RoActemra® (tocilizumab) for Rheumatoid Arthritis (RA) and Giant Cell Arteritis (GCA) RoActemra ACTPen®

(162 mg solution for injection in pre-filled pen)

What you should know about RoActemra and RoActemra ACTPen

This brochure provides key information to assist in the patient's understanding of the benefits and risks associated with RoActemra therapy

This educational material is provided by Roche Products Limited and is mandatory as a condition of the marketing authorisation of RoActemra 162mg solution for injection in a pre-filled pen for the treatment of Rheumatoid Arthritis or GCA in adult patients in order to further minimise important selected risks.

For more information on RoActemra, please see the Patient Information Leaflet (PIL) that comes with your medicine. If you have any further questions, please ask your doctor, nurse or pharmacist.

What you should know about RoActemra

Finding the right treatment for Rheumatoid Arthritis (RA), a chronic autoimmune disease, or Giant Cell Arteritis (GCA), an autoimmune disease that causes inflammation and swelling of the arteries, is very important.

All medications carry both potential benefits and potential risks to our health and it is important to understand these. Finding the balance between the two will lead you to a treatment that works best for you. RoActemra might be that treatment.

RoActemra initially in combination with steroids, can be used to treat GCA in adult patients.

This brochure will answer some questions you may have about the side effects and potential risks of RoActemra. Talk to your doctor, nurse or pharmacist if you have any questions or problems.

This brochure does not take the place of speaking to your doctor, nurse or pharmacist.

Medicines are sometimes prescribed for purposes other than those listed. Only take RoActemra as directed for the condition for which it was prescribed.

What you should know about RA and RoActemra

What causes RA?

The exact cause of RA is not known. In RA, the body's immune system doesn't work the way it should.The immune system is supposed to attack only foreign substances like germs. But when it doesn't work right, it can also attack the body itself. Diseases in which this happens, like RA, are called autoimmune diseases. When the immune system attacks the body, it can lead to the symptoms such as joint pain, swelling, stiffness and fatigue.

What is IL-6?

Interleukin-6 (IL-6) is a protein that is made by the immune system. The body uses IL-6 to manage inflammation and infections. IL-6 also plays a major role in the signs and symptoms of RA. Some people with RA have too much IL-6.

What is RoActemra?

RoActemra is a biologic drug (a type of therapy made from living cells) that contains the active substance tocilizumab, which is a protein made from specific immune cells (monoclonal antibody), that blocks the action of IL-6.

How has RoActemra been studied in RA?

RoActemra has been studied in adults with RA. It has been studied alone and in combination with oral medications for RA.

How is RoActemra used in RA?

RoActemra is used to treat adults with moderate to severe active RA, an autoimmune disease, if previous therapies did not work well enough. RoActemra is usually given in combination with methotrexate. However, RoActemra can be given alone if your doctor determines that methotrexate is inappropriate. RoActemra can also be used to treat adults who have not had previous methotrexate treatment if they have severe, active and progressive RA. RoActemra has not been studied with other biologic medicines for RA. Because of the possibility of increased risk of infection, RoActemra should not be used with other biologic medicines for RA. These other biologic medicines for RA include drugs such as:

Enbrel® (etanercept), Humira® (adalimumab), Remicade® (infliximab), MabThera® (rituximab), Orencia® (abatacept), Cimzia® (certolizumab pegol), Kineret® (anakinra), Olumiant® (baricitinib), Xeljanz® (tofacitinib) and Kevzara® (sarilumab).

What you should know about GCA and RoActemra

What causes GCA?

No one knows for sure. In GCA, the body's immune system doesn't work the way it should. The immune system is supposed to attack only foreign substances like germs. But when it doesn't work right, it can also attack the body itself. Diseases in which this happens, like GCA, are called autoimmune diseases. When the immune system attacks the body, it can lead to the symptoms people with GCA have. In GCA these may include headaches and vision loss.

How has RoActemra been studied in GCA?

RoActemra has been studied in adults with GCA in combination with a gradual reduction of steroids.

How is RoActemra used in GCA?

RoActemra can be used in combination with a gradual reduction of steroids; RoActemra can also be used alone following discontinuation of steroids.

How is RoActemra given in GCA?

RoActemra is administered as a subcutaneous (under the skin) (SC) injection using a pre-filled syringe or pre-filled pen. Please refer to the relevant section below for more specific information on how RoActemra is administered.

What is ACTPen?

ACTPen is an autoinjector that contains RoActemra (tocilizumab) 162 mg solution for injection in a pre-filled pen-type syringe and is given under the skin (subcutaneously).

Autoinjectors are needle-based drug delivery devices and are designed to help patients self-inject. Some patients may find autoinjectors easier to use than standard syringes.

How is RoActemra ACTPen given in GCA?

ACTPen is a 162 mg solution for injection in pre-filled pen given under the skin (subcutaneously).

At the start, your doctor or nurse will inject RoActemra with ACTPen. However, your doctor may decide that you (or your caregiver) may inject ACTPen. In this case you will get training on how to inject ACTPen yourself. Please refer to the relevant section below for more specific information on how to use ACTPen.

The ACTPen:

- Dosing is set at 162 mg of RoActemra, regardless of body weight
- Injection site is your abdomen, thigh, or upper arm
- Is given once per week (unless instructed otherwise by your healthcare professional)

What do I do if I miss a dose of ACTPen?

It is very important to use ACTPen exactly as prescribed by your doctor and to keep track of your doses.

- If you miss your weekly dose within 7 days, take your dose on the next scheduled day
- If you are prescribed a once-every-other-weekly dose, and should you miss your dose and are within 7 days of when the missed dose was due,
  - Take the missed dose immediately and take your next dose as usual on the next scheduled day
- If you miss your weekly or every-other-weekly dose by more than 7 days or are not sure when to inject ACTPen, call your doctor, nurse or pharmacist.

How is ACTPen packaged?

Each pack of ACTPen contains 4 pre-filled pens.

How should I store ACTPen?

- You must keep your unused pre-filled pens in the original carton and keep in the refrigerator at 2°C to 8°C (36°F to 46°F). It is important that you do not freeze them
- The pre-filled pen should be kept in the outer carton to protect them from light.
- The pre-filled pen should be kept out of sight and reach of children
- Inspect the pre-filled pen visually for particulate matter and discolouration prior to administration. It should be clear and colourless to pale yellow.

What do I do after I take ACTPen out of the refrigerator?

- Once you remove your ACTPen from the refrigerator, you must administer it within 8 hours. You should make sure it is not kept above 30°C.
- Allow ACTPen to reach room temperature (18°C to 28°C) by waiting for 45 minutes after removing it from the refrigerator.
- Do not speed up the warming process in any way, such as using the microwave or placing the ACTPen in warm water.
- Do not leave the ACTPen to warm up in direct sunlight.
- Once ACTPen has achieved room temperature:
  - Remove the needle-cap,
  - Start the injection within 3 minutes to prevent the medicine from drying out and blocking the needle.
    - Dispose of the pre-filled pen in a puncture-resistant container if you do not use the pre-filled pen within 3 minutes of the cap removal,
    - In this case, you must use a new pre-filled pen.
- **Do not** re-attach the needle-cap after removal.

What else should I know during my ACTPen injection?

- Step by Step detailed instructions are provided in Step-by-Step Dosing and Administration Guide found later in this pamphlet.
- If the purple indicator does not move after you press the activation button:
  - You must dispose of the pre-filled pen in a puncture resistant container.
  - **Do not** try to re-use the ACTPen.
  - **Do not** repeat the injection with another ACTPen. You may have received a partial dose with an unknown amount medication
  - Call your healthcare provider for help.

What do I do with my ACTPen after I have used it?

- Dispose of the ACTPen in a puncture-resistant container,
  - Any unused product or waste material should be disposed of in a puncture-resistant container.
- 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.

Step--by--Step Dosing and Administration Guide

Read and follow the Instructions for use that come with your RoActemra ACTPen before you start using it and each time you get a prescription refill.

Make sure your healthcare provider shows you the right way to use it before you use the ACTPen for the first.

Important:

- **Keep your unused ACTPen in the original carton**
- **Keep in the refrigerator at 2˚C to 8˚C (36˚F to 46˚F). Do not freeze.**
- **Do not remove the ACTPen cap until you are ready to inject ACTPen.**
- **Do not try to take apart the ACTPen at any time.**
- **Do not reuse the same ACTPen.**
- **Do not use the ACTPen through clothing.**
- **Do not leave the ACTPen unattended.**
- **Keep out of the reach of children.**

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

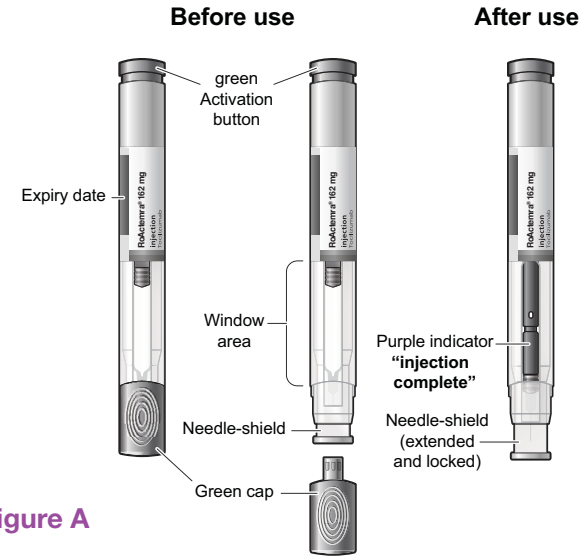


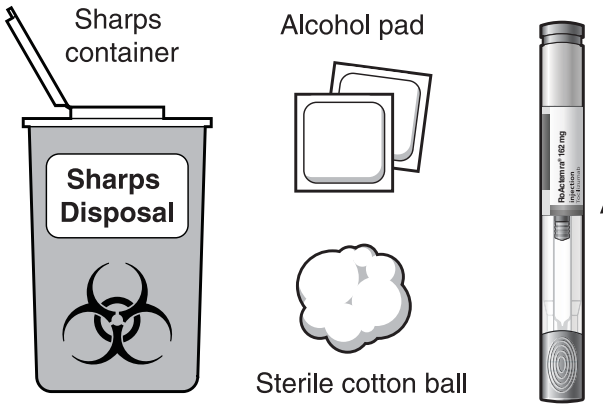
Figure A

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

You will need:

- One RoActemra pre-filled pen
- One Alcohol pad / Cleansing wipes
- One Sterile cotton ball or gauze
- One 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 an ACTPen Injection

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

Take the box containing the ACTPen out of the refrigerator.

Do not use the ACTPen if the box looks like it has already been opened.

Make sure that the box is properly sealed if you are opening the box for the first time.

Check that the pre-filled pen box is not damaged. Do not use ACTPen if the box looks damaged.

Check the expiration date on the ACTPen 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 **ACTPen** from the box.

Return any remaining **ACTPen** in the box to the refrigerator **(See Figure A)**

Check the expiration date on the ACTPen (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 ACTPen in a sharps container and get a new one.

Check the ACTPen to make sure it is not damaged. Do not use the ACTPen if it appears to be damaged or if you have accidentally dropped the ACTPen.

Place the ACTPen on a clean, flat surface and let the ACTPen warm up for 45 minutes to allow it to reach room temperature. If the ACTPen 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 ACTPen in warm water.
- **Do not** leave the ACTPen to warm up in direct sunlight.

Do not remove the green cap while allowing your ACTPen to reach room temperature.

Hold your ACTPen with the green cap pointing down **(See Figure C)**.

Look in the clear Window area to check the liquid in the ACTPen **(See Figure C)** that should be clear and colorless to pale yellow.

Do not inject ACTPen if the liquid is cloudy, discolored, or has lumps or particles in it because it may not be safe to use. In this case, safely dispose of the ACTPen in a sharps container and get a new one.

- Wash your hands well with soap and water.

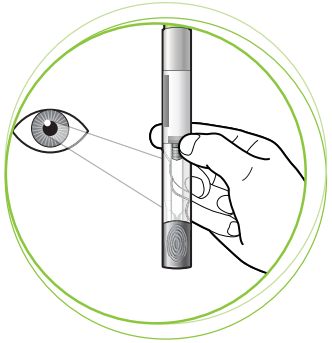


Figure C

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)**.

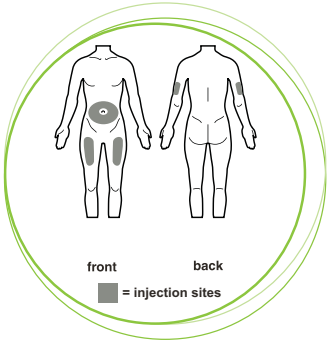


Figure D

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.

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 ACTPen

Hold the ACTPen 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.
- **Ask** a caregiver for help or contact your healthcare provider, if you cannot remove the green cap

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

Figure E

- Throw away the green cap in a sharps container.
- After you remove the green cap, the ACTpen is ready for use.
- If the ACTpen is not used within 3 minutes of the cap removal, the ACTpen should be disposed of in the sharps container and a new pre-filled pen should be used.

Do not reattach the green cap after removal.

Hold the ACTpen comfortably in 1 hand by the upper part, so that you can see the Window area of the pre-filled pen **(See Figure F)**.

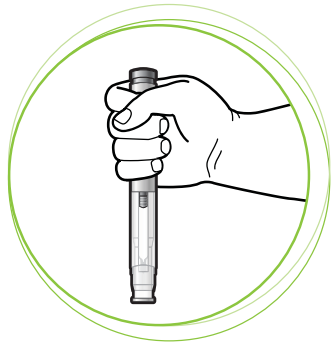


Figure F

Figure G

Use your other hand to gently pinch the area of skin you cleaned, to prepare a firm injection site **(See Figure G)**. The ACTpen 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.

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.

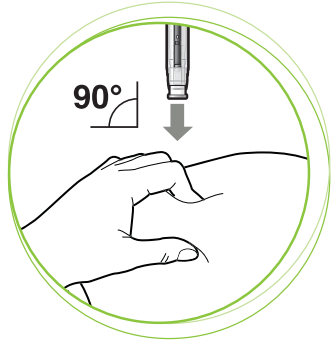


Figure H

Step 3. Inject ACTPen (Continued)

Unlock the green Activation Button

- You first have to unlock the green Activation Button to use the ACTpen,
- **Press** the ACTpen firmly against your pinched skin until the needle-shield is completely pushed in to unlock it. **(See 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 ACTpen in place.

Figure I

Figure J

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 ACTpen pressed firmly against your skin (See Figure J).
- Ask for help from a caregiver or contact your healthcare provider, if you cannot start the injection.

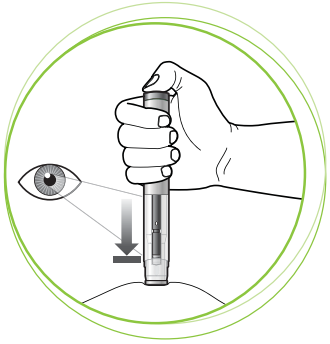


Figure K

- 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.

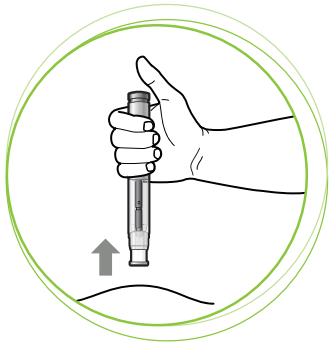


Figure L

- 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.

Release the green button, when the purple indicator has stopped moving,

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)**.

- 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 ACTpen, 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 ACTPen

- Do not reuse the ACTPen.
- 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 ACTPen.

Step 4. Dispose of ACTPen (Continued)

If your injection is given by another person, this person must also be careful when removing the pre-filled pen and disposing it of to prevent accidental needle stick injury and passing infection.

Figure M

How do I dispose of used pre-filled pens?

- **Put** your used ACTPen and green cap in a sharps disposal container right away after use (**See Figure M)**.

Do not throw away (dispose of) the ACTPen and the green cap in your 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.

Keep the ACTPen 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 ACTPen, talk to your healthcare provider familiar with RoActemra ACTPen.

What tests will be done when I am receiving treatment with RoActemra?

At each visit to see your doctor or nurse, they may test your blood to help guide your treatment. Here are some things they may look at:

Neutrophils
Having enough neutrophils is important to help our bodies fight infections. RoActemra works on the immune system and can cause the number of neutrophils, a form of white blood cells, to drop. For this reason, your doctor may test to make sure you have enough neutrophils and monitor for signs and symptoms of infection.

Platelets
Platelets are small blood components that help stop bleeding by forming clots. Some people taking RoActemra had a drop in the number of platelets in their blood. In clinical trials, the drop in platelets was not associated with any serious bleeding.

Liver enzymes
Liver enzymes are proteins produced by your liver which may be released into your blood, sometimes indicating liver damage or disease. Some people who have taken RoActemra have had a rise in liver enzymes, which could be a sign of liver damage. Rises in liver enzymes were seen more often when medications that could be harmful to the liver were used with RoActemra. If this happens to you, your doctor should take care of this right away. Your doctor may decide to change your dose of RoActemra, or of other medication, or potentially stop treatment with RoActemra altogether.

Cholesterol
Some people who have taken RoActemra have had a rise in blood cholesterol, which is a type of lipid (fat). If this happens, your doctor may prescribe a cholesterol-lowering medication.

Can patients have vaccinations during treatment with RoActemra?

RoActemra is a medication that affects the immune system and may lower the body's ability to fight infection. Immunisation with live or live-attenuated vaccines (which contain very small amounts of the actual germ or weakened germs), should not be given during treatment with RoActemra. Patients should be brought up to date with all immunisations before starting RoActemra.

What are the most common side effects of RoActemra?

Most common side effects reported by patients in clinical trials were usually mild and usually did not result in the patient having to stop using the medication. Side effects could occur 3 months or more after your last dose of RoActemra.

These common side effects were:

- Upper respiratory tract infections (with typical symptoms such as cough, blocked nose, runny nose and sore throat and headache)
- Headache
- High blood pressure
- Rash
- Dizziness – if you experience dizziness, you should not drive or use machines until it has resolved
- Injection site reactions (including erythema, pruritus, pain and hematoma)
  - These are more common when RoActemra is given subcutaneously than when given by infusion

What are the serious side effects of RoActemra?

Infections
RoActemra is a medication that affects your immune system. Your immune system is important because it helps you fight infections. Your ability to fight infections may be lowered with RoActemra. Some infections may become serious while on RoActemra. Serious infections may require treatment and hospitalisation and in some cases may lead to death. It is very important to report any signs of infection to your doctor or nurse right away

Seek immediate medical attention if you develop signs/symptoms of infection such as:

- Fever and chills
- Persistent cough
- Weight loss
- Throat pain or soreness
- Wheezing
- Red or swollen skin or mouth blisters, skin tears or wounds
- Severe weakness or tiredness

Allergic reactions
Most allergic reactions occur during injection or within 24 hours of RoActemra administration, although allergic reactions can occur at any time. Serious allergic reactions including anaphylaxis have been reported in association with RoActemra. Such reactions may be more severe, and potentially fatal in patients who have experienced allergic reactions during previous treatment with RoActemra. Fatal anaphylaxis has been reported after marketing authorisation during treatment with intravenous RoActemra.

If an anaphylactic reaction or other serious allergic reaction occurs, administration of RoActemra should be stopped immediately, appropriate medical treatment initiated and RoActemra should be permanently discontinued.

Your doctor will assess you (or your caregiver) for your suitability to use RoActemra injections at home.

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 receiving RoActemra, if you are administering at home and you experience any symptoms suggestive of an allergic reaction.

Seek immediate medical attention if you notice any of the following signs or symptoms of allergic reactions after receiving RoActemra:

- Rash, itching or hives
- Shortness of breath or trouble breathing
- Swelling of the lips, tongue or face
- Chest pain or chest tightness
- Feeling dizzy or faint
- Severe stomach pain or vomiting
- Very low blood pressure

Abdominal pain
Patients taking RoActemra have on rare occasions experienced serious side effects in their stomach and intestines. Symptoms may include fever and persistent abdominal pain with change in bowel habits. **Seek immediate medical attention** if you develop stomach pain or colic, or notice blood in your stool.

Malignancies
Medicines which act on the immune system, like RoActemra, may increase the risk of malignancy.

Summary and contact information
This patient brochure reviews some of the most important information about RoActemra. Medicines are sometimes prescribed for purposes other than those listed. Do not use RoActemra for a condition for which it was not prescribed.

Tell your doctor, nurse or pharmacist about any side effect you experience, bothers you or that does not go away. These side effects listed in this brochure are not all of the possible side effects that you could experience with RoActemra. Ask your doctor, nurse or pharmacist for more information. Talk to your doctor, nurse or pharmacist if you have any questions or problems.

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 the package leaflet. Reporting forms and information can be found at www.medicinesauthority@gov.mt Adverse events should also be reported to Roche Products Ltd.

Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44 (0)1707 367554. By reporting side effects you can help provide more information on the safety of this medicine.

Detailed information on this medicine is available on the European Medicines Agency website (www.ema.europa.eu).

Pre-Administration Checklist for GCA - Before each administration of RoActemra, please review the points below

RoActemra may not be right for you. Before starting RoActemra, and before each administration of RoActemra, please review the points below, and tell your doctor or nurse if you checked 'yes' for any of the following:

	YES	NO
Infections		
Do you have an infection or feel unwell? (Signs of an infection may include: fever, cough, headache, open wounds or sores (as in chicken pox or shingles)	❑	❑
Are you being treated for an infection or get a lot of infections?	❑	❑
Do you have tuberculosis (TB) or have you been in close contact with someone who has had TB? (Your doctor should test you for TB before starting RoActemra.)	❑	❑
Have you had or currently have viral hepatitis or any disease of the liver?	❑	❑
Do you have diabetes or other conditions that increase the chance of infections?	❑	❑
Allergic Reactions		
Have you had any allergic reactions to previous medications, including RoActemra?	❑	❑
Gastrointestinal Complications		
Have you had or currently have gastrointestinal ulcers or diverticulitis (inflammation in parts of your large intestine)? (Symptoms my include abdominal pain and unexplained changes in bowel habits, with fever)	❑	❑
Medical History		
Have you had or do you now have impaired lung function? (For example, interstitial lung disease, where inflammation and scarring in the lungs make it difficult to get enough oxygen)	❑	❑
Have you ever had cancer?	❑	❑
Do you have heart or circulatory disease? (Examples include raised blood pressure or cholesterol levels)	❑	❑
Do you have kidney problems?	❑	❑
Do you have persistent headaches?	❑	❑

	YES	NO
Pregnancy		
Are you pregnant, possibly pregnant or do you intend to become pregnant? (Women of childbearing potential must use effective contraception during (and up to 3 months after)) treatment. RoActemra should not be used during pregnancy unless absolutely necessary).	❑	❑
Are you breast-feeding or do you intend to breast-feed?	❑	❑
Medications		
Have you recently had a vaccination (immunisation), or are scheduled to have one?	❑	❑
Are you taking other medications? Tell your doctor or nurse about all the medicines you take. This includes prescription (such as steroids) and non-prescription medications, vitamins and herbal medicines	❑	❑
You can take other medications if your doctor has told you it is okay to take them while you are taking RoActemra. RoActemra may interact with some medications. This may affect the dose you need of that medication. No effect of cumulative corticosteroid dose on RoActemra exposure was observed In GCA patients.		
Tell your doctor if you are taking the following medicines:		
atorvastatin, used to reduce cholesterol levels	❑	❑
calcium channel blockers (e.g. amlodipine), used to treat raised blood pressure	❑	❑
theophylline, used to treat asthma	❑	❑
warfarin, used as a blood-thinning agent	❑	❑
phenytoin, used to treat convulsions	❑	❑
ciclosporin, used to suppress the immune system during organ transplants	❑	❑
benzodiazepines (e.g. temazepam), used to relieve anxiety	❑	❑

RXUKACTE00065c April 2018 Ver1.0