Dosing and administration guide

Not actual size

Indication

CRYSVITA® (burosumab-twza) is a fibroblast growth factor 23 (FGF23) blocking antibody indicated for:

- The treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
- The treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.

Important Safety Information

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.

Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

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Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

DOSAGE & ADMINISTRATION CONSIDERATIONS

Dosing and administration for CRYSVITA® in adult and pediatric patients

Important dosage and administration information[1]

BEFORE initiating CRYSVITA[1]

- Discontinue oral phosphate and/or active vitamin D analogs (eg, 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
- In patients at high risk for hypercalcemia (eg, pre-existing hyperparathyroidism, prolonged immobilization, dehydration, hypervitaminosis D, or renal impairment) assess serum calcium and parathyroid hormone levels prior to starting CRYSVITA

- CRYSVITA is administered by subcutaneous injection and should be administered by a healthcare provider
- The maximum volume of CRYSVITA per injection is 1.5 mL. If multiple injections are required, administer at different injection sites

Missed dose[1]

- If a patient misses a dose, resume CRYSVITA as soon as possible at the prescribed dose
- To avoid missed doses, treatments may be administered 3 days before or after the scheduled treatment date

Not actual size

25-hydroxyvitamin D supplementation[1]

- Monitor 25-hydroxyvitamin D levels. Supplement with cholecalciferol or ergocalciferol to maintain 25-hydroxyvitamin D levels in the normal range for age
- Do not administer active vitamin D analogs during CRYSVITA treatment

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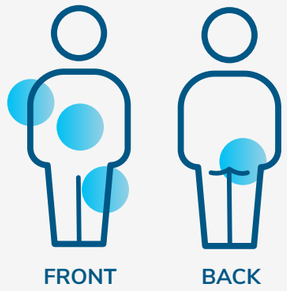
CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

Administering and handling CRYSVITA®

General considerations for subcutaneous administration[1]



Injection sites should be rotated, with each injection administered at a different anatomic location than the previous injection. Injection site locations include:

- Upper arms
- Upper thighs
- Buttocks
- Any quadrant of the abdomen

Do not inject into moles, scars, or areas where the skin is tender, bruised, red, hard, or not intact.

- If a given dose on a dosing day requires multiple vials of CRYSVITA, contents from 2 vials can be combined for injection
- The maximum volume of CRYSVITA per injection is 1.5 mL. If multiple injections are required on a given dosing day, administer at different injection sites. Monitor for signs of reactions
- 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

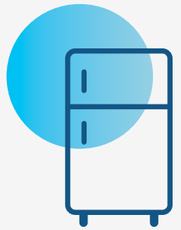
How CRYSVITA is supplied[1]

- CRYSVITA injection for subcutaneous administration is supplied as a sterile, preservative-free, clear to slightly opalescent and colorless to pale brown-yellow solution
- **The product is available as 1 single-dose vial per carton in the following strengths:**

10 mg/mL
(NDC# 42747-102-01)

20 mg/mL
(NDC# 42747-203-01)

30 mg/mL
(NDC# 42747-304-01)



Storage and handling[1]

CRYSVITA vials must be stored in the original carton until the time of use under refrigerated conditions at 36°F to 46°F (2°C to 8°C). Keep the CRYSVITA vial in the original carton to protect it from light until the time of use.

- Do not freeze or shake CRYSVITA
- Do not use CRYSVITA beyond the expiration date stamped on the carton
- CRYSVITA vials are single-dose only. Discard any unused product

Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

Dosing for children with XLH

Dosing schedule[1]

CRYSVITA®

1

dose every 2 weeks

CRYSVITA is administered by an HCP every 2 weeks and its dose is based on the patient's body weight.

Recommended starting dosage (6 months to <18 years)[1]

Patients who weigh **<10 kg**

Starting dose regimen is 1 mg/kg of body weight, rounded to the nearest 1 mg, administered every 2 weeks.

Patients who weigh **≥10 kg**

Starting dose regimen is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every 2 weeks. The minimum starting dose is 10 mg up to a maximum dose of 90 mg.

AFTER initiating CRYSVITA[1]

- Measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment and thereafter, as appropriate
- If fasting serum phosphorus is above the lower limit of the reference range for age and below 5 mg/dL, continue treatment with the same dose
- To maintain fasting serum phosphorus within the reference range, follow dose adjustment schedule to the right

CRYSVITA dosing is based on a patient's weight. Continue to monitor their weight and make any dose adjustments as indicated in this guide.[1]

Guidelines for dose adjustments with CRYSVITA

Reassessment every **4 weeks** is key

When making dose adjustments for your patients, take note of the following[1]:

- Reassess fasting serum phosphorus level 4 weeks after dose adjustment
- Do not adjust CRYSVITA more frequently than every 4 weeks

INCREASING DOSES

For patients who weigh **<10 kg**[1]

If fasting serum phosphorus is **below the reference range for age:**

- The dose may be increased to 1.5 mg/kg, rounded to the nearest 1 mg, administered every 2 weeks

If additional dose increases are needed:

- The dose may be increased to the maximum dose of 2 mg/kg, rounded to the nearest 1 mg, administered every 2 weeks

For patients who weigh **≥10 kg**[1]

If fasting serum phosphorus is **below the reference range for age:**

- The dose may be increased stepwise up to approximately 2 mg/kg, administered every 2 weeks (maximum dose of 90 mg) according to the dosing schedule shown to the right

XLH pediatric dose schedule for stepwise dose increase for patients ≥10 kg[1]

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	90	90	90

DECREASING DOSES

If fasting serum phosphorus is **>5 mg/dL**[1]:

- Withhold the next dose and reassess the serum phosphorus level in 4 weeks. The patient must have serum phosphorus below the reference range for age to reinitiate CRYSVITA
- Once serum phosphorus is below the reference range for age, treatment may be restarted

For patients who weigh **<10 kg**[1]

Restart CRYSVITA at 0.5 mg/kg of body weight, rounded to the nearest 1 mg, administered every 2 weeks.

For patients who weigh **≥10 kg**[1]

Restart CRYSVITA according to the dose schedule shown in the table to the right.

XLH pediatric dose schedule for reinitiation of therapy for patients ≥10 kg[1]

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

After a dose decrease, reassess serum phosphorus level 4 weeks after the dose adjustment. If the level remains below the reference range for age after the reinitiation dose, the dose can be adjusted as outlined above under **Increasing Doses**.

Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

XLH DOSING FOR ADULTS

Dosing for adults with XLH

Dosing schedule[1]

CRYSVITA®

1

dose every 4 weeks

CRYSVITA is administered by an HCP every 4 weeks and its dose is based on the patient's body weight.

Recommended starting dosage (≥18 years)[1]

1 mg/kg body weight, rounded to the nearest 10 mg, administered every 4 weeks

Doses may be increased up to 90 mg, administered every 4 weeks

AFTER initiating CRYSVITA[1]

- 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 fasting serum phosphorus is within the normal range, continue with the same dose

CRYSVITA dosing is based on a patient's weight. Continue to monitor their weight and make any dose adjustments as indicated in this guide.[1]

Guidelines for dose adjustments with CRYSVITA

Reassess **2 weeks** after dose adjustment

When making dose adjustments for your patients, take note of the following[1]:

- Reassess fasting serum phosphorus level 2 weeks after dose adjustment
- Do not adjust CRYSVITA more frequently than every 4 weeks

DECREASING DOSES

If fasting serum phosphorus is **above the normal range[1]:**

- Withhold the next dose and reassess the fasting serum phosphorus level after 4 weeks
- The patient must have fasting serum phosphorus below the normal range to be able to reinitiate CRYSVITA

Once fasting serum phosphorus is **below the normal range[1]:**

- Reinitiate CRYSVITA at approximately half the initial starting dose, up to a maximum dose of 40 mg every 4 weeks, according to the dose schedule shown in the table below

Previous dose (mg)	Reinitiation dose (mg)
40	20
50	20
60	30
70	30
≥80	40

Reassess fasting serum phosphorus 2 weeks after any change in dose.[1]

Monitor for nephrocalcinosis[1]

- When serum phosphorus increases above the upper limit of normal, there is an increased risk of nephrocalcinosis
- For patients already taking CRYSVITA, dose interruption and/or dose reduction may be required based on a patient's fasting serum phosphorus levels

Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

TIO DOSING FOR CHILDREN

Dosing for children with TIO

Dosing schedule[1]

CRYSVITA®

1

dose every 2 weeks

CRYSVITA is administered by an HCP every 2 weeks and its dose is based on the patient's body weight.

Recommended starting dosage (2 years to <18 years)[1,a]

0.4 mg/kg body weight, rounded to the nearest 10 mg, administered every 2 weeks

Doses may be increased up to 2 mg/kg (not to exceed 180 mg), administered every 2 weeks

[a]Safety and effectiveness of CRYSVITA in pediatric patients 2 years of age and older with TIO are supported by evidence from the studies in adult patients with TIO with additional modeling and simulation of pharmacokinetic data from adult and pediatric patients with XLH and adult patients with TIO to inform dosing. Safety and effectiveness for CRYSVITA in pediatric patients with TIO below the age of 2 years have not been established.[1]

AFTER initiating CRYSVITA[1]

- 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 fasting serum phosphorus is within the reference range for age, continue with the same dose
- To maintain fasting serum phosphorus within the reference range for age, follow the dose adjustment schedule on the right

CRYSVITA dosing is based on a patient's weight. Continue to monitor their weight and make any dose adjustments as indicated in this guide.[1]

Guidelines for dose adjustments with CRYSVITA

i Reassess **4 weeks** after dose adjustment

When making dose adjustments for your patients, take note of the following[1]:

- Reassess fasting serum phosphorus level 4 weeks after dose adjustment
- Do not adjust CRYSVITA more frequently than every 4 weeks

INCREASING DOSING

If fasting serum phosphorus is **below the reference range[1]:**

- The dose should be titrated up, per the table below, to the maximum dose of 2 mg/kg every 2 weeks. The maximum dose should not exceed 180 mg

TIO pediatric dose schedule for stepwise dose increase for patients ≥10 kg[1]

Body weight (kg)	Starting dose (mg)	First dose increase to (mg)	Second dose increase to (mg)	Third dose[b] increase to (mg)
10-14	5	10	15	20
15-18	5	10	20	25
19-31	10	20	25	30
32-43	10	30	40	50
44-56	20	40	50	70
57-68	20	50	70	90
69-80	30	60	80	100
81-93	30	70	100	120
94-105	40	80	110	140
≥106	40	90	130	160

[b]The table shows a dose increase up to 1.5 mg/kg. Further dose increases to a maximum of 2 mg/kg, not to exceed 180 mg, administered every 2 weeks should be calculated by the physician.

DECREASING DOSES

If fasting serum phosphorus is **above the reference range for age[1]:**

- Withhold the next dose and reassess the serum phosphorus level in 4 weeks
- The patient must have fasting serum phosphorus below the reference range for age to reinitiate CRYSVITA at approximately half the initial starting dose, up to a maximum dose of 180 mg, administered every 2 weeks for pediatric patients
- Reassess fasting serum phosphorus level 4 weeks after the dose adjustment
- If the level remains below the reference range for age after the reinitiation dose, the dose can be adjusted according to the table above

INTERRUPTING DOSES

If a patient undergoes treatment of the underlying tumor (ie, surgical excision or radiation therapy)[1]:

- CRYSVITA treatment should be interrupted and fasting serum phosphorus reassessed after treatment has been completed
- CRYSVITA dose should be restarted at the patient's initiation dose if fasting serum phosphorus remains below the lower limit of normal
- To maintain fasting serum phosphorus within the reference range for age, follow the dose adjustment schedule above

Please click to see Important Safety Information on pages 15 and 16 and full Prescribing Information.

CRYSVITA® burosumab-twza Injection 10, 20, 30 mg/mL

TIO DOSING FOR ADULTS

Dosing for adults with TIO

Dosing schedule for starting treatment[1]

CRYSVITA®

1

dose every 2 or 4 weeks

CRYSVITA is administered by an HCP and its dose is based on the patient's body weight.

Recommended starting dosage (≥18 years)[1]

0.5 mg/kg body weight, rounded to the nearest 10 mg, administered every 4 weeks

Dose may be increased up to 2 mg/kg (not to exceed 180 mg), administered every 2 weeks

AFTER initiating CRYSVITA[1]

- 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 fasting serum phosphorus is within the normal range, continue with the same dose
- To maintain fasting serum phosphorus within the reference range for age, follow the dose adjustment schedule to the right

CRYSVITA dosing is based on a patient's weight. Continue to monitor their weight and make any dose adjustments as indicated in this guide.[1]

Guidelines for dose adjustments with CRYSVITA

Reassess **2 weeks** after dose adjustment

When making dose adjustments for your patients, take note of the following[1]:

- Reassess fasting serum phosphorus level 2 weeks after dose adjustment
- Do not adjust CRYSVITA more frequently than every 4 weeks

INCREASING DOSING

If fasting serum phosphorus is **below the normal range**[1]:

- The dose should be titrated up, per the table below, to the maximum dose of 2 mg/kg not to exceed 180 mg, administered every 2 weeks
- For those individuals not reaching a fasting serum phosphorus greater than the lower limit of the normal range, consider dividing total dose administered every 4 weeks and administering every 2 weeks

TIO dose schedule[c] for stepwise[d] dose increase for adults[1]

	Starting dose	First dose increase[e]	Second dose increase[e]	Third dose increase[e]	Fourth dose increase	Fifth dose increase (maximum dose)
If serum phosphorus 2 weeks post-dose adjustment is below lower limit of normal	0.5 mg/kg every 4 weeks	**Increase to:** 1 mg/kg every 4 weeks **OR** 0.5 mg/kg every 2 weeks	**Increase to:** 1.5 mg/kg every 4 weeks[f] **OR** 0.75 mg/kg every 2 weeks	**Increase to:** 2 mg/kg every 4 weeks[f] **OR** 1 mg/kg every 2 weeks	**Increase to:** 1.5 mg/kg not to exceed 180 mg every 2 weeks	**Increase to:** 2 mg/kg not to exceed 180 mg every 2 weeks

[c]Rounded to the nearest 10 mg.
[d]Do not adjust CRYSVITA more frequently than every 4 weeks.
[e]For those individuals not reaching a fasting serum phosphorus greater than the lower limit of the normal range, physicians may consider dividing total dose administered every 4 weeks and administering every 2 weeks.
[f]In patients with high body weight, if the calculated dose is greater than 180 mg every 4 weeks, move to a divided dose every 2 weeks.

DECREASING DOSES

If fasting serum phosphorus is **above the normal range**[1]:

- Withhold the next dose and reassess the serum phosphorus level in 4 weeks
- The patient must have fasting serum phosphorus below the reference range to reinitiate CRYSVITA at approximately half the initial starting dose, up to a maximum dose of 180 mg, administered every 2 weeks for adults
- After a dose decrease, reassess fasting serum phosphorus level 2 weeks after the dose adjustment
- If the level remains below the reference range after the reinitiation dose, the dose can be adjusted per the table above

INTERRUPTING DOSING

If a patient undergoes treatment of the underlying tumor (ie, surgical excision or radiation therapy)[1]:

- CRYSVITA treatment should be interrupted and fasting serum phosphorus reassessed after treatment has been completed
- CRYSVITA dose should be restarted at the patient's initiation dose if fasting serum phosphorus remains below the lower limit of normal
- To maintain fasting serum phosphorus within the reference range, follow the dose adjustment schedule above

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CRYSVITA®
burosumab-twza
Injection 10, 20, 30 mg/mL

Indication and Important Safety Information

Indication

CRYSVITA® (burosumab-twza) is a fibroblast growth factor 23 (FGF23) blocking antibody indicated for:

- The treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
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Important Safety Information

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.
- Patients with TIO who undergo treatment of the underlying tumor should have dosing interrupted and adjusted to prevent hyperphosphatemia.

Hypercalcemia

- Increases in serum calcium have been reported in patients treated with CRYSVITA. Patients with risk factors such as pre-existing hyperparathyroidism, prolonged immobilization, dehydration, hypervitaminosis D, or renal impairment, are at higher risk of hypercalcemia. Monitor these patients for serum calcium and parathyroid hormone levels before and during CRYSVITA treatment for moderate to severe hypercalcemia. In patients with moderate to severe hypercalcemia, CRYSVITA should not be administered until hypercalcemia is adequately managed.

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
Pediatric Patients

- Adverse reactions reported in 10% or more of CRYSVITA-treated pediatric XLH patients across three studies are: pyrexia (55%, 44%, and 62%), injection site reaction (52%, 67%, and 23%), cough (52%), vomiting (41%, 48%, and 46%), pain in extremity (38%, 46%, and 23%), headache (34% and 73%), tooth abscess (34%, 15%, and 23%), dental caries (31%), diarrhea (24%), vitamin D decreased (24%, 37%, and 15%), toothache (23% and 15%), constipation (17%), myalgia (17%), rash (14% and 27%), dizziness (15%), and nausea (10%).

Adult Patients

- Adverse reactions reported in more than 5% of CRYSVITA-treated adult XLH patients and in at least 2 patients more than placebo in one study are: back pain (15%), headache (13%), tooth infection (13%), restless legs syndrome (12%), vitamin D decreased (12%), dizziness (10%), constipation (9%), muscle spasms (7%), and blood phosphorus increased (6%).
- Spinal stenosis is prevalent in adults with XLH, and spinal cord compression has been reported. It is unknown if CRYSVITA therapy exacerbates spinal stenosis or spinal cord compression.
- Adverse reactions reported in more than 10% of CRYSVITA-treated adult TIO patients in two studies are: tooth abscess (19%), muscle spasms (19%), dizziness (15%), constipation (15%), injection site reaction (15%), rash (15%), and headache (11%).

USE IN SPECIFIC POPULATIONS

- There are no available data on CRYSVITA use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Serum phosphorus levels should be monitored throughout pregnancy. Report pregnancies to the Kyowa Kirin, Inc. Adverse Event reporting line at 1-844-768-3544.
- There is no information regarding the presence of CRYSVITA in human milk or the effects of CRYSVITA on milk production or the breastfed infant. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CRYSVITA and any potential adverse effects on the breastfed infant from CRYSVITA or from the underlying maternal condition.

PATIENT COUNSELING INFORMATION

- Advise patients not to use any oral phosphate and/or active vitamin D analog products.
- Instruct patients to contact their physician if hypersensitivity reactions, injection site reactions, and restless legs syndrome induction or worsening of symptoms occur.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Kyowa Kirin, Inc. at 1-844-768-3544.

For important risk and use information, please see the full Prescribing Information for CRYSVITA.

Reference:

1. CRYSVITA (burosumab-twza). US Prescribing Information. Kyowa Kirin, Inc.; August 2025.

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Injection 10, 20, 30 mg/mL

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