VOXZOGO®
(vosoritide) for injection

Dosing and Administration Guide for Healthcare Providers

VOXZOGO is indicated to increase linear growth in pediatric patients with achondroplasia and open growth plates.[1]

Learn how VOXZOGO is administered so you can help prepare caregivers, patients, and families for daily injections at home.

Review the full Prescribing Information and Instructions for Use with caregivers and patients.

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.

Visit **voxzogo.com/dosing-administration-video** for the full dosing and administration video

Please see Important Safety Information throughout as well as the full Prescribing Information.

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A healthcare provider should show caregivers how to administer VOXZOGO® (vosoritide) before they use it for the first time. Clinical Coordinators are available to provide additional education at home for caregivers along the way.[2]

Patients and caregivers may also receive a Welcome Kit with additional information, including the Instructions for Use for VOXZOGO, to be reviewed before the patient receives their first injection and each time their prescription is refilled. A copy of the Instructions for Use is included with every 10-pack of VOXZOGO.

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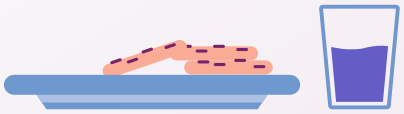
Administration Process

Getting Started

To help establish a daily routine, encourage caregivers to administer VOXZOGO® (vosoritide) around the same time each day. Guiding caregivers through each step will help them feel more confident and organized for the injection.

Ensure caregivers have[1,2]:

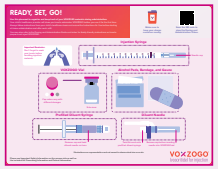
- A **calm and clean environment** where the patient and caregiver feel comfortable.
- Given your patient something to **drink** (about 8 to 10 ounces) and made sure your patient is **well fed** within 1 hour before the injection. This will reduce the signs and symptoms of potential decreases in blood pressure.



Use this time to let the VOXZOGO vial reach room temperature.

- Hands washed with **soap and water**.

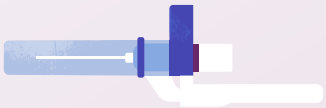
- A clean, flat surface or placemat to keep everything clearly laid out.



- A **vial with medicine powder at room temperature**. Show the caregiver how to confirm the correct dose by checking the label and color of the vial's cap, how to check the expiration date, and how to inspect for damage or contamination.

  VOXZOGO comes in 3 strengths, indicated by white, magenta, and gray colored caps. Dosing is based on body weight and may be adjusted as part of regular check-ins. For complete dosing information, refer to the back cover of this guide.

- The **diluent needle**.



- The **prefilled diluent syringe** containing sterile water. Show the caregiver how to check the expiration date and do not use if expired.

- An **injection syringe** with a capped needle.

- **Alcohol pads, gauze, bandages**, and a **sharps container**.

Show caregivers how to inspect the vial and materials for any sign of damage or contamination, such as discolored medicine or bent syringes. Remind them not to use VOXZOGO or the prefilled diluent syringe if they are expired.

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Preparing the Injection

Remind caregivers to **wash their hands** before handling materials[2]

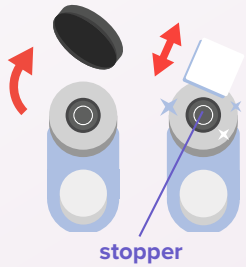
How to mix the sterile water with the medicine powder to prepare the injection syringe[2]

Most caregivers will not be familiar with reconstituting medications, so it is vital they feel comfortable with the following steps.

Step 1

- Begin by demonstrating how to flip off the cap of the **vial** (shown in the image) and wipe the top with an alcohol pad

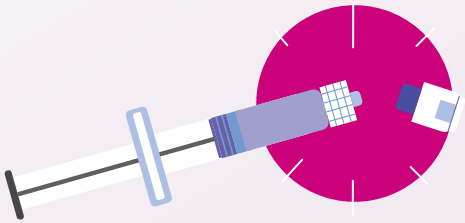
Remind caregivers not to touch the vial stopper once cleaned.



Step 2

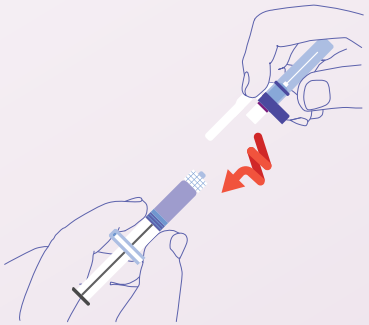
- Take the **prefilled diluent syringe** and gently bend the cap back and forth so it snaps off

Do not twist the cap.



Step 3

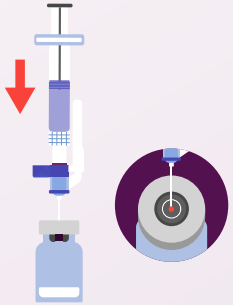
- Hold the **prefilled diluent syringe** and twist the **diluent *needle*** straight onto it until it no longer twists
- Make sure the syringe and the needle are tightly attached to prevent leakage



Inform caregivers not to use the prefilled diluent syringe to administer the injection.

Step 4

For this next part, emphasize the importance of safe needle handling—make sure caregivers know not to point the needle at anyone, including themselves.



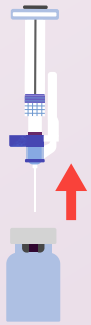
- Explain how to remove the **needle cap** by pulling it straight off while pointing the needle away from anyone
- Insert the needle **straight down** into the middle of the "bull's-eye" on the **vial's stopper**—instructing caregivers not to insert at an angle or touch the side walls
- Be careful not to touch the needle tip

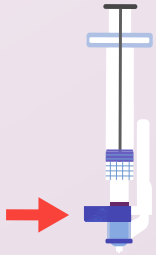
- ***Slowly*** push the plunger rod down to inject all of the **sterile water** into the vial. Pushing too quickly will cause air bubbles

Step 5

Make sure caregivers are careful not to push the blue tab until all the sterile water is in the vial, or the needle will retract too soon.

- Once there is no more **sterile water** in the syringe, remove the **diluent needle** from the **vial**





- Press the blue tab to retract the **needle**

- Instruct caregivers to dispose of the used **diluent needle** and **syringe** in the **sharps container**

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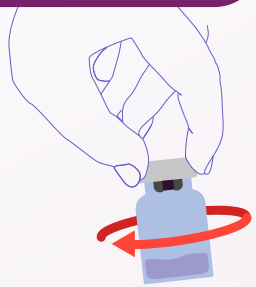
Step 6



- ***Gently*** swirl the **vial** until the powder is completely dissolved and solution is clear[2]

Remind caregivers not to shake the vial or touch the vial's stopper.[2]

- Examine the **vial** to make sure the medicine is[2]:
  - clear to yellow
  - not cloudy
  - particle free

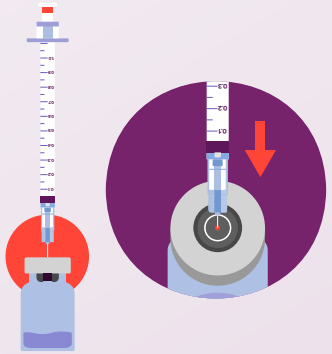
Instruct caregivers to discard the vial if the medicine looks cloudy, discolored, or contaminated with particles. Once mixed, the medicine must be used within 3 hours.[1,2]

Step 7

- Take the **injection syringe**. Remove and discard the cap that covers the needle by pulling it straight up and off. Remind caregivers about safe needle handling—be careful not to point it at anyone[2]

- Show caregivers how to completely insert the needle **straight through the middle** of the "bull's-eye" on the **vial's stopper[2]**

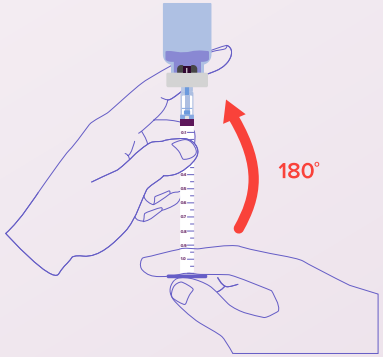
Explain how best not to touch the stopper sides or bend the injection needle.



Step 8

- **Securely and carefully** hold the **vial** and **syringe** together in place[2]
- Turn them upside down so the **vial's bottom** points at the ceiling[2]

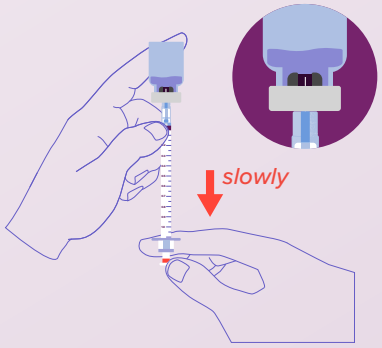
Show caregivers how to hold the vial using their index finger.[2]



Step 9

- Indicating the center channel, illustrate how to keep the **needle tip** in the **medicine** while **slowly** pulling the plunger rod back to draw the prescribed dose into the syringe, avoiding air bubbles[2]

Remind caregivers to continue to support the vial to avoid bending the needle.



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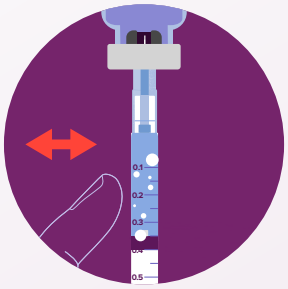
Step 10

- Show caregivers how to closely examine the **injection syringe** for bubbles[2]
- Demonstrate how to remove large air bubbles by gently *tapping* the base of the **syringe** and carefully *pushing* the plunger to get air bubbles back into the **vial**[2]

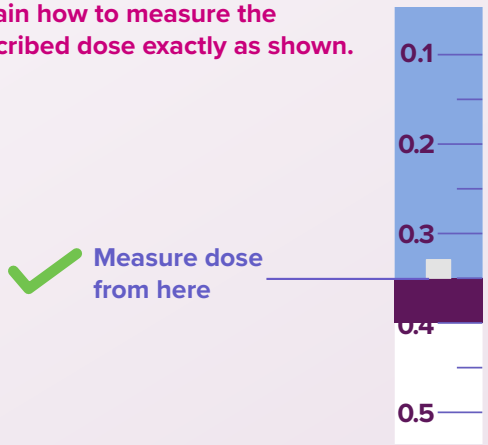
1 or 2 small bubbles are acceptable.



Step 11

- Instruct caregivers to repeat steps 9 and 10 until the **injection syringe** has the prescribed dose with no large bubbles. 1 or 2 small bubbles are acceptable[2]
- Double-check to make sure the dose in the **injection syringe** matches the prescribed dose. It is not necessary to prime the needle[2]

Explain how to measure the prescribed dose exactly as shown.



Step 12

- Once caregivers have confirmed the prescribed dose in the syringe, they should remove the **vial** by pulling it straight off the needle and discard it in the nearby **sharps container**, even if there's leftover liquid[2]

Next, it's important to review with caregivers how to prepare the injection site and administer VOXZOGO while being careful not to contaminate the needle or drop the syringe.

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VOXZOGO®
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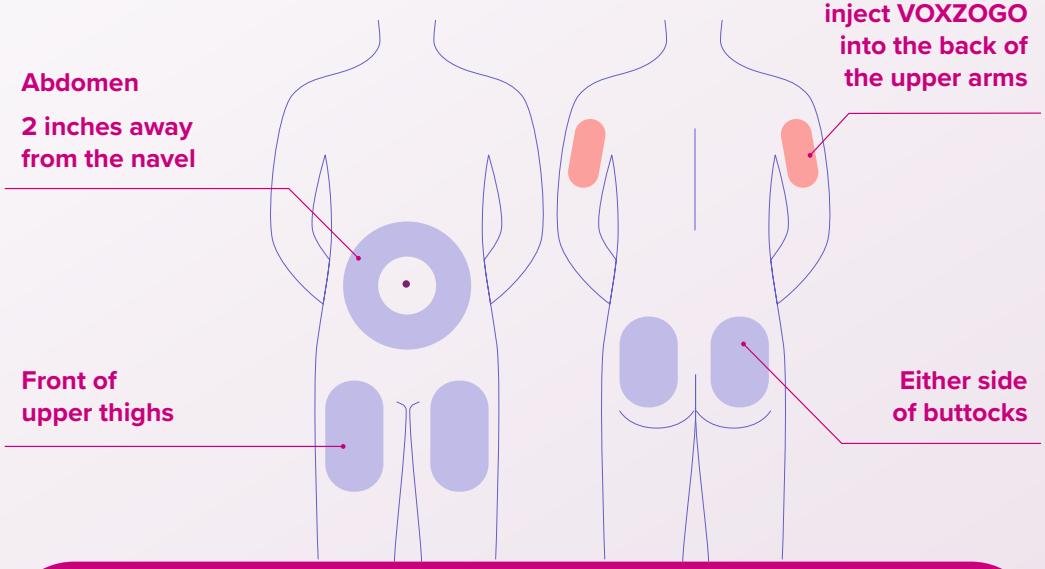
Administration

Step 13

There are 7 places caregivers can inject VOXZOGO® (vosoritide)[2]:



Remind caregivers not to inject into the same site 2 times in a row.

Step 14

Clean the site[2]

Wipe the injection site with an alcohol pad and let the skin air-dry. Do not touch or blow on the area again before the injection.

Inform caregivers not to inject through clothes.

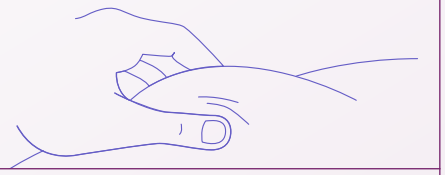
Caregivers should not inject VOXZOGO into sites that are swollen, sore, red, bruised, scarred, or hardened.

Ready to administer VOXZOGO[2]

Now that the VOXZOGO® (vosoritide) syringe has been prepared and they've selected and cleaned the injection spot, encourage caregivers to check in with their child to make sure they're both ready and comfortable. Once everyone is ready to go, the caregiver can go ahead and inject VOXZOGO.

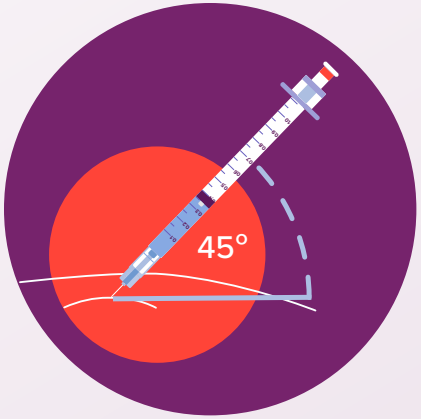
Step 15

- After they wipe the selected injection site with an alcohol pad, instruct caregivers to pinch the skin up around the injection site



Step 16

- Show caregivers how to quickly insert the **injection needle** all the way into the skin at a 45-degree angle

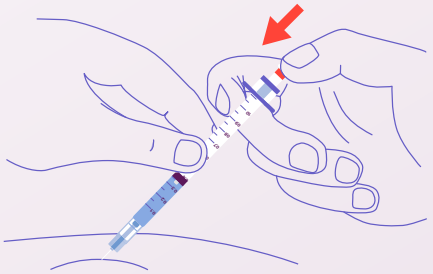


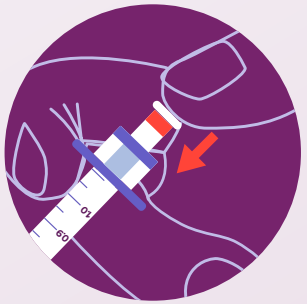
Step 17

- **Release the pinch**

Instruct caregivers how to use both hands: one to stabilize the syringe and the other to push the plunger.

- **Slowly** push the plunger rod until all the medicine is injected and the syringe is empty. Caregivers will feel a slight resistance when the syringe is empty

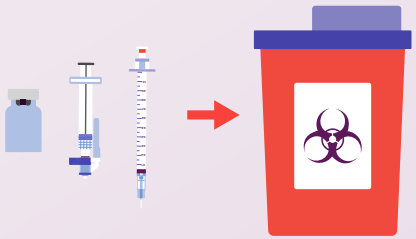




- Next, give a final push on the plunger to retract the needle into the syringe

Step 18

- Remind caregivers to dispose of the **vial, injection syringe**, and **needle** in their **sharps container**



See how to dispose of VOXZOGO in the following section.

Please see Important Safety Information throughout as well as the full Prescribing Information.

VOXZOGO®
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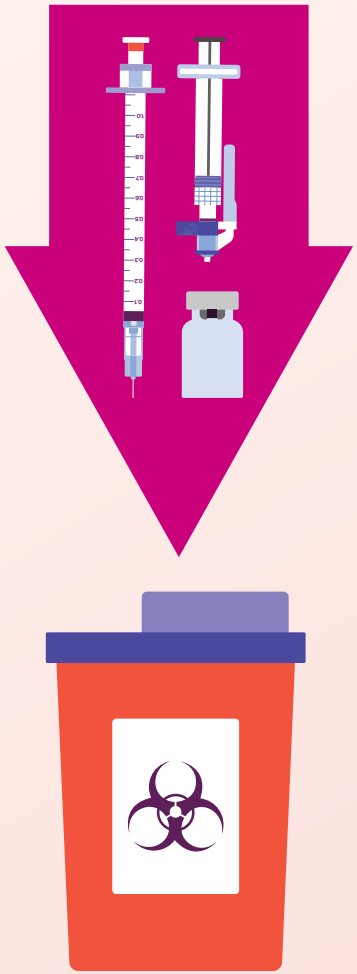
Clean and Careful

Storage and Safety Information

- Store VOXZOGO® (vosoritide) in a refrigerator at 36°-46° F (2°-8° C)[2]
- Do not freeze[2]
- Store in the original package to protect from light[1,2]
- If necessary, VOXZOGO may be stored (before mixing) at room temperature at 68°-77° F (20°-25° C) for up to 90 days[2]
- Do not return VOXZOGO to the refrigerator once it has reached room temperature[2]
- Do not use VOXZOGO after the expiration date[2]
- Reconstituted VOXZOGO must be administered within 3 hours of reconstitution[1]

Dispose of used or expired vials, needles, and syringes in an approved sharps container immediately after use[2]



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VOXZOGO®
(vosoritide) for injection

At-Home Management

Helpful Hints

Encourage communication between your patient and caregiver after administration[2]

After every injection, it's helpful for the caregiver to have a short talk with their child about how they feel. If their child experiences signs of decreased blood pressure, advise caregivers to call you and to lay their child down with their legs raised. The caregiver should inspect the injection site—if slight bleeding occurs, they can gently press a gauze pad on it for a few seconds or apply a bandage. Caregivers should not rub the injection site.

Let parents and caregivers know to contact you if their child experiences any adverse reactions, including signs and symptoms of potential decreases in blood pressure, while taking VOXZOGO® (vosoritide).

If a dose is missed, it can be administered within 12 hours of the scheduled time of administration. After that, the missed dose should be skipped. Instruct caregivers to resume their daily schedule by giving the prescribed dosage.

VOXZOGO is indicated to increase linear growth in patients with achondroplasia of all ages and open growth plates. Because keeping up with daily injections is important to get the most out of VOXZOGO, remind your families to consult the Instructions for Use as well as their take-home administration guide for tips that may help make the process easier.

Every family is unique. Empower caregivers to incorporate VOXZOGO into their child's daily routine in a way that's successful for them.

For medical information inquiries:
- **Email: medinfo@bmrn.com**
- **Phone: 1-800-983-4587**

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VOXZOGO®
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Resources for Caregivers and Patients

BioMarin Clinical Coordinators can provide one-to-one product education and support to help caregivers feel confident about giving their child VOXZOGO® (vosoritide) at home. Clinical Coordinators provide families with:

- Product education support tailored to the family and child's needs while the child is on treatment
- Ongoing injection reinforcement education and reminders for families
- Coordination with the specialty pharmacy for the delivery of the medication

If your patient enrolls in BioMarin RareConnections™ after receiving a prescription for VOXZOGO, a Clinical Coordinator can deliver a Welcome Kit to the patient's family with resources to help them along their treatment journey, including:

- VOXZOGO Patient Dosing and Administration Guide
- Injection Placemat
- VOXZOGO Instructions for Use
- Daily Injection Tracker
- and more!

Additional resources to support caregivers and patients are available at VOXZOGO.com

Use this QR code for the full dosing and administration video

Please see Important Safety Information throughout as well as the full Prescribing Information.

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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.

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Dose Monitoring and Adjustment

Injection volume is based on body weight and concentration of reconstituted VOXZOGO® (vosoritide)[1]

Actual Body Weight*	Vial Strength for Reconstitution**	Dose	Injection Volume
3 kg	0.4 mg	0.096 mg	0.12 mL
4 kg		0.12 mg	0.15 mL
5 kg		0.16 mg	0.2 mL
6-7 kg		0.2 mg	0.25 mL
8-11 kg		0.24 mg	0.3 mL
12-16 kg	0.56 mg	0.28 mg	0.35 mL
17-21 kg		0.32 mg	0.40 mL
22-32 kg		0.4 mg	0.5 mL
33-43 kg	1.2 mg	0.5 mg	0.25 mL
44-59 kg		0.6 mg	0.3 mL
60-89 kg		0.7 mg	0.35 mL
≥90 kg		0.8 mg	0.4 mL

* Intermediate body weights that fall within these weight bands should be rounded to the nearest whole number.

** The concentration of vosoritide in reconstituted 0.4 mg vial and 0.56 mg vial is 0.8 mg/mL. The concentration of vosoritide in reconstituted 1.2 mg vial is 2 mg/mL.

Adjust dose based on body weight

Regular check-ins will ensure appropriate dosing from early childhood through teenage years. Assess patient weight every 3 to 6 months to determine the appropriate dose.

References:

1. VOXZOGO [package insert]. Novato, CA: BioMarin Pharmaceutical Inc; 2023. **2.** VOXZOGO Instructions for Use. Novato, CA: BioMarin Pharmaceutical Inc; 2023.

This guide is intended for medical professionals who will be training caregivers on daily VOXZOGO administration. This resource is not intended for non-medical audiences.

Visit VOXZOGO.com/hcp for more information about achondroplasia and VOXZOGO.

Please see Important Safety Information throughout as well as the full Prescribing Information.

VOXZOGO®
(vosoritide) for injection

BIOMARIN®