VOXZOGO®
(vosoritide) for injection

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]: $(\text{Height at Recent Visit} - \text{Height at Previous Visit}) \times \frac{365.25}{\text{Days Between Visits}}$ **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

For more information, contact your BioMarin Account Manager or Field Reimbursement Manager

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.

Please see Important Safety Information on the next page as well as the full Prescribing Information.

INDICATION AND IMPORTANT SAFETY INFORMATION

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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.

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.

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