Abbreviated Prescribing Information (PI) (INTL): VOXZOGO® ▼ (vosoritide)

Refer to Summary of Product Characteristics for full information.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Presentation: VOXZOGO® 0.4 mg powder and solvent for solution for injection. VOXZOGO® 0.56 mg powder and solvent for solution for injection. VOXZOGO® 1.2 mg powder and solvent for solution for injection. **Therapeutic indications:** VOXZOGO® is indicated for the treatment of achondroplasia in patients 4 months of age and older whose epiphyses are not closed. The diagnosis of achondroplasia should be confirmed by appropriate genetic testing. **Posology:** Treatment with vosoritide should be initiated and directed by a physician appropriately qualified in the management of growth disorders or skeletal dysplasias. VOXZOGO is given as a daily subcutaneous injection. The volume of vosoritide to be administered at the recommended dose is based on the patient's weight and is approximately between 15–30 µg/kg, where the higher dose is given to smallest children. The dose can be administered using either mL graduated syringes or Unit (U) graduated syringes (see table below). The measurements for the Unit graduated syringes are equivalent to mL as follows: 0.1 mL = 10 Units. For practicality reasons and to account for weight-related PK changes, the following dosing is recommended.

Body weight (kg)	**Dose**	**Vosoritide 0.4 mg solvent (water for injections): 0.5 mL concentration: 0.8 mg/mL**		**Vosoritide 0.56 mg solvent (water for injections): 0.7 mL concentration: 0.8 mg/mL**		**Vosoritide 1.2 mg solvent (water for injections): 0.6 mL concentration: 2 mg/mL**	
		Daily injection volume					
		mL	Units	mL	Units	mL	Units
4	0.12 mg	0.15 mL	15 U				
5	0.16 mg	0.20 mL	20 U				
6–7	0.20 mg	0.25 mL	25 U				
8–11	0.24 mg	0.30 mL	30 U				
12–16	0.28 mg			0.35 mL	35 U		
17–21	0.32 mg			0.40 mL	40 U		
22–32	0.40 mg			0.50 mL	50 U		
33–43	0.50 mg					0.25 mL	25 U
44–59	0.60 mg					0.30 mL	30 U
60–89	0.70 mg					0.35 mL	35 U
≥ 90	0.80 mg					0.40 mL	40 U

Duration of treatment: Treatment with this medicinal product should be stopped upon confirmation of no further growth potential, indicated by a growth velocity of <1.5 cm/year and closure of epiphyses. *Missed dose:* If a dose of vosoritide is missed, it can be administered within 12 hours. If more than 12 hours have passed since the original dosing schedule, the missed dose should NOT be administered. Patients/caregivers should be advised to continue with the next scheduled dose the following day. *Growth monitoring:* Patients should be monitored and assessed regularly every 3–6 months to check body weight, growth and physical development. Dose should be adjusted according to the patient's body weight (see Table). *Patients with renal or hepatic impairment:* The safety and efficacy of vosoritide in patients with renal or hepatic impairment has not been evaluated. *Paediatric population:* The safety and efficacy of VOXZOGO® in children aged less than 4 months is limited, no recommendation on a posology can be made. **Administration:** VOXZOGO® is for subcutaneous single use only. This medicinal product must be administered within 3 hours of reconstitution. Prior to injecting, a healthcare professional should: train caregivers on the preparation and subcutaneous injection of this medicinal product; train caregivers and patients to recognise signs and symptoms of decreased blood pressure; inform caregivers and patients what to do in the event of symptomatic decreases in blood pressure. Patients and caregivers should be instructed to rotate sites for subcutaneous injections. Recommended injection sites on the body include the front middle of the thighs, the lower part of the abdomen except for 5 cm directly around the navel, top of the buttocks or the back of the upper arms. The same injection area should not be used on two consecutive days. VOXZOGO® should not be injected into sites that are red, swollen, or tender. Patients should be well hydrated at the time of injection. It is recommended patients eat a light snack and drink an adequate amount of fluid (e.g., water, milk, juice, etc.) about 30 minutes before injecting. This is to reduce the signs and symptoms of potential decreases in blood pressure (dizziness, fatigue and/or nausea) occurring. If possible, this medicinal product should be injected at approximately the same time each day. **Contraindications:** Hypersensitivity to the active substance(s) or to any of the excipients. **Warnings and precautions:** *Traceability:* In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded. *Blood pressure effects:* Patients with significant cardiac or vascular disease and patients on anti-hypertensive medicinal products were excluded from participation in premarketing clinical trials. To reduce the risk of a potential decrease in blood pressure and associated symptoms (dizziness, fatigue and/or nausea), patients should be well hydrated at the time of injection. *Sodium:* This medicinal product contains less than 1 mmol sodium (23 mg) per unit volume, essentially 'sodium-free'. **Interaction with other medicinal products:** *In vitro* cytochrome P450 (CYP) inhibition and induction studies and *in vitro* transporter inhibition studies have been performed. Results suggested that vosoritide is unlikely to cause CYP- or transporter-mediated drug-drug interactions in humans when the medicinal product is administered concomitantly with other medicinal products. No other interaction studies have been performed. Because it is a recombinant human protein, vosoritide is an unlikely candidate for drug-drug interactions. **Fertility, pregnancy and lactation:** *Pregnancy:* There are no or limited amount of data from the use of vosoritide in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of vosoritide during pregnancy. *Breast-feeding:* Available pharmacodynamic/toxicological data in animals have shown excretion of vosoritide in milk. A risk to newborns/infants cannot be excluded. Vosoritide should not be used during breast-feeding. *Fertility:* No impairment of male or female fertility has been observed in nonclinical studies. **Effects on ability to drive and use machines:** VOXZOGO® has moderate influence on the ability to drive, cycle and use machines. Vosoritide may cause transient decreases in blood pressure that are usually mild but syncope, pre-syncope, and dizziness, as well as other signs and symptoms of decreased blood pressure have been reported as adverse reactions with VOXZOGO®. The patient's response to treatment should be considered and if appropriate, advised not to drive, cycle or use machines for at least 60 minutes after injection. **Overdose:** In clinical trials, doses of vosoritide were explored up to 30 µg/kg/day. Two patients received up to 3 times the recommended daily dose of 15 µg/kg/day for up to 5-weeks. No signs, symptoms or adverse reactions associated with the higher than intended dose were observed. In the event a patient takes more than they should, the patient should contact their healthcare professional. **Summary of the safety profile:** The most common adverse reactions to vosoritide were injection site reactions (85%), vomiting (27%), and decreased blood pressure (13%). **Tabulated list of adverse reactions:** Adverse reactions are listed below by MedDRA system organ class and by frequency. Frequencies are defined as very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. See the Voxzogo SmPC for full details of adverse reactions.

System organ class	**Very common**	**Common**	**Uncommon**
Nervous system disorders		Syncope	
		Pre-syncope	
		Dizziness	
Vascular disorders	Hypotension[a]		
Gastrointestinal disorders	Vomiting	Nausea	
Skin and subcutaneous disorders			Hypertrichosis
General disorders and administration site conditions	Injection site reaction[b]	Fatigue	
Investigations	Increased alkaline phosphatase		

[a.] Hypotension includes both asymptomatic and symptomatic adverse reactions.

[b.] Injection site reactions include the preferred terms; injection site erythema, injection site reaction, injection site swelling, injection site urticaria, injection site pain, injection site bruising, injection site pruritus, injection site haemorrhage, injection site discolouration, and injection site induration.

Special precautions for storage: Store in a refrigerator (2 °C – 8 °C). Do not freeze. Store in the original package in order to protect from light. VOXZOGO® may be stored at room temperature below 30 °C for a single period up to 90 days, but not beyond the expiry date. Do not return VOXZOGO® to refrigerator after storage at room temperature. If not used immediately, VOXZOGO® must be administered within 3 hours of reconstitution. **Marketing authorisation holder:** BioMarin International Limited. Shanbally, Ringaskiddy, County Cork, Ireland. **Marketing authorisation number(s):** EU/1/21/1577/001 - EU/1/21/1577/002 - EU/1/21/1577/003 Detailed information on this medicinal product is available on the website of the European Medicines Agency: http://www.ema.europa.eu/ - **Date of first authorisation:** August 2021. **Latest aPI revision:** June 2024. VOXZOGO® is a trademark of BioMarin Pharmaceutical Inc. from whom further information is available. **Legal classification:** Prescription-Only Medicine.

Healthcare professionals should report adverse events in accordance with their local requirements.

Adverse events should also be reported to BioMarin on + 1 415 506 6179 or drugsafety@bmrn.com

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