Package leaflet: Information for the user

Avtozma 162 mg solution for injection in pre-filled pen
tocilizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Avtozma.

What is in this leaflet:

1. What Avtozma is and what it is used for
2. What you need to know before you use Avtozma
3. How to use Avtozma
4. Possible side effects
5. How to store Avtozma
6. Contents of the pack and other information
7. Instructions for use

1. What Avtozma is and what it is used for

Avtozma 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. Avtozma 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.

  Avtozma helps to reduce RA symptoms such as pain and swelling in your joints and can also improve your performance of daily tasks. Avtozma 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.

  Avtozma is usually given in combination with another medicine for RA called methotrexate. However, Avtozma 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.

Avtozma 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 Avtozma 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.

  Avtozma 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.

  Avtozma 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 Avtozma

Do not use Avtozma
- 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). (See special warnings at the end of this section under subtitle "Avtozma contains polysorbate")
- 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 Avtozma.

Warnings and precautions

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

- 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 Avtozma 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. Avtozma 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 Avtozma. 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 Avtozma, 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 Avtozma. Certain types of vaccines should not be given while receiving Avtozma.

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

- 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 Avtozma.

- 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 Avtozma, to determine if you have a low white blood cell count, low platelet count or high liver enzymes.

Children and adolescents
Avtozma pre-filled pen is not recommended for use in children under 12 years of age. Avtozma 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 Avtozma.

Other medicines and Avtozma
Tell your doctor if you are taking any other medicines, or have recently taken any. Avtozma 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, tocilizumab is not recommended for use with other biological medicines for the treatment of RA, sJIA, pJIA, or GCA.

Pregnancy, breast-feeding and fertility

Avtozma 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 Avtozma, 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 Avtozma is passed into breast milk.

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

Avtozma contains polysorbate
This medicine contains 0.2 mg of polysorbate 80 in each pre-filled pen. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Avtozma

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 Avtozma 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 Avtozma 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.

Avtozma is given by injection under the skin (*subcutaneously*). At the start, your doctor or nurse may inject Avtozma. However, your doctor may decide that you may inject Avtozma yourself. In this case you will get training on how to inject Avtozma yourself. Parents and carers will get training on how to inject Avtozma 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 Avtozma than you should
Because Avtozma 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 Avtozma 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 Avtozma, call your doctor or pharmacist.

If an adolescent with pJIA misses or forgets a dose
It is very important to use Avtozma 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 Avtozma, call the doctor or pharmacist.

If you stop using Avtozma
You should not stop using Avtozma 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, Avtozma can cause side effects, although not everybody gets them. Side effects could occur 3 months or more after your last dose of Avtozma.

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 1 000 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 to1in 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Avtozma

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 3 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 yellow, 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 needle cover the orange 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. The pre-filled pen is locked and the needle is covered inside the needle cover when trying to re-use. 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 Avtozma 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-Threonine, L-Methionine, polysorbate 80 and water for injections.

What Avtozma looks like and contents of the pack
Avtozma is a solution for injection. The solution is colourless to yellow.

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

The Avtozma pre-filled pen for patient use is available in packs containing:

- 1 pre-filled pen
- 4 pre-filled pens
- 12 (3 packs of 4) pre-filled pens (Multipacks)

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Celltrion Healthcare United Kingdom Limited
The Charter Building, Charter Place,
Uxbridge UB8 1JG
United Kingdom

Manufacturer
Nuvisan France SARL
2400, Route des Colles,
06410, Biot,
France

Midas Pharma GmbH
Rheinstr. 49,
55218 Ingelheim,
Germany

KYMOS S.L.
Ronda Can Fatjó, 7B.
08290 Cerdanyola del Vallès,
Barcelona,
Spain

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

United Kingdom
Celltrion Healthcare United Kingdom Limited
Tel: +44 (0)1753 983500

This leaflet was last revised in 12/2024

7. Instructions for use

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

Important Information

- **Do not** remove the pre-filled pen cap until you are ready to inject Avtozma.
- **Do not** try to take apart the pre-filled pen at any time.
- **Do not** reuse the same pre-filled pen.
- **Do not** shake the pre-filled pen
- **Do not** use the pre-filled pen if it has been dropped or damaged.
- **Patient advice regarding hypersensitivity reactions (or anaphylaxis):** 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 injection you should seek emergency care immediately.

Storing Avtozma

- Store the unused pre-filled pen in the original carton in a refrigerator between 2°C to 8ºC. **Do not** freeze.
- Once removed from the refrigerator, Avtozma can be stored up to 3 weeks at or below 30°C. If not used within the 3 weeks, Avtozma should be discarded.
- Keep the pre-filled pen out of direct sunlight.
- **Do not** remove the pre-filled pen from its original carton during storage.
- **Do not** leave the pre-filled pen unattended.
- Keep the pre-filled pen out of the reach of children. Contains small part.

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

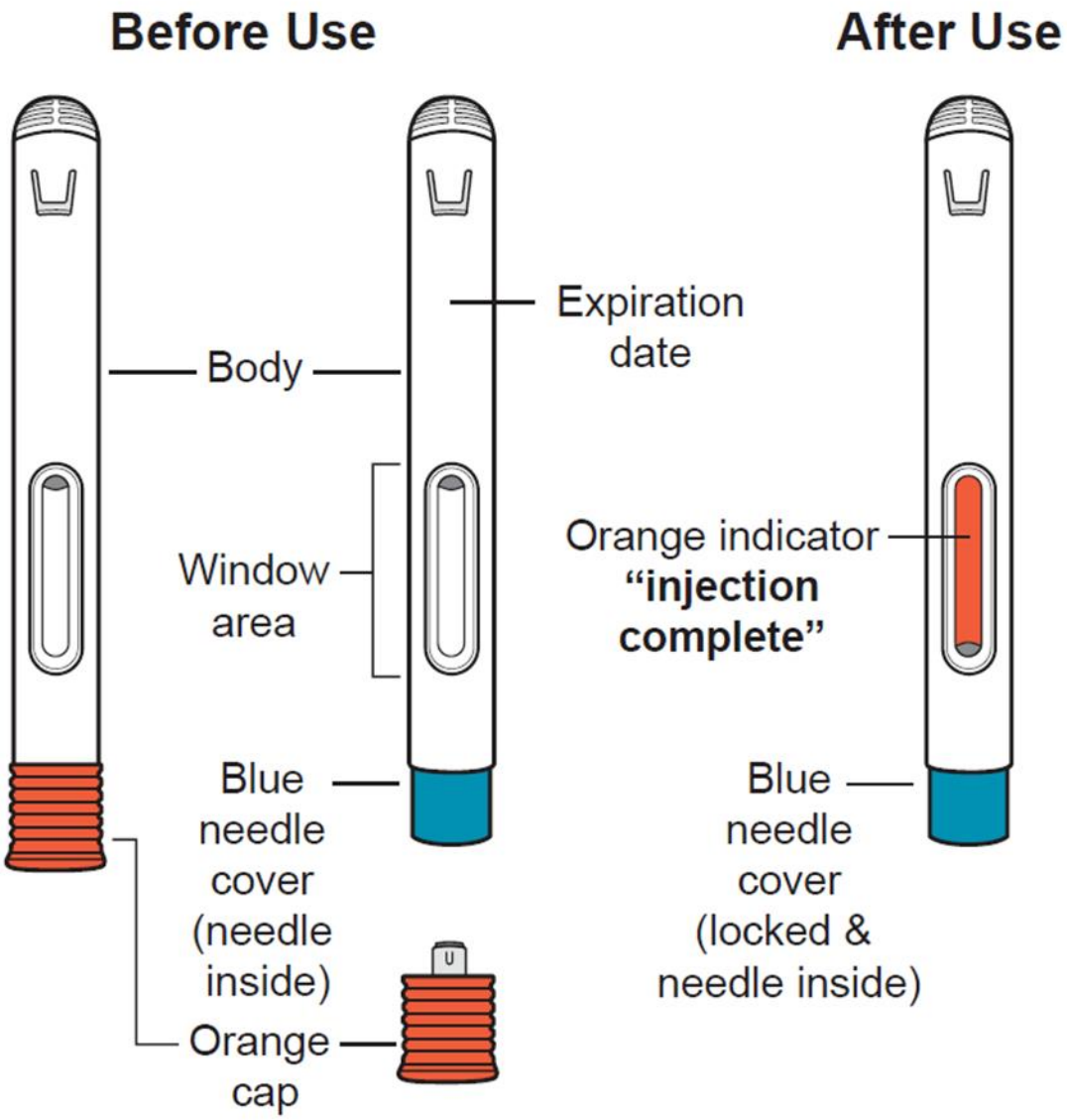

Figure A

Preparing for the Injection

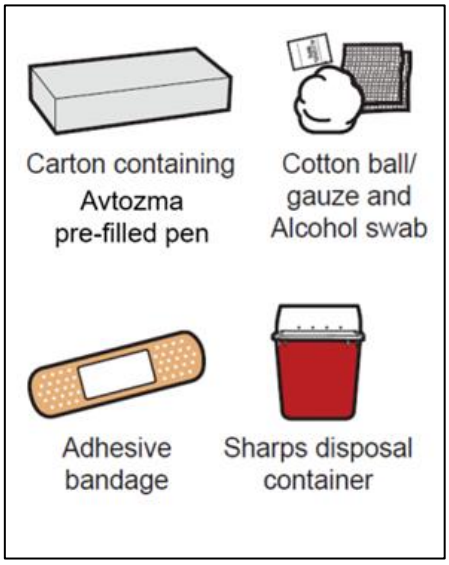

Figure B

1. Gather the supplies for the injection.

a. Prepare a clean, flat surface, such as a table or countertop, in a well-lit area.

b. Take the carton containing the pre-filled pen out of the refrigerator.

c. Make sure you have the following supplies (see **Figure B**):

- Carton containing Avtozma pre-filled pen

Not included in the carton:

- Cotton ball or gauze
- Adhesive bandage
- Sharps disposal container
- Alcohol swab

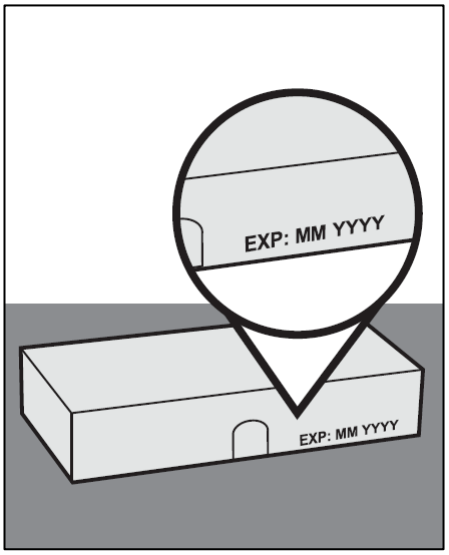

Figure C

2. Inspect the carton

a. Look at the carton and make sure you have the correct medicine and dose strength. (Avtozma)

b. Check the expiration date on the carton to make sure the date has not passed.

- **Do not** use the pre-filled pen if the expiration date has passed.
- If you are opening the carton for the first time, check to make sure that it is properly sealed.
- **Do not** use the pre-filled pen if the carton looks like it has been opened or damaged.

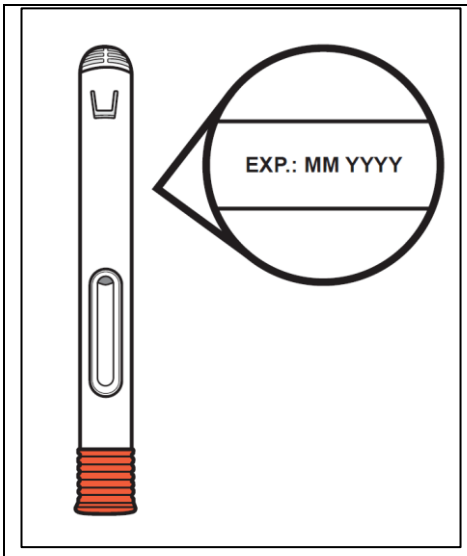

Figure D

3. Inspect the pre-filled pen.

a. Open the carton and remove one single-dose pre-filled pen from the carton. Return any remaining Avtozma pre-filled pens in the box to the refrigerator.

b. Check the expiration date on the Avtozma pre-filled pen (**see Figure D**).

- **Do not** use the pre-filled pen if the expiration date has passed. If the expiration date has passed, safely dispose of the pre-filled pen in your sharps disposal container and get a new one.

c. Check the pre-filled pen to make sure it is not damaged, and shows no sign of leakage.

- **Do not** use the pre-filled pen if it has been dropped, damaged, or has leaked.

Note: A small gap between the orange cap and injector body is normal.

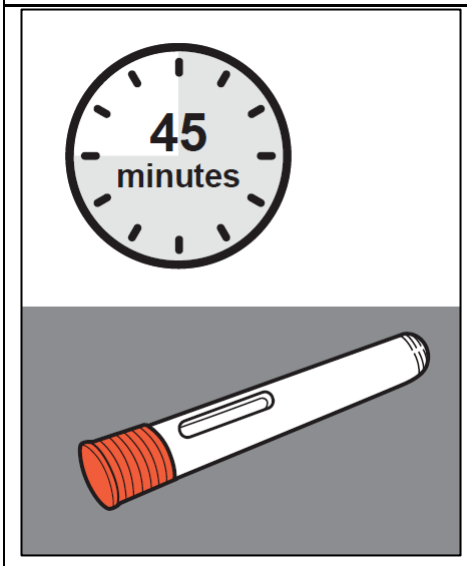

Figure E

4. Wait 45 minutes.

a. Leave the pre-filled pen outside of the carton at room temperature 20°C to 25°C for 45 minutes to allow it to warm up (see **Figure E**).

- **Do not** warm the pre-filled pen using heat sources such as hot water or a microwave.
- **Do not** leave the pre-filled pen in the direct sunlight.
- **Do not** remove the cap while allowing your pre-filled pen to reach room temperature.
- If the pre-filled pen does not reach room temperature, this could cause discomfort.

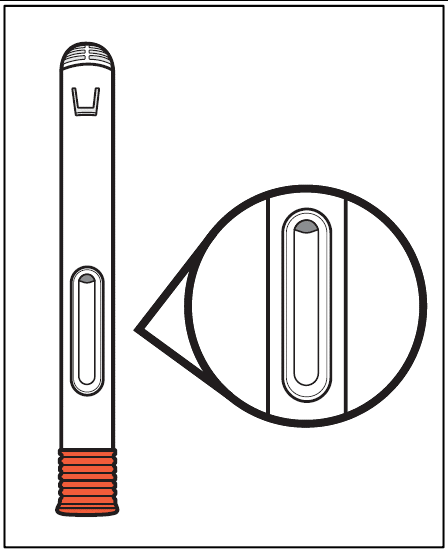

Figure F

5. Inspect the medication.

a. Hold your Avtozma with the cap pointing down.

b. Look at the medicine and confirm that the liquid is clear to slightly opalescent and colourless to yellow and does not contain any particles or flakes (see **Figure F**).

- **Do not** use the pre-filled pen if the liquid is discoloured, cloudy, or has particles or flakes in it. Safely dispose of the pre-filled pen in a sharps disposal container and use a new one.
- Air bubbles are normal.

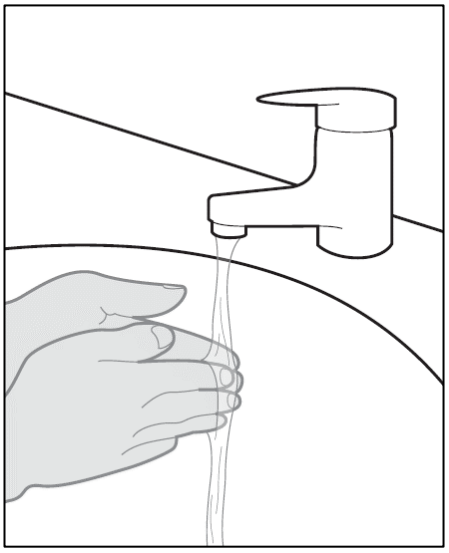

Figure G

6. Wash your hands.

a. Wash your hands with soap and water and dry them thoroughly (see **Figure G**).

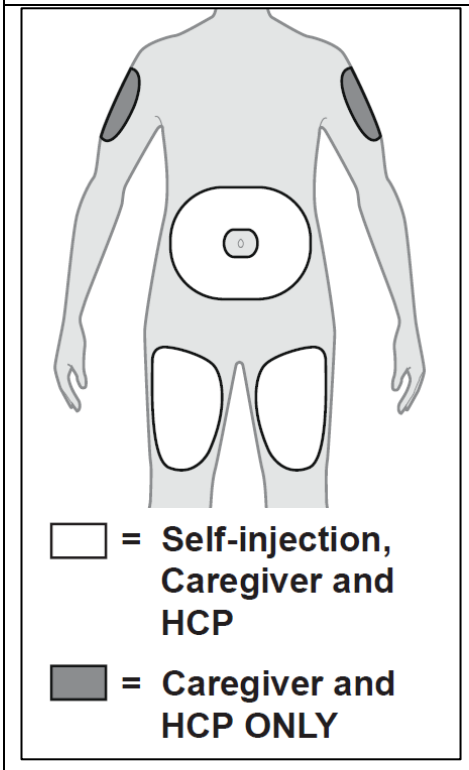

Figure H

7. Choose an appropriate injection site (see Figure H).

a. You may inject into

- The front of the thighs
- The abdomen, except for the 5 cm around the belly button.
- The outer area of the upper arm (only if you are a caregiver or healthcare professional (HCP).

- **Do not** inject into the upper arm by yourself.
- Choose a different injection site for each new injection at least 2.5 cm from the last area you injected.
- **Do not** inject into moles, scares, bruises, or areas where the skin is tender, red, hard or not intact.

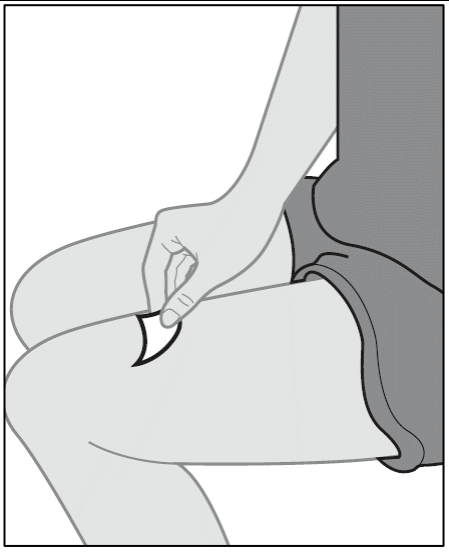

Figure I

8. Clean the injection site.

a. Wipe the injection site with an alcohol swab and let it air dry (see **Figure I**). This will 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.

Administering the Injection

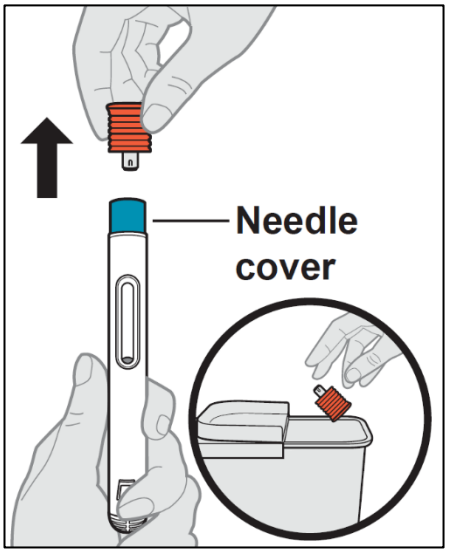

Figure J

9. Remove the cap.

a. Hold the pre-filled pen by the injector body with the cap on top using one hand.
Gently pull the cap straight off with the other hand (see **Figure J**).

Note: If you cannot remove the cap, you should ask a caregiver for help or contact your healthcare provider.

b. Dispose of the cap right away in your sharps disposal container (see **step 14** and **Figure O**)

- **Do not** re-cap the pre-filled pen.
- **Do not** touch the needle shield at the tip of the pre-filled pen to avoid accidental needle stick injury.
- After you remove the cap, the pre-filled pen is ready for use. If the pre-filled pen is not used within 3 minutes of cap removal, throw away the pre-filled pen in a sharps disposal container and use a new pre-filled pen.

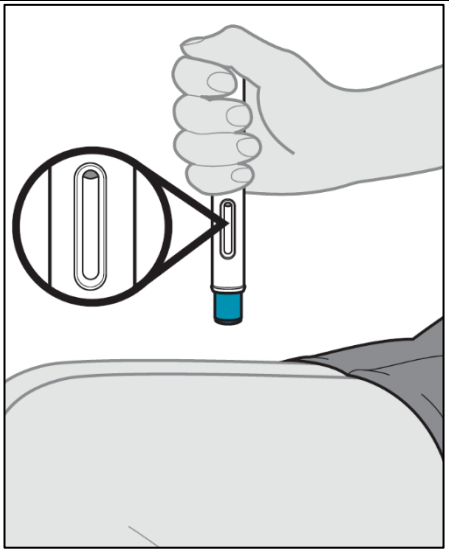

Figure K

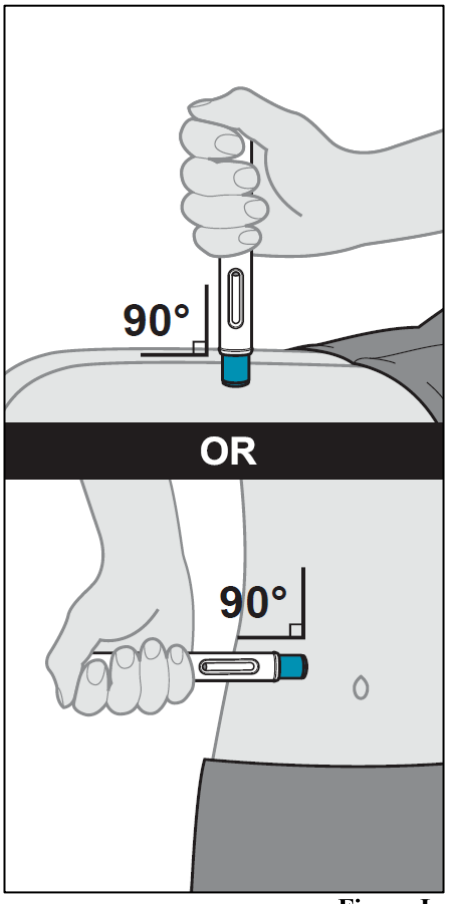

Figure L

10. Place the pre-filled pen on the injection site.

a. Hold the pre-filled pen comfortably in one hand so that you can see the window (see **Figure K**).

b. Without pinching or stretching the skin, place the pre-filled pen against the skin at a 90-degree angle (see **Figure L**).

Note: 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.

- **Do not** administer into muscle or a blood vessel.

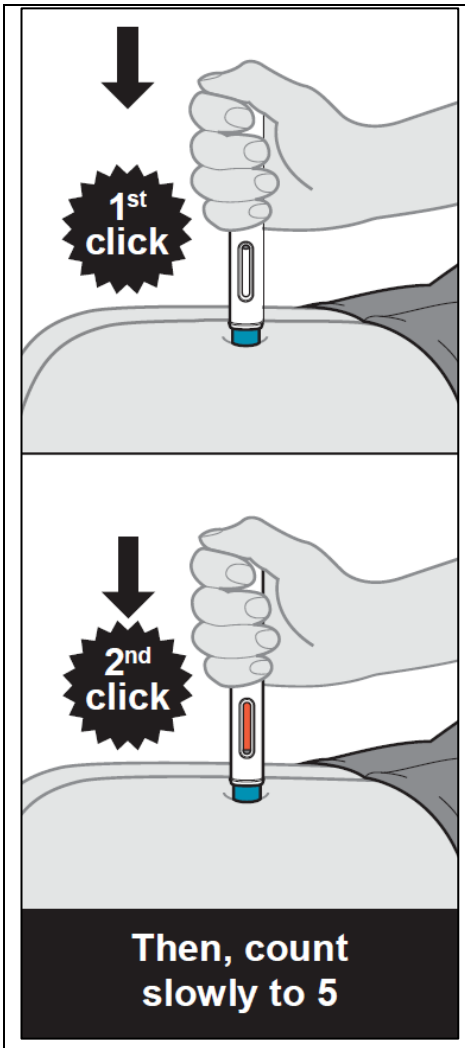

Figure M

11. Give the injection.

a. Firmly press the pre-filled pen into the skin to begin the injection.

b. When the injection starts you will hear the 1st "click" and the orange indicator will begin to fill the window (see **Figure M**).

c. Keep holding the pre-filled pen firmly against the skin and listen for the 2nd "click".

d. After you hear the 2nd "click", continue to hold the pre-filled pen firmly against the skin and **count slowly to 5** to make sure you inject the full dose (see **Figure M**).

e. Watch the orange indicator until it stops moving and has reached the end of the window to be sure the full dose of medicine is injected.
Note: If the orange indicator does not move, discard the pre-filled pen and use a new one.

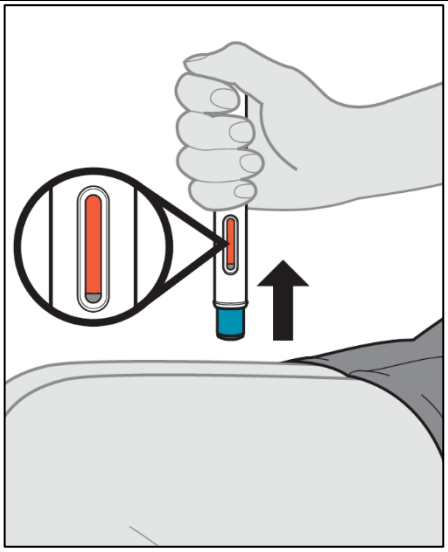

Figure N

12. Remove the pre-filled pen from the injection site.

a. When the orange indicator has stopped moving, lift the pre-filled pen straight off of the injection site at a 90-degree angle to remove the needle from the skin.

- The needle cover will automatically move out and lock into place covering the needle (see **Figure N**).

Note: If the window has not turned completely orange or if the medicine is still injecting, this means you have not received a full dose. Carefully place the pre-filled pen into the sharps disposal container and call your healthcare provider immediately.

- **Do not** touch the needle cover of the pre-filled pen.
- **Do not** try to re-use the pre-filled pen.
- **Do not** repeat the injection with another pre-filled pen.

After the Injection

13. Care for the injection site.

a. If a little bleeding occurs, treat the injection site by gently pressing, not rubbing, a cotton ball or gauze to the site and apply an adhesive bandage if needed.

- **Do not** rub the injection site

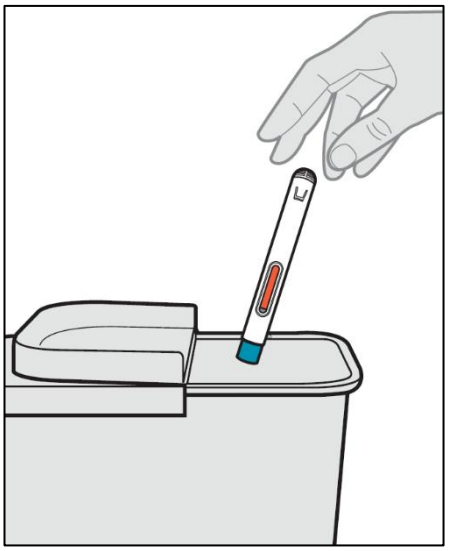

Figure O

14. Dispose of Avtozma.

a. Put the used pre-filled pen in your sharps disposal container right away after use (see **Figure O)**.

Note: 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.

- **Do not** re-use the pre-filled pen.
- **Do not** put the cap back onto the pre-filled pen.
- **Do not** dispose of your used sharps disposal container in your household trash.
- **Do not** recycle your used sharps disposal container.
- Keep the Avtozma pre-filled pen and disposal container out of the reach of children.
- Dispose of the full container as instructed by your healthcare provider or pharmacist. If you do not have a sharps disposal container, you may use a household container that is closable and puncture resistant. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

15. Record your injection.

a. Write the date, time, and specific part of your body where you injected yourself.