

## Early Access to Medicines Scheme – Treatment protocol – Information for patients

### Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation) to UK patients that have a high unmet clinical need. The medicines included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life threatening conditions where there are no adequate treatment options. More information about the scheme can be found here:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The information below is intended for you, the patient, and is provided by the pharmaceutical company that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation). More information about medicines licensing can be found here:

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm>

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. This is known as Informed consent and should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine outweigh any potential risks.

### Information for the patient

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

- Keep this protocol. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This EAMS 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.

### What is in this protocol

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

#### 1. What volanesorsen is and what it is used for

Volanesorsen is a medicine, which helps to treat a condition called familial chylomicronemia syndrome (FCS). FCS is a genetic disease which causes certain types of fats called triglycerides to be present in the blood at abnormally high levels. This can lead to inflammation of your pancreas, causing severe pain and may be life-threatening. Together with a controlled low fat diet, Volanesorsen helps your body to lower the levels of triglycerides in your blood.

#### 2. What you need to know before you use volanesorsen

**Do not use volanesorsen if:**

- you are allergic to volanesorsen sodium or any of the other ingredients in this medicine (listed in Section 6).
- If you bleed longer than usual due to a very low number of platelets in your blood - a condition called thrombocytoepenia

Do not use volanesorsen if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or a nurse before using volanesorsen.

### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before using volanesorsen if you have or have had any of the following medical problems:

- Very high triglyceride levels which are not due to FCS.
- A lack of platelets, cells in your blood that stick together to help it clot (thrombocytopenia); your doctor will do a blood test before you start using volanesorsen to check the number of platelets in your blood. After starting treatment with volanesorsen, your doctor will check the number of platelets in your blood. Depending on the number of platelets in your blood following treatment with volanesorsen, your doctor may also decide to repeat the blood tests at regular intervals. Your doctor will discuss the frequency of these blood tests with you. You must attend these blood tests as advised by your doctor.
- Any liver or severe kidney problems.

### **Children and adolescents**

Do not use volanesorsen if you are under 18 years old. This product is intended for patients aged 18 years and above.

### **Other medicines and volanesorsen**

Tell your doctor or pharmacist if you are taking, have recently taken, or are considering taking any other medicines when you are taking volanesorsen. Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines. It is important that you inform your doctor if you are already being treated with any of the following:

- Medicines to prevent blood clots or that lower the platelet numbers in your blood, e.g., aspirin or warfarin.
- Other medicines that may change how your blood clots.

### **Taking volanesorsen with food and drink**

The following may also cause interactions with your medicine, and should be avoided during your treatment.

- Foods containing high levels of fat should be avoided whilst taking volanesorsen. Other interactions with foods or drinks have not been established.
- Interactions with herbal products have not been established.

It is not advisable to drink alcohol if you have FCS. Alcohol should not be taken whilst undergoing treatment with volanesorsen.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to become pregnant, discuss this with your doctor or pharmacist before using this medicine. You should not be given volanesorsen if you are pregnant unless clearly necessary. It is not known whether volanesorsen passes into breast milk. It is recommended that you discuss breast-feeding with your doctor to see what is best for you and your child.

### **Driving and using machines**

Volanesorsen has not been shown to affect the ability of the user to drive or use machinery.

## **3. How to use Volanesorsen**

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

- Before starting volanesorsen, you should be on a diet designed to help lower triglyceride levels in your blood.
- It is important that you maintain this triglyceride-lowering diet, and do not drink alcohol whilst using volanesorsen.

You or your caregiver will be trained on how to use volanesorsen according to the instructions in this protocol. Volanesorsen should be injected under your skin in the way the doctor, nurse or pharmacist has shown you, and making sure you inject all of the liquid in the syringe. This method of injection is also known as subcutaneous injection, and is sometimes abbreviated to “s.c.”. Each dose of volanesorsen is contained within a single-use, pre-filled syringe, which delivers a dose of 300 mg in 1.5 mL. This means that, when you fully depress the plunger of the syringe, you will inject the required amount to get your full dose of volanesorsen.

Your doctor will do a blood test before you start using volanesorsen to check the number of platelets you have, and then at regular intervals once you have started using volanesorsen to keep a check on the platelet levels. Your doctor will discuss the frequency of these blood tests with you. You must attend these blood tests as advised by your doctor. If necessary, your doctor may change how often you use volanesorsen, or may stop its use for a period of time.

Before you inject your volanesorsen, it is important to allow your syringe to come to room temperature by removing it from the refrigerator for at least 30 minutes before you plan to use it. Volanesorsen should be injected on the same day of the week as previous doses.

**Before using volanesorsen, it is important that you read, understand, and closely follow the Instructions for Use.**

### **Instructions for Use**

Volanesorsen is an injection given under the skin with a single-use, disposable, prefilled syringe.

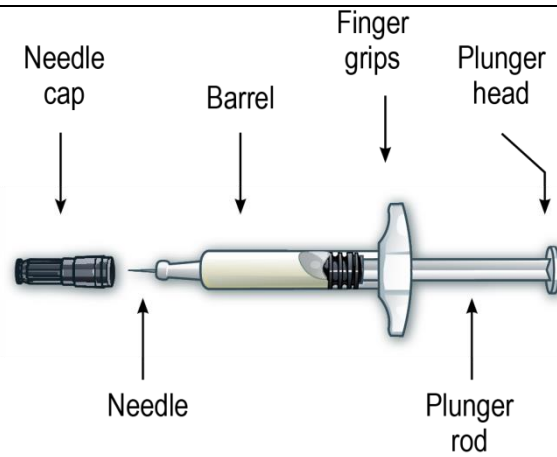
**Do not** use volanesorsen until you completely understand the procedure described below. If you have any questions about how to use volanesorsen, please contact your doctor or pharmacist.

### **Introduction to volanesorsen**

Volanesorsen is an injection given under the skin with a single-use, disposable, prefilled syringe. Before using your volanesorsen Prefilled Syringe, it is important that you read, understand, and closely follow these instructions.

Do not use the volanesorsen Prefilled Syringe until you completely understand the procedure. If you have any questions about how to use the volanesorsen Prefilled Syringe, please contact your doctor or specialist nurse.

### **Prefilled Syringe Components**



**Important Storage Information**

Store the volanesorsen Prefilled syringe in the refrigerator, or at room temperature for up to 6 weeks, before use. Refer to the “Storage” section at the end of these instructions for additional storage information.

**Important Disposal Informations**

**Do not** dispose of used syringes in the household waste. Dispose into a sharps container. For more information about device disposal refer to the section titled “After the Injection”.

**Get Ready to Inject**

**1. Wash Hands and Gather Supplies**

Wash and dry your hands well. Place these supplies on a clean, flat surface in a well-lit area (Figure A).

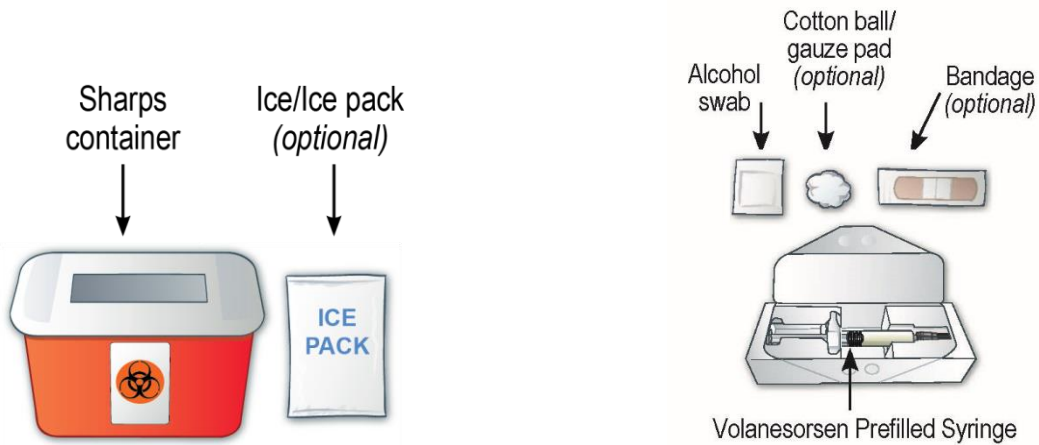


Figure A

**2. Allow to Warm to Room Temperature**

If the syringe was in the refrigerator, allow the prefilled syringe to come to room temperature for at least 30 minutes prior to the injection.

An injection with cold liquid may cause injection site reactions such as pain, redness, or swelling.

**Do not** warm syringe in any other way, such as by microwave or warm water.



### 3. Check the Expiration Date

Check the expiration date on the carton (Figure B).

The expiration date on the package refers to the life of the product when refrigerated.

**Do not** take volanesorsen if the expiration date has passed or if it was stored for longer than 6 weeks at room temperature.

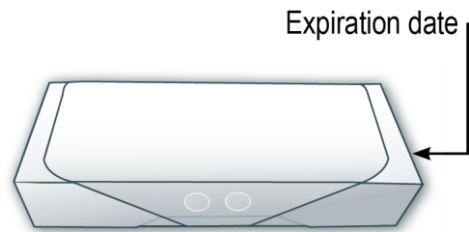


Figure B

### 4. Remove the Syringe and Inspect the Medication

Open the carton and remove the syringe by grasping the syringe barrel and pulling straight out (Figure C).

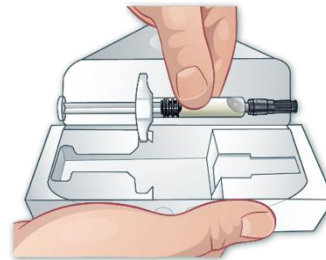


Figure C

Look at the liquid medication in the syringe. The medicine should not have particles and should be clear to slightly yellow in color. It is normal to see a large air bubble (Figure D).

**Do not** attempt to remove the air bubble.

**Do not** use the prefilled syringe if the liquid is cloudy or has floating particles.

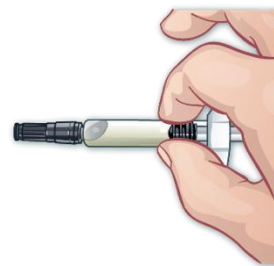


Figure D

### 5. Choose an Injection Site

#### If self-injecting:

Stomach – Stomach area as shown, except for 2 inches around the belly button.

Thighs – Front, middle area as shown (Figure E).

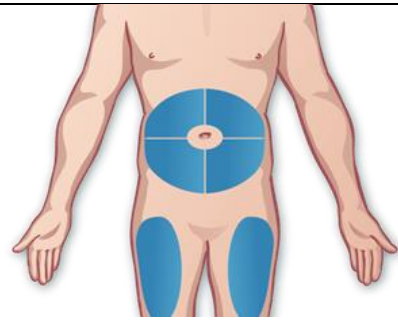


Figure E

**If administering an injection to someone else as a caregiver:**

Arms – Back of upper area as shown (Figure F).

Alternate the injection area for each injection.

Avoid injecting at the waistline where your clothing may rub or press the injection area.

**Do not** inject into tattoos, moles, scars, birthmarks, bruises, rashes, or areas where the skin is tender, red, hard, damaged, burned, or inflamed.

Talk to your healthcare provider if you are unsure of where to inject.

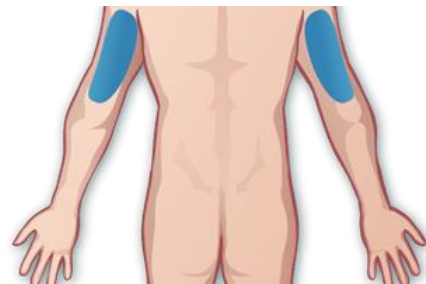


Figure F

**Injecting**

**6. Prepare Injection Site**

Ice may be applied at the injection site before injection

Clean your chosen injection site with an alcohol pad (Figure G).

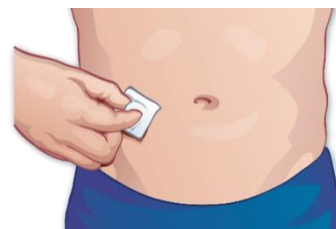


Figure G

**7. Remove Needle Cap**

Remove the needle cap by holding the barrel of the syringe with the needle pointing away from you and pulling the needle cap straight off (Figure H).

It is normal to see a drop of liquid at the tip of the needle following removal of the needle cap.

**Do not** hold the plunger rod and/or the plunger head while removing the needle cap.

**Do not** use the prefilled syringe if the needle appears damaged.

**Do not** use the prefilled syringe if it is dropped with the needle cap removed.

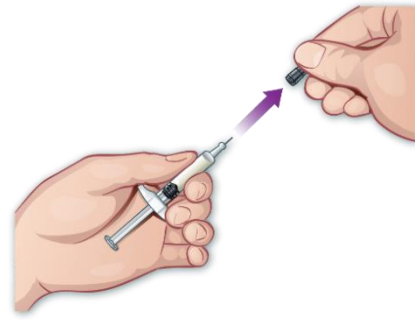


Figure H

## 8. Pinch the Skin

Using your free hand, pinch the skin around the injection site (Figure I).



Figure I

## 9. Insert Needle

Insert the needle into the injection site with a quick, firm motion without touching the plunger head (Figure J).



Figure J

## 10. Inject volanesorsen

Inject the liquid by holding the syringe with your thumb on the plunger, and **slowly push** the plunger down as far as it will go, until the syringe is completely empty (Figure K).

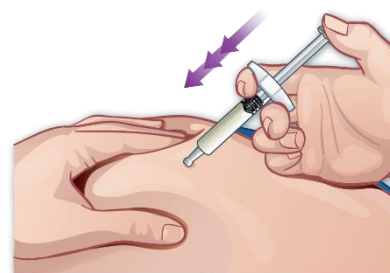


Figure K

The injection is complete when the plunger has been pressed all the way down and the liquid is injected (Figure L).



## 11. Remove Needle

Pause before removing the needle to ensure that the drug is dispensed

Remove the needle from the injection site by pulling out at the same angle it was inserted (Figure M).

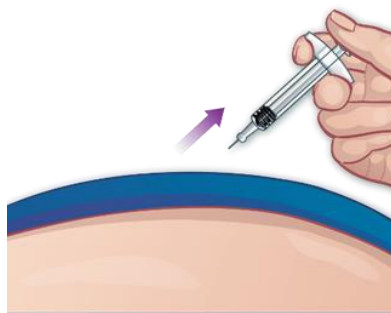


Figure M

### After the Injection

## 12. Dispose of the Use Syringe into a Sharps Container

Immediately after the injection, dispose of the used syringe as instructed by your healthcare professional or into a sharps disposal container (Figure N) by following these steps.

Throw away the needle cap after injecting.

**Do not** recap the syringe.

If you do not have a sharps disposal container, you may use a household container that is:

- Made of heavy-duty plastic,
- Capable of being closed with a tight-fitting, Puncture-resistant lid, without sharps being able to come out,
- Upright and stable during use,
- Leak-resistant,
- Properly labeled to warn of hazardous waste inside the container.



Figure N

When your sharps disposal container is almost full, you will need to follow your community guidelines for proper disposal of the sharps container. There may special local laws regarding how you should throw away used needles and syringes. See your local public health government website for more details on how you should dispose of sharps in your location.

**Do not** dispose of your used sharps disposal container in your household trash.

**Do not** recycle your used sharps disposal container.

**Always keep your sharps container away from children and pets.**

## 13. Treat the Injection Site



If you see drops of blood where you've injected, press the site lightly with the sterile cotton ball or gauze and bandage if needed (Figure O).

**Do not** rub the site after you've injected.



Figure O

You may also apply ice to the injection site to reduce pain, redness, or discomfort (Figure P).



Figure P

## Storage

### Storage Information

Store volanesorsen Prefilled Syringes in their packaging in either:

- The refrigerator 2°C-8°C (Figure Q), or
- At room temperature 8°C-30°C in a cool dry place, out of direct sunlight, for up to 6 weeks.

**Do not** freeze the volanesorsen Prefilled Syringe.

**Do not** take out of the packaging or remove the needle cap until you are ready to inject.

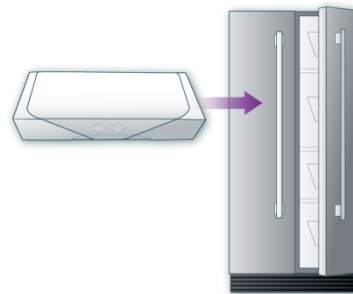


Figure Q

### If you use more volanesorsen than you should

Please contact your doctor or pharmacist, or attend a hospital emergency department immediately, even if there are no symptoms.

### If you forget to use volanesorsen, or miss a dose

If a dose is missed, take the missed dose as soon as possible. If the next scheduled dose is within 48 hours, then the missed dose should be skipped and the next planned injection taken.

### If you stop using volanesorsen

Do not stop using volanesorsen unless you have discussed stopping your medicine with your doctor.

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

The side effects that may occur with volanesorsen include:

### The most common side effects of volanesorsen include

- Low counts of platelets in your blood (platelets are cells important for blood clotting)
- Injection site reactions (pain, redness, swelling, itching, or a burning feeling at the injection site)

**Other common side effects include**

- Abdominal pain
- Headache
- Common cold
- Fatigue
- Loss of energy
- Nausea
- Vomiting
- Diarrhoea
- Localized muscle pain
- Pain in extremity
- Nose bleeds and other minor bleeding
- Round spots that appear on the skin as a result of bleeding
- Joint pains
- Diabetes

Report to your physician immediately if you experience any signs of bleeding, which can include round spots on the skin, spontaneous bruising, red blood vessels showing in the eyes, nosebleeds, bleeding from gum, blood in stools or unusually heavy menstrual bleeding, neck stiffness, atypical severe headache, or any prolonged bleeding.

**5. How to store volanesorsen**

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 carton and syringe label after 'EXP'. Please note that the expiry date refers to the last day of that month.

Volanesorsen should be stored in a refrigerator, between 2° to 8°C and within the original carton to protect from light.

Volanesorsen can also be kept at room temperature (up to 30°C) in the original carton for up to 6 weeks. If it is not used within the 6 weeks after removing from the refrigerator, the syringe should be discarded. If the expiry date on the syringe label is exceeded during the 6 week period at room temperature, the syringe should not be used and should be discarded.

Do not use this medicine if you can see that the solution is cloudy or contains particles; it should be clear and colourless to slightly yellow.

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 volanesorsen contains**

- The active substance is volanesorsen sodium.

The other ingredients are saline solution, which is made using water for injections Ph. Eur sodium hydroxide Ph. Eur., and hydrochloric acid Ph. Eur.

**What volanesorsen looks like and contents of the pack**

Volanesorsen (volanesorsen sodium injection) is provided in a carton as a single-dose syringe with needle and needle cap, prefilled with a clear, colourless to slightly yellow solution.

Volanesorsen is filled to deliver 300 mg of volanesorsen sodium in 1.5 mL of solution upon full

depression of the syringe's plunger. Each syringe carton contains this Patient Information Protocol.

Volanesorsen is available as either a carton containing 1 prefilled syringe, or as a carton containing 4, 1-pack cartons of prefilled syringes. The needle is covered with a needle cap, which is to be removed before use. Do not attempt to put the needle back in to the needle cap after use.

### **Scientific Opinion Holder**

Akcea Therapeutics UK Ltd.  
First Floor West, Davidson House,  
Forbury Square,  
Reading  
RG1 3EU

### **Additional information:**

#### **Informed Consent Form**

All patients will have the Early Access to Medicines Scheme (EAMS) explained to them using the informed consent form. The patient will be asked to sign this form and a copy will be given to them to keep.

#### **Patient Alert Card**

Each patient must be given a Patient Alert Card before they start treatment with volanesorsen. The patients must keep this alert card with them at all times during the treatment and for at least 5 months after completing their treatment with volanesorsen. The card summarises that they are currently receiving volanesorsen, the important side effects for which patients need to seek assistance should they occur, details of the patients treating physician managing their treatment, out of hours contact details and the company contact details.

### **Contact information**

#### **Contact details for reporting Adverse Events/Special Situations/Pregnancies:**

Email: [drugsafety@pharsafer.com](mailto:drugsafety@pharsafer.com)

Tel number: +44 1483 212150

Fax number: +44 1483 212178

#### **Contact email for the EAMS programme (excluding AE reporting):**

[EAMS@CALIGORRX.COM](mailto:EAMS@CALIGORRX.COM)