

Package leaflet: Information for the user

CRYSVITA 10 mg solution for injection
CRYSVITA 20 mg solution for injection
CRYSVITA 30 mg solution for injection

burosumab

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

1. What CRYSVITA is and what it is used for

What CRYSVITA is

CRYSVITA contains the active substance burosumab. This is a type of medicine called a human monoclonal antibody.

What is CRYSVITA used for

CRYSVITA is used to treat X-linked hypophosphataemia (XLH). It is used in children and adolescents aged 1 to 17 years, and in adults.

What is X-Linked Hypophosphataemia (XLH)

X-Linked Hypophosphataemia (XLH) is a genetic disease.

- People with XLH have higher levels of a hormone called fibroblast growth factor 23 (FGF23).
- FGF23 lowers the amount of phosphate in the blood.
- The low level of phosphate may:
 - lead to bones that may not harden properly and, in children and adolescents, cannot grow properly
 - result in pain and stiffness in bones and joints

How CRYSVITA works

CRYSVITA attaches to FGF23 in the blood which stops FGF23 from working and increases the phosphate levels in the blood so that normal levels of phosphate can be achieved.

2. What you need to know before you use CRYSVITA

Do not use CRYSVITA if

- you are allergic to burosumab or any of the other ingredients of this medicine (listed in section 6)
- you are taking any phosphate supplements or certain vitamin D supplements (that contain so called active vitamin D, e.g. calcitriol)
- you already have a high level of phosphate in your blood (“hyper-phosphataemia”)
- you have severe kidney disease or kidney failure.

Allergic reactions

Stop taking CRYSVITA and contact your doctor straight away if you have any of the following side effects, as they could be signs of an allergic reaction:

- rash and itching all over the body
- severe swelling of eyelids, mouth or lips (angio-oedema)
- shortness of breath
- rapid heartbeat
- sweating.

Do not take CRYSVITA if any of the above apply to you. If you are not sure, talk to your doctor before using CRYSVITA.

Warnings and precautions

Skin reactions

You may get skin reactions where the injection is given, see section 4 for more information. If these reactions are severe, tell your doctor.

Tests and checks

Your doctor will check the phosphate and calcium levels in your blood and urine and may also do a renal ultrasound during your treatment in order to reduce the risk of hyperphosphataemia (too much phosphate in the blood) and ectopic mineralisation (a build-up of calcium in tissues such as the kidneys). Your serum parathyroid hormone level will also be checked from time to time.

Children under 1 year

CRYSVITA should not be given to children under 1 year of age because the safety and effects of the medicine have not been studied in this age group.

Other medicines and CRYSVITA

Tell your doctor if you are taking, have recently taken, or might take any other medicines.

Do not take CRYSVITA and tell your doctor if you are taking:

- phosphate supplements
- certain vitamin D supplements (that contain so called active vitamin D, e.g. calcitriol). There are some vitamin D supplements you can continue or start to use and your doctor will advise which ones these are.

Talk to your doctor before taking CRYSVITA if you are taking:

- medicines that work in the same way as calcium in the body (“calcimimetics”). If used together they may lower blood calcium.

Pregnancy and breastfeeding

If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. This is because it is not known if CRYSVITA will affect the baby.

CRYSVITA is not recommended in pregnancy.

If you could get pregnant, you must use an effective method of contraception (birth control) while using CRYSVITA. You should discuss this with your doctor.

It is not known if CRYSVITA passes into breast milk, and a risk to newborns or infants cannot be ruled out. You should discuss this with your doctor.

Driving, riding a bike and using machines

It is possible that CRYSVITA could cause dizziness and affect you being able to ride a bike, use any tools or machines or to drive. If you think you are affected, do not ride a bike, use any tools or machines or drive, and tell your doctor.

CRYSVITA contains sorbitol

This medicine contains 45.91 mg of sorbitol in each vial which is equivalent to 45.91 mg/ml.

3. How to use CRYSVITA

CRYSVITA should be given by injection under the skin (subcutaneous use) in the upper arm, abdomen, buttock or thigh. This medicine will be given to you or your child by a . healthcare provider. Alternatively, your doctor may recommend that you inject yourself or your child. A healthcare provider will show you how to do this. The first self-injection after start of treatment or after any dose change should be carried out in front of them. A detailed 'Instructions for Use' section is provided at the end of this leaflet. Always follow these instructions carefully when giving yourself or your child the CRYSVITA injection.

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

How much CRYSVITA you will need

The dose is based on your body weight. Your doctor will work out the right dose for you.

Your CRYSVITA dose will need to be injected:

- every two weeks in children and adolescents aged 1 - 17 years
- every four weeks in adults

Your doctor will perform checks to make sure that you are getting the right dose and may change your dose if needed.

The maximum dose you will be given is 90 mg.

If you have been given more CRYSVITA than you should

If you think that you have been given too much CRYSVITA, tell your doctor straight away.

If you miss a dose of CRYSVITA

If a dose is missed, talk to your doctor straight away. The missed dose should be given as soon as possible and your doctor will re-arrange future doses accordingly.

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

4. Possible side effects

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

Side effects in children and adolescents

Very common (may affect more than 1 in 10 children and adolescents)

- Tooth abscess (infection)
- Cough
- Headache
- Dizziness
- Vomiting
- Nausea
- Diarrhoea
- Constipation
- Tooth decay or cavities
- Rash
- Pain in muscles (myalgia) and hands and feet
- Reactions where the injection was given, which may include:
 - redness or rash
 - pain or itching
 - swelling
 - bleeding or bruisingThese injection site reactions are usually mild and occur within a day after the injection and usually get better in around 1 to 3 days.
- Fever
- Low vitamin D in your blood

Not known (frequency cannot be estimated from the available data)

- Increased phosphate in your blood

Side effects in adults

Very common (may affect more than 1 in 10 adults)

- Tooth abscess (infection)
- Headache
- Dizziness
- Restless legs syndrome (irresistible urge to move your legs to stop uncomfortable, painful or odd sensations in the legs especially prior to sleep or at night time)
- Pain in back
- Muscle spasm
- Low vitamin D in your blood

Common (may affect up to 1 in 10 adults)

- Constipation
- Increased phosphate in your blood

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via 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 CRYSVITA

Keep CRYSVITA out of the sight and reach of children.

Do not use CRYSVITA after the expiry date which is stated on the carton and label after “EXP”.

The expiry date refers to the last day of that month.

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

Keep the vial in the outer carton in order to protect from light.

Do not use CRYSVITA if it contains visible particles.

Do not throw away any medicines via wastewater or household waste. These measures will help protect the environment.

If self-injecting, see step 5 of the ‘Instructions for Use’ in the end of the Package Leaflet for instructions on disposal of unused medicines and supplies.

If you have questions on how to throw away medicines you no longer use, ask your healthcare provider or pharmacist.

6. Contents of the pack and other information

What CRYSVITA contains

The active substance is burosumab. Each vial contains either 10, 20 or 30 mg of burosumab.

The other ingredients are L-histidine, D-sorbitol (E420), polysorbate 80, L-methionine, 10%, hydrochloric acid, and water for injections. (See “CRYSVITA contains sorbitol” in section 2 for more information).

What CRYSVITA looks like and contents of the pack

CRYSVITA comes as a clear to slightly opalescent, colourless to pale yellow/brown solution for injection in a small glass vial. Each pack contains 1 vial.

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INSTRUCTIONS FOR USE

Read these Instructions for Use carefully before you use CRYSVITA:

- Only inject yourself or your child if you have been told to do so by your doctor.
- You should only inject after you have been trained in injection technique. The first self-injection after start of treatment or after any dose change should be carried out in front of a healthcare provider.
- Always use this medicine exactly as your doctor, pharmacist or nurse (healthcare provider) has told you. Check with your healthcare provider if you are not sure.
- Your doctor will prescribe your correct dose. Your dose is measured in milligrams (mg). CRYSVITA is available in three different strength vials: 10 mg, 20 mg, and 30 mg. Each vial is for single use only. Always use a new CRYSVITA vial for each injection, see step 5 on how to dispose used vials and other supplies.
- Your healthcare provider will tell you how much CRYSVITA to give yourself or your child. You or your child may be given more than one vial to get the correct dose.
- If your healthcare provider tells you that more than one injection is needed to give your required dose, you must repeat the following Steps 2-5 for each injection. Use new supplies and a different site on the body for each injection.
- Only use the syringe and needles provided or prescribed by your healthcare provider to give the injection.
 - Always use the large needle to withdraw the liquid and remember to change to the small needle to inject the liquid.
 - Using the wrong syringe or needle can lead to a mistake in your dose or make the injection more painful.
- When giving CRYSVITA to a young child, it may be helpful to have another person present to provide support.
- Do not use CRYSVITA if allergic to any ingredients of this medicine. Stop using CRYSVITA if you have any allergic reaction during or after the injection and contact your healthcare provider straightaway. See section 2 of the package leaflet for more information.

Step 1. Gather and Inspect Supplies

Remove the CRYSVITA vials you need from the refrigerator.

Check the strength on the label of each vial.

Make sure that you have the correct number of vials to match the dose in mg as advised by your healthcare provider.

If you are not sure, ask your healthcare provider for advice.

Let the vials warm to room temperature for 30 minutes. Do not warm the vials in any other way, such as with hot water or a microwave oven. Do not put the vials in direct sunlight.

Check the expiry date (shown after EXP) on the label of the vial.

Inspect the liquid in the vial. Do not shake.

Do not use the vial if it is:

- past the expiry date
- discoloured, cloudy or contains any particles. CRYSVITA liquid should be clear to slightly opalescent, colourless to pale brown-yellow.



Place all the items you will need on a clean, flat surface. For each injection you will need:

- A. Vial(s) of CRYSVITA for injection
- B. One syringe with plunger
- C. One large syringe needle to withdraw CRYSVITA
- D. One small syringe needle to inject CRYSVITA
- E. Alcohol wipes
- F. Sharps container
- G. Plaster (if required)
- H. Gauze pad or cotton wool

Contact your healthcare provider if you do not have these supplies.

Your healthcare provider will explain the use of different needles.

The **large needle** is used for withdrawing CRYSVITA from the vial.

The **small needle** is used for injecting CRYSVITA.

If you are not sure, ask your healthcare provider for advice before use.

Do not use any items that have missing pieces or are damaged in any way.

Do not remove the caps from the needles until you are ready to use them.

Wash your hands thoroughly with soap and water before going to Step 2.

STEP 2. Withdraw CRYSVITA and Prepare Injection

Remove the sealing cap from the vial to reveal the rubber stopper.

Clean the rubber stopper with an alcohol wipe and let it dry. Don't touch the rubber stopper after cleaning it.



Select the **large** needle and remove from the sterile packaging but do not remove the cap covering the needle.

To attach the needle to the syringe, hold the **large** needle by the protective cap in one hand and the syringe by the barrel in the other hand.

Depending on the supplies you have been given;

- you will need to push the needle down and turn clockwise onto the syringe until tight
- **or** push the needle down until it is firmly attached.

Do not touch the needle itself or the end of the syringe where the needle attaches.

Once the needle is firmly attached, hold the syringe by the barrel with the needle pointing up. Remove the needle cap by pulling it straight off.

Do not throw the needle cap away.

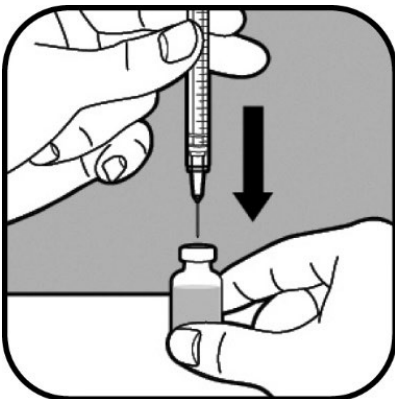
Do not touch the needle or allow the needle to touch any surface once the cap has been removed.
Do not use the syringe if you drop it after removing the cap or if the needle appears damaged.



Your healthcare provider will tell you how much liquid you need to inject. This will normally be 1ml for each injection. Your healthcare provider will show you which mark to use if you need to inject less than 1ml.

Always use the mark equal to your dose. If you are not sure, ask your healthcare provider for advice before use.

Pull back the syringe plunger until the end of the plunger lines up with mark equal to your dose. This fills the syringe with air.



Keep the vial on a flat surface.

Slowly insert the large needle through the rubber stopper and into the vial.

Do not let the tip of the needle touch the liquid in the vial.

If the tip of the needle touches the liquid, slowly pull the needle until it no longer touches the liquid.

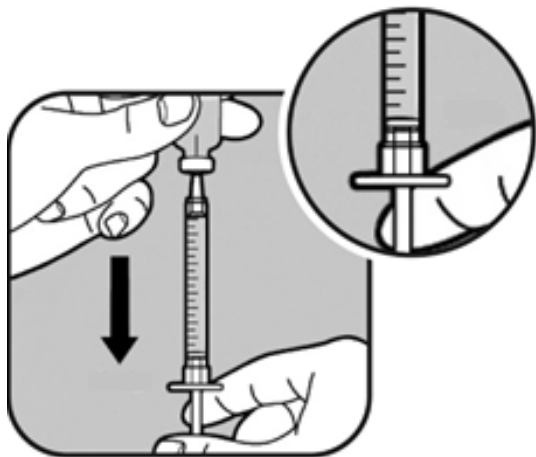
Slowly push the plunger into the syringe.

This pushes air from the syringe into the vial.

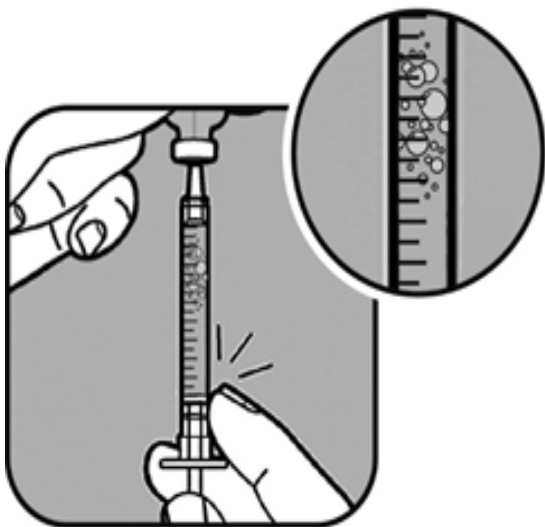


Keep the needle in the vial and turn the vial upside down.

Make sure the tip of the needle is at the bottom of the liquid.



Slowly pull back the plunger to fill the syringe until the end of the plunger lines up with the mark equal to your dose.
Keep the tip of the needle in the liquid at all times.



Check the liquid in the syringe for air bubbles.

If you see bubbles,

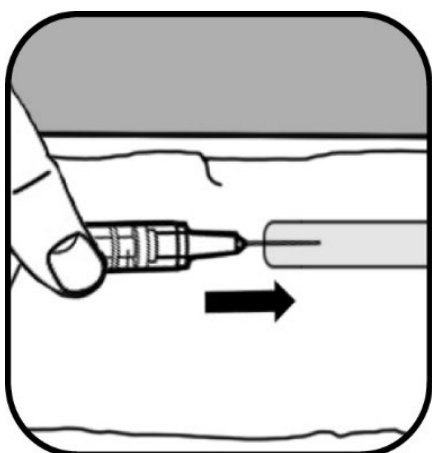
- keep the syringe upright with the needle still inside the vial,
- gently tap the barrel with your finger to move the air bubbles,
- when the air bubbles are at the top, slowly push the plunger to push out the air bubbles.

Check your dose again against the markings on the syringe.

If required, withdraw some more liquid to line up with the mark equal to your dose.

Check again for bubbles and repeat the process if required.

When there are no bubbles in the syringe, pull the syringe and needle straight down out of the vial.



Remove the large needle from the syringe.

- To do this, take the large needle cap and place on a flat surface.
- Using one hand, slide the large needle into the cap and scoop upward to cover the needle without using your other hand to avoid injury. Then use your other hand to secure the cap and snap into place.
- Depending on your supplies, you will;
 - need to twist the capped large needle anti-clockwise to remove from the syringe
 - or pull the capped large needle straight from the syringe and place in the sharps container.

Select the **small** needle and remove from the sterile packaging but do not remove the cap covering the needle.

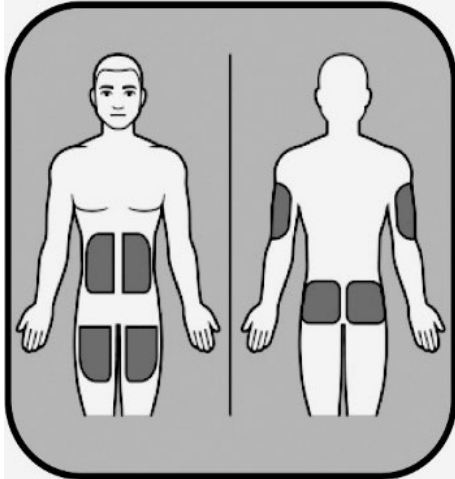
To attach the needle to the syringe, hold the **small** needle by the protective cap in one hand and the syringe by the barrel in the other hand.

Depending on the supplies you have been given,

- you will need to push the needle down and turn clockwise onto the syringe until tight
- **or** push the needle down until it is firmly attached.

Do not touch the needle itself or the end of the syringe where the needle attaches.

Step 3. Prepare the Injection Site



The injection must be given into the fatty layer just below the skin. You will need to choose an injection site. If you are giving the injection to yourself, suitable areas are:

- stomach area, upper thighs

If you are giving the injection to someone else, suitable areas are:

- stomach area, upper thighs, outer area of upper arms, buttocks

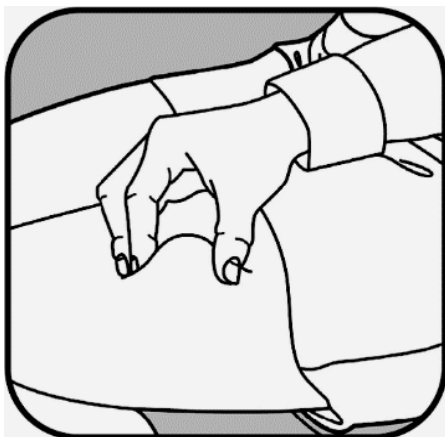
Do not inject:

- an area that is sore, red, bruised or where the skin is broken
- an area that has stretch marks or scars (including burns)
- directly into a mole, or an area around a mole

If you are giving more than one injection, use a different site for each injection. Clean each injection site with a new alcohol wipe and leave the skin to dry.

CRYSVITA should be injected into clean dry skin.

Step 4. Inject CRYSVITA



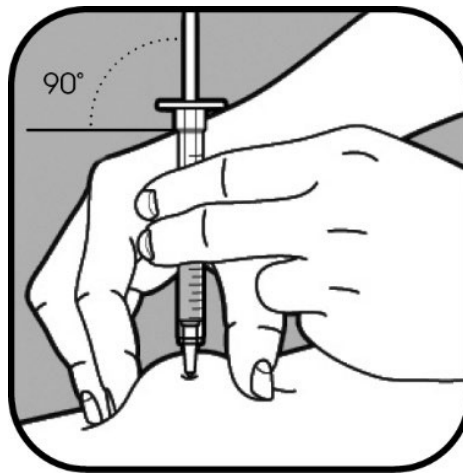
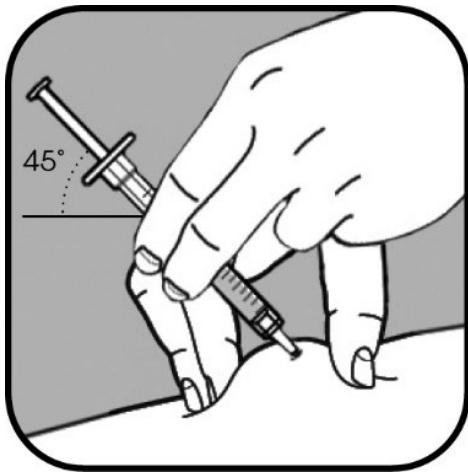
Remove the small needle cap by pulling it straight off.

Pinch the skin firmly between your thumb and fingers, creating an area about 5 cm wide.

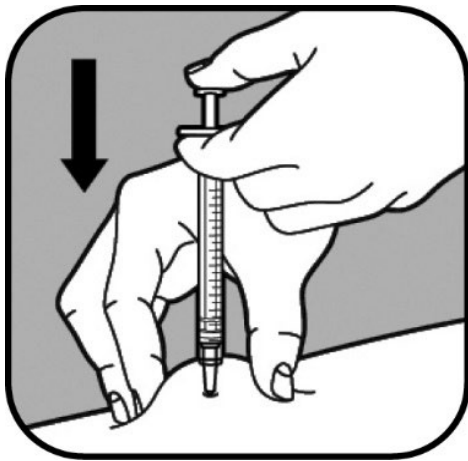
Hold the syringe between the thumb and index finger of your dominant hand.

The needle should be inserted into the skin at a 45° angle or 90° angle.

Your healthcare provider will show you which angle you should use.

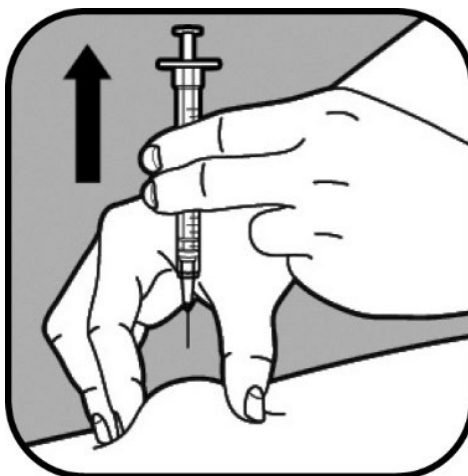


Use a quick 'dart-like' motion to insert the needle into the pinched skin.
Do not push the plunger when inserting the needle.



When the needle is inserted do not move it around.

Keep pinching the skin.
Slowly push the plunger into the syringe, for up to 30 seconds, until the syringe is empty.



After you have given the full dose, remove the injection by gently pulling the syringe straight out.

Release the pinched skin.
Press the injection site with a cotton ball or gauze pad for a few seconds to stop bleeding. Apply a plaster if needed.

Do not rub the injection site.

To avoid any injury, do not put the cap back on the small needle. Place the uncapped needle in the sharps disposal container.

Step 5. After each injection

Put your used needles, caps and syringes in the sharps disposal container; vials should be discarded according to your local guidelines.

Do not throw away needles or syringes in your household waste.

Do not save vials with leftover medicine for future use or pass it on to others.

When your sharps container is almost full, you will need to follow your local guidelines to request another container and to dispose of it correctly.

Reminder: If you are giving more than one injection, repeat steps 2-5 for each injection.

Use new supplies for each injection.

Note the date of the injection and all the areas where you have injected so that you use different sites for the next injection.

A video showing you how to prepare and give the injection is available on the following link:

www.myinject.eu