vosoritide (Voxzogo™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO248

Description

Vosoritide (Voxzogo) is a daily subcutaneously administered C type natriuretic peptide.

Length of Authorization

- Initial: Six months
- Renewal: Six months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
vosoritide (Voxzogo)	0.4 mg vials	To increase linear growth, in pediatric patients with achondroplasia	30 vials/30 days
	0.56 mg vials		
	1.2 mg vials		

Initial Evaluation

I. **Vosoritide (Voxzogo)** may be considered medically necessary when the following criteria are met:
   A. Member is one month or older; **AND**
   B. Member weighs 3kg or more; **AND**
   C. Medication is prescribed by, or in consultation with, a pediatric specialist in one of the following areas: neurology, orthopedic surgery, endocrinology, genetics; **AND**
   D. A diagnosis of **achondroplasia**; **AND**
      1. Provider attestation to the following:
         i. Genetic testing has been done to confirm diagnosis; **AND**
         ii. Epiphyses are open, as confirmed by radiographic imaging completed in the previous three months; **AND**
         iii. Member will not receive growth hormone treatment (e.g., Genotropin, Norditropin) concurrently with vosoritide (Voxzogo); **AND**
         iv. Limb lengthening surgery has not been performed in the past 18 months; **AND**
         v. At the time of vosoritide (Voxzogo) request, limb lengthening surgery is not planned to occur prior to closure of the epiphyses; **AND**

II. Vosoritide (Voxzogo) is considered investigational when used for all other conditions, including but not limited to:
   A. Forms of dwarfism other than achondroplasia
   B. For growth in patients with achondroplasia when epiphyses are closed

C. Combination therapy with growth hormone treatment or limb-lengthening surgery

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Provider attestation to the following:
   A. If the member is 12 years of age or older or if epiphyses could be closed (e.g., precocious puberty, no height gained in previous few months): radiographic imaging on long bones has been completed within the past year to confirm epiphyses remain open (i.e., potential for growth still remains); **AND**
   B. Member will not receive growth hormone treatment (e.g., Genotropin, Norditropin) concurrently with vosoritide (Voxzogo); **AND**
   C. Limb lengthening surgery has not been performed in the past 18 months; **AND**
   D. At the time of vosoritide (Voxzogo) request, limb lengthening surgery is not planned to occur prior to closure of the epiphyses; **AND**

IV. Provider attestation that the most recent annualized growth velocity (AGV) is greater than the baseline AGV

Supporting Evidence

I. Vosoritide (Voxzogo), is FDA-approved to increase linear growth in pediatric patients with achondroplasia. It is a daily subcutaneous (SC) injection with dose based on patient body weight. In 2023, it was evaluated for safety and efficacy in patients at least one month of age and older, receiving FDA-approval in this age group. This expands the original label of those five and older with achondroplasia.

II. Achondroplasia is a condition of disproportionate short stature and affects 1:20,000 births. Gene mutations permanently activate the FGFR3 receptors, inhibit chondrocyte proliferation, and impair bone formation. Vosoritide (Voxzogo) is the first pharmacotherapy FDA-approved for this condition. There are no formal U.S. guidelines for the treatment of achondroplasia; however, management is highly specialized. Thus, a specialist prescriber is required.

III. Achondroplasia is caused by variants in the FGFR3 gene, and is recognized on genetic testing. Vosoritide (Voxzogo) targets the root cause of the condition, and safety and efficacy in other causes of forms of dwarfism are unknown, and is not expected to increase linear growth in other conditions. To rule out other causes or forms of dwarfism, genetic testing is required.

IV. Outside of lifestyle management (e.g., adaptation of home and school environments) and adjunctive care (e.g., treatment for sleep apnea), limb lengthening surgery may be considered.

Surgery may be performed at any time, prior to or after epiphyses (i.e., growth plate) close. Evidence suggests there is greater success with surgery after epiphyses have closed. Therapy has not been evaluated for safety and efficacy in those that have received limb lengthening surgery within the past 18 months, or in conjunction with limb lengthening surgery. If surgery has been completed, vosoritide (Voxzogo) therapy should not be used within an 18-month window of surgery, to realize the benefits of surgical intervention. Furthermore, safety and efficacy of this therapy in conjunction with or to prepare for surgery has not been evaluated. Additionally, it is unknown if use of vosoritide (Voxzogo) will have additive effects if used prior to surgery; thus, if surgery is planned or expected prior to final height being reached (e.g., closed epiphyses), therapy should be discontinued.

V. Vosoritide (Voxzogo) is not expected to provide further linear growth after epiphyses close. FDA and manufacturer guidance indicate that if epiphyses close, therapy should be discontinued at this time. Additionally, therapy should not be initiated in patients that have epiphysial closure. Routine imaging should be completed to evaluate medical necessity for therapy, and is required for initiation of therapy, as well as for renewal evaluation in patients of 12 years of age and older given the greater potential of epiphysial closure at in adolescence.

VI. Growth hormone therapy is controversial in patients with achondroplasia. It is not commonly used in the U.S. as evidence suggests this may exacerbate the disproportionate stature; however, evidence is conflicting. Dual therapy has not been evaluated for safety or efficacy; thus, concurrent use is not allowed.

VII. Vosoritide (Voxzogo) was evaluated in a Phase 3, randomized, blinded, placebo-controlled trial in 121 patients that were at least five years of age. Baseline AGV was around 4 cm/year for all patients. The primary outcome was an increase in annualized growth velocity (AGV) over baseline, which was statistically significant for vosoritide (Voxzogo) over placebo with an increase in AGV of 1.71 cm/year, compared to 0.13 cm/year. Therapy was also evaluated in a one-year, open-label extension trial where patients could continue therapy, and those originally randomized to placebo were switched to vosoritide (Voxzogo). The crossover group achieved an AGV of 1.62 cm/year, further supporting the pivotal trial results that therapy may influence an increase a 1.5-1.6 cm increase in AGV. Vosoritide (Voxzogo) has not yet shown to improve other disease manifestations, function, QoL, or reduction surgical intervention need. Vosoritide (Voxzogo) was granted Priority Review, Accelerated Approval, and Orphan Drug Designations. There will be a long-term, open-label trial to evaluate the drug's impact on final height. To assess if there has been an increase in AGV for patients on vosoritide (Voxzogo) therapy, a recently measured baseline AGV is required prior to initiation, as well as upon each renewal to determine if there is a continued treatment effect. In absence of continued treatment effect, continuation of therapy is not warranted at this time.

VIII. In 2023, vosoritide (Voxzogo) received approval by the FDA for an age expansion into those one month of age and older. This approval was based on a 52-week, phase 2, double-blind, placebo-controlled trial (Study 111-206) which evaluated the safety and efficacy in children with achondroplasia 0-60 months of age. There was a total of 75 patients, 43 received vosoritide and 32 placebo; patients were enrolled over three cohorts which assessed two different doses. Primary endpoints assessed the safety and tolerability, as well as the change from baseline in

length/height Z-score. The change from baseline in AGV was measured as a secondary endpoint. Vosoritide (Voxzogo) was well tolerated with a safety profile consistent with those patients over five years of age. All patients had one adverse event with the most common being injection pain pain/redness. Over all patients in the 52-week period, there was an improvement of over 0.3 standard deviations (95% CI 0.07, 0.54) in height Z-score with vosoritide (n=43) versus placebo (n=32). This change was consistent with those children over five in the pivotal trial and across the three cohorts. Additionally, there was an increase in AGV of 0.92cm/year (95% CI 0.24, 1.59) with vosoritide compared to placebo. Vosoritide (Voxzogo) is weight based; thus, a recent weight from growing pediatric patients is required for initial and renewal coverage considerations for appropriate dose calculation. There is no data or experience in treating those under 3 kilograms.

Investigational or Not Medically Necessary Uses

I. Vosoritide (Voxzogo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Forms of dwarfism other than achondroplasia. Vosoritide (Voxzogo) counteracts the genetic mutation that causes achondroplasia. In addition to lack of evidence for safety and efficacy, there is no expectation that therapy would be effective for other conditions, including other forms of dwarfism or short stature (e.g., growth hormone deficiency, Turner syndrome).
   B. For growth in patients with achondroplasia when epiphyses are closed
   C. Combination therapy with growth hormone treatment or limb-lengthening surgery

References

1. Voxzogo [Prescribing Information]. BioMarin Pharmaceutical Inc., Novato, CA. December 2021. Revised October 2023.
2. 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.
3. Randel A. Aap guidelines on health supervision of patients with achondroplasia. AFP. 2006;73(6):1112.
4. Coste J, et al. Height and health-related quality of life: a nationwide population study. J Clin Endocrinol Metab. 2012;97(9):3231–3239.
5. Vosoritide product dossier. BioMarin. November 30, 2023.

Policy Implementation/Update:

Action and Summary of Changes	Date
Update to the policy and supporting evidence to include age expansion in those one month and older; removed requirement of documentation of current AGV and weight on initial and renewal	02/2024
Policy created	02/2022