navepegritide (Yuviwel®) and vosoritide (Voxzogo™)
EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO248

Description
Navepegritide (Yuviwel) and vosoritide (Voxzogo) are subcutaneously administered C type natriuretic peptide (CNP) agents.

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		
navepegritide (Yuviwel)	1.3 mg vials	To increase linear growth, in pediatric patients with achondroplasia	4 vials/28 days
	2.8 mg vials		
	5.5 mg vials		

Initial Evaluation

I. **Navepegritide (Yuviwel) and vosoritide (Voxzogo)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, a pediatric specialist in one of the following areas: neurology, orthopedic surgery, endocrinology, genetics; **AND**
   B. Vosoritide (Voxzogo) and navepegritide (Yuviwel) will not be used in combination with each other; **AND**
   C. 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 navepegritide (Yuviwel) or vosoritide (Voxzogo); **AND**
         iv. Limb lengthening surgery has not been performed in the past 18 months; **AND**
         v. At the time of request, limb lengthening surgery is not planned to occur prior to closure of the epiphyses; **AND**
   D. The request is for vosoritide (Voxzogo); **AND**
      1. Member is one month or older; **AND**

2. Member weighs 3 kg or more; **OR**

E. The request is for navepegritide (Yuviwel); **AND**
   1. Member is 2 years of age or older; **AND**
   2. Member weighs 8 kg or more; **AND**
   3. Documentation the member experienced intolerance, hypersensitivity, or has a contraindication to vosoritide (Voxzogo) that is not expected to occur with navepegritide (Yuviwel) as confirmed by a Moda Health pharmacist/clinician.

II. Navepegritide (Yuviwel) and vosoritide (Voxzogo) are 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. Documentation of radiographic imaging on long bones has been completed within the past year to confirm epiphyses remain open (i.e., potential for growth still remains) 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); **AND**
IV. Provider attestation to the following:
   A. Member will not receive growth hormone treatment (e.g., Genotropin, Norditropin) concurrently with navepegritide (Yuviwel) or vosoritide (Voxzogo); **AND**
   B. Limb lengthening surgery has not been performed in the past 18 months; **AND**
   C. At the time of request, limb lengthening surgery is not planned to occur prior to closure of the epiphyses; **AND**
V. 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) and navepegritide (Yuviwel) target 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)/ navepegritide (Yuviwel) 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)/ navepegritide (Yuviwel) 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)/ navepegritide (Yuviwel) are not expected to provide further linear growth after epiphyses close. The 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. Available guidelines for achondroplasia have no specific recommendations for therapy and guidance focuses on disease monitoring and treatment for the medical complications related to achondroplasia. Due to a lack of evidence that one agent is more beneficial than the other and the significant cost difference between vosoritide (Voxzogo) and navepegritide (Yuviwel), use of vosoritide (Voxzogo) is required before allowing treatment with navepegritide (Yuviwel).

VIII. 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.

IX. 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 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, and 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.

X. Navepegritide (Yuviwel) is FDA-approved to increase linear growth in pediatric patients with achondroplasia aged 2 years of age or older. It is given as a once weekly subcutaneous injection with dose based on patient weight. This was approved under an accelerated pathway and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

XI. Navepegritide (Yuviwel) was evaluated in a Phase 2b trial (ApproaCH) and subsequent open-label extension (OLE) that enrolled a total of 84 children aged 2 through 11 years and a clinical diagnosis of achondroplasia with genetic confirmation. Baseline characteristics included mostly males (53.6%) with a median age of 5.5 years, median height of 89 cm, achondroplasia-specific mean height Z-score of 0.1 and mean annualized growth velocity (AGV) of 3.9 cm/year.

XII. Participants were randomized 2:1 to receive 100mcg/kg/week of navepegritide (Yuviwel) or weekly placebo. The primary endpoint was annualized growth velocity (AGV) at week 52 and the secondary endpoint was the change from baseline in achondroplasia-specific height Z-score

at week 52. The AGV for navepegritide (Yuviwel) was 5.89 cm/year compared to placebo at 4.41 cm/year at week 52. The difference between treatment AGV at week 52 was considered statistically significant (1.49; 95% CI, 1.05 to 1.93; p<0.001), along with the change in achondroplasia-specific height Z-score from baseline to week 52 (0.28; 95% CI, 0.18 to 0.39; p<0.001).

XIII. Health-related quality of life measures using the achondroplasia child experience measure (ACEM) also showed improvement from baseline in physical functioning. However, these results are subjective, and their long-term clinical relevance remains unclear. The OLE enrolled all the participants who completed the initial blinded trial and either continued treatment or switched from placebo to navepegritide (Yuviwel). The results in week 104 showed sustained mean, AGV increase (5.65 cm/year), and the crossover group achieved an increase in mean AGV (5.42 cm/year), which supports the reproducibility of the treatment.

XIV. Although the primary endpoint was statistically significant compared with placebo, annualized growth velocity is a surrogate endpoint, and its impact on final adult height, functional outcomes, complications, and quality of life remains uncertain. Health-related quality of life (HRQoL) measures such as the achondroplasia child experience measure (ACEM) showed improvement from baseline, but these findings are subjective and their long-term clinical relevance is unclear. The open-label extension study supports reproducibility of growth findings through two years of therapy; however, longer-term efficacy and safety remain unestablished. The overall quality of evidence is low because clinically meaningful long-term outcomes, including the impact on final adult height and quality of life has not yet been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Investigational or Not Medically Necessary Uses

I. Navepegritide (Yuviwel) and vosoritide (Voxzogo) have 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. These agents counteract the genetic mutation that causes achondroplasia. In addition to lack of evidence for safety and efficacy, there is no expectation that these therapies 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

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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.
6. Yuviwel product dossier. Ascendis Pharma; March 2026.
7. Yuviwel. Package Insert. Ascendis Pharma; February 2026.
8. Savarirayan R, McDonnell C, Bacino CA, et al. Once-Weekly Navepegritide in Children With Achondroplasia: The APPROACH Randomized Clinical Trial. JAMA Pediatr. 2026;180(1):18–25. doi:10.1001/jamapediatrics.2025.4771
9. Savarirayan R, McDonnell C, Bacino CA, et al. O04: Growth outcomes and safety of navepegritide in children with achondroplasia: Results of the ApproaCH trial open label extension. Genetics in Medicine Open, 4.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy to include navepegritide (Yuviwel) for the treatment of linear growth in pediatric patients two years and older with open epiphyses. Updates made to align policy with newer formatting and verbiage.	08/2026
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