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

Start Guide for Healthcare Professionals

Helping your patients begin their CRYSVITA treatment journey

- Step-by-step guidance, from patient enrollment to treatment initiation
- Overview of the prior authorization process
- Resources for prescribers and staff

For Important Safety Information, please see pages 2-3. For important risk and use information, please click to see full Prescribing Information for CRYSVITA.

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[1]
- 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

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

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%)
- Postmarketing experience reported in CRYSVITA-treated pediatric XLH patients: blood phosphorus increased

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 click to see full Prescribing Information for CRYSVITA.

The decision to prescribe CRYSVITA® (burosumab-twza) has been made. Now what?

From enrollment and authorization of coverage to product acquisition and delivery, getting patients from prescription to a first injection may take several weeks. This guide is designed to help prescribers and office staff get through the steps as efficiently as possible.

Dosing and Administration:
CRYSVITA is a subcutaneous injection administered by a healthcare provider and given on a schedule as prescribed. CRYSVITA dosing is based on a patient's weight and fasting serum phosphorus levels. Continue to monitor their weight and make any dose adjustments as indicated in the Dosing and Administration Guide or refer to the Prescribing Information.

Dosing and Administration Guide
DOWNLOAD

1 ENROLLMENT

Download the **enrollment form**, fill it out with your patient's information, sign it, and fax it to 833-552-3299.

Enrollment Form
DOWNLOAD

Provide complete and accurate information to reduce additional follow-up and potential treatment delay

- Completing confirmatory testing prior to submitting a completed enrollment form may prevent delays. (And testing may be required by patient's health plan)

Set expectations with your patient

- Patient consent is needed to facilitate Kyowa Kirin Cares access services and financial assistance options for those who qualify. If the patient or care partner wishes to consent, be sure to have them sign the **Patient Authorization on the enrollment form**

Annotated Enrollment Form
ASK A REP

- Alternatively, a Case Manager can send the patient an enrollment form and assist them with the process over the phone
- Use the **Patient Next Steps guide** to help your patient understand the process and the role they play

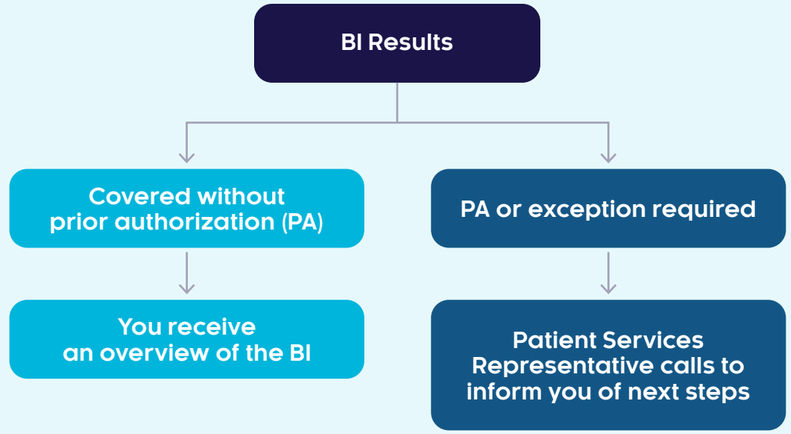
Patient Next Steps
ASK A REP

WHY SUBMIT AN ENROLLMENT FORM?

Kyowa Kirin Cares can help get your patient from prescription to treatment with an overview of insurance coverage, financial assistance options, and shipment coordination. Patients must opt-in to Kyowa Kirin Cares by signing the Patient Authorization section of the enrollment form.

2 AUTHORIZATION

Upon receiving the completed enrollment form, Kyowa Kirin Cares will begin the benefits investigation (BI) process for the patient, then inform you of results within two business days.



A dedicated Case Manager will call the patient to review insurance coverage. They will inform the patient of the copay program and other assistance options.

Support Brochure
DOWNLOAD

3 PROCUREMENT

A dedicated Patient Access Liaison (PAL) will work with you to coordinate a procurement option based on your patient's BI results. CRYSVITA can be procured by an authorized Specialty Distributor or from a select group of Specialty Pharmacies, and ordering requirements may differ based on the patient's coverage.

Access and Reimbursement Guide
ASK A PAL

Questions? Ask a representative, or call Kyowa Kirin Cares at 833-KK-CARES (833-552-2737) Monday through Friday, 8 AM to 8 PM (ET).

Understanding Prior Authorization

The list on the opposite page shows documents and other criteria commonly required by health plans to cover CRYSVITA. A dedicated Patient Access Liaison (PAL) will contact you with your patient's plan-specific drug requirements.

Provide all documentation required by the patient's health plan to prevent delays and denials

- Health plans may require documentation of past and current disease management interventions, such as use of supplement therapy or growth hormone, or orthopedic/dental surgery

Schedule testing

- Your patient's health plan may have specific testing requirements
- A dedicated PAL can help you determine plan-specific criteria
- Timely submission of test results will facilitate the PA process

Monitor communications with the patient's health plan and answer any additional requests or questions promptly

Your patient's plan may require genetic testing. A PAL can help you navigate diagnostic documentation and other plan requirements for your patient. **Contact Kyowa Kirin Cares by calling 833-KK-CARES (833-552-2737).**

Template Letter of Medical Necessity
ASK A PAL

Template Letter of Appeal
ASK A PAL

Questions? Ask a representative, or call Kyowa Kirin Cares at 833-KK-CARES (833-552-2737) Monday through Friday, 8 AM to 8 PM (ET).

*The common PA requirements on the following page are based on a composite of PA requirements from several leading health insurance plans. Specific PA requirements may vary based on your patient's health plan. Please contact a PAL for more information.

Common PA Requirements for CRYSVITA

For informational purposes only.

Common ICD-10 and CPT Codes

ICD-10 Codes[2]		
XLH	E83.31	Familial hypophosphatemia
	E83.39	Other disorders of phosphorus metabolism
TIO	M83.8	Other adult osteomalacia

CPT Codes[2]		
XLH or TIO	96401	Chemotherapy administration, subcutaneous or intramuscular, nonhormonal antineoplastic
	96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

Home Health Care Nursing Codes[3]		
XLH or TIO	99601	Home Infusion Procedures and Services - Use this code for up to the first two hours of a visit
	99602	Home Infusion Procedures and Services - Use this code for each additional hour of the visit after the first two hours

Use of the above ICD-10 or CPT codes does not guarantee that claims related to the treatment of patients with XLH or TIO will be reimbursed by a health plan. Please refer to the specific health plan when deciding how to submit a claim for care.

This checklist should be used for educational purposes only. Many health insurers have developed specific policies and criteria for their prior authorization process when it comes to approving the use of CRYSVITA to treat patients with XLH and TIO. Please refer to the patient's health plan for specific criteria and documentation requirements. This prior authorization checklist is not intended as a diagnostic tool for XLH or TIO and should not be a substitute for a healthcare provider's clinical expertise.

Common Documentation for Diagnosis of XLH

The following diagnosis criteria are a representation of common signs and symptoms that may help diagnose XLH and meet some common payer requirements. This is not to suggest that use of CRYSVITA will improve these clinical symptoms. Additional documentation may be required.

Biochemical Markers[a]	Clinical Presentation	Genetic Testing	Additional Requirements
☐ Low fasting serum phosphate ☐ Elevated alkaline phosphatase (ALP) (patients aged <18 years) ☐ Elevated bone-specific alkaline phosphatase (BAP) (patients aged ≥18 years) ☐ Decreased TmP/GFR ☐ Elevated or inappropriately normal FGF23 levels[b] ☐ Low or inappropriately normal $1,25(OH)_2D$	☐ Rickets in pediatrics ☐ Osteomalacia in adults ☐ Skeletal deformities ☐ Fractures/ pseudofractures ☐ Past orthopedic surgeries ☐ Enthesopathy ☐ Frequent dental abscesses that may lead to tooth loss ☐ Growth impairment	☐ Confirmed *PHEX* mutation[b] ☐ Confirmed *PHEX* mutation in directly related family member	☐ Prescribed by, or in consultation with, an endocrinologist, nephrologist, geneticist, or other specialist experienced in the treatment of metabolic bone disorders ☐ Individual does not have severe renal impairment or end stage renal disease ☐ Office visit notes

Prior/Current Disease Management Interventions

☐ Use of oral phosphate agent
☐ Use of active vitamin D therapy

Documentation That May Be Used for Reauthorization/Continuation of Therapy

Biochemical Markers	Clinical Presentation
☐ Increased/normalized fasting serum phosphate[c] ☐ Reduction in serum alkaline phosphatase in pediatrics ☐ Increased TmP/GFR from baseline	☐ Notes on patient's clinical presentation and additional documentation as required by payer

[a]Appropriate for age and gender.

[b]Many current health plan policies require the testing of either *PHEX* mutations or FGF23 levels for approval.

[c]For adults: check monthly, 2 weeks post-dose for the first 3 months of treatment, and thereafter as appropriate. For pediatric patients: check every 4 weeks for the first 3 months of treatment, and thereafter as appropriate.

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

Common Documentation for Diagnosis of TIO

The following diagnosis criteria are a representation of common signs and symptoms that may help diagnose TIO and meet some common payer requirements. This is not to suggest that use of CRYSVITA will improve these clinical symptoms. Additional documentation may be required.

Biochemical Markers[a]	Clinical Presentation	Imaging	Additional Requirements
☐ Decreased fasting serum phosphate level for age ☐ Decreased TmP/GFR ☐ Elevated or inappropriately normal FGF23 levels	☐ Disease is associated with a phosphaturic mesenchymal tumor that cannot be curatively resected or identified/localized ☐ Osteomalacia, fractures, musculoskeletal pain, fatigue	☐ Functional/ anatomical imaging	☐ Prescribed by, or in consultation with, an endocrinologist, nephrologist, rheumatologist, or specialist in TIO ☐ Individual does not have severe renal impairment or end stage renal disease ☐ Office visit notes

Prior/Current Disease Management Interventions

☐ History of inadequate response, contraindication, or intolerance to oral phosphate, active vitamin D, or both

Documentation That May Be Used for Reauthorization/Continuation of Therapy

Biochemical Markers	Clinical Presentation
☐ Patient achieved and sustained an improvement in serum phosphate levels[b]	☐ Notes on patient's clinical presentation and additional documentation as required by payer

[a]Appropriate for age and gender.

[b]For adults and pediatric patients: check monthly, 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.

Notes

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

Support at every step

Here are the Kyowa Kirin staff who are available to help answer your questions.

Access questions

Ask a dedicated Kyowa Kirin Cares Case Manager (CM) and/or Patient Access Liaison (PAL) or call 833-KK-CARES (833-552-2737) Monday through Friday, 8 AM to 8 PM (ET).

General questions about CRYSVITA

Ask a Kyowa Kirin Rare Disease Specialist (RDS) (sales representative).

Medical questions

For medical questions, please contact medical information. Email KyowaKirin-US@medinfodept.com.

Kyowa Kirin Cares helps to get your patients from prescription to treatment

While a dedicated PAL is supporting you, a Case Manager is available to assist your patient. Please share the Patient Next Steps guide with your patient to help them understand their role in getting on therapy. For more information please visit kyowakirincares.com.

LEARN MORE

Reference: 1. CRYSVITA. Prescribing Information. Kyowa Kirin Inc. Princeton, NJ. **2.** American Academy of Professional Coders. ICD-10-CM 2023. Salt Lake City, UT: American Academy of Professional Coders; 2022. **3.** American Medical Association. *CPT 2023 Professional Edition.* Chicago, IL: American Medical Association; 2022.

KYOWA KIRIN