

Package leaflet: Information for the user

MIRCERA

30 micrograms/0.3 ml solution for injection in pre-filled syringe
40 micrograms/0.3 ml solution for injection in pre-filled syringe
50 micrograms/0.3 ml solution for injection in pre-filled syringe
60 micrograms/0.3 ml solution for injection in pre-filled syringe
75 micrograms/0.3 ml solution for injection in pre-filled syringe
100 micrograms/0.3 ml solution for injection in pre-filled syringe
120 micrograms/0.3 ml solution for injection in pre-filled syringe
150 micrograms/0.3 ml solution for injection in pre-filled syringe
200 micrograms/0.3 ml solution for injection in pre-filled syringe
250 micrograms/0.3 ml solution for injection in pre-filled syringe
360 micrograms/0.6 ml solution for injection in pre-filled syringe

methoxy polyethylene glycol-epoetin beta

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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What MIRCERA is and what it is used for

This medicine is prescribed to you because you have anaemia caused by your chronic kidney disease and associated with typical symptoms, such as tiredness, weakness and shortness of breath. This means that you have too few red blood cells and your haemoglobin level is too low (your body's tissues might not receive enough oxygen).

MIRCERA is indicated to treat only the symptomatic anaemia caused by chronic kidney disease in adult patients and in paediatric patients (aged 3 months to less than 18 years) on erythropoiesis stimulating agent (ESA) maintenance treatment after their haemoglobin level was stabilised with the previous ESA.

MIRCERA is a medicine produced by gene-technology. Like the natural hormone erythropoietin, MIRCERA increases the number of red blood cells and haemoglobin level in your blood.

2. What you need to know before you use MIRCERA

Do not use MIRCERA

- if you are allergic to methoxy polyethylene glycol-epoetin beta or to any of the other ingredients of this medicine (listed in section 6)
- if you have high blood pressure that cannot be controlled

Warnings and precautions

The safety and efficacy of MIRCERA therapy in other indications, including anaemia in patients with cancer, has not been established.

The safety and efficacy of MIRCERA therapy in paediatric patients have only been established in patients whose haemoglobin level has been previously stabilised by treatment with an ESA.

Before treatment with MIRCERA

- A condition called Pure Red Cell Aplasia (PRCA, stopped or reduced production of red blood cells) due to anti-erythropoietin antibodies was observed in some patients treated with erythropoiesis stimulating agents (ESAs), including MIRCERA.
- If your doctor suspects or confirms that you have these antibodies in your blood, you must not be treated with MIRCERA.
- If you are a patient with hepatitis C and you receive interferon and ribavirin you should discuss this with your doctor because a combination of ESAs with interferon and ribavirin has led to a loss of effect and development of PRCA, a severe form of anaemia, in rare cases. ESAs are not approved in the management of anaemia associated with hepatitis C.
- If you are a patient with chronic kidney disease and anaemia treated with an ESA and are also a cancer patient you should be aware that ESAs, might have a negative impact on your condition. You should discuss options for anaemia treatment with your doctor.
- It is not known if MIRCERA has a different effect in patients with haemoglobinopathies (disorders associated with abnormal haemoglobin), past or present bleeding, seizures or with a high blood platelet count. If you have any of these conditions, your doctor will discuss it with you and must treat you with caution.
- Healthy people should not use MIRCERA. Using it can lead to too high haemoglobin levels and cause problems with the heart or blood vessels that may be life-threatening.

During treatment with MIRCERA

- If you are a patient with chronic renal failure, and particularly if you do not respond properly to MIRCERA, your doctor will check your dose of MIRCERA because repeatedly increasing your dose of MIRCERA if you are not responding to treatment may increase the risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.
- Your doctor may initiate treatment with MIRCERA if your haemoglobin level is 10 g/dl (6.21 mmol/l) or less. After initiation of therapy, your doctor will seek to maintain your haemoglobin level between 10 and 12 g/dl (7.45 mmol/l).
- Your doctor will check the amount of iron in your blood before and during MIRCERA treatment. If the amount is too low your doctor may give you an additional iron supplement.
- Your doctor will check your blood pressure before and during your MIRCERA treatment. If your blood pressure is high and cannot be controlled, either by appropriate medicines or a special diet, your doctor will interrupt your MIRCERA treatment or reduce the dose.
- Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin could put you at risk of having a problem of the heart or the blood vessels and could increase risk of thrombosis, including pulmonary embolism, myocardial infarction, stroke and death.
- Contact your doctor if you feel tired, weak or have shortness of breath, because this could mean that your MIRCERA treatment is not effective. Your doctor will check that you do not have other causes of anaemia and may perform blood tests or examine your bone marrow. If you have developed PRCA, your MIRCERA treatment will be discontinued. You will not receive another ESA and your doctor will treat you for this condition.

Children and adolescents

MIRCERA can be used for the treatment of children and adolescents, 3 months of age to less than 18 years, with anaemia associated with chronic kidney disease. They should be stabilised on ESA maintenance treatment prior to switching to MIRCERA and may or may not be receiving dialysis. Talk to your doctor, pharmacist or nurse before you are given this medicine if you, or your child, are under 18 years of age.

Take special care with other products that stimulate red blood cell production: MIRCERA is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional will always record the exact product you are using.

Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.

If you develop a serious rash or another of these skin symptoms stop taking Mircera and contact your doctor or seek medical attention immediately.

Other medicines and MIRCERA

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. No interaction studies have been performed. There is no evidence that MIRCERA interacts with other medicines.

MIRCERA with food and drink

Food and drink do not affect MIRCERA.

Pregnancy, breast-feeding and fertility

Ask your doctor or pharmacist for advice before taking any medicine.

MIRCERA has not been studied in pregnant or breast-feeding women.

Tell your doctor if you are pregnant, think you are pregnant or intend to become pregnant. Your doctor will consider what is the best treatment for you during pregnancy.

Tell your doctor if you are breast-feeding or intend to breast-feed. Your doctor will advise if you should stop or continue breast-feeding and stop or continue your treatment.

MIRCERA has not shown evidence of impaired fertility in animals. The potential risk for humans is unknown.

Driving and using machines

MIRCERA does not affect your ability to drive and use machines.

Important information about some of the ingredients of MIRCERA

This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say it is essentially 'sodium-free'.

3. How to use MIRCERA

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to MIRCERA, your doctor will check your dose and will inform you if you need to change doses of MIRCERA.

Treatment with MIRCERA must be started under the supervision of a healthcare professional. Further injections can be given by a healthcare professional or, after you have been trained, as an adult, you can inject MIRCERA yourself. Children and adolescents less than 18 years should not self-inject MIRCERA, the administration should be performed by a healthcare professional or trained adult caregiver (follow the instructions at the end of this leaflet on how to use MIRCERA pre-filled syringe to give to yourself or another individual an injection.)

MIRCERA can be injected under the skin in the abdomen, arm or thigh; or into a vein. Your doctor will decide which is best for you.

Your doctor will carry out regular blood tests to monitor how your anaemia is responding to treatment by measuring your haemoglobin level.

- **If you are an adult not currently treated with an ESA**

If you are not on dialysis, the recommended starting dose of MIRCERA is 1.2 micrograms for every kilogram of your body weight to be administered under the skin once every month as a single injection. Alternatively, your doctor may decide to administer a starting dose of MIRCERA of 0.6 micrograms for every kilogram of your body weight. The dose is to be administered once every two weeks as a single injection under the skin or into a vein. Once your anaemia is corrected your doctor may change your dosing to once a month administration.

If you are on dialysis, the recommended starting dose is 0.6 micrograms for every kilogram of your body weight. The dose is to be administered once every two weeks as a single injection under the skin or into a vein. Once your anaemia is corrected your doctor may change your dosing to once a month administration.

Your doctor may increase or decrease your dose or temporarily stop your treatment to adjust your haemoglobin level, as appropriate for you. Dose changes will not be made more often than once a month.

- **If you are currently being treated with another ESA**

Your doctor may replace your current medicine with MIRCERA. Your doctor will decide to treat you with MIRCERA administered as a single injection once a month. Your doctor will calculate your MIRCERA starting dose based on the last dose of your previous medicine. The first MIRCERA dose will be given on the planned injection day of your previous medicine.

Your doctor may increase or decrease your dose or temporarily stop your treatment to adjust your haemoglobin to an appropriate level for you. Dose changes will not be made more often than once a month.

If you use more MIRCERA than you should

Please contact your doctor or pharmacist if you used too large a dose of MIRCERA as it may be necessary to perform some blood tests and interrupt your treatment.

If you forget to use MIRCERA

If you miss a dose of MIRCERA administer the missed dose as soon as you remember and talk to your doctor about when to use the next doses.

If you stop using MIRCERA

Treatment with MIRCERA is normally long-term. It can, however, be stopped on the advice of your doctor at any time.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The frequency of possible side effects listed below:

A common side effect (may affect up to 1 in 10 people) is hypertension (high blood pressure).

Uncommon side effects (may affect up to 1 in 100 people) are:

- headache
- vascular access thrombosis (blood clots in your dialysis access).
- thrombocytopenia
- thrombosis

Rare side effects (may affect up to 1 in 1000 people) are:

- hypertensive encephalopathy (very high blood pressure that can result in headache, especially sudden, stabbing, migraine-like headache, confusion, speech disturbances, fits or convulsions).
- pulmonary embolism.
- maculo-papular rash (red skin reaction that can include pimples or spots)
- hot flush
- hypersensitivity (allergic reaction that can cause unusual wheezing or difficulty in breathing; swollen tongue, face or throat, or swelling around the injection site, or make you feel light-headed, faint or cause you to collapse).

If you have these symptoms please contact your doctor immediately to receive treatment.

During clinical studies patients had a slight decrease in their platelet blood counts. There have been reports of platelet counts below the normal range (thrombocytopenia) in the post-marketing setting.

Hypersensitivity reactions, including cases of anaphylactic reaction and serious skin rashes including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using Mircera if you develop these symptoms and contact your doctor or seek medical attention immediately, see also section 2.

As with other ESAs, cases of thrombosis, including pulmonary embolism, have been reported in the post-marketing setting.

A condition called Pure Red Cell Aplasia (PRCA, stopped or reduced production of red blood cells) due to anti-erythropoietin antibodies was observed in some patients treated with ESAs, including MIRCERA.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: 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 MIRCERA

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 outer carton and pre-filled syringe label after 'EXP'. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C). Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

You may remove your MIRCERA pre-filled syringe from the refrigerator and store it at a room temperature not above 30 °C for a single period of one month. During this period when you have stored MIRCERA at a room temperature not above 30 °C you may not put MIRCERA back in the refrigerator before use. Once you have removed your medicine from the refrigerator you must use it within this period of one month.

Only solutions which are clear, colourless to slightly yellowish and free of visible particles must be injected.

Do not throw away any medicines via wastewater or household waste.
Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What MIRCERA contains

- The active substance is methoxy polyethylene glycol-epoetin beta. One pre-filled syringe contains:
30, 40, 50, 60, 75, 100, 120, 150, 200 or 250 micrograms in 0.3 ml and 360 micrograms in 0.6 ml.
- The other ingredients are sodium dihydrogen phosphate monohydrate, sodium sulphate, mannitol (E421), methionine, poloxamer 188 and water for injections.

What MIRCERA looks like and contents of the pack

MIRCERA is a solution for injection in pre-filled syringe.

The solution is clear, colourless to slightly yellowish and free of visible particles.

MIRCERA comes in pre-filled syringes with laminated plunger stopper and tip cap with one needle 27G1/2. Each pre-filled syringe contains 0.3 ml or 0.6 ml. Pre-filled syringes are not designed for administration of partial doses. MIRCERA is available, for all strengths, in pack sizes of 1 and also pack size of 3 for the strengths 30, 50, 75 micrograms/0.3ml. 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

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MIRCERA pre-filled syringe

Instructions For Use

The following instructions explain how to use the MIRCERA pre-filled syringe to give yourself or another individual an injection.

It is important to read and follow these instructions carefully so that you are able to use the pre-filled syringe correctly and safely.

Do not attempt to administer an injection until you are sure that you understand how to use the pre-filled syringe, if in doubt contact a healthcare professional. Children and adolescents less than 18 years **should not** self-inject MIRCERA, the administration should be performed by a healthcare professional or trained adult caregiver.

Always follow all directions in these Instructions For Use as they may differ from your experience. These instructions will allow preventing incorrect treatments or risks such as needle stick injury or an early activation of the needle safety device, or problems related to the attachment of the needle.

IMPORTANT INFORMATION

- Only use MIRCERA pre-filled syringe if you have been prescribed this medication.
- Read the packaging and ensure you have the dose prescribed by your healthcare professional.
- **Do not** use MIRCERA if the syringe, the box or the plastic tray containing the syringe appears to be damaged.
- **Do not** touch the activation guards (see Figure A) as this may damage the syringe and make it unusable.
- **Do not** use the syringe if the contents are cloudy, hazy or contain particles.
- Never attempt to take the syringe apart.
- Never handle or pull on the syringe by its plunger.
- **Do not** remove the needle shield until you are ready to perform an injection.
- **Do not** swallow the medicine in the syringe.
- **Do not** inject through clothing.
- Never re-use a syringe.
- Pre-filled syringes are not designed for administration of partial doses.
- Keep syringe, needle and supplies out of the reach of children.

STORAGE

Keep the pre-filled syringe and the puncture-resistant/ sharps container out of the reach of children.

Store the syringe in its original box until ready to use.

Always store the syringe in a refrigerator at a temperature of 2 - 8°C (35.6 - 46.4°F).
Do not allow the medicine to freeze, and protect the medicine from light. Keep the syringe dry.

MATERIALS INCLUDED IN THE PACK (Figure A):

- A pre-filled syringe containing MIRCERA
- A separate injection needle

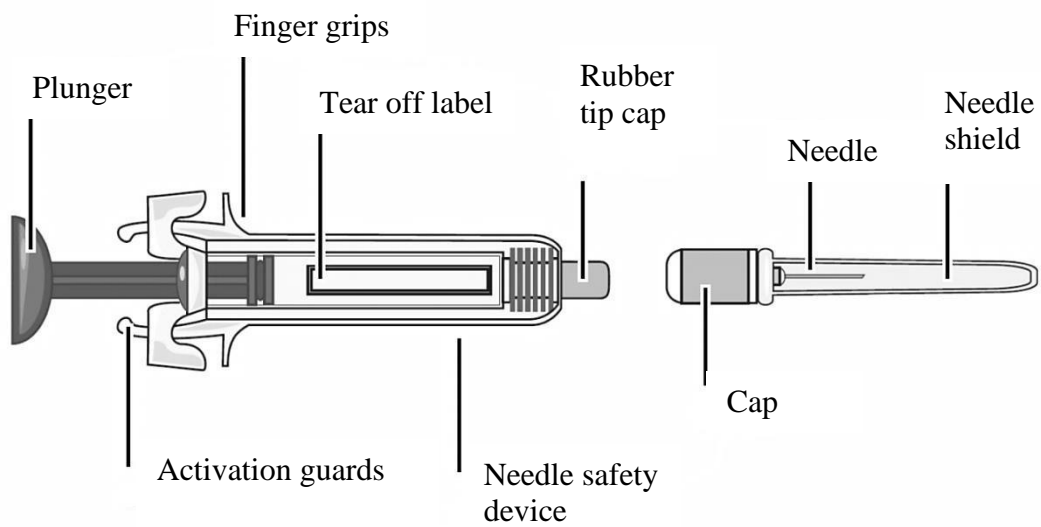


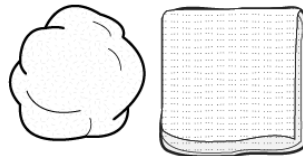
Figure A

MATERIALS NOT INCLUDED IN THE PACK (Figure B):

Cleansing
alcohol swabs



Sterile cotton
ball or gauze



Puncture-resistant container or
sharps container for safe disposal
of needle and used syringe



Figure B

Assemble all of the supplies you will need for an injection on a clean, well-lit flat surface such as a table.

HOW TO GIVE THE INJECTION

Step 1: Allow the syringe to adjust to room temperature

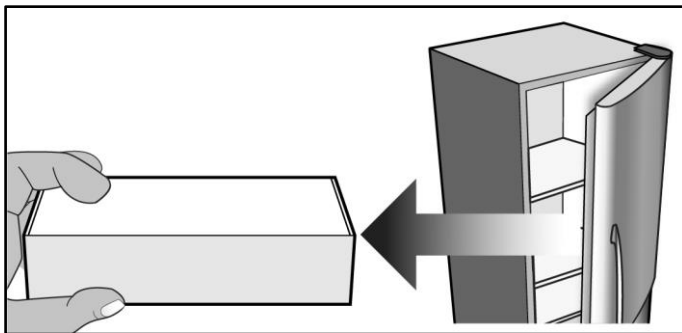


Figure C

Carefully remove the box containing the MIRCERA pre-filled syringe from the refrigerator. Keep the syringe in the box to protect it from light and allow it to reach room temperature for at least 30 minutes (Figure C).

- Not allowing the medicine to come to room temperature could result in an uncomfortable injection, and it may be difficult to depress the plunger.
- **Do not** warm up the syringe in any other way.

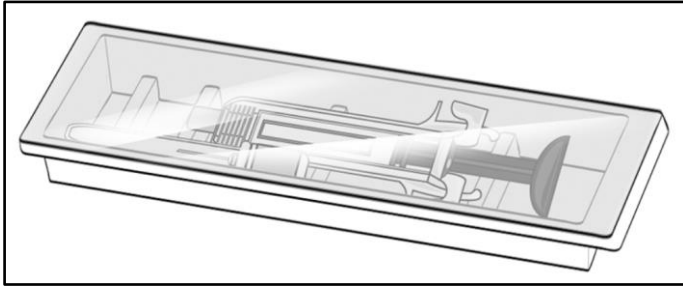


Figure D

Open the box and Remove the plastic tray with the MIRCERA pre-filled syringe without peeling back the protective film (Figure D).

Step 2: Clean your hands



Figure E

Disinfect your hands well with soap and warm water or hands sanitizer (Figure E).

Step 3: Unpack and visually inspect the pre-filled syringe

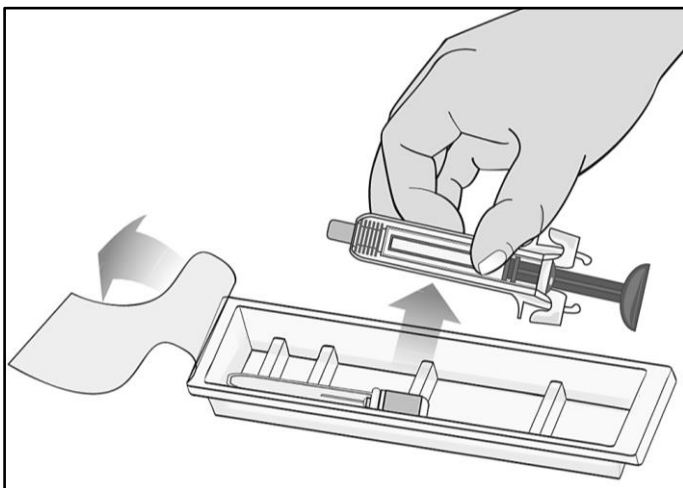


Figure F

Peel back the protective film from the plastic tray and remove the packed needle and the syringe, holding the syringe by the middle of the body without touching the activation guards (Figure F).

Only handle the syringe by the body, because any contact with the activation guards could cause premature release of the safety device.

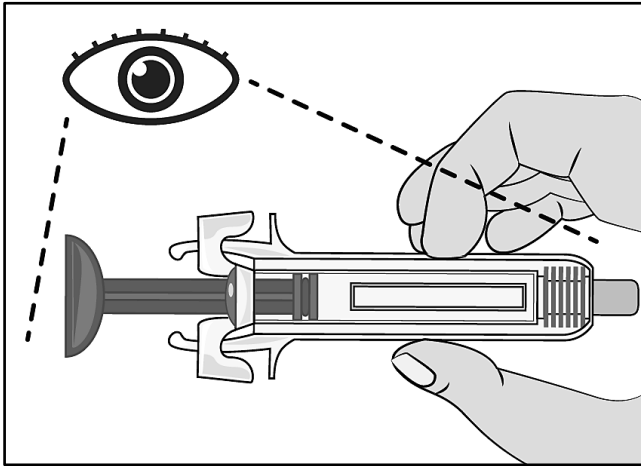


Figure G

Examine the syringe for damage and check the expiration date on the syringe and box. This is important to ensure that the syringe and medicine are safe to use (Figure G).

Do not use the syringe if:

- You have accidentally dropped the syringe.
- Any part of the syringe appears to be damaged.
- The contents are cloudy, hazy or contain particles.
- If the colour is other than colourless to slightly yellowish.
- The expiration date has passed.

Step 4. Attach the needle to the syringe

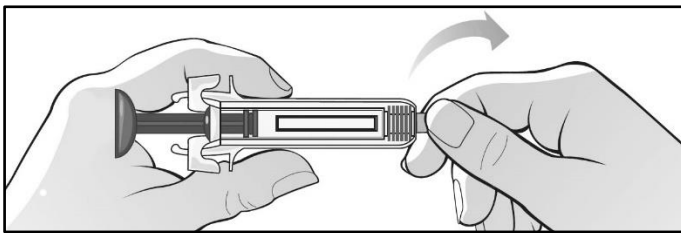


Figure H

Grasp the syringe in the middle of the body, hold the rubber tip cap firmly, and remove the rubber tip cap from the syringe (bend and pull) (Figure H).

- Once removed, immediately dispose of the rubber tip cap in the sharps/ puncture-resistant container.
- **Do not** touch the activation guards.
- **Do not** push the plunger.
- **Do not** pull on the plunger.

Grasp the packaged needle firmly in both hands. Break the seal of the needle, using a twisting motion, and remove the needle cap (Figure I).

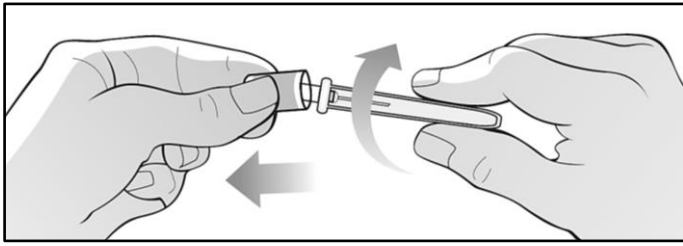


Figure I

Immediately throw away the needle cap in the sharps / puncture-resistant container or sharps container.

Do not remove the needle shield that protects the needle.

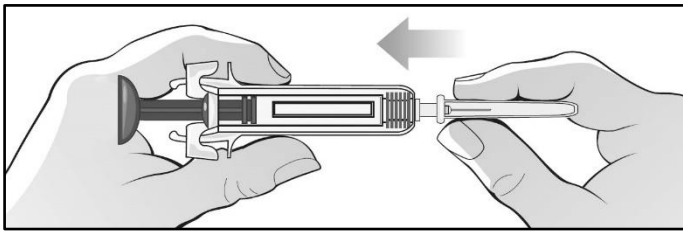


Figure J

Attach the needle to the syringe by pushing it firmly straight onto the syringe and by twisting or turning it slightly (Figure J).

Step 5. Remove the needle shield and prepare for injection

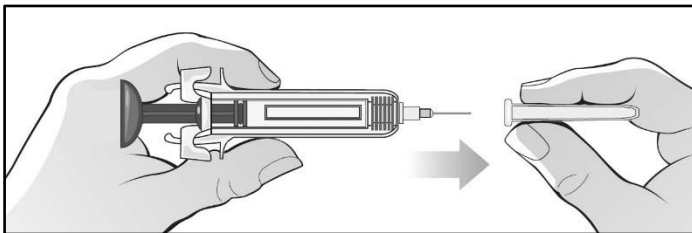


Figure K

Hold the syringe firmly with one hand in the middle of the body and pull the needle shield straight off with the other hand. Throw away the needle shield in the sharps/ puncture-resistant container or sharps container (Figure K).

- Once the needle shield is removed **do not** touch the needle or let it touch any surface, as the needle may become contaminated and may cause injury and pain if touched.
- You may see a drop of liquid at the end of the needle. This is normal.
- Never reattach the needle shield after removal.

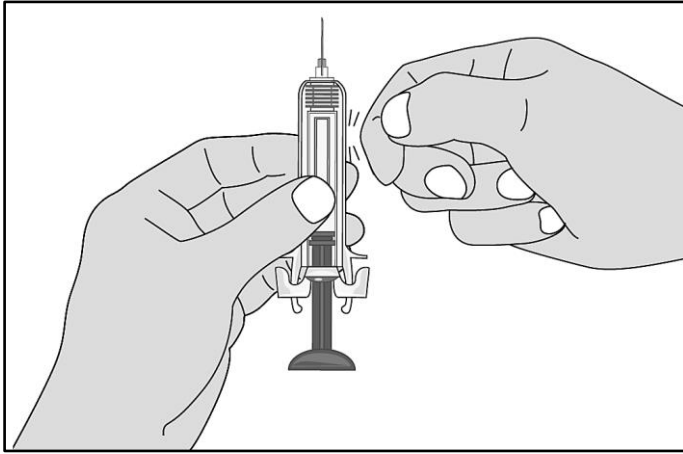


Figure L

To remove air bubbles from the pre-filled syringe, hold the syringe with the needle pointing up.

Tap the syringe gently to bring any bubbles to the top (Figure L and M).

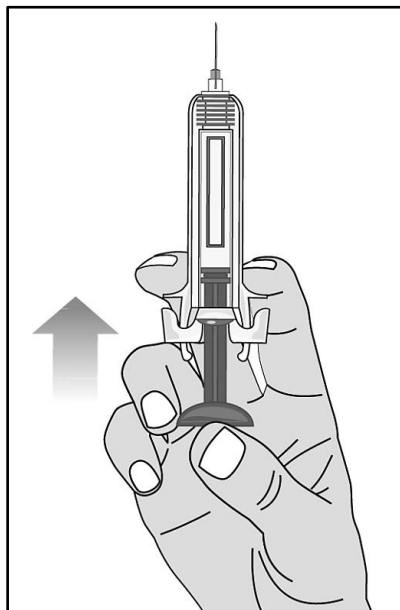


Figure M

Push the plunger up slowly to remove all air, as shown to you by a healthcare professional. (Figure M).

Step 6. Perform the injection

There are two different ways (routes) to inject MIRCERA into your body. Follow the recommendations of your healthcare professional about how you should inject MIRCERA.

SUBCUTANEOUS ROUTE:

If you are advised to inject MIRCERA under your skin, please administer your dose as described below.

Choose one of the recommended injection sites as shown.

You may inject MIRCERA into the upper arm, thigh or abdomen, but not in the area around the navel (belly button) (Figure N).

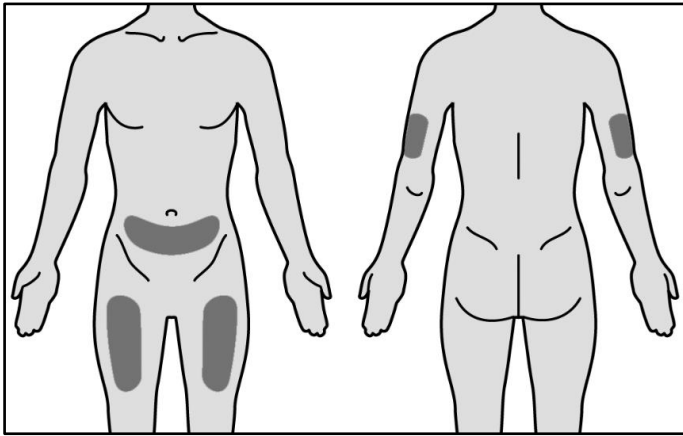


Figure N

The back of the upper arm is not a recommended site for self-injection. Use this injection site only if you inject someone else.

When selecting an injection site:

- You should use a different injection site each time you administer an injection, at least three centimeters from the area you used for the previous injection.
- **Do not** inject into areas that could be irritated by a belt or waistband.
- **Do not** inject into moles, scars, bruises, or areas where the skin is tender, red, hard or not intact.



Figure O

Clean the chosen injection site area using an alcohol pad to reduce the risk of infection; carefully follow the instructions of the alcohol pad (Figure O).

- Let the skin dry for approximately 10 seconds.
- Be sure not to touch the cleaned area prior to the injection and **do not** fan or blow on the clean area.
- Immediately throw away the alcohol pad.

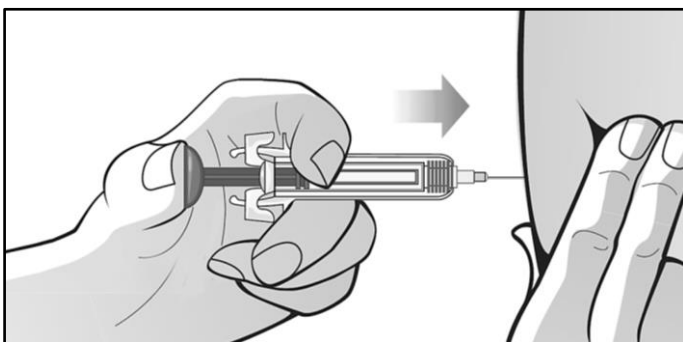


Figure P

Adopt a comfortable posture before performing an injection of MIRCERA.

To be sure the needle can be inserted correctly under the skin, use your free hand to pinch a fold of loose skin at the clean injection site. Pinching the skin is important to ensure that you inject under the skin (into fatty tissue) but not any deeper

(into muscle). Injection into muscle could result in an uncomfortable injection (Figure P).

Carefully fully insert the needle into the skin at an angle of 90° in a quick, “dart-like” motion. Then keep the syringe in position and let go of the pinch of skin.

Do not move the needle while it is inserted in the skin.

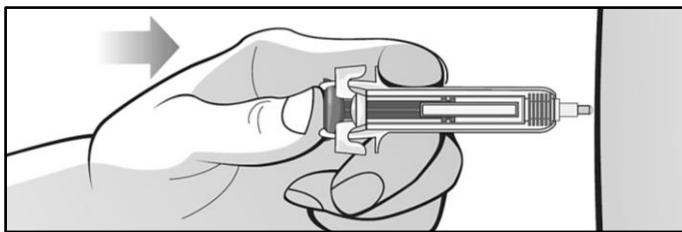


Figure Q

Once the needle is fully inserted into the skin, slowly push the plunger with your thumb while holding the syringe with the forefinger and the middle finger against the finger grips until all the medicine is injected. The plunger rod should be fully pushed down (depressed) and you should hear a click indicating the activation of the needle guard (Figure Q).

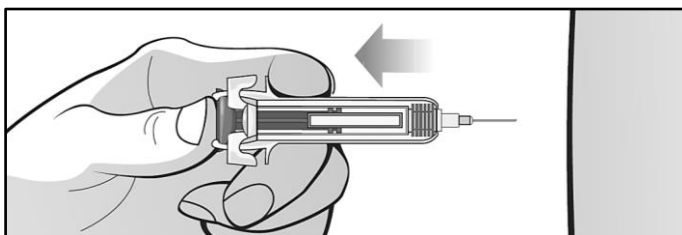


Figure R

Do not release the plunger before the end of injection or before the plunger is completely depressed.

Take the needle out of the skin **WITHOUT** releasing the plunger (Figure R).

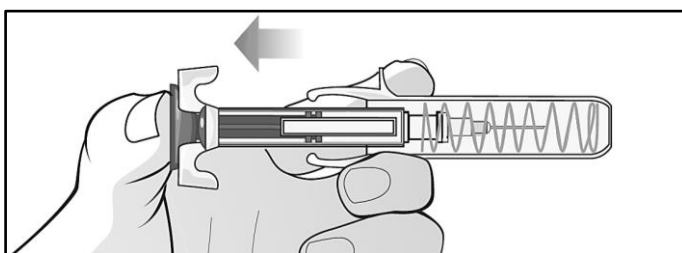


Figure S

Release the plunger, allowing the needle guard to protect the needle (Figure S).

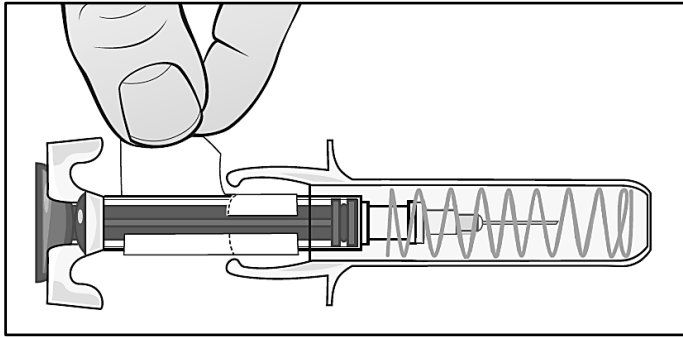


Figure T

Now, the tear-off label can be removed, if necessary (Figure T).

After the injection:

- Place a sterile cotton ball or gauze over the injection site and press for several seconds.
- Immediately throw away the cotton ball or the gauze after use.
- **Do not** rub the injection site with a dirty hand or cloth.
- If needed, you may cover the injection site with a small bandage.

Dispose of the syringe:

- Throw away used syringes in a sharps/ puncture-resistant container.
- **Do not** try to replace the needle shield on the needle.
- **Do not** throw away used syringes or the sharps/ puncture-resistant container in household trash and **do not** recycle them.
- Dispose of the full sharps/ puncture resistant container.

INTRAVENOUS ROUTE:

If your healthcare professional has recommended injection of MIRCERA into a vein, you should follow the procedure described below.

After preparation of the syringe as described in steps 1 to 5:

Clean the venous port of the hemodialysis tubing with an alcohol swab as instructed by the provider or manufacturer. Immediately throw away the alcohol swab after use.

Insert the needle of the pre-filled syringe into the **cleaned** venous port (Figure U).

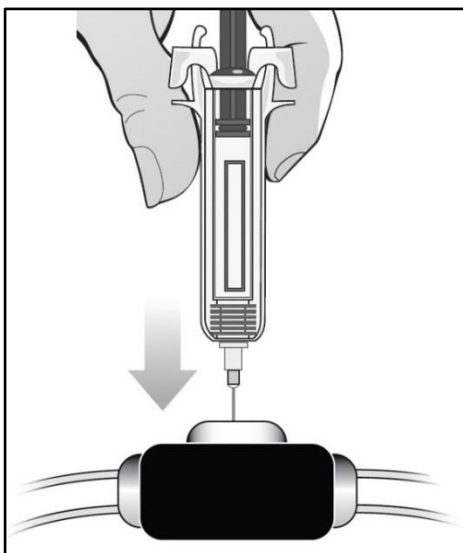


Figure U

Do not touch the injection site of the venous port

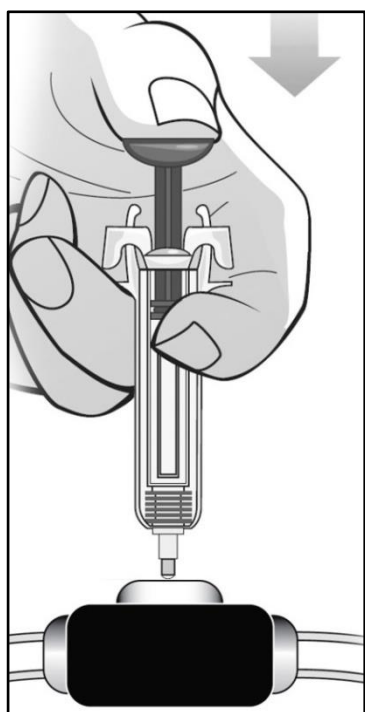


Figure V

Push the plunger with the thumb while holding the syringe with the forefinger and the middle finger against the finger grips until all the medicine is injected (Figure V).

Remove the pre-filled syringe from the venous port **WITHOUT** releasing the plunger.

Once removed release the plunger, allowing the needle guard to protect the needle.

Now, the tear-off label can be removed, if necessary (See Figure T).

Step 7: Dispose of the syringe

- Throw away used syringes in a sharps/ puncture-resistant container.
- **Do not** try to replace the needle shield on the needle.
- **Do not** throw away used syringes or the sharps/ puncture-resistant container in household trash and **do not** recycle them.

- Dispose of the full sharps/ puncture resistant container.