CRYSVITA®
burosumab

DOSING AND ADMINISTRATION GUIDE IN PEDIATRIC AND ADULT PATIENTS

CRYSVITA® (burosumab) injection for subcutaneous use

INDICATION

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

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

Fasting serum phosphorus 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 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.

Sample Starting Dose Calculation – Pediatric (1 to <18 years)

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

Example: 23 kg x 0.8 mg/kg = 9.2 mg **(Round to nearest 10 mg)**
Starting dose CRYSVITA® = 10 mg

STARTING AND STAYING ON TRACK WITH CRYSVITA® IN PEDIATRIC 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 phosphorus 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 phosphorus 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 phosphorus 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 phosphorus level **If CRYSVITA® was administered at Week 4, and fasting serum phosphorus 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 phosphorus test to reassess level in **4 weeks** **If CRYSVITA® was NOT administered at Week 4, and fasting serum phosphorus levels are BELOW the normal range at Week 8:** • Restart CRYSVITA® at a lower dose, as recommended (see page 6) • Reassess **fasting** serum phosphorus 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 phosphorus level, as appropriate • Reassess **fasting** serum phosphorus level 4 weeks after any change in dose. Do not adjust CRYSVITA® more frequently than every 4 weeks

To avoid large fluctuations in phosphorus 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.

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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 phosphorus 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 phosphorus** monthly. Measure at 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.

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 phosphorus level should be below the normal range prior to initiation of treatment.

WEEK 0/ DAY 1	• Administer first dose
WEEK 2	• Measure **fasting** serum phosphorus level **WITHIN range:** • Administer next dose in 2 weeks • Maintain dosage **ABOVE range:** • Withhold the next dose • Reassess fasting serum phosphorus level in **4 weeks**. Do not administer CRYSVITA® until serum phosphorus 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 phosphorus level, as appropriate • Reassess fasting serum phosphorus level 2 weeks after any change in dose

To avoid large fluctuations in phosphorus 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.

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DOSE ADJUSTMENTS FOR PEDIATRIC PATIENTS[1]

Dose Increase

If serum phosphorus 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 **Pediatric Dose Schedule for Stepwise Dose Increase** dosing schedule shown on the right.

Reassess **fasting** serum phosphorus 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 **Pediatric Dose Schedule for Stepwise Dose Increase** dosing schedule shown on the right.

PEDIATRIC DOSE SCHEDULE
Pediatric 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

Dose Decrease

If serum phosphorus is **above** 5 mg/dL, withhold the next dose and reassess the serum phosphorus level in 4 weeks.

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

Reassess serum phosphorus level 4 weeks after dose adjustment.

PEDIATRIC DOSE SCHEDULE
Pediatric Dose Schedule for Re-Initiation of Therapy

Previous Dose (mg)	Re-initiation 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 phosphorus is **above** the normal range, withhold the next dose and reassess **fasting** serum phosphorus level after 4 weeks.

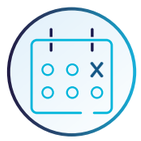
Serum phosphorus must be below the normal range to be able to re-initiate CRYSVITA®. Once serum phosphorus is below the normal range, CRYSVITA® treatment may be restarted at approximately half the initial starting dose up to a maximum dose of 40 mg every 4 weeks according to the **Adult Dose Schedule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

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

ADULT DOSE SCHEDULE FOR RE-INITIATION OF THERAPY

Previous Dose (mg)	Re-Initiation Dose(mg)
40	20
50	20
60	30
70	30
80 and greater	40

MISSED DOSE[1]



If a patient misses a dose, resume CRYSVITA® as soon as possible at the previously prescribed dose.

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

Please refer to the full prescribing information before prescribing.

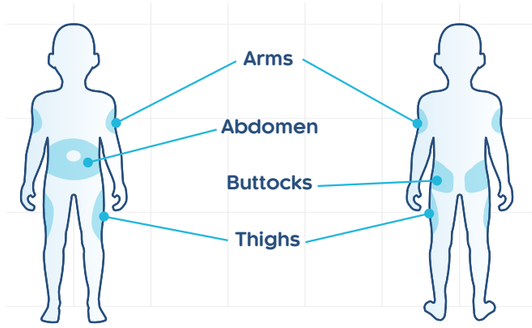
CRYSVITA® ADMINISTRATION FOR SUBCUTANEOUS USE AND STORAGE[1]

CRYSVITA® should be administered subcutaneously by a healthcare professional

- Inject in the 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.

Abbreviated Prescribing Information:

CRYSVITA® (Burosumab)

Based on Singapore Package Insert. Kyowa Kirin Asia Pacific Pte. Ltd. 2021.

Please refer to the full Prescribing Information before prescribing.

Indications and usage:
CRYSVITA® is indicated for the treatment of X-linked hypophophatemia (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 active vitamin D analogs 1 week prior to initiation of treatment. Fasting serum phosphorus concentration should be below the reference range for age prior to initiation of treatment. 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 tr eatment with CRYSVITA®, measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. 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.

Contraindications:
Do not use CRYSVITA® with oral phosphate and active vitamin D analogs. Do not initiate CRYSVITA® treatment if serum phosphorus is within or above the normal range for age. CRYSVITA® is contraindicated 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:
Adverse reactions (>10%) reported in pediatric patients during clinical trials were: injection site reactions, cough, headache, pyrexia, pain in extremity, vomiting, tooth abscess, vitamin D decreased, diarrhoea, rash, nausea, constipation, dental caries, dizziness and myalgia. Adverse reactions (>5%) reported in adult patients during clinical trials were: back pain, headache, tooth infection, restless legs syndrome, vitamin D decrease and dizziness, constipation and blood phosphorus increased.

Reference 1: CRYSVITA® (burosumab). Based on Singapore Package Insert. Kyowa Kirin Asia Pacific Pte Ltd; 2021

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