COVERAGE AUTHORIZATION GUIDE

VOXZOGO® (vosoritide)

INDICATION

VOXZOGO® (vosoritide) is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates.

MECHANISM OF ACTION

In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (*FGFR3*). Binding of VOXZOGO to natriuretic peptide receptor-B (NPR-B) antagonizes *FGFR3* downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, VOXZOGO, like C-type natriuretic peptide (CNP), acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation.

SELECT IMPORTANT SAFETY INFORMATION

Transient decreases in blood pressure were observed in clinical studies. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, fatigue, and/or nausea), patients should be well fed and hydrated in the hour prior to VOXZOGO administration.

VOXZOGO®
(vosoritide) for injection

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

BIOMARIN®

INDICATION

VOXZOGO® (vosoritide) is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

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Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

INTRODUCTION AND DISCLAIMER

VOXZOGO® (vosoritide) is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates. BioMarin, the manufacturer of VOXZOGO, would like to assist every patient with achondroplasia who is eligible for therapy to have access to the product. We can help you and your staff understand the process of securing insurance coverage authorization for patients prescribed VOXZOGO. We offer patients and their caregivers assistance through our support services hub, BioMarin RareConnections™. We also work directly with patients and healthcare providers to provide education on the safe and appropriate use of BioMarin products.

Every insurance plan provides different individual and family health benefits, so it is important to contact the patient/caregiver's plan for assistance when interpreting drug policies, billing processes and appropriate codes, and payment. These items can vary greatly and are subject to change with or without notice because of frequently changing guidelines, laws, rules, and regulations. Additionally, some patients/caregivers may switch insurance plans during the year because of new life events and/or job changes, so it is important to verify current insurance information at each patient visit. If your patient encounters coverage issues or receives a denial for treatment, consult the insurance plan to help interpret the coverage policy and/or denial language, and provide the necessary information and documentation requested by the plan in a timely manner.

Disclaimer

BioMarin has compiled this guide with information gathered from third-party sources and experienced insurance reimbursement experts to serve as a source of information to assist your practice in obtaining approval and prior authorization for VOXZOGO treatment. While we have included some best practices for working with BioMarin RareConnections, insurance companies, and specialty pharmacies in this guide, BioMarin makes no guarantee that the use of this information will prevent denials, delays, or differences of opinion with insurance plans as to the correct information to submit for VOXZOGO authorization, or forms of billing that will expedite payment to providers of service.

The coding information provided in this guide is general in nature and subject to change without notice. Coding determinations are at the discretion of the provider and should be made in accordance with applicable regulations and payer guidance. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the healthcare provider to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient. Providers should contact third-party payers for specific information on their coding, coverage, and payment policies. Information provided should in no way be considered a guarantee of coverage or reimbursement for any product or service. BioMarin provides this information as a convenience; it does not constitute legal advice or a recommendation regarding medical practice.

This guide provides assistance for US Food and Drug Administration (FDA)-approved indications that are documented in the VOXZOGO full Prescribing Information. Where reimbursement is sought for prescribed use and/or administration of this product that may be inconsistent with, or not expressly specified in, the FDA-cleared or FDA-approved labeling outlined in the VOXZOGO full Prescribing Information, consult with your practice's billing advisers or the patient's insurance plan on handling such issues.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

GETTING STARTED

Does your patient have access to VOXZOGO® (vosoritide)?

Now that your patient/caregiver and you have chosen VOXZOGO® (vosoritide), it is important to understand how to gain access to this specialty medication.

VOXZOGO is delivered through a once-daily subcutaneous injection administered at home by the trained caregiver. In order to secure coverage for VOXZOGO, many health insurance plans may request prior authorization (PA) steps that could include diagnostic confirmation of a patient's genotype, baseline assessments, and thorough review of medical and treatment history, as well as confirmation of medical necessity and authorization for treatment. Health plans may also request ongoing medical documentation that demonstrates the long-term impact of VOXZOGO on growth parameters.

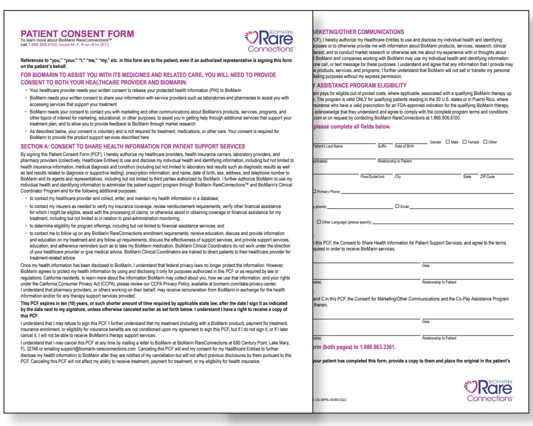
The following pages provide a detailed view of the steps to securing access for your patient and how BioMarin RareConnections™ can provide education and assistance throughout the VOXZOGO treatment journey

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

INTRODUCTION TO BIOMARIN RARECONNECTIONS™

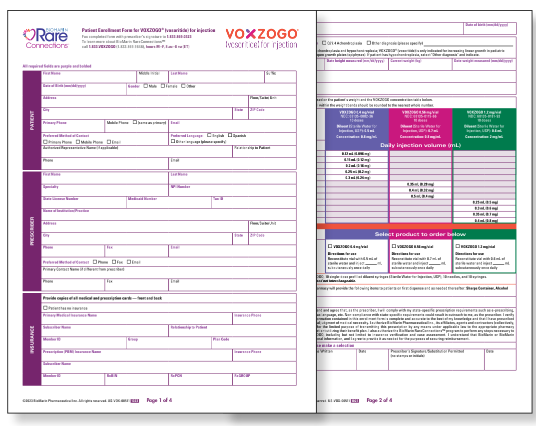
BioMarin RareConnections is a resource for patients, caregivers, clinics, and your staff

- BioMarin RareConnections is a personalized product support program for patients taking VOXZOGO® (vosoritide), their caregivers, and you. Our dedicated and experienced BioMarin RareConnections Case Managers and Field Reimbursements Managers will provide guidance to help gain access to VOXZOGO. We can educate patients/caregivers, you, and your staff about insurance coverage and PA requirements, provide education on appeals, identify financial assistance options for eligible patients/caregivers, and work with the specialty pharmacy to coordinate ordering and delivery logistics
- To enroll your patient into BioMarin RareConnections, including assistance with investigating the patient's insurance benefits, submit both the Patient Consent Form (PCF) and the Patient Enrollment Form (PEF), as well as the front and back images of the patient/policy holder's medical and pharmacy benefit insurance card(s). The forms are located on the BioMarin RareConnections VOXZOGO HCP website and can be submitted electronically to BioMarin RareConnections via QUICK ENROLL. If preferred, the forms can also be downloaded, printed, completed and faxed. Make sure the images are clear, otherwise BioMarin RareConnections will need to call you to verbally verify the information or request a legible copy of the information



The Patient Consent Form (PCF)

The PCF provides HIPAA (Health Insurance Portability and Accountability Act) authorization that allows BioMarin RareConnections access to patient-level information to communicate with health insurance providers and specialty pharmacies. The PCF is completed by the caregiver on behalf of the patient. It is also available in Spanish.



The Patient Enrollment Form (PEF)

The PEF provides clinical and insurance information and authorization for BioMarin RareConnections to provide access to services. The PEF is completed by the clinic and serves as the VOXZOGO prescription.

BIOMARIN RareConnections™

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

INTRODUCTION TO BIOMARIN RARECONNECTIONS™ (continued)

After submitting the PCF and PEF, BioMarin RareConnections Case Managers can provide assistance during coverage authorization and prescription fulfillment. We will reach out to you and the patient/caregiver to assist with any of the following:

- Providing an in-depth overview of BioMarin RareConnections services
- Conducting and sending the benefits investigation (BI) results
- Providing PA forms to be completed by your clinic
- Providing information about the Letter of Medical Necessity (LMN) to submit with the PA
- Providing education about denials and appeals
- Directing the prescription to the appropriate in-network specialty pharmacy covered by the patient's insurance

BioMarin RareConnections Field Reimbursement Managers (FRMs) can also work directly with you and your staff to provide education for navigating the VOXZOGO® (vosoritide) reimbursement and specialty pharmacy processes. The FRM works in coordination with the patient's BioMarin RareConnections Case Manager and is your one-to-one informational resource for seeking access to VOXZOGO for your patient. BioMarin RareConnections FRMs can facilitate communication for issues that arise during the enrollment and fulfillment process, for example:

- Discussing expectations for starting a patient on VOXZOGO
- Reviewing and summarizing the available BioMarin RareConnections support services and programs
- Answering access, financial assistance, and product distribution questions
- Providing insurance plan insights to help you understand a patient's coverage benefits and plan coverage policies
- Explaining the details of the LMN and PA requirements
- Discussing the management of denials and the insurance plan appeals process
- Reviewing the VOXZOGO Coverage Authorization Guide with you and your staff

BioMarin RareConnections is helping patients access VOXZOGO®[1]
- 97% of insured patients* have secured coverage for VOXZOGO

BioMarin RareConnections provides support to help you and your staff understand how to access VOXZOGO. When you are ready to start your patient on VOXZOGO, contact BioMarin RareConnections at 1.833.VOXZOGO (1.833.869.9646), email at VOXZOGOsupport@biomarin-rareconnections.com, or visit biomarin-rareconnections.com/hcp/VOXZOGO

*BioMarin RareConnections Data on File. VOXZOGO patients included are eligible VOXZOGO patients who have enrolled in BioMarin RareConnections and are on commercial therapy. BioMarin RareConnections data from April through December 2023.

REFERENCE: 1. Data on file. BioMarin Pharmaceutical Inc.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

BioMarin RareConnections™ and Specialty Pharmacy PATIENT PATHWAY FOR CLINICS

Patient Enrollment PEF + PCF

- ✓ Clinic submits PEF and is notified of receipt
- ✓ Patient/caregiver submits PCF and is notified of receipt
- ✓ Follow-up with clinic on missing information

Explaining Coverage Options

- ✓ Determination of coverage and PA requirements through BI
- ✓ Patient/caregiver welcome call with notification of BI results
- ✓ Clinic notification of BI results & PA requirements

Financial Assistance Support

- ✓ Co-pay program eligibility* screening
- ✓ Identification of additional support options, if needed

Specialty Pharmacy Triage & Shipment Coordination

- ✓ Verification of prescription and validation of insurance coverage
- ✓ Shipment coordination with patient/caregiver
- ✓ Packaging and delivery logistics

Maintaining Therapy†

- ✓ Reauthorization
- ✓ Prescription expiration
- ✓ Refill reminders

*As appropriate for eligible patients.
†Specialty pharmacy–dependent processes.

BIOMARIN Rare Connections™

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

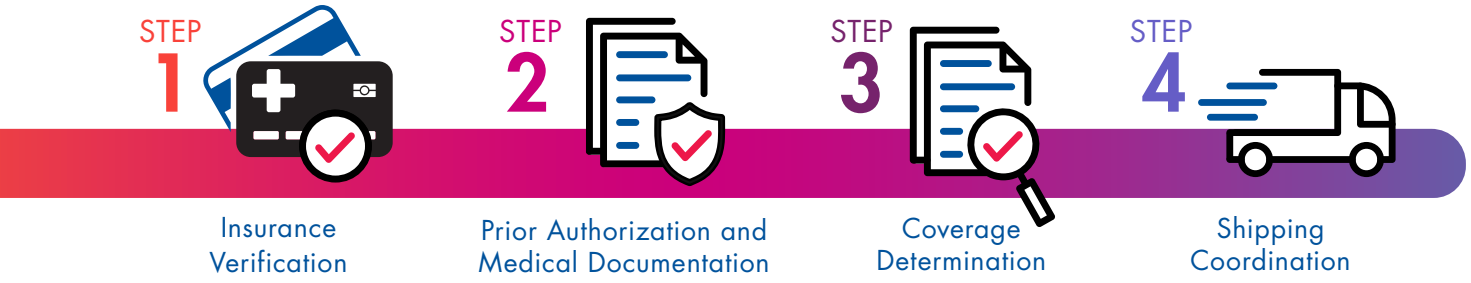
VOXZOGO® (vosoritide) TREATMENT AUTHORIZATION

Requesting insurance approval and coverage for VOXZOGO

VOXZOGO® (vosoritide) for injection is a specialty medication and insurance plans require extra verification steps to establish that your patient is a candidate for treatment. The insurance plan manages access to specialty medications to ensure they are used in the appropriate patient population.

Treatment authorization can be an intricate process, and **you may need to advocate for your patient throughout the various steps**. It is critical that you and your staff monitor all communication with the patient's insurance plan and answer any additional requests or questions. Typically, the insurance plan needs the additional information within a specified time frame, and failure to do so may result in you needing to restart the process or may make it more difficult for your patient to gain access to VOXZOGO. If you or your staff need help, a BioMarin RareConnections™ Case Manager or Field Reimbursement Manager can provide information and education along the way.

Proactive advocacy for your patient throughout the VOXZOGO treatment journey and monitoring for communication from the patient's insurance plan are crucial



STEP 1 Insurance Verification

After you determine VOXZOGO is appropriate for your patient, be sure to gather the following information, especially if they are a new patient or were referred to your office to discuss VOXZOGO:

- Enrollment forms
- Primary and secondary insurance information
- Patient/policy holder's medical and pharmacy insurance benefit cards, front and back
- Complete contact information for patient and family/caregiver(s), including home/work/cell phone numbers and email addresses

After BioMarin RareConnections completes the benefits investigation (BI), a summary of that BI will be sent to your clinic that includes information about the patient's benefits and their potential co-pay or co-insurance for VOXZOGO. This BI will also include information about further documentation that is required by the plan for authorization. BioMarin RareConnections will typically send a prior authorization (PA) form from the insurance plan that your clinic must complete to verify the medical necessity of VOXZOGO for your patient.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

VOXZOGO® (vosoritide) TREATMENT AUTHORIZATION (continued)

STEP 2 Prior Authorization and Medical Documentation

A PA is a request created by the patient/caregiver's insurance plan to determine if your patient is a suitable candidate for VOXZOGO® (vosoritide). It is usually a 1- to 2-page document that may ask a series of questions to confirm diagnosis, treatment history, treatment selection, and if medical management will be by a licensed and qualified specialist healthcare provider. In addition to completing the PA form, the insurance plan may also require that you provide documentation of the patient's medical and treatment history, genetic testing, and/or diagnostic and baseline assessments. When completing a PA form for VOXZOGO, the information required may include, but is not limited to, the following:

The insurance plan may request a PA for VOXZOGO, medical documentation, and genetic testing to determine a patient's eligibility for treatment

Checklist of information typically required to complete a PA form

ITEM	√	INFORMATION
Medical history		ICD-10-CM diagnosis (Q77.4)
		Patient weight
Genetic testing (if required)		Molecular test for achondroplasia-specific mutations in the fibroblast growth factor receptor 3 (*FGFR3*) gene
Additional measurements and testing		• Baseline growth velocity (cm/year) at time of treatment initiation • Height z-score • Radiographic evidence or physician attestation of open epiphyses • Pubertal status (Tanner stage)
VOXZOGO information		VOXZOGO full Prescribing Information
		Copy of VOXZOGO FDA approval letter

Ensure the PA form is complete as denials can occur if questions are unanswered. The submission timing of the PA is also important and varies by plan; you may need to restart the authorization process if you do not submit the PA in a timely manner.

Ensure the PA form is complete; denials can occur if questions are unanswered or incomplete

Letter of Medical Necessity for VOXZOGO

Some insurance plans may require a written request for treatment, usually called a Letter of Medical Necessity (LMN). The LMN is composed by the treating physician, and depending on the insurance plan, submitted along with the completed PA and supporting medical documentation.

Examples of relevant LMN content:

- Personal details about the patient, based on your clinical assessment and the patient's disease history
- A description of achondroplasia, including any relevant information about its causes, disease course, and burden of illness
- The healthcare provider's medical opinion and personal experience of helping the patient and caregiver manage the disease, which is important context for the insurance plan

An example LMN is provided on page 12 of this guide.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

VOXZOGO® (vosoritide) TREATMENT AUTHORIZATION (continued)

Some Payers have policies that require VOXZOGO to be prescribed by, or in consultation with, a provider who is considered an expert in growth disorders. Please check the relevant payer policy to determine what specialist the payer considers eligible to prescribe VOXZOGO. If your specialty is not listed in the policy, it may be helpful when writing your LMN, when submitting the PA, to explain your experience in treating growth disorders and why you are a qualified provider to prescribe VOXZOGO. You may want to remind the payer that a VOXZOGO pivotal, Phase 3 clinical trial included Principal Investigators who are specialists in pediatric orthopedics, pediatric endocrinology, and genetics.[1]

You may choose to reference the study here and either provide this study link or download the study and attach it to the LMN.

Submitting an LMN with the PA allows you to provide additional medical documentation, coordinating care information, and your personal history managing the patient's achondroplasia

STEP 3 Coverage Determination

After you send the LMN, PA, and medical documentation to the patient's insurance plan, they will review all the information and provide a coverage determination (approval or denial). It is very important for you and your staff to monitor the phone, fax, email, and/or mail for any communication from the insurance plan; the patient/caregiver should monitor their phone, text, email, or mail as well. At this stage the insurance plan may request specific medical documentation in addition to what was sent in your original submission. Be sure to provide this information to the health plan as soon as possible to avoid any delays.

Monitor for any communication from the insurance plan

Denials and Appeals

If the insurance plan denies VOXZOGO® (vosoritide), BioMarin RareConnections™ will reach out to your clinic and the patient/caregiver to discuss the contents of the denial letter and provide appeal options as determined by the payer. Additional details regarding the appeal process and a sample letter can be found on pages 13-15 in this guide. If you or the patient/caregiver requests assistance with appealing the denial, BioMarin RareConnections can provide information and education about the appeal process.

It is possible that your patient's insurance may exclude coverage for VOXZOGO, meaning they do not provide coverage for the treatment at all. BioMarin RareConnections can provide support to determine possible next steps.

STEP 4 Shipping Coordination

Once VOXZOGO is approved, BioMarin RareConnections can assist eligible patient/caregivers with financial assistance programs as needed. The specialty pharmacy and BioMarin RareConnections will contact the patient/caregiver to discuss all requirements for shipping, handling, storage, and shipment coordination to the home.

REFERENCE: 1. Savarirayan R, Tofts L, Irving M, et al. Once daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo controlled, multicentre trial. *The Lancet.* 2020;396(10252):684-692.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

SAMPLE LETTER OF MEDICAL NECESSITY FOR VOXZOGO® (vosoritide) FOR SUBCUTANEOUS INJECTION

- ✔ Date
- ✔ Health plan contact name
- ✔ Health plan name
- ✔ Address
- ✔ City, State, ZIP Code
- ✔ Patient (first and last name)
- ✔ Policy number
- ✔ Group number
- ✔ Claim number, if relevant to request

RE: Authorization of VOXZOGO® (vosoritide) Treatment

Dear [Contact name]:

I am writing this letter of medical necessity on behalf of my patient, [insert patient name], in support of [initiating/continuing] treatment with VOXZOGO. Achondroplasia is a genetic condition characterized by [provide description of typical burden and progression of achondroplasia and impact of not being treated here]. Based on my patient's underlying genetic condition, I believe that [insert patient name] is an excellent candidate for VOXZOGO treatment and that treatment is warranted and medically necessary. Below, this letter outlines [patient name]'s medical history and prognosis, and the rationale for treatment with VOXZOGO.

Summary of patient's medical history and rationale for treatment

[Exercise your medical judgment and discretion when providing a characterization of the patient's condition and clinical rationale for treatment. Consider including the following in this section of the letter:

- Achondroplasia diagnosis (include ICD-10-CM code) and *FGFR3* genetic testing results (if needed)
- Relevant medical history (height, growth velocity/height z-score, confirmation of open epiphyses)
- Other factors that impact the treatment decision]

In brief, based on my patient's status and the clinical data available to date, [initiating/continuing] treatment with VOXZOGO for [patient name] is warranted, appropriate, medically necessary, and should be covered.

About VOXZOGO

VOXZOGO is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates. In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (*FGFR3*). Binding of VOXZOGO to natriuretic peptide receptor-B (NPR-B) antagonizes *FGFR3* downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, VOXZOGO, like C-type natriuretic peptide (CNP), acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation.

[Healthcare professionals to include relevant clinical trial/real-world observational information to justify use of VOXZOGO for this patient specific to their medical condition and criteria. For additional information, refer to the VOXZOGO full Prescribing Information.]

I have also attached the full Prescribing Information for VOXZOGO, which was approved by the US Food and Drug Administration (FDA) on October 20, 2023. The VOXZOGO dose is based on the patient's body weight, and the trained caregiver will administer the subcutaneous VOXZOGO injections for my patient at home.

Conclusion

In conclusion, I am requesting that you approve treatment for my patient, [insert patient name], with VOXZOGO. I will personally monitor my patient's progress and manage their treatment while they are under my care. Please contact me with any additional questions or if you require additional information.

Sincerely,

[Insert prescriber name, credentials, contact information]

Possible enclosures:

- Copy of patient's insurance cards
- VOXZOGO FDA approval letter
- VOXZOGO full Prescribing Information
- VOXZOGO published clinical studies
- Detailed patient medical history covering patient's complete experience with achondroplasia, clinical notes, and genetic tests confirming diagnosis
- Relevant growth records (confirmation of open epiphyses, growth velocity, z-score, etc)

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

MANAGING DENIALS AND APPEALS

BioMarin RareConnections™ can help you understand a payer's reasons for denials and appeal options

Denials occur when the insurance plan does not have enough information to confirm a patient is the right candidate for a specialty treatment or the plan does not provide coverage for a particular treatment. Denials also occur if the patient does not meet the clinical criteria for approval, as specified by the insurance plan. Specialty drugs are commonly denied following an initial prior authorization (PA) request and reversing the outcome of the denial will require supplementary effort from you. **To advocate for your patient to gain access to VOXZOGO® (vosoritide), you have the option of writing an appeal letter or, if available through the payer, conducting a peer-to-peer discussion between yourself and the patient's insurance plan to help petition for authorization of VOXZOGO treatment.**

If you receive a denial, work with BioMarin RareConnections to help understand why the PA was denied and how to appeal the decision

The insurance plan is required, by law, to provide a written rationale for the treatment denial, which is usually sent by mail to the patient/caregiver and you. Read these letters carefully, as they will provide the explicit reasons for the denial, methods for appeal, and time frame to request an appeal. The denial letter may stipulate the additional medical documentation required, including but not limited to supplemental medical records, laboratory work, genetic testing records, other baseline assessments, and/or your medical rationale for selecting VOXZOGO as medically necessary for the patient.

If you do not understand the denial letter, contact the patient's insurance plan to request additional information. BioMarin RareConnections can assist with the following:

- Obtaining the reason for the payer's denial of VOXZOGO
- Reviewing the appeal options available through the patient/caregiver's insurance plan
- Providing information about the methods and time frame for appealing
- Contacting the insurance plan to learn what additional information is being requested
- Contacting the insurance plan to identify all appeal options and which option is preferred by the plan

An example appeal letter can be found on page 15.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

MANAGING DENIALS AND APPEALS (continued)

Types of Appeals

Some insurance plans may have more than one level of appeal available. Written appeal letters are usually the first option, but if a peer-to-peer discussion is available, this is the preferred and most expeditious means of appealing a denial.

A peer-to-peer discussion can be the preferred and most expeditious means of appealing a denial

1 

Peer-to-peer discussion: A teleconference call in which the healthcare provider has the opportunity to advocate on behalf of the patient, verbally provide the missing data to the insurance plan reviewer, and explain their rationale for selecting a particular treatment. This can be employed as the first or second level of appeal, depending on the health plan. Approval for coverage may be provided during the call or issued in letter format within a specified time, as stated by the insurance plan reviewer during the call. **If approved on the call, request the approval authorization number from the reviewer before ending the call. If the reviewer does not specify when the insurance plan will make a coverage determination, be sure to request a time frame before ending the call.**

2 

Appeal letter: A formal written letter submitted to the insurance plan by the healthcare provider is the usual and customary first level of appeal. The letter is intended to answer and/or provide all additional information requested by the insurance plan in the denial letter. Adjudication for coverage authorization will be returned in letter format.

3 

Expedited appeal: An expedited appeal is a teleconference call in which the prescriber has the opportunity to verbally request emergency and immediate coverage for a treatment. Some insurance plans may only provide access to expedited appeals for certain conditions. Speak with the patient's insurance plan to understand your options; VOXZOGO® (vosoritide) may not qualify for an expedited appeal.

External review: After your clinic has exhausted these appeal options the patient/caregiver can appeal to an external court or Administrative Law Judge (ALJ) for a complete review of the insurance plan's ongoing decision to deny treatment authorization. This is typically the highest level of appeal, and the external reviewer is not affiliated with the insurance plan. The ruling will be based on evidence and legal and binding determinations, and the insurance plan is required by law to follow the decision of the external reviewer. External reviewers are used when the patient has non-Medicare insurance.

It might be helpful to include the patient and caregiver directly in the appeal process. Ask the caregiver to include their own letter, or a letter from their child, explaining why VOXZOGO treatment is important to them.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

SAMPLE APPEAL LETTER FOR VOXZOGO® (vosoritide) FOR SUBCUTANEOUS INJECTION

- ✔ Date
- ✔ Health plan contact name
- ✔ Health plan name
- ✔ Address
- ✔ City, State, ZIP Code
- ✔ Patient (first and last name)
- ✔ Policy number
- ✔ Group number
- ✔ Claim number, if relevant to request

RE: Appeal of denial of coverage for VOXZOGO® (vosoritide) treatment

Dear [Contact name]:

I am writing this letter on behalf of my patient, [insert patient name] to appeal the [insert date] denial for coverage of treatment with VOXZOGO. Achondroplasia is a genetic condition characterized by [provide description of typical burden and progression of achondroplasia here]. Non-coverage of treatment will result in [provide impact of not being treated here]. This letter provides the additional information requested by [insert insurance plan name] in your denial letter and is a formal and urgent request for expedited review and approval of my request for VOXZOGO for my patient.

Summary of patient's medical history and rationale for treatment

[Provide a characterization of the patient's condition and clinical rationale for treatment. Consider including the following in this section:

- Achondroplasia diagnosis (include ICD-10-CM code) and *FGFR3* genetic testing results (if needed)
- Information to address reasons for payer denial
- Relevant medical history (height, growth velocity/height z-score, confirmation of open epiphyses)
- Other factors that impact the treatment decision (eg, detailed medical history, unmet need and treatment priorities, etc)]

In brief, based on my patient's status and the clinical data available to date, [initiating/continuing] treatment with VOXZOGO for [patient name] is warranted, appropriate, medically necessary, and should be covered.

About VOXZOGO

VOXZOGO is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates. In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (*FGFR3*). Binding of VOXZOGO to natriuretic peptide receptor-B (NPR-B) antagonizes *FGFR3* downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, VOXZOGO, like C-type natriuretic peptide (CNP), acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation.

[Healthcare professionals to include relevant clinical trial/real-world observational information to justify use of VOXZOGO for this patient specific to their medical condition and criteria. For additional information, refer to the VOXZOGO full Prescribing Information.]

I have also attached the full Prescribing Information for VOXZOGO, which was approved by the US Food and Drug Administration (FDA) on October 20, 2023. The VOXZOGO dose is based on the patient's body weight, and the trained caregiver will administer the subcutaneous VOXZOGO injections for my patient at home.

Conclusion

In light of the additional information I am providing in this appeal letter, I am requesting that you please reassess your denial decision and approve my request for treatment of [insert patient name] with VOXZOGO.

Please contact me with any additional questions or if you require more information.

Sincerely,

[Insert prescriber name, credentials, contact information]

Suggested enclosures:

- Copy of denial letter
- Copy of patient's insurance cards
- VOXZOGO FDA approval letter
- VOXZOGO full Prescribing Information
- VOXZOGO published clinical studies
- Detailed patient medical history covering patient's complete experience with achondroplasia, clinical notes, and genetic tests confirming diagnosis
- Relevant growth records (confirmation of open epiphyses, growth velocity, z-score, etc)

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

FINANCIAL ASSISTANCE SUPPORT

BioMarin RareConnections™ can provide patients/caregivers with financial assistance information

VOXZOGO® (vosoritide) Co-Pay Assistance Program

The VOXZOGO® (vosoritide) Co-Pay Assistance Program is a BioMarin program that assists eligible*, commercially insured patients with cost sharing needs. The BioMarin RareConnections Case Manager and specialty pharmacy can help educate the patient/caregiver on their cost sharing requirements and determine eligibility for the program. The program can cover up to 100% of co-pay/co-insurance and deductible costs depending on the patient's benefit design, up to the VOXZOGO Co-Pay Assistance Program's annual maximum benefit.

The VOXZOGO Co-Pay Assistance Program is for commercially insured patients only, and certain terms and conditions may apply.

Identification of Additional Options

BioMarin RareConnections may also be able to identify additional options, if any, for the caregiver to consider for financial support.

Additional BioMarin Programs

BioMarin RareConnections can provide information about any other applicable BioMarin programs that may apply, such as possible product assistance in the event of an insurance delay during reauthorization or the loss of insurance.

With the VOXZOGO Co-Pay Assistance Program, eligible commercially insured patients may pay as little as $0 for VOXZOGO prescriptions*[1]

- 96% of participants paid $0 out-of-pocket for their prescription†

*Valid only for those patients with commercial prescription insurance coverage for VOXZOGO who meet eligibility criteria. Offer not valid for prescriptions reimbursed, in whole or in part, by any federal, state, or government-funded insurance programs (for example, Medicare, Medicare Advantage, Medigap, Medicaid, VA, DoD, or TRICARE), for cash-paying patients, where product is not covered by patient's commercial insurance, where patient's commercial insurance plan reimburses them for entire cost of their prescription drug, or where prohibited by law or by the patient's health insurance provider. If at any time a patient begins receiving prescription drug coverage under any such federal, state, or government-funded healthcare program, patient will no longer be able to use the VOXZOGO Co-Pay Assistance Program and patient must notify BioMarin RareConnections at 1.833.869.9646 to stop participation. Patients may not seek reimbursement for the value of the out-of-pocket expense amount covered by the program from any third-party payer, whether public or private. Valid only in the United States and Puerto Rico. This program is not health insurance. Offer may not be combined with any other rebate, coupon, or offer. Co-payment assistance under the program is not transferable. BioMarin Pharmaceutical Inc. reserves the right to rescind, revoke, or amend the program without notice. Patient/caregiver certifies responsibility for complying with applicable limitations, if any, of any commercial insurance and reporting receipt of program rewards, if necessary, to any commercial insurer. This program is subject to termination or modification at any time. The VOXZOGO Co-Pay Assistance Program will cover up to the annual maximum co-pay assistance benefit per calendar year for eligible patients. Some restrictions apply.

†BioMarin RareConnections Data on File. VOXZOGO patients included are eligible VOXZOGO patients who have enrolled in BioMarin RareConnections and are on commercial therapy. BioMarin RareConnections data from January through December 2023. Out of pocket costs may vary.

REFERENCE: 1. Data on file. BioMarin Pharmaceutical Inc.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

SPECIALTY PHARMACY AND VOXZOGO® (vosoritide) SHIPMENT COORDINATION

BioMarin RareConnections™ coordinates with the specialty pharmacy

Ordering VOXZOGO

Once coverage is secured, BioMarin RareConnections will work with the appropriate specialty pharmacy (SP) to coordinate the shipment of VOXZOGO® (vosoritide) to the patient's home.

BioMarin has selected a limited network of SPs designed to promote efficiency while ensuring that we cover the greatest number of payer plans nationwide.

- For new patients, SPs will reverify the prescription, insurance authorization, and dosage, collect the patient's co-payment/co-insurance, and coordinate shipment and logistics for ongoing refill management
- For prescription renewals, SPs can provide case management for VOXZOGO reauthorizations, prescriptions changes, and dose modifications

We are contracted with Accredo, CVS Caremark, Optum Frontier Therapies, Acaria, and Axium (in Puerto Rico)

VOXZOGO is delivered directly to the patient's home. At the time of ordering, the SP will confirm if ancillary supplies or sharps containers are needed and may provide these items as requested. The SP will educate the patient/caregiver on the special handling and refrigeration requirements for VOXZOGO to ensure proper storage, care, and disposal of the product.

It is important that your clinic educate patients/caregivers and reinforce that the distribution of VOXZOGO will be different than what they have become accustomed to with other medications; it is not distributed by a local or neighborhood retail pharmacy. Coordination happens behind the scenes with the assistance of BioMarin RareConnections. VOXZOGO can only be shipped by the SP. The patient/caregiver is responsible for answering SP phone calls, accepting VOXZOGO shipments, storing the medication, administering injections appropriately each day, and reordering as needed.

SPs focus on handling specialty products; they are licensed across the United States and Puerto Rico. They can provide case management on VOXZOGO treatment authorization, as well as coordinate shipment and logistics for delivery. Many large health plans own or are partnered with SPs to manage specialty drugs for their patient populations.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

FOLLOW-UP VISITS AND TREATMENT REAUTHORIZATION

Monitoring your patient after VOXZOGO® (vosoritide) injections

Patient monitoring and reauthorization of VOXZOGO® (vosoritide) is the ongoing responsibility of your clinic and the specialty pharmacy (SP). You will be responsible for managing coverage authorization for prescription renewals, so it is important to work with your SPs on reauthorization requirements. BioMarin RareConnections™ is available if your clinic has additional questions during this stage.

Follow-up Visits

Insurance plans may expect a high level of monitoring and oversight by the healthcare providers (HCPs) of patients being treated with VOXZOGO, and may also request ongoing medical documentation and observation notes demonstrating the long-term impact of VOXZOGO on growth and any other key metrics. Be sure to check with your patient's insurance company to understand what relevant baseline and follow-up measurements they will require you to document during treatment.

Prescription Renewal and Reauthorization

Insurance plans usually authorize treatment for 6-12 months, and typically require the HCP to issue a renewal prescription and/or complete a reauthorization or new prior authorization (PA) form. The patient/caregiver's insurance plan may request additional documentation at this time, including your assessment of the patient's treatment and growth progress on VOXZOGO. BioMarin encourages you to thoroughly document the patient's baseline measurements prior to treatment and record the patient's progress while on VOXZOGO. It may also be helpful for the patient/caregiver to keep a journal and track the progress on VOXZOGO.

The SPs provide reauthorization and renewal monitoring services for patients. They can also do the following to assist with renewing the prescription and/or PA:

- Inform the patient/caregiver and HCP of upcoming prescription renewal and/or reauthorization by the insurance plan
- Reconfirm patient's insurance information and identify any insurance plan or coverage changes
- Request and submit prescription and PA documentation to the insurance plan
- Monitor for approvals and help the HCP manage questions or denials from the insurance plan
- Inform the patient/caregiver and HCP of approvals and continue to coordinate VOXZOGO shipments and delivery to the patient's home

Checklist of information typically required to complete a reauthorization form

ITEM	√	INFORMATION
Update medical history		Reconfirm ICD-10-CM diagnosis (Q77.4)
		Patient's weight
Updated measurements and testing		• Growth velocity (cm/year) and height z-score versus baseline measures • Radiographic evidence or physician attestation of open epiphyses • Pubertal status (Tanner stage)
Other		Additional progress notes, and benefits and impact of treatment as seen during follow-up visits and as reported by patient/caregiver

For more information on understanding the growth metrics payers may require for reauthorizations, see page 19.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

FOLLOW-UP VISITS AND TREATMENT REAUTHORIZATION (continued)

Reporting growth for patients on VOXZOGO: Understanding the metrics payers may require.

VOXZOGO® (vosoritide) is indicated to increase linear growth in pediatric patients with achondroplasia and open growth plates.

- This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

At treatment initiation[1]

Baseline height	Standing height
Baseline growth velocity	Baseline growth velocity may be captured by looking back at the patient's growth velocity during a time period prior to treatment initiation.[2] It requires two measurements: (1) the previous 6-12 months before treatment was initiated and (2) at treatment initiation • May require requesting growth charts and notes from other clinicians if you were not previously treating the patient • May be used as the basis for measuring benefit over time; therefore, capturing a baseline growth velocity as close to treatment initiation is important[3]
	Annualized growth velocity (AGV): The difference in standing height over the course of a year is calculated as follows:[3] $\text{(Height at Recent Visit – Height at Previous Visit)} \times \frac{365.25}{\text{Days Between Visits}}$ **Use this online AGV calculator:** biomarin-rareconnections.com/hcp/voxzogo/agv-calculator Assess a patient's growth rate by recording height at two different visits at least 3 to 6 months apart, and preferably 6 to 12 months apart, to account for growth spurts.[2]
Growth plate status	Confirmation of open epiphyses • Often required for authorization and reauthorization. Clinician attestation is often sufficient, but in some cases, radiographic imaging may be required
Height Z-score	Standing height converted to age- and sex-appropriate standard deviation scores relative to average stature children
Pubertal status	Tanner stage
Genetic testing	Molecular test confirming specific pathogenic variants
Renal clearance	Confirmation of no renal impairment. Not recommended in patients with eGFR < 60 mL/min/1.73[1]

At treatment follow-up for ongoing reauthorization[1]

- AGV on treatment
- Growth plate status
- Height Z-score
- Pubertal status

Other quick tips

- **Careful documentation:** Thorough documentation of the patient's baseline measurements and progress while on VOXZOGO is important in support of any payer requests
- **Information gathering:** A referring physician or pediatrician may have retrospective metrics
- **Scheduling:** Consider payer's reauthorization period (3, 6, or 12 months) and required data when scheduling a patient's follow-up visits

REFERENCES: 1. BioMarin. Voxzogo (vosoritide) Prescribing Information. 2023. 2. Barstow C, Rerucha C. Evaluation of short and tall stature in children. Am Fam Physician. 2015;92(1):43-50. 3. Savarirayan R, Tofts L, Irving M, et al. Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. Lancet. 2020;396(10252):684-692. Supplementary Appendix available from https://doi.org/10.1016/S0140-6736(20)31541-5.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

ADDITIONAL INFORMATION AND RESOURCES

VOXZOGO® (vosoritide) Product Information

For additional information about VOXZOGO® (vosoritide) for injection resources, visit VOXZOGO.com/hcp.
The following materials are available:

- VOXZOGO Efficacy and Safety Information
- VOXZOGO Instructions for Use
- VOXZOGO Resources

BioMarin RareConnections™

If you or your staff wish to utilize BioMarin RareConnections resources, you will need to complete a Patient Enrollment Form (PEF).
For your patients and their caregivers to enroll in BioMarin RareConnections they will need to complete the Patient Consent Form (PCF).
All VOXZOGO forms as well as additional BioMarin RareConnections materials are available at biomarin-rareconnections.com/hcp/VOXZOGO.

BioMarin RareConnections contact information:

- Phone: 1.833.VOXZOGO (1.833.869.9646)
- Fax: 1.833.869.0323
- Email: VOXZOGOsupport@biomarin-rareconnections.com
- Hours: Monday to Friday, 8AM to 8PM ET

BioMarin Clinical Coordinator Support

The BioMarin VOXZOGO Patient Support Program helps patients gain access to and start therapy and provides ongoing product education throughout their treatment journey. The BioMarin Clinical Coordinator is available to the patient/caregiver throughout VOXZOGO treatment. They coordinate with the BioMarin RareConnections Case Manager to share insurance coverage information with the patient/caregiver. Additionally, Clinical Coordinators provide one-to-one family support with:

- Product education throughout the child's treatment journey
- Education on the dosing and administration of VOXZOGO
- Ongoing injection reinforcement education
- Coordination of specialty pharmacy shipments
- Ongoing reminders for product refills and shipment updates

BIOMARIN Rare Connections™

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

ADDITIONAL INFORMATION AND RESOURCES (continued)

Coding

The following list is not inclusive of all potential codes that may be used and is provided for consideration only. Although the codes are provided by BioMarin, they are not a guarantee for reimbursement.

While the ICD-10-CM code for achondroplasia is shared by hypochondroplasia and osteosclerosis congenita, VOXZOGO® (vosoritide) is a prescription medicine used to increase linear growth in children with achondroplasia and open growth plates.

CODE TYPE	CODE	DESCRIPTOR(S)
ICD-10-CM[1]	Q77.4	Achondroplasia Hypochondroplasia Osteosclerosis congenita
VOXZOGO National Drug Codes	68135-0082-36	VOXZOGO® (vosoritide) 0.4 mg Kit (10 doses)
	68135-0119-66	VOXZOGO® (vosoritide) 0.56 mg Kit (10 doses)
	68135-0181-93	VOXZOGO® (vosoritide) 1.2 mg Kit (10 doses)

Caregivers may inject VOXZOGO subcutaneously after proper training by a healthcare professional on the preparation and administration of VOXZOGO. Some insurance plans may allow healthcare providers to bill for training the patient; contact the patient's health insurance plan to discuss coding options.

REFERENCE: 1. Centers for Disease Control and Prevention. National Center for Health Statistics website. Index to diseases and injuries. https://icd10cmtool.cdc.gov/?fy=FY2023&query=achondroplasia. Last Reviewed July 29, 2023. Accessed September 12, 2023.

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

ACRONYMS

Acronyms used in the VOXZOGO® (vosoritide) Coverage Authorization Guide

BI	Benefits investigation
CNP	C-type natriuretic peptide
FDA	US Food and Drug Administration
FGFR3	Fibroblast growth factor receptor 3
HCP	Healthcare provider
HIPAA	Health Insurance Portability and Accountability Act
ICD-10-CM	International Classification of Disease, 10th Revision, Clinical Modification
LMN	Letter of Medical Necessity
NPR-B	Natriuretic peptide receptor-B
PA	Prior authorization
PCF	Patient Consent Form
PEF	Patient Enrollment Form
SP	Specialty pharmacy

Please see Important Safety Information on page 23 and full Prescribing Information for VOXZOGO here.

INDICATION AND IMPORTANT SAFETY INFORMATION

VOXZOGO® (vosoritide) is indicated to increase linear growth in pediatric patients with achondroplasia and open growth plates.

- This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Warnings and Precautions for Risk of Low Blood Pressure

Transient decreases in blood pressure were observed in clinical studies. Patients with significant cardiac or vascular disease and patients on anti-hypertensive medicinal products were excluded from participation in VOXZOGO clinical trials. To reduce the risk of a decrease in blood pressure and associated symptoms (dizziness, fatigue, and/or nausea), patients should be well hydrated, have adequate food intake, and drink approximately 8-10 ounces of fluid in the hour prior to VOXZOGO administration.

In a 52-week, randomized, double-blind, placebo-controlled trial in 121 subjects with achondroplasia, subjects aged from 5.1 to 14.9 years, (Study 1) eight (13%) of 60 patients treated with VOXZOGO had a total of 11 events of transient decrease in blood pressure, compared to 3 (5%) of 61 patients on placebo, over a 52-week treatment period. The median time to onset from injection was 31 (18 to 120) minutes, with resolution within 31 (5 to 90) minutes in VOXZOGO-treated subjects. Two out of 60 (3%) VOXZOGO-treated patients each had one symptomatic episode of decreased blood pressure with vomiting and/or dizziness compared to 0 of 61 (0%) patients on placebo.

Adverse Reactions:

Adverse reactions that occurred in ≥5% of patients treated with VOXZOGO and at a rate greater than that of placebo in the phase 3 study are injection site reactions (including erythema, swelling, urticaria, pain, bruising, pruritus, hemorrhage, discoloration, and induration), vomiting, arthralgia, decrease in blood pressure, gastroenteritis, diarrhea, dizziness, ear pain, influenza, fatigue, seasonal allergy, and dry skin. VOXZOGO-treated patients had an increase in alkaline phosphatase levels (17%), and was noted as a laboratory abnormality.

Injection site reactions: In Study 1, injection site reactions occurred in 51 (85%) subjects receiving VOXZOGO and 50 (82%) subjects receiving placebo over a 52-week period of treatment. Patients receiving VOXZOGO experienced a total of 6983 events of injection site reactions, while patients receiving placebo experienced a total of 1776 events of injection site reactions, over a 52-week period, representing 120.4 events per patient/year exposure and 29.2 events per patient/year exposure, respectively. Two patients in the VOXZOGO arm discontinued treatment due to adverse events of pain and anxiety with injections.

Pediatric Patients 0 to <5 Years:

The safety of VOXZOGO in pediatric patients 0 to <5 years with achondroplasia was evaluated in a 52-week randomized, double-blind, placebo-controlled study (Study 2). In this study, 64 patients from birth to <5 years of age were randomized to receive either a daily vosoritide dose with similar exposure to that characterized to be safe and effective in children with ACH aged ≥5 years old, or placebo. An additional 11 patients received open-label treatment as part of this study. The most common adverse reactions (>10%) reported in pediatric patients 0 to <5 years were injection site reactions (86%) and rash (28%). The overall safety profile of VOXZOGO in pediatric patients 0 to <5 years was similar to that seen in older pediatric patients.

Administration and Monitoring:

VOXZOGO is administered as a daily subcutaneous injection. Prior to use, instruct caregivers on proper preparation and administration of VOXZOGO, and ensure caregivers have demonstrated the ability to perform a subcutaneous injection.

Monitor and assess patient body weight, growth, and physical development regularly every 3-6 months. Adjust dosage according to the patient's actual body weight. Permanently discontinue treatment with VOXZOGO upon confirmation of no further growth potential, indicated by closure of epiphyses.

Special Populations:

- There are no available data on the use of VOXZOGO in pregnant women, or data on the presence of VOXZOGO in human milk, the effects on the breastfed infant, or the effects on milk production.
- The influence of renal impairment on the pharmacokinetics of VOXZOGO has not been evaluated. No dosage adjustment is needed for patients with eGFR ≥60 mL/min/1.73 m^2. VOXZOGO is not recommended for patients with eGFR <60 mL/min/1.73 m^2.

You may report side effects to the FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch**. You may also report side effects to BioMarin at **1-866-906-6100**.

Please see additional safety information in the full Prescribing Information.

VOXZOGO® (vosoritide) for injection

BIOMARIN®

VOXZOGO®
(vosoritide) for injection