

Package leaflet: Information for the user

CRYSVITA 10 mg solution for injection in pre-filled syringe
CRYSVITA 20 mg solution for injection in pre-filled syringe
CRYSVITA 30 mg solution for injection in pre-filled syringe

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

CRYSVITA 10 mg solution for injection in pre-filled syringe: This medicine contains 15.30 mg sorbitol in each pre-filled syringe.

CRYSVITA 20 mg solution for injection in pre-filled syringe: This medicine contains 30.61 mg sorbitol in each pre-filled syringe.

CRYSVITA 30 mg solution for injection in pre-filled syringe: This medicine contains 45.91 mg sorbitol in each pre-filled syringe.

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 can be given to you by a healthcare provider, or alternatively, your doctor may recommend that you or your caregiver can inject CRYSVITA. If you are suggested to self-inject, a healthcare provider will provide training to show you or your caregiver the correct way to use CRYSVITA before the first self-injection.

The first self-injection after start of treatment or after any dose change should be carried out in front of the healthcare provider. A detailed 'Instructions for Use' section for using the pre-filled syringe is provided at the end of this leaflet. 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 or frequency of dose if needed.

The maximum dose you will be given for the treatment of XLH 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 with XLH***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 bruising

These 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 with XLH***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)
- Constipation
- Pain in back
- Muscle spasm
- Reactions where the injection was given, which may include pain or swelling.
- Low vitamin D in your blood

Common (may affect up to 1 in 10 adults)

- Rash
- 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 pre-filled syringe 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 4 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.

10 mg pre-filled syringe:

Each pre-filled syringe contains 10 mg of burosumab in 0.33 ml solution.

20 mg pre-filled syringe:

Each pre-filled syringe contains 20 mg of burosumab in 0.67 ml solution.

30 mg pre-filled syringe:

Each pre-filled syringe contains 30 mg of burosumab in 1 ml solution.

The other ingredients are L-histidine, D-sorbitol (E 420), 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 pre-filled syringe. Each pack contains 1 pre-filled syringe.

The different strengths of the medicinal product can be identified by a different coloured plunger rod: 10 mg (blue), 20 mg (red), and 30 mg (green).

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INSTRUCTIONS FOR USE

The following Instructions for Use are intended for:

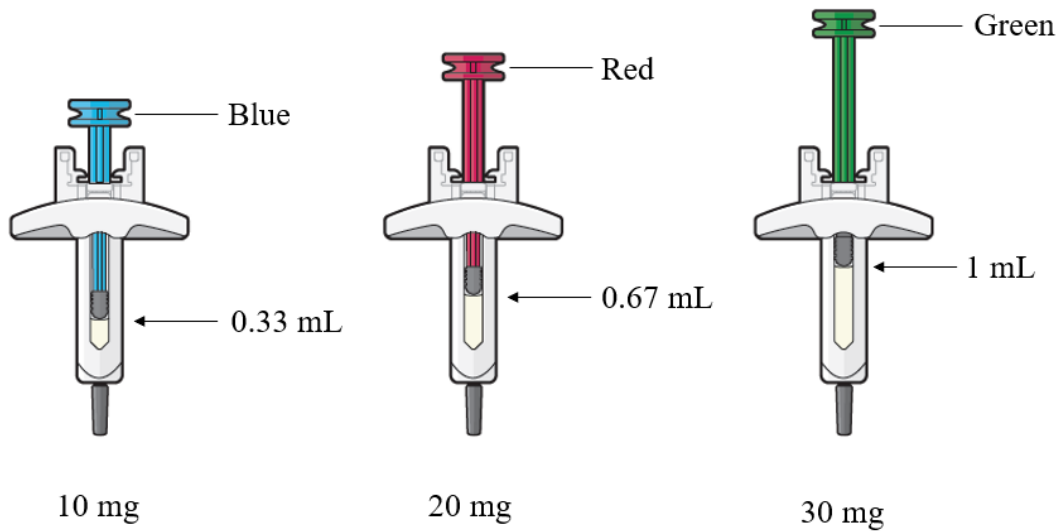
- **self-administration**
- **administration by a caregiver or healthcare professional**

Read these Instructions for Use carefully before you use CRYSVITA:

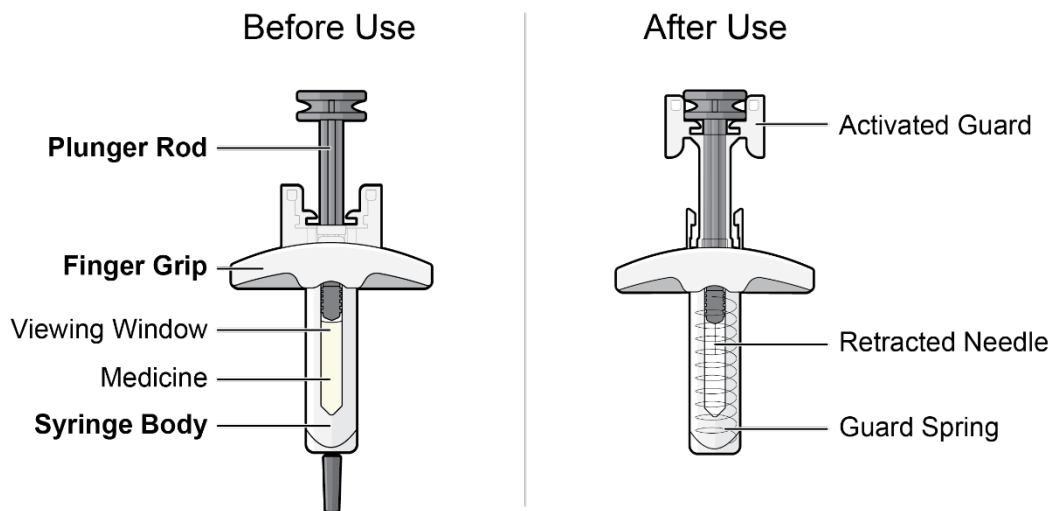
- Only give this medicine to yourself or someone else if you have been told to do so by your doctor.
- You should only give this medicine to yourself or someone else after you have been trained in injection technique. The first self-injection after start of treatment or after any dose change should be carried out in front of a doctor, pharmacist, or nurse (healthcare provider).
- Always use this medicine exactly as your 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).
- Your healthcare provider will tell you how much CRYSVITA to give yourself or someone else. You may need more than one pre-filled syringe 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 2-4 for each injection.
- Use new supplies for each injection.
- Each pre-filled syringe is for single use only. Always use a new CRYSVITA pre-filled syringe for each injection, see step 4 on how to dispose used syringes and other supplies.
- When possible, use a different site on the body for each injection.
- 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.

CRYSVITA is available in three different strengths of pre-filled syringe: 10 mg (blue), 20 mg (red), and 30 mg (green). The amount of liquid in the pre-filled syringes varies per strength. The syringes you will be given will depend upon your prescribed dose.

These instructions are used for all three strengths.



The parts of the CRYSVITA pre-filled syringe are shown below:



Step 1. Gather and Inspect Supplies

CRYSVITA should be stored in a refrigerator before use. When you need to give CRYSVITA to yourself or someone else, take CRYSVITA out of the refrigerator, but keep it in the carton. Place the carton on a clean, flat surface.

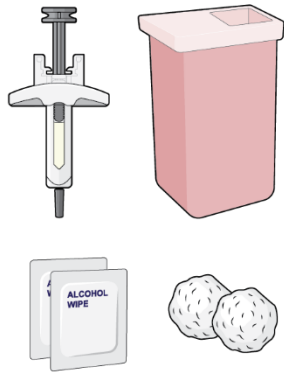
Look at the CRYSVITA cartons to check the strength of each pre-filled syringe you have been given. Make sure that you have the correct number of syringes, and correct strengths of each pre-filled syringes to match the dose in mg as advised by your healthcare provider. If you are not sure, ask your healthcare provider for advice.

Let the pre-filled syringe carton warm to room temperature **for 45 minutes**. **Do not** warm the pre-filled syringe in any other way, such as with hot water or a microwave oven. **Do not** put the pre-filled syringe in direct sunlight.

After 45 minutes, open the carton and remove the plastic tray. Gently grasp the pre-filled syringe by the syringe body and remove from the tray.

Do not lift the syringe by the plunger rod or needle cap.

Do not touch the plunger rod or remove the needle cap until you are ready to use them.



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

- CRYSVITA pre-filled syringe
- Alcohol wipes
- Sharps container
- Gauze pad or cotton wool

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

Do not use the pre-filled syringe if the needle cap is missing or not securely attached.

Do not use the pre-filled syringe if it is cracked or broken in any way.

Check the strength on the label of each pre-filled syringe.

Check the expiry date (shown after EXP) on the label of each pre-filled syringe.

Do not use the pre-filled syringe if it is past the expiry date.

Inspect the liquid in the pre-filled syringe. Do not shake.

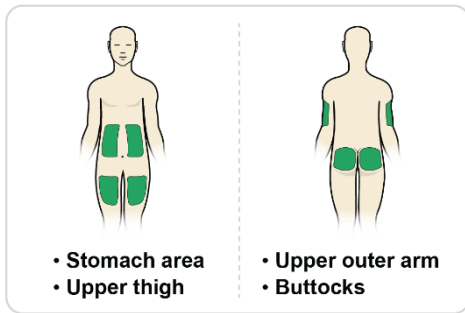
CRYSVITA liquid should be clear to slightly opalescent, colourless to pale brown-yellow.

Note: It is normal for the medicine to have air bubbles. Air bubbles will not harm you or affect your dose.

Do not use the pre-filled syringe if the liquid is discoloured, cloudy or contains any particles.

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

Step 2. 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:

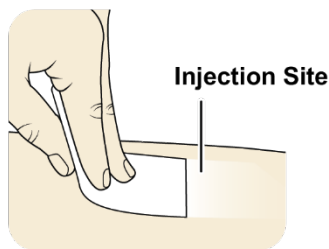
- stomach area, upper thighs

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



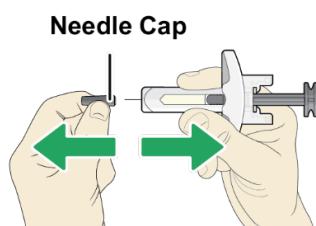
Clean the injection site with an alcohol wipe and let it air dry.

Do not touch or blow on the clean injection site.

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 air dry.

CRYSVITA should be injected into clean dry skin.

Step 3. Inject CRYSVITA



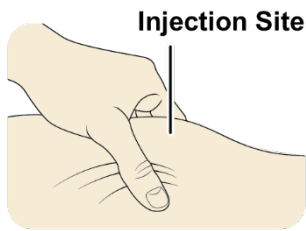
Hold by the **syringe body** with one hand and with the **needle cap pointed away from you**.

Pull the **needle cap straight off** with your other hand.

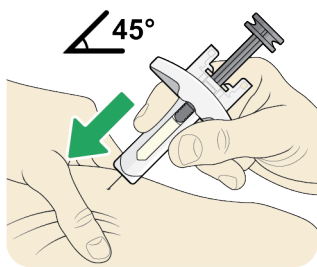
Do not twist the needle cap.

Throw the needle cap away in an approved sharps container.

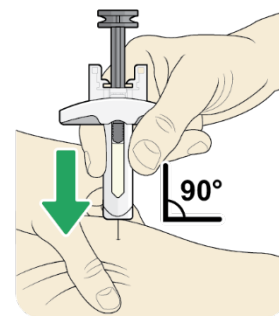
- **Do not touch the needle or plunger rod.**
- **Do not allow the needle to touch any surface once the cap has been removed.**
- **Do not use the syringe if you drop it after removing the cap or if the needle appears damaged.**



Without touching the clean injection site, pinch the surrounding skin firmly between your thumb and fingers, creating an area about 5 cm wide.

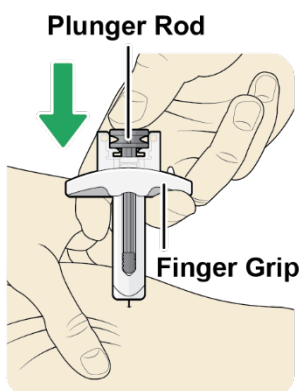


OR



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 tell 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. Grasp the **finger grip** with one hand and **slowly and steadily push** the **plunger rod** all the way down until the syringe is empty.

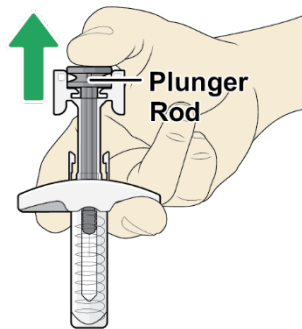
Do not remove the needle yet.

After you have given the full dose, **keep the syringe at the same injection angle** and remove by gently pulling the syringe straight out.

Do not tilt the syringe while removing it.

Do not rub the injection site.

Release the pinched skin.



Release the plunger rod. The guard will activate and cover the needle.

To avoid any injury, **do not** put the cap back on the needle.

Do not touch any exposed needle.

If there is any bleeding, press the injection site with a cotton ball or gauze pad for a few seconds.

Step 4. After each injection

Put your used caps and syringes in the sharps disposal container.

Do not throw away syringes in your household waste.

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 2-4 for each injection. Use new supplies for each injection.

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