**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

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

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- 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

**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 tell 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 in the arm, abdomen, buttock or thigh by a trained healthcare provider.

**How much CRYSVITA you will be given**
The dose is based on your body weight. Your doctor will work out the right dose for you.

CRYSVITA will 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
- 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

***Common (may affect up to 1 in 10 children and adolescents)***
- Dizziness

***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.
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.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 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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**This leaflet was last revised in September 2020**

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.

The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

**Other sources of information**
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.