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# Crysvita (*burosumab*)

An overview of Crysvita and why it is authorised in the EU

## What is Crysvita and what is it used for?

Crysvita is a medicine used for the treatment of X-linked hypophosphataemia, a hereditary disorder characterised by low levels of phosphate in the blood (hypophosphataemia). Phosphate is essential to build bones and teeth and to maintain their strength, so patients may develop rickets and other bone deformities and growth problems. Crysvita can be used to treat children and adolescents between 1 and 17 years of age when signs of bone disease are seen on X-rays, and in adults.

Crysvita is also used to treat osteomalacia (softening and weakening of the bones) caused by phosphaturic mesenchymal tumours. This type of tumour produces hormones, particularly a substance called fibroblast growth factor 23 (FGF23), which cause the body to lose phosphate. Crysvita is used in patients from 1 year of age, when the tumour cannot be located or removed by surgery.

Crysvita contains the active substance burosumab.

These diseases are rare, and Crysvita was designated an 'orphan medicine' (a medicine used in rare diseases). Further information on the orphan designations can be found on the European Medicines Agency's website (X-linked hypophosphataemia: 15 October 2014; phosphaturic mesenchymal tumour: 16 April 2018).

## How is Crysvita used?

The medicine can only be obtained with a prescription and treatment should be started by a doctor experienced in the management of patients with bone diseases caused by alterations in the body's chemical processes.

Crysvita is given as an injection under the skin every two or four weeks, depending on the patient's age. The recommended starting dose depends on the disease being treated and on the patient's age and weight. The dose is also adjusted according to the patient's phosphate levels in the blood.

For further information about using Crysvita, see the package leaflet or contact your doctor or pharmacist.

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## How does Crysvita work?

Phosphate levels are largely controlled by the kidneys, which either remove excess phosphate or returns it to the bloodstream when needed. Patients with X-linked hypophosphataemia or tumour-induced osteomalacia have abnormally high levels of FGF23, which causes the kidneys to stop returning phosphate into the bloodstream.

Crysvita is a monoclonal antibody (a type of protein) designed to recognise and attach to the FGF23 protein. By attaching to the FGF23 protein, the medicine blocks its activity, allowing the kidneys to return phosphate and restore normal levels of phosphate in the blood.

## What benefits of Crysvita have been shown in studies?

**X-linked hypophosphataemia**

Crysvita reduced the severity of rickets (bone deformities) as shown in X-rays in patients with X-linked hypophosphataemia.

The medicine was assessed in one main study in 52 children aged between 5 and 12 years. All the children received Crysvita either every two weeks or every four weeks. The main measure of effectiveness was a reduction in the severity of rickets in the wrist and knee measured on a scale from 0 (normal) to 10 (severe). The average score before treatment (baseline score) was 1.9 points in children given Crysvita every 2 weeks, and this fell by 1.0 point after 64 weeks of treatment; in those given the medicine every 4 weeks the baseline score of 1.7 fell by 0.8 point. In addition, phosphate levels in the blood improved over time in both groups, particularly those given Crysvita every 2 weeks. A study in 13 younger children shows that Crysvita is effective in those aged between 1 and 4 years.

Another study investigated the use of Crysvita in 134 adults. Patients were given Crysvita or placebo (a dummy treatment) every four weeks for 24 weeks, and the main measure of effectiveness was the normalisation of phosphate levels in the blood. The study showed that blood phosphate levels returned to normal values in 94% of patients given Crysvita, compared with 8% of patients on placebo.

**Tumour-induced osteomalacia**

Crysvita has been shown to increase phosphate levels in the blood and improve bone health in adults with tumour-induced osteomalacia, where the tumour could not be located or removed by surgery.

In a first study in 14 adults with tumour-induced osteomalacia, 7 patients achieved normal levels of phosphate in the blood after about 6 months of treatment. In addition, improvement in bone health was observed after about a year of treatment.

In a second study in 13 adults with tumour-induced osteomalacia, phosphate levels in the blood increased to normal levels and remained stable throughout the study (up to 2.7 years).

Based on data available in patients under 18 years of age with X-linked hypophosphataemia and the fact that both conditions are caused by high levels of FGF23, Crysvita is expected to also be effective in children and adolescents with tumour-induced osteomalacia.

## What are the risks associated with Crysvita?

In children, the most common side effects with Crysvita (which may affect more than 1 in 10 people) are injection site reactions (such as skin redness, itching, rash, pain and bruising), cough, headache, fever, pain in arms and legs, vomiting, tooth abscess, decreased vitamin D level, diarrhoea, rash, nausea (feeling sick), constipation, dental caries (cavities) and muscle pain.

In adults, the most common side effects (which may affect more than 1 in 10 people) are back pain, injection site reactions, headache, tooth infection, restless legs syndrome, muscle spasms, constipation, decreased vitamin D level and dizziness.

Oral phosphate and active forms of vitamin D (such as calcitriol) must not be used during treatment with Crysvita. Also, Crysvita must not be used in patients with high phosphate levels in the blood or in patients with severe kidney disease.

For the full list of side effects and restrictions with Crysvita see the package leaflet.

## Why is Crysvita authorised in the EU?

Crysvita was shown to reduce the severity of bone deformities in the wrist and knee and improve the level of phosphate in the blood of children with X-linked hypophosphataemia. The medicine was also effective at improving phosphate blood levels in adults. Crysvita was further shown to have beneficial effects on phosphate levels and bone health in patients with tumour-induced osteomalacia. The medicine's side effects are considered manageable. The European Medicines Agency therefore decided that Crysvita's benefits are greater than its risks and recommended that it can be authorised for use in the EU.

## What measures are being taken to ensure the safe and effective use of Crysvita?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Crysvita have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Crysvita are continuously monitored. Side effects reported with Crysvita are carefully evaluated and any necessary action taken to protect patients.

## Other information about Crysvita

Crysvita received a conditional marketing authorisation valid throughout the EU on 19 February 2018. This was switched to a full marketing authorisation on 21 September 2022.

Further information on Crysvita can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/crysvita

This overview was last updated in 09-2022.