CRYSVITA®
burosumab

DOSING AND ADMINISTRATION GUIDE IN PAEDIATRIC AND ADULT PATIENTS

CRYSVITA® (burosumab) injection for subcutaneous use

INDICATION

CRYSVITA® (burosumab) is indicated for the treatment of X-linked hypophosphataemia (XLH) in adults, adolescents and children 1 year of age or older.[1]

PLEASE REFER TO THE FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.

This material is for Healthcare Professionals Only

Kyowa KIRIN

CRYSVITA® DOSING SCHEDULE IN PAEDIATRIC PATIENTS[1]

All patients should discontinue oral phosphate and active vitamin D analogues 1 week prior to initiation of CRYSVITA® treatment.

Fasting serum phosphate concentration should be below the reference range for age prior to initiation of treatment.

Dosing in children (≥1 year) 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** up to a **maximum dose of 90 mg.**

After initiating CRYSVITA®, measure **fasting serum phosphate** every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. If serum phosphate is within the reference range for age, continue with the same dose.

Sample Starting Dose Calculation – Paediatric (1 to <18 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 PAEDIATRIC PATIENTS[1]

HEALTHCARE PROVIDER

Patients should discontinue oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) 1 week prior to initiation of CRYSVITA® treatment. **Fasting** serum phosphate level should be below the normal range prior to initiation of treatment.

WEEK 0/ DAY 1

- Administer first dose

WEEK 2

- Administer next dose. Maintain dosage

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
- Schedule a **fasting** serum phosphate test to reassess level in **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
- Schedule a **fasting** serum phosphate test to reassess level in **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® at a lower dose, as recommended (see page 6)
- Reassess **fasting** serum phosphate level in **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
- Reassess **fasting** serum phosphate level 4 weeks after any change in dose. Do not adjust CRYSVITA® 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.

Always monitor for signs of reactions with every injection of CRYSVITA®.

Always rotate injection site to a different anatomic location (upper arms, upper thighs, buttocks, or any quadrant of abdomen) than the previous injection.

Please refer to the full prescribing information before prescribing.

CRYSVITA® DOSING SCHEDULE IN ADULT PATIENTS[1]

All patients should discontinue oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) 1 week prior to initiation of CRYSVITA® treatment.

Fasting serum phosphate concentration should be below the reference range for age prior to initiation of treatment.

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

Recommended starting dose: **1 mg/kg** of body weight, **rounded to the nearest 10 mg** up to a **maximum dose: 90 mg**

After initiating CRYSVITA®, measure **fasting serum phosphate** every 4 weeks. Measure at 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate. If serum phosphate is within the normal range, continue with the same dose.

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

Patients should discontinue oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol) 1 week prior to initiation of CRYSVITA® treatment. **Fasting** serum phosphate level should be below the normal range prior to initiation of treatment.

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:** • Withhold the next dose • Reassess fasting serum phosphate level in **4 weeks**. Do not administer CRYSVITA® until serum phosphate level is below the normal range. Restart treatment at approximately half the initial starting dose, as recommended (see page 6)
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 • Reassess fasting serum phosphate level 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.

Always monitor for signs of reactions with every injection of CRYSVITA®.

Always rotate injection site to a different anatomic location (upper arms, upper thighs, buttocks, or any quadrant of abdomen) than the previous injection.

Please refer to the full prescribing information before prescribing.

CRYSVITA® burosumab

DOSE ADJUSTMENTS FOR PAEDIATRIC PATIENTS[1]

Dose Increase

If serum phosphate level is **below** the reference range for age, the CRYSVITA® dose may be increased stepwise up to approximately 2 mg/kg, administered every two weeks (maximum dose of 90 mg) according to the **Paediatric Dose Schedule for Stepwise Dose Increase** dosing schedule shown on the right.

Reassess **fasting** serum phosphate level 4 weeks after dose adjustment. If the level remains below the reference range for age after the re-initiation dose, the dose can be adjusted according to the **Paediatric Dose Schedule for Stepwise Dose Increase** dosing schedule shown on the right.

PAEDIATRIC DOSE SCHEDULE
Paediatric Dose Schedule for Stepwise Dose Increase

Body Weight (kg)	Starting Dose (mg)	First Dose Increase to (mg)	Second Dose Increase to (mg)
10-14	10	15*	20
15-18	10	20	30
19-31	20	30	40
32-43	30	40	60
44-56	40	60	80
57-68	50	70	90
69-80	60	90	90
81-93	70	90	90
94-105	80	90	90
106 and greater	90	90	90

*This dose increase is an exception to rounding to the nearest 10 mg

Dose Decrease

If serum phosphate is **above** the reference range for age, withhold the next dose and reassess the serum phosphate level in 4 weeks.

Fasting serum phosphate must be **below** the reference range for age to reinitiate CRYSVITA®. Once serum phosphate is below the reference range for age, treatment may be restarted according to the **Paediatric Dose Schedule for Re-Initiation of Therapy** dosing schedule shown on the right.

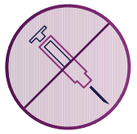
Reassess serum phosphate level 4 weeks after dose adjustment.

PAEDIATRIC DOSE SCHEDULE
Paediatric Dose Schedule for Re-Initiation of Therapy

Previous Dose (mg)	Reinitiation Dose (mg)
10	5
15	10
20	10
30	10
40	20
50	20
60	30
70	30
80	40
90	40

DOSE ADJUSTMENTS FOR ADULT PATIENTS[1]

Dose Decrease



If serum phosphate is **above** the normal range, withhold the next dose and reassess **fasting** serum phosphate level after 4 weeks.

Serum phosphate must be below the normal range to be able to reinitiate CRYSVITA®. Once serum phosphate is below the normal range, CRYSVITA® treatment may be restarted at approximately half the initial starting dose up to a maximum dose of 40 mg every 4 weeks according to the **Adult Dose Schedule for Reinitiation of Therapy** dosing schedule shown on the right.

Reassess **fasting** serum phosphate level 2 weeks after any change in dose.

ADULT DOSE SCHEDULE FOR REINITIATION OF THERAPY

Previous Dose (mg)	Reinitiation Dose (mg)
40	20
50	20
60	30
70	30
80 and greater	40

MISSED DOSE[1]

To avoid missed doses, treatments may be administered 3 days either side of the scheduled treatment date.

Do not adjust CRYSVITA® more frequently than every 4 weeks.

Please refer to the full prescribing information before prescribing.

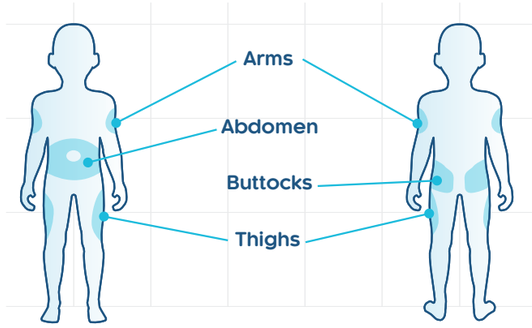
CRYSVITA® ADMINISTRATION FOR SUBCUTANEOUS USE AND STORAGE[1]

CRYSVITA® should be administered subcutaneously by a healthcare provider

- 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 CRYSVITA® should be split and administered at two 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 and 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.

CRYSVITA® burosumab

Minimum Prescribing Information:

CRYSVITA® (burosumab)

▽ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems Adverse events can be reported at pv.kkau.2r@kyowakirin.com

THERAPEUTIC INDICATION:
CRYSVITA® (burosumab) is indicated for the treatment of X-linked hypophosphataemia (XLH) in adults, adolescents and children 1 year of age or older.

DOSE AND ADMINISTRATION:
The recommended starting dose regimen for paediatrics (children 1-11yrs and adolescents 12-17yrs) is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, every 2 weeks, up to a maximum dose of 90 mg. The recommended dose regimen in adults (18yrs and older) is 1 mg/kg of body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every 4 weeks. Treatment should be initiated and monitored by specialist medical practitioners experienced in the management of patients with metabolic bone disease. Fasting serum phosphate concentration should be below the reference range for age prior to initiation of treatment. CRYSVITA® is administered by subcutaneous injection and should be administered by a healthcare provider. The maximum volume of CRYSVITA® per injection site is 1.5 mL. If multiple injections are required, administer at different injection sites.

CONTRAINDICATIONS:
Hypersensitivity to CRYSVITA® or to any of the excipients. Concurrent administration with oral phosphate and / or active vitamin D analogues. Serum phosphate level within or above the normal range for age at initiation of treatment. Severe renal impairment or end stage renal disease.

PRECAUTIONS:
Discontinue oral phosphate and active vitamin D analogues at least 1 week prior to initiating CRYSVITA® treatment. Monitor for signs and symptoms of nephrocalcinosis, hyperphosphatemia, ectopic mineralisation, and serious hypersensitivity reactions. Administration should be interrupted in any patient experiencing severe injection site reactions. Discontinue if serious hypersensitivity reaction occurs. Monitoring for signs and symptoms of nephrocalcinosis due to ectopic mineralisation, e.g. by renal ultrasonography, is recommended at the start of treatment and every 6 months for the first 12 months of treatment, and annually thereafter. Monitoring of urine calcium and phosphate is suggested every 3 months. Monitoring of plasma alkaline phosphatase, calcium, parathyroid hormone (PTH) and creatinine is recommended every 6 months (every 3 months for children 1 - 2 years) or as indicated

INTERACTIONS:
Concurrent administration of CRYSVITA® with oral phosphate and active vitamin D analogues is contraindicated as it may cause an increased risk of hyperphosphatemia and hypercalcaemia. Caution should be exercised when combining CRYSVITA® with calcimimetic medicinal products

ADVERSE EFFECTS:
Very common adverse reactions (>10%) reported in paediatric patients (≥1-17yrs) during clinical trials who had received at least 1 dose of CRYSVITA® were: injection site reactions, cough, headache, pyrexia, pain in extremity, vomiting, tooth abscess, vitamin D decreased, diarrhoea, rash, nausea, constipation, dental caries and myalgia. Common adverse reactions (≤10%) reported in paediatric patients ≥1 year of age during clinical trials who had received at least 1 dose of CRYSVITA® were: dizziness and blood phosphate increased. Very common adverse reactions (>10%) reported in adult patients (≥18yrs) who had received at least 1 dose of CRYSVITA® during clinical trials were: back pain, headache, tooth infection, restless legs syndrome, muscle spasms, vitamin D decrease and dizziness. Common adverse reactions (≤10%) reported in adult patients who had received at least 1 dose of CRYSVITA® during clinical trials were: constipation and blood phosphate increased. Content based on full CRYSTVITA® Product Information. Date Approved: 10 Sept 2021.

Reference: 1. Australian Product Information for Crysvita® (burosumab) approved Sept 2021. Available at: https://www.kyowakirin.com/australia/our_medicines/doc/crysvita_product_information_leaflet.pdf. Last accessed June 2022.

PBS INFORMATION: This product is listed on the PBS as a Section 100 item. Refer to PBS Schedule for full authority information.

CRYSVITA®
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KYOWA KIRIN

Kyowa Kirin Australia Pty Ltd, 68 York Street, Sydney.
https://www.kyowakirin.com/australia/index.html.
Date of Preparation July 2022. KKAU-XLH-2207141
Report adverse events to pv.kkau.2r@kyowakirin.com