

Abbreviated Prescribing Information: **CRYSVITA® (Burosumab)**

Based on Singapore Package Insert. Kyowa Kirin Asia Pacific Pte. Ltd. (Date of Revision: FEB 2023)

Indications and usage:

CRYSVITA is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.

Dosage and Administration:

CRYSVITA is administered by subcutaneous injection and should be administered by a healthcare provider. Discontinue oral phosphate and/or active vitamin D analogs (e.g. calcitriol, paricalcitol, doxercalciferol, calcifediol) 1 week prior to initiation of treatment. Fasting serum phosphorus concentration should be below the reference range for age prior to initiation of treatment. The maximum volume of CRYSVITA per injection is 1.5 mL. If multiple injections are required, administer at different injection sites.

For pediatric patients (1 to less than 18 years of age), the recommended starting dose regimen is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks. The minimum starting dose is 10 mg up to a maximum dose of 90 mg. After initiation of treatment with CRYSVITA, measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is above the lower limit of the reference range for age and below 5 mg/dL, continue treatment with the same dose. Follow dose adjustment schedule below to maintain serum phosphorus within the reference range for age.

For adult patients (18 years of age and older), the recommended dose regimen is 1 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every four weeks. After initiation of treatment with CRYSVITA, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is within the normal range, continue with the same dose.

CONTRAINDICATIONS

CRYSVITA is contraindicated:

- In concomitant use with oral phosphate and/or active vitamin D analogs (e.g. calcitriol, paricalcitol, doxercalciferol, calcifediol) due to the risk of hyperphosphatemia.

- When serum phosphorus is within or above the normal range for age
- In patients with severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism.

Warnings and Precautions:

Hypersensitivity: Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients with CRYSVITA. Discontinue CRYSVITA if serious hypersensitivity reactions occur and initiate appropriate medical treatment.

Hyperphosphatemia and Risk of Nephrocalcinosis: Increases in serum phosphorus to above the upper limit of normal may be associated with an increased risk of nephrocalcinosis. For patients already taking CRYSVITA, dose interruption and/or dose reduction may be required based on a patient's serum phosphorus levels.

Injection Site Reactions: Administration of CRYSVITA may result in local injection site reactions. Discontinue CRYSVITA if severe injection site reactions occur and administer appropriate medical treatment.

Adverse Reactions:

The following adverse reactions are described below and elsewhere in the labeling:

- Hypersensitivity
- Hyperphosphatemia and Risk of Nephrocalcinosis
- Injection Site Reactions

Adverse reactions (≥10%) reported in paediatric patients during clinical trials were: Pyrexia, Injection site reaction, Cough, Vomiting, Pain in extremity, Headache, Tooth abscess, Dental caries, Diarrhea, Vitamin D decreased, Constipation, Rash, Nausea, Myalgia, Toothache and Dizziness.

Adverse reactions (>5%) reported in adult patients during clinical trials were: Back pain, Headache, Tooth infection, Restless legs syndrome, Vitamin D decreased, Dizziness, Muscle spasms, Constipation and Blood phosphorus increased.

PLEASE REFER TO FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.



INSTRUCTIONS FOR USE

CRYSVITA® (burosumab)
injection for subcutaneous use

CRYSVITA® is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.¹



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This material is for Healthcare Professionals Only



INSTRUCTIONS FOR USE

CRYSVITA® (burosumab) injection for subcutaneous use



Before you begin

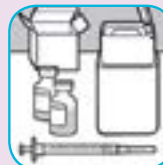
Although you and your staff may be familiar with the preparation of drug suspensions and the administration of depot injections, it is important that you read all the instructions below for specifically administering burosumab. Please refer to the burosumab Prescribing Information for the recommended weight-based dose regimen. This dose is measured in milliliters (mL). Use the needle(s) indicated in the guidance below.

Important information

Before you use burosumab, read this important information:

- **If, based on the dose regimen, you need to inject more than one vial of medicine, repeat Steps 2–4 in these Instructions for Use**
- Burosumab should only be administered by a trained healthcare professional, using aseptic technique and sterile disposable syringes and injection needles
- When administering the injection to a young child, it may be helpful to have a colleague, parent or carer present to provide support. Keep all medicines out of the sight and reach of children
- Store in a refrigerator (2°C to 8°C).¹ Do not freeze. Keep the vial in the outer carton in order to protect from light
- **DO NOT** use any part that has missing pieces, appears to have been tampered with or is damaged or broken
- **DO NOT** shake the vial before use
- Each vial is for single use only. Do not re-use
- **ALWAYS** use one needle to draw medicine into the syringe and a **new** needle to administer burosumab to the patient

STEP 1



Gather and inspect supplies

Remove the number of medicine vials you will need from the refrigerator. Place the medicine vial or vials and the additional supplies listed in the previous section on a clean, flat surface. If you are giving a second injection, you will need four needles, two syringes and two medicine vials for each patient.

DO NOT use the same needles or syringe for the second injection.

DO NOT remove the needle cover until you are ready to inject.

Check the expiration date on the label of the medicine vial. **DO NOT** use a medicine vial if it is past the expiration date.

Inspect the medicine in the vial. Only use the medicine if it is clear to slightly opalescent, colourless to pale yellow/brown, and free of visible particles. **DO NOT** shake.

Let the medicine vial warm to room temperature for 30 minutes. **DO NOT** try to warm the kit in any other way, such as with hot water or a microwave.

00:30

Wash your hands thoroughly with soap and water.



STEP 2

NOTE: You will repeat this step if you are giving a second injection.



Remove the sealing cap from the medicine vial.



Clean the rubber stopper of the vial with an alcohol wipe. Be careful not to touch the rubber stopper after cleaning it.



Remove the needle cover by pulling it straight off. **DO NOT** twist the needle cover. **DO NOT** touch the needle after the needle cover has been removed.



Pull back the plunger until it is even with the dose you have calculated using the burosumab Prescribing Information. This fills the syringe with air. **DO NOT** twist or bend the needle. **DO NOT** use the syringe if you drop it after removing the needle cap or if the needle appears damaged.



With the medicine vial right side up on the work surface, slowly insert the needle through the rubber stopper and into the medicine vial. **DO NOT** let the tip of the needle go into the medicine. If the needle does go into the medicine, withdraw the needle/syringe from the vial until the needle is no longer in the medicine before continuing.



Slowly push the plunger into the syringe. This pushes air from the syringe into the medicine vial. Doing this will help you draw the medicine into the syringe.



Turn the medicine vial, with the needle/syringe still in it, upside down.

STEP 2 CONTINUED



Hold the medicine vial and needle/syringe straight up and down. Make sure the needle is in the medicine. This will help stop air bubbles from getting into the syringe.



Slowly pull the medicine into the syringe by pulling back the plunger until the volume is equivalent to that of the dose you have calculated, according to the patient's weight and the information in the Prescribing Information.¹



If there are no bubbles in the syringe, pull the needle out of the medicine vial. Be careful not to touch the needle

If you see bubbles in the syringe, lightly tap the syringe to bring the air bubbles to the top. Then gently push the plunger in slightly to push the air out of the syringe.

Make sure that the right amount of medicine is still in the syringe. If you need to add medicine, insert the needle/syringe into the medicine vial, turn it upside down, and pull back the plunger until you have the correct amount.

Put the needle cap on a clean, flat surface with something firm to 'push' the needle cap against. Insert the needle/syringe into the cap and push the capped needle against a firm object to fit the cap firmly onto the needle. Carefully remove the needle/cap from the syringe and replace it with a new, identical needle before moving to Step 3.



Clean each injection site with a new alcohol wipe.

STEP 3

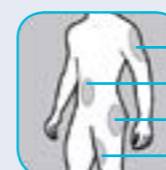
NOTE: You will repeat this step if you are giving a second injection.

Prepare the injection site

Choose an injection site.

You can use:

- Arm
- Abdomen
- Buttock
- Thigh



DO NOT inject into an area that is tender, red, bruised, hard, or that has stretch marks.

The maximum volume per injection site is 1.5 mL. If more than 1.5 mL is required, the total volume of burosumab should be split and administered at two different injection sites.¹

STEP 4

NOTE: You will repeat this step if you are giving a second injection.

Inject

The injection site must be firm so that the needle goes into the fatty tissue.

You can make the injection site firm by using the pinch method as shown:

Pinch method

Pinch the skin firmly between your thumb and fingers, creating an area about 2 inches (5 centimeters) wide.

Hold the pinch throughout the injection.

Hold the syringe between your thumb and index finger. Use a quick 'dart-like' motion to insert the needle straight (90° angle) into the fatty tissue of the injection site. The entire needle should go all the way into the skin.

Push the plunger down until the syringe is empty.

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

DO NOT recap the needle.

REMINDER: If you are giving a second injection, repeat Steps 2–4.

Use new needles, syringe and medicine vial.

Choose a different injection site.

STEP 5

Clean up

Immediately after the injection(s), put the used needle(s)/syringe(s) into a sharps container.

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

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