CRYSVITA®
burosumab

DOSING AND ADMINISTRATION GUIDE IN PEDIATRIC AND ADULT PATIENTS

CRYSVITA® (burosumab) solution for injection

INDICATION

CRYSVITA® is indicated for the treatment of X-linked hypophosphataemia (XLH), in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.[1]

PLEASE REFER TO THE FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.

This material is for Healthcare Professionals Only

Kyowa KIRIN

CRYSVITA® DOSING SCHEDULE IN PEDIATRIC PATIENTS[1]

Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. Vitamin D replacement or supplementation with inactive forms may be started or continued as per local guidelines under monitoring of serum calcium and phosphate.[1]

At initiation, fasting serum phosphate concentration should be below the reference range for age.[1]

Dosing in children and adolescents aged 1 to 17 years old is every 2 weeks.

Recommended starting dose: **0.8 mg/kg** of body weight, **rounded to the nearest 10 mg.** The **minimum starting dose is 10 mg. The maximum dose of 90 mg.**

After initiating treatment with burosumab, **fasting serum phosphate** should be measured every 2 weeks for the first month of treatment, every 4 weeks for the following 2 months and thereafter as appropriate. **fasting serum phosphate** should also be measured 4 weeks after any dose adjustment. If **fasting serum phosphate** is within the reference range for age, the same dose should be maintained.[1]

Sample Starting Dose Calculation – Pediatric (1 to 17 years)

Patient weight (kg) x Recommended starting dose (0.8mg/kg)

Example: 23 kg x 0.8 mg/kg = 18.4 mg **(Round to nearest 10 mg)**
Starting dose CRYSVITA® = 20 mg

STARTING AND STAYING ON TRACK WITH CRYSVITA® IN PEDIATRIC PATIENTS[1]

HEALTHCARE PROVIDER

Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. Vitamin D replacement or supplementation with inactive forms may be started or continued as per local guidelines under monitoring of serum calcium and phosphate. At initiation, **fasting** serum phosphate concentration should be below the reference range for age.[1]

WEEK 0/ DAY 1	• Administer first dose
WEEK 2	• Administer next dose. Maintain dosage (see page 6) • Measure **fasting** serum phosphate level
WEEK 4	• Measure **fasting** serum phosphate level **WITHIN range:** • Administer next dose. Maintain dosage **BELOW range:** • Increase dose stepwise, as recommended (see page 6) **ABOVE range:** • Withhold doses at Week 4 and Week 6 • **Fasting** serum phosphate reassessed within **4 weeks**
WEEK 6	**If dose was administered at Week 4:** • Administer next dose. Maintain dosage **If dose was NOT administered at Week 4:** • Withhold dose
WEEK 8	• Measure **fasting** serum phosphate level **If CRYSVITA® was administered at Week 4, and fasting serum phosphate levels are:** **WITHIN range:** • Administer next dose. Maintain dosage **BELOW range:** • Increase dose stepwise, as recommended (see page 6) **ABOVE range:** • Withhold doses at Week 8 and Week 10 • **Fasting** serum phosphate test reassessed within **4 weeks** **If CRYSVITA® was NOT administered at Week 4, and fasting serum phosphate levels are BELOW the normal range at Week 8:** • Restart CRYSVITA®, increase dose stepwise, as recommended (see page 6) • **Fasting** serum phosphate reassessed within **4 weeks**
WEEK 10	• Repeat steps outlined at Week 6, as appropriate
WEEK 12 AND BEYOND	• Repeat steps outlined at Week 8, as appropriate • Continue to administer the next dose every 2 weeks • Assess **fasting** serum phosphate level, as appropriate • **Fasting** serum phosphate should be measured 4 weeks after dose adjustment. Burosumab should not be adjusted more frequently than every 4 weeks.

To avoid large fluctuations in phosphate levels and for optimal efficacy results, patients should adhere as closely as possible to the established CRYSVITA® treatment schedule.

Carefully monitored for signs of potential reactions.

Always rotate injection site to a different anatomic location (upper arms, abdomen, buttock or thigh) than the previous injection.

Please refer to the full prescribing information before prescribing.

CRYSVITA® burosumab

CRYSVITA® DOSING SCHEDULE IN ADULT PATIENTS[1]

Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. Vitamin D replacement or supplementation with inactive forms may be started or continued as per local guidelines under monitoring of serum calcium and phosphate.[1]

At initiation, fasting serum phosphate concentration should be below the reference range for age.[1]

Dosing in adult patients (≥18 years of age) is every 4 weeks

The recommended starting dose in adults is **1.0 mg/kg** of body weight, **rounded to the nearest 10 mg** up to a **maximum dose of 90 mg.**

After initiation of treatment with burosumab, **fasting serum phosphate** should be measure every 2 weeks for the first month of treatment, every 4 weeks for the following 2 months and thereafter as appropriate. **Fasting serum phoshate** should be measured 2 weeks after the previous dose of burosumab. If serum phosphate is within the normal range, the same dose should be continued.

Sample Starting Dose Calculation: Adult patient (≥18 years of age)

Patient weight (kg) x Recommended starting dose (1 mg/kg)

Example: 77 kg x 1 mg/kg = 77 mg **(Round to nearest 10 mg)**
Starting dose CRYSVITA® = 80 mg

STARTING AND STAYING ON TRACK WITH CRYSVITA® IN ADULT PATIENTS[1]

HEALTHCARE PROVIDER

Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. Vitamin D replacement or supplementation with inactive forms may be started or continued as per local guidelines under monitoring of serum calcium and phosphate. At initiation, **fasting** serum phosphate concentration should be below the reference range for age.[1]

WEEK 0/ DAY 1	• Administer first dose
WEEK 2	• Measure **fasting** serum phosphate level **WITHIN range:** • Administer next dose in **2 weeks** • Maintain dosage **ABOVE range:** • Withold the next dose • Serum phosphate level reassessed within **2 weeks**. The patient must have serum phosphate below the normal range before restarting burosumab. • Once serum phosphate is below the normal range, treatment may be restarted at half the initial starting dose up to a maximum dose of 40 mg every 4 weeks. Serum phosphate should be reassessed **2 weeks** after any change.
WEEK 4	• Administer next dose • Maintain dosage
WEEK 6	• Repeat steps as outlined at Week 2, as appropriate
WEEK 8	• Repeat steps as outlined at Week 4, as appropriate
WEEK 10	• Repeat steps as outlined at Week 6, as appropriate
WEEK 12 AND BEYOND	• Assess **fasting** serum phosphate level, as appropriate • Serum phosphate should be reassessed 2 weeks after any change in dose.

To avoid large fluctuations in phosphate levels and for optimal efficacy results, patients should adhere as closely as possible to the established CRYSVITA® treatment schedule.

Carefully monitored for signs of potential reactions.

Always rotate injection site to a different anatomic location (upper arms, abdomen, buttock or thigh) than the previous injection.

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CRYSVITA® burosumab

DOSE ADJUSTMENTS FOR PEDIATRIC PATIENTS[1]

Dose Increase

If serum phosphate level is **below** the reference range for age, the dose may be increased stepwise by 0.4 mg/kg up to a maximum dose of 2.0 mg/kg (maximum dose of 90 mg). **Fasting** serum phosphate should be measured 4 weeks after dose adjustment. Burosumab should not be adjusted.

Dose Decrease

If fasting serum phosphate is **above** the reference range for age, the next dose should be withheld and the fasting serum phosphate reassessed within 4 weeks.

The patient must have fasting serum phosphate **below** the reference range for age to restart burosumab at half of the previous dose, rounding the amount as described above.

Dose Conversion at age 18 years

Children and adolescents aged 1 to 17 years should be treated using the dosing guidance outlined above. At **18 years of age** the patient should **convert** to the **adult dose** and dosing regimen as outlined below.

DOSE ADJUSTMENTS FOR ADULT PATIENTS[1]

Dose Decrease

If serum phosphate is **above** the upper limit of normal range, the next dose should be withheld and the serum phosphate level reassessed within 2 weeks. The patient must have serum phosphate below the normal range before restarting burosumab. Once serum phosphate is below the normal range, treatment may be restarted at half the initial starting dose up to a maximum dose of 40 mg every 4 weeks. Serum phosphate should be reassessed 2 weeks after any change in dose.

MISSED DOSE[1]

Treatments may be administered 3 days either side of the scheduled treatment date if needed for practical reasons. If a patient misses a dose, burosumab should be resumed as soon as possible at the prescribed dose.

Burosumab should not be adjusted more frequently than every 4 weeks.

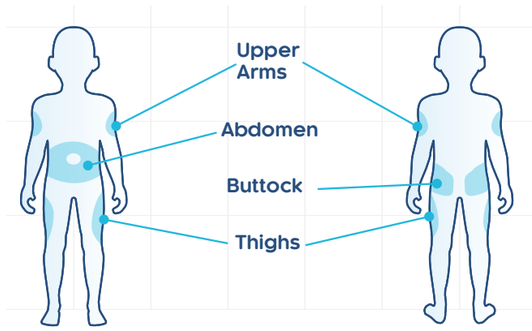
CRYSVITA® ADMINISTRATION FOR SUBCUTANEOUS USE AND STORAGE[1]

CRYSVITA® should be administered subcutaneously by a healthcare professional

- Inject in the upper arm, abdomen, buttock or thigh.
- Do not inject into moles, scars, or areas where the skin is tender, bruised, red, hard, or not intact.

The maximum volume of CRYSVITA® per injection site is 1.5 ml If more than 1.5 ml is required on a given dosing day, the total volume of medicinal product must be split and administered at two or more different injection sites.

Injections sites should be rotated and carefully monitored for signs of potential reactions.



CRYSVITA® Storage

- Visually inspect CRYSVITA® for particulate matter and discoloration prior to administration.
- CRYSVITA® is a sterile, preservative-free, clear to slightly opalescent, colorless to pale brown-yellow solution for subcutaneous injection.
- Do not use if the solution is discolored or cloudy or if the solution contains any particles or foreign particulate matter
- The product is available as one single-dose vial per carton in the following strengths : **10, 20, 30 mg/ml.**

Store in original package to protect from light until use, under refrigerated conditions at **2°C to 8°C.**

Do not freeze or shake. Do not use CRYSVITA® after the expiry date which is stated on the package and label. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Please refer to the full prescribing information before prescribing.

CRYSVITA® Abbreviated Product Information

CRYSVITA® (burosumab) Malaysia Package Insert. September 2022, Version 1

INDICATIONS AND USAGE: CRYSVITA® is indicated for the treatment of X-linked hypophosphataemia, in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.

DOSAGE AND ADMINISTRATION: Treatment should be initiated by a physician experienced in the management of patients with metabolic bone diseases. Oral phosphate and active vitamin D analogues (e.g. calcitriol) should be discontinued 1 week prior to initiation of treatment. The recommended starting dose in children and adolescents aged 1 to 17 years is 0.8 mg/kg of body weight given every two weeks. Doses should be rounded to the nearest 10 mg. The maximum dose is 90 mg. After initiation of treatment with burosumab, fasting serum phosphate should be measured every 2 weeks for the first month of treatment, every 4 weeks for the following 2 months and thereafter as appropriate. Fasting serum phosphate should also be measured 4 weeks after any dose adjustment. If fasting serum phosphate is within the reference range for age, the same dose should be maintained. The recommended starting dose in adults is 1.0 mg/kg of body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, given every 4 weeks. After initiation of treatment with burosumab, fasting serum phosphate should be measured every 2 weeks for the first month of treatment, every 4 weeks for the following 2 months and thereafter as appropriate. Fasting serum phosphate should be measured 2 weeks after the previous dose of burosumab. If serum phosphate is within the normal range, the same dose should be continued. For subcutaneous use.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of Package Insert. Concurrent administration with oral phosphate, active vitamin D analogs (see section 4.5 of Package Insert). Fasting serum phosphate above the normal range for age due to the risk of hyperphosphatemia (see section 4.4 of Package Insert). Patients with severe renal impairment or end stage renal disease.

WARNINGS AND PRECAUTIONS: Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded within the patient's records. Ectopic mineralization: Ectopic mineralization, as manifested by nephrocalcinosis, has been observed in patients with XLH treated with oral phosphate and active vitamin D analogs; these medicinal products should be stopped at least 1 week prior to initiating burosumab treatment (see section 4.2 of Package Insert). Hyperphosphataemia: Levels of fasting serum phosphate should be monitored due to the risk of hyperphosphatemia. Serum parathyroid hormone: Increases in serum parathyroid hormone have been observed in some XLH patients during treatment with burosumab. Periodic measurement of serum parathyroid hormone is advised. Injection site reactions: Administration of burosumab may result in local injection site reactions. Administration should be interrupted in any patient experiencing severe injection site reactions (see section 4.8 of Package Insert) and appropriate medical therapy administered. Hypersensitivity: Burosumab must be discontinued if serious hypersensitivity reactions occur and appropriate medical treatment should be initiated. Excipient with known effect: This medicine contains 45.91 mg of sorbitol in each vial which is equivalent to 45.91 mg/ml.

UNDESIRABLE EFFECTS: The most common (>10%) adverse drug reactions reported in pediatric patients treated for up to 64 weeks during clinical trials were: injection site reactions (56%), cough (56%), headache (50%), pyrexia (43%), pain in extremity (40%), vomiting (39%), tooth abscess (35%), vitamin D decreased (32%), diarrhea (25%), rash (24%), nausea (15%), constipation (11%), dental caries (11%) and myalgia (11%). The most common adverse drug reactions reported in adult patients during clinical trials were: back pain (23%), headache (21%), tooth infection (19%), restless legs syndrome (13%), muscle spasms (12%), vitamin D decrease (15%) and dizziness (11%).

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REFERENCE 1. CRYSVITA® (burosumab) Malaysia Package Insert. September 2022, Version 1

CRYSVITA® burosumab

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