition and treatment to limit risk of a serious infection

Be alert for the first signs of infection such as:

- body aches, fever, chills
- cough, chest discomfort/tightness, shortness of breath
- redness, heat, unusual swelling of skin or joint
- abdominal pain/tenderness and/or change in bowel function

Call your doctor and seek medical attention without delay if you think you might be developing an infection.

If you have any concerns or questions about your syringe, contact your healthcare provider or pharmacist for assistance.