Package leaflet: Information for the user

RoActemra 162 mg solution for injection in pre-filled pen (ACTPen®)
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 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 12 years 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 12 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 pre-filled pen (ACTPen®) is not recommended for use in children under 12 years 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 with RA or GCA for all adults is 162 mg (the content of 1 pre-filled pen) given once a week.

Adolescents with sJIA (aged 12 years 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 pen) once every 2 weeks
- If the patient weighs **30 kg or more**: the dose is 162 mg (the content of 1 pre-filled pen) once every week

The pre-filled pen should not be used to treat children less than 12 years of age.

Adolescents with pJIA (aged 12 years 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 pen), **once every 3 weeks**
- If the patient weighs **30 kg or more**: the dose is 162 mg (the content of 1 pre-filled pen), **once every 2 weeks.**

The pre-filled pen should not be used to treat children less than 12 years of age.

RoActemra is given by injection under the skin (*subcutaneously*). At the start, your doctor or nurse may inject RoActemra (ACTPen®). 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.

Talk to your doctor if you have any questions about giving yourself or an adolescent 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 pen, 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 an 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 other week 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 weekly or once every other week dose by more than 7 days or you are not sure when to inject RoActemra, call your doctor or pharmacist.

If an 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.

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 pen 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 pen can be stored up to 2 weeks at or below 30°C.

Keep the pre-filled pens 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 pen appears to be damaged.

The pen should not be shaken. After removing the cap the injection must be started within 3 minutes to prevent the medicine from drying out and blocking the needle. If the pre-filled pen is not used within 3 minutes of cap removal, you must dispose of it in a puncture resistant container and use a new pre-filled pen.

If following pressing the activation button the purple indicator does not move, you must dispose of the pre-filled pen in a puncture resistant container. **Do not** try to re-use the pre-filled pen. Do not repeat the injection with another pre-filled pen. Call your healthcare provider for help.

6. Contents of the pack and other information

What RoActemra contains

- The active substance is tocilizumab.
  Each pre-filled pen 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 pen containing 162 mg tocilizumab solution for injection.

Each pack contains 4 pre-filled pens **with multipacks containing 12 (3 packs of 4) pre-filled pens. 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

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What you need to know to use your RoActemra pre-filled pen (ACTPen) safely.

Read and follow the Instructions for Use that come with your RoACTEMRA pre-filled pen before you start using it and each time you get a prescription refill. Before you use the RoACTEMRA pre-filled pen for the first time, make sure your healthcare provider shows you the right way to use it.

Important: Keep your unused pre-filled pens in the original carton and keep in the refrigerator at 2˚C to 8˚C. **Do not** freeze.

Once removed from the refrigerator, the pre-filled pen can be stored up to 2 weeks at or below 30°C. Always keep the pre-filled pens in the outer carton in order to protect from light and moisture.

- **Do not remove the pre-filled pen cap until you are ready to inject RoACTEMRA.**
- **Do not try to take apart the pre-filled pen at any time.**
- **Do not reuse the same pre-filled pen.**
- **Do not use the pre-filled pen through clothing.**
- **Do not leave the pre-filled pen unattended.**
- **Keep out of the reach of children.**

Parts of your RoACTEMRA pre-filled pen **(See Figure A).**

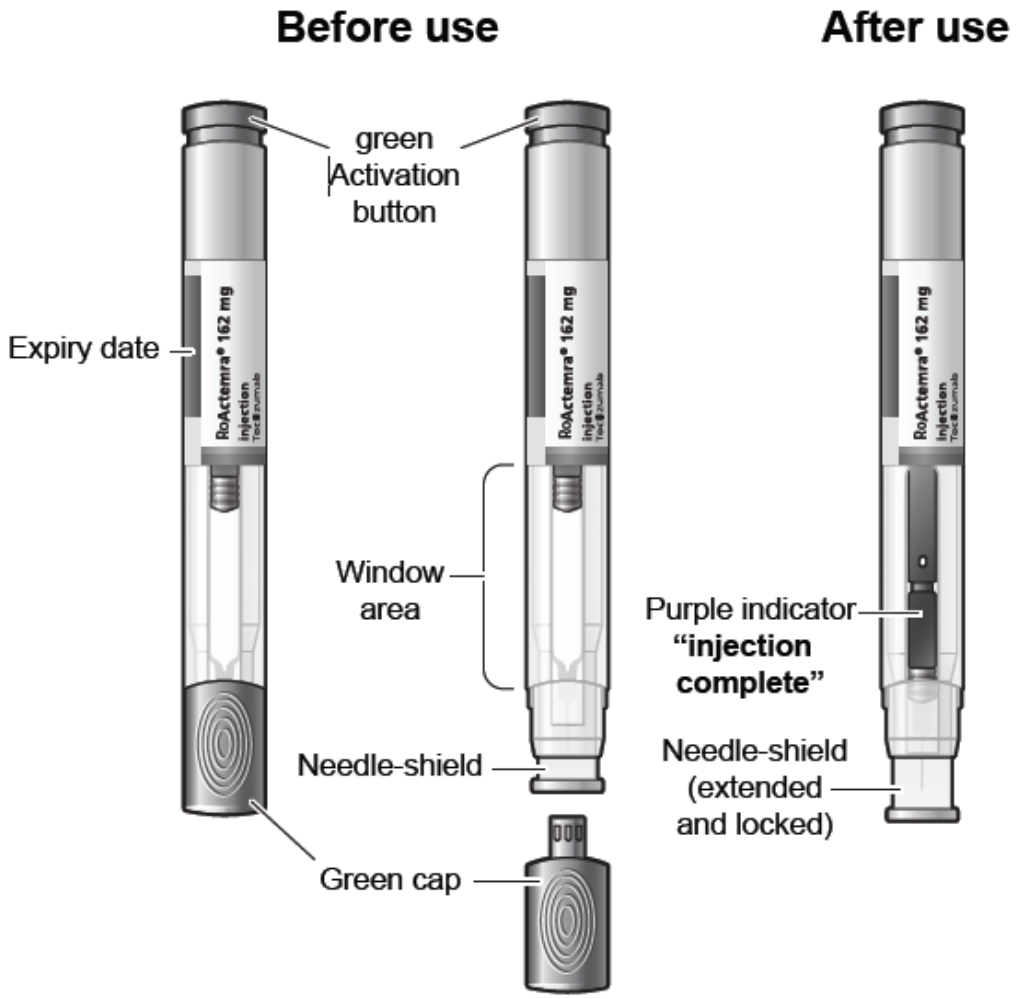

Figure A

Supplies needed for an injection using your RoACTEMRA pre-filled pen (See Figure B):

- 1 RoACTEMRA pre-filled pen
- 1 Alcohol pad
- 1 Sterile cotton ball or gauze
- 1 Puncture-resistant container or sharps container for safe disposal of pre-filled pen cap and used pre-filled pen (see **Step 4 "Dispose of the pre-filled pen")**

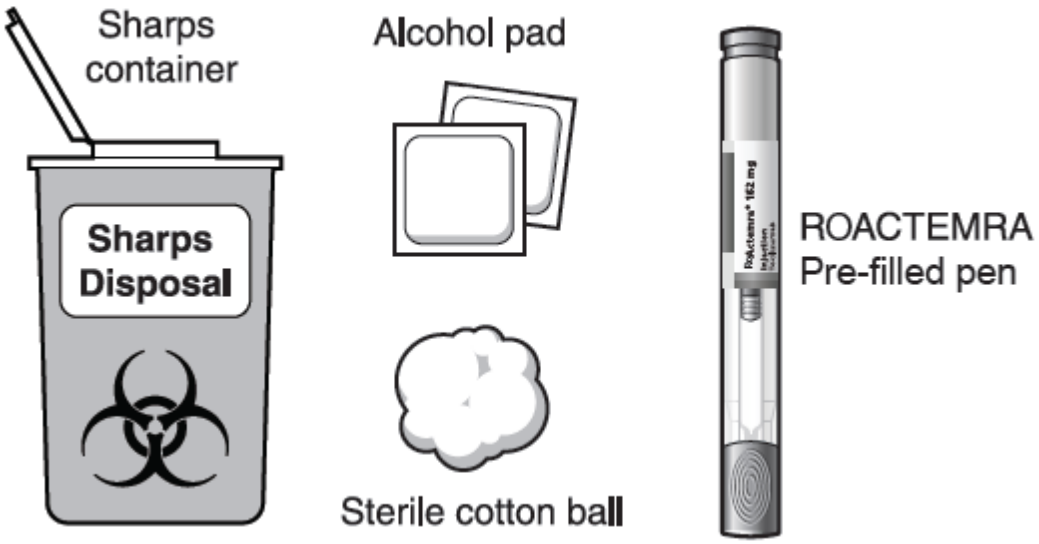

Figure B

Step 1. Preparing for a RoACTEMRA Injection

Find a comfortable space with a clean, flat, working surface.

- Take the box containing the pre-filled pen out of the refrigerator.
- If you are opening the box for the first time, check to make sure that it is properly sealed. **Do not** use the pre-filled pen if the box looks like it has already been opened.
- Check that the pre-filled pen box is not damaged. **Do not** use RoActemra pre-filled pen if the box looks damaged.
- **Check the expiration date on the pre-filled pen box**. **Do not** use the pre-filled pen if the expiration date has passed because it may not be safe to use.
- Open the box, and remove 1 single-use RoACTEMRA pre-filled pen from the box.
- Return any remaining pre-filled pens in the box to the refrigerator.
- **Check the expiration date on the RoACTEMRA pre-filled pen (See Figure A). Do not** use it if the expiration date has passed because it may not be safe to use. If the expiration date has passed, safely dispose of the pre-filled pen in a sharps container and get a new one.
- **Check the pre-filled pen to make sure it is not damaged.** Do not use the pre-filled pen if it appears to be damaged or if you have accidentally dropped the pre-filled pen.
- Place the pre-filled pen on a clean, flat surface and let the pre-filled pen warm up for 45 minutes to allow it to reach room temperature. If the pre-filled pen does not reach room temperature, this could cause your injection to feel uncomfortable and it could take longer to inject.
    - **Do not** speed up the warming process in any way, such as using the microwave or placing the pre-filled pen in warm water.
    - **Do not** leave the pre-filled pen to warm up in direct sunlight.

Do not remove the green cap while allowing your RoACTEMRA pre-filled pen to reach room temperature.

- Hold your RoACTEMRA pre-filled pen with the green cap pointing down **(See Figure C).**

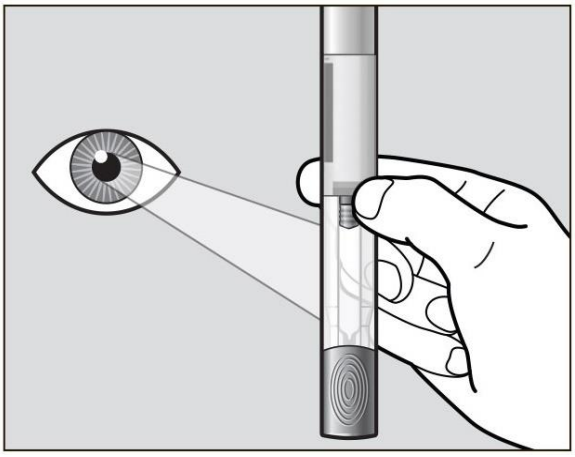

Figure C

- Look in the clear Window area. Check the liquid in the RoACTEMRA pre-filled pen **(See Figure C)**. It should be clear and colourless to pale yellow. **Do not** inject RoACTEMRA if the liquid is cloudy, discoloured or has lumps or particles in it because it may not be safe to use. Safely dispose of the pre-filled pen in a sharps container and get a new one.
- Wash your hands well with soap and water.

Step 2. Choose and Prepare an Injection Site

Choose an Injection Site

- The front of your thigh or your abdomen except for the 2-inch (5cm) area around your navel are the recommended injection sites **(See Figure D).**
- The outer area of the upper arms may also be used only if the injection is being given by a caregiver. Do not attempt to use the upper arm area by yourself **(See Figure D).**

Rotate Injection Site

- Choose a different injection site for each new injection at least 1 inch (2.5cm) from the last area you injected.
- Do not inject into moles, scars, bruises, or areas where the skin is tender, red, hard or not intact.

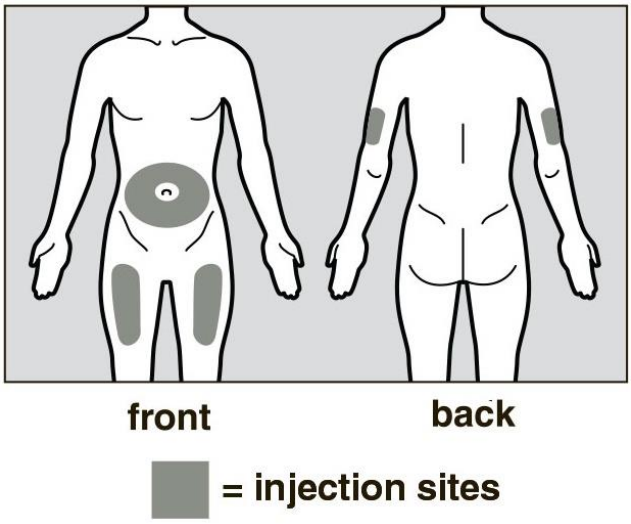

Figure D

Prepare the Injection Site

- Wipe the injection site with an alcohol pad in a circular motion and let it air dry to reduce the chance of getting an infection. **Do not** touch the injection site again before giving the injection.
- **Do not** fan or blow on the clean area.

Step 3. Inject RoACTEMRA

- Hold the RoACTEMRA pre-filled pen firmly with one hand. Twist and pull off the green cap with the other hand **(See Figure E).** The green cap contains a loose fitting metal tube.
- If you cannot remove the green cap you should ask a caregiver for help or contact your healthcare provider.

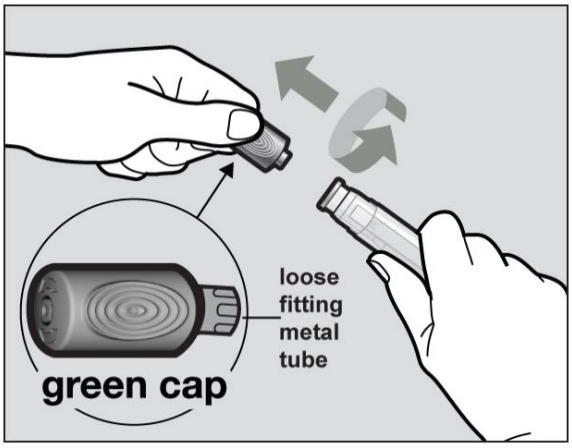

Figure E

Important: Do not touch the needle shield which is located at the tip of the pre-filled pen below the Window area (see Figure A), to avoid accidental needle stick injury.

- Throw away the green cap in a sharps container.
- After you remove the green cap, the pre-filled pen is ready for use. If the pre-filled pen is not used within 3 minutes of the cap removal, the pre-filled pen should be disposed of in the sharps container and a new pre-filled pen should be used.
- Never reattach the green cap after removal.
- Hold the pre-filled pen comfortably in 1 hand by the upper part, so that you can see the Window area of the pre-filled pen **(See Figure F).**

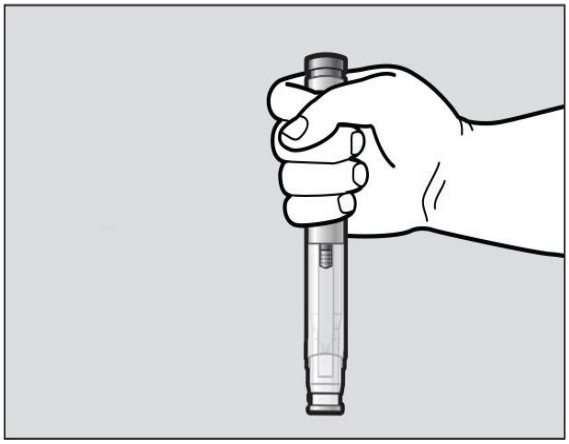

Figure F

- Use your other hand to gently pinch the area of skin you cleaned, to prepare a firm injection site **(See Figure G).** The pre-filled pen requires a firm injection site to properly activate.

- Pinching the skin is important to make sure that you inject under the skin (into fatty tissue) but not any deeper (into muscle). Injection into muscle could cause the injection to feel uncomfortable.

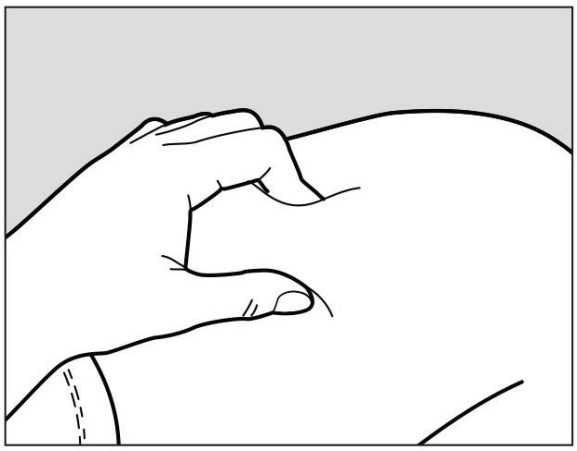

Figure G

- **Do not** press the green activation button yet.
- Place the needle-shield of the pre-filled pen against your pinched skin at a 90° angle **(See Figure H).**
- It is important to use the correct angle to make sure the medicine is delivered under the skin (into fatty tissue), or the injection could be painful and the medicine may not work.

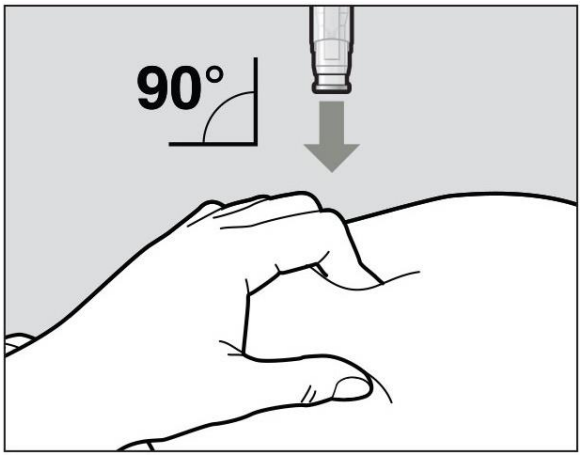

Figure H

- To use the pre-filled pen, you first have to unlock the green Activation button.
- To unlock it, press the pre-filled pen firmly against your pinched skin until the needle-shield is completely pushed in **(See Figure I)**.

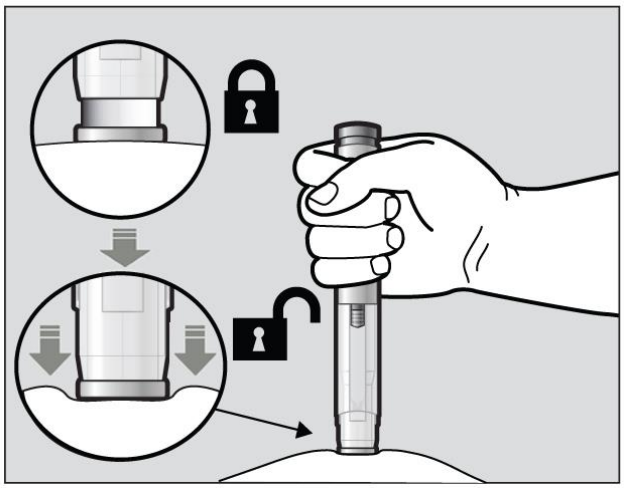

Figure I

- Continue to keep the needle-shield pushed in.
- If you don’t keep the needle-shield completely pushed against the skin, the green Activation button will not work.
- Continue to pinch the skin while you keep the pre-filled pen in place.
- Press the green Activation button to start the injection. A “click” sound indicates the start of the injection. Keep the green button pressed in and continue holding the pre-filled pen pressed firmly against your skin **(See Figure J).** If you cannot start the injection you should ask for help from a caregiver or contact your healthcare provider.

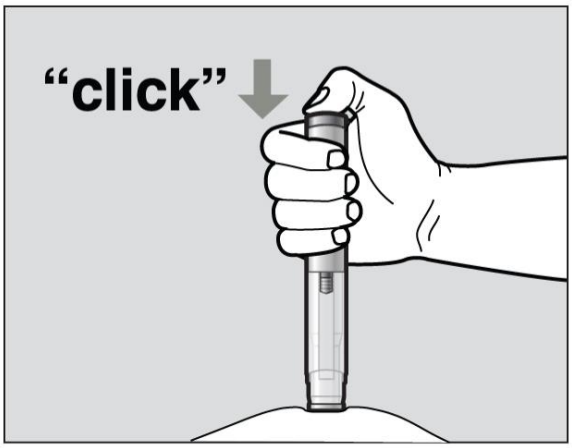

Figure J

- The purple indicator will move along the Window area during the injection **(See Figure K).**
- Watch the purple indicator until it stops moving to be sure the full dose of medication is injected.

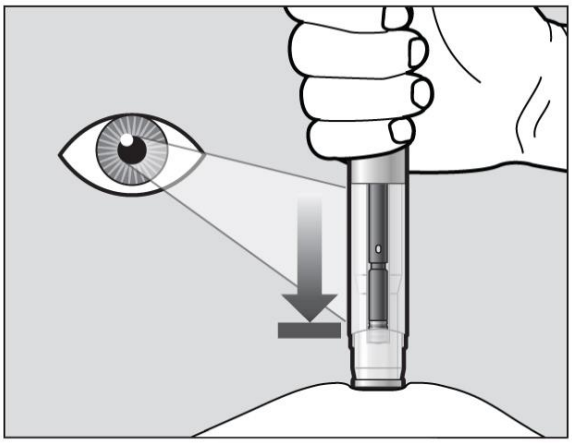

Figure K

- The injection may take up to **10 seconds**.
- You may hear a second "click" during the injection but you should continue to hold the pre-filled pen firmly against your skin until the purple indicator stops moving.
- When the purple indicator has stopped moving, release the green button. Lift the pre-filled pen straight off of the injection site at a 90° angle to remove the needle from the skin. The needle-shield will then move out and lock into place covering the needle **(See Figure L)**.

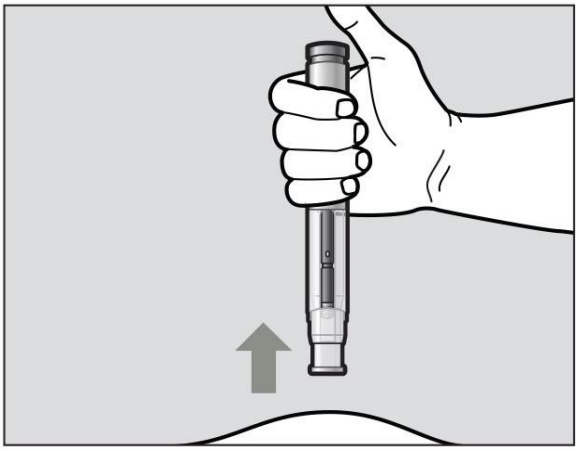

Figure L

- Check the Window area to see that it is filled with the purple indicator **(See Figure L).**
- If the Window area is not filled by the purple indicator then:
    - The needle-shield may not have locked. **Do not** touch the needle-shield of the pre-filled pen, because you may stick yourself with the needle. If the needle is not covered, carefully place the pre-filled pen into the sharps container to avoid any injury with the needle.
    - You may not have received your full dose of RoACTEMRA. **Do not** try to re-use the pre-filled pen. Do not repeat the injection with another pre-filled pen. Call your healthcare provider for help.

After the Injection

- There may be a little bleeding at the injection site. You can press a cotton ball or gauze over the injection site.
- **Do not** rub the injection site.
- If needed, you may cover the injection site with a small bandage.

Step 4. Dispose of the pre-filled pen

- The RoACTEMRA pre-filled pen should not be reused.

- Put the used pre-filled pen into your sharps container (see **"How do I dispose of used pre-filled pens?")**
- **Do not** put the cap back on the pre-filled pen.
- **If your injection is given by another person, this person must also be careful when removing the pre-filled pen and disposing of it to prevent accidental needle stick injury and passing infection.**

How do I dispose of used pre-filled pens?

- Put your used RoACTEMRA pre-filled pen and green cap in a sharps disposal container right away after use **(See Figure M).**
- **Do not throw away (dispose of) the pre-filled pen and the green cap in your household trash and do not recycle them.**

Figure M

- 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.

Keep the RoACTEMRA pre-filled pen and disposal container out of the reach of children.

Record your Injection

- Write the date, time, and specific part of your body where you injected yourself. It may also be helpful to write any questions or concerns about the injection so you can ask your healthcare provider.

If you have any questions or concerns about your RoACTEMRA pre-filled pen, talk to your healthcare provider familiar with RoACTEMRA.