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Drug Class Update with New Drug Evaluation: C-Type Natriuretic Peptides

Date of Review: August 2026

Generic Name: Navepegritide

Date of Last Review: April 2022
Dates of Literature Search: 01/01/1946 – 05/13/2026
Brand Name (Manufacturer): YUVIWEL (Ascendis Pharma)
Dossier Received: no

Current Status of PDL Class:

See **Appendix 1**.

Purpose for Class Update:

Assess the evidence for efficacy and safety of YUVIWEL (navepegritide), a C-type natriuretic peptide (CNP) pro-drug recently approved by the Food and Drug Administration (FDA) to increase linear growth in children aged 2 years and older with achondroplasia and open epiphyses. In addition, new evidence for VOXZOGO (vosoritide), a CNP analog indicated for the management of bone growth in children with achondroplasia will be evaluated.

Plain Language Summary:

- Achondroplasia is a rare condition that affects the growth of bones in childhood. It is caused by a mutation, or change, in a gene that is responsible for bone development. The bones in the arms and legs are mostly affected, which causes short-limbed dwarfism or short stature.
- Other features of the achondroplasia include enlarged head, short fingers, spinal curvature, and bowed legs. Complications of this condition are frequent ear infections which can affect hearing development, brief periods of stopped breathing while sleeping (apnea), back pain, numbness, leg weakness, and slowed development of motor skills such as sitting and walking.
- YUVIWEL (navepegritide) is a new medicine approved by the FDA to stimulate bone growth in children aged 2 years and older with achondroplasia. A similar medicine, VOXZOGO (vosoritide), was approved in 2021 to also stimulate bone growth in children with achondroplasia. Vosoritide must be given once a day by an injection under the skin (subcutaneously), while navepegritide is given once a week by a subcutaneous injection. The two medicines have not been studied together so it is not known if one medicine is more safe or effective than the other medicine.
- A clinical study conducted over one year found that navepegritide added an additional 0.6 inches of height in children who received the medicine instead of placebo. However, final the effect on final adult height measurements have not yet been determined.
- The most common side effects with navepegritide injections are redness, swelling or rash at the site where the medicine was given (injection site reactions).
- The Oregon Health Plan should offer coverage of navepegritide similar to vosoritide in children enrolled in the plan who have achondroplasia after the prescriber documents medical need through a process called prior authorization.

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Research Questions:

1. What is the efficacy and effectiveness of navepegritide in reducing symptoms, avoiding complications, and improving functional outcomes in patients with achondroplasia?
2. What are the harms of navepegritide in the treatment of patients with achondroplasia?
3. Are there populations based on demographic characteristics, such as age, gender, ethnicity, comorbidities, who would benefit from or be harmed by navepegritide?

Conclusions:

- No new high-quality systematic reviews or clinical guidelines were identified for this drug class update.
- The FDA approved an expanded indication for vosoritide for all pediatric patients with achondroplasia and open epiphyses in October 2023.[1] Prior to the expanded indication, vosoritide was only approved in children aged 5 years and older.[1] The expanded approval is based on results from a 52-week, double-blind, placebo-controlled, phase 2 randomized controlled trial (RCT) evaluating the efficacy and safety of vosoritide in 64 children younger than 5 years (range: 4.4 months to 59.8 months).[2] The study was not powered to detect significant changes in primary endpoints. The least-squares mean difference (LSMD) from baseline to 52 weeks in height Z-score between the vosoritide (-0.06) and placebo (-0.31) was 0.25 (95% CI -0.02 to 0.53; low-quality evidence).[2] Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]
- In February 2026, a new CNP pro-drug, navepegritide, received FDA approval to increase linear growth in pediatric patients 2 years or older with achondroplasia with open epiphyses.[3] This indication was approved under accelerated approval based on an improvement in annualized growth velocity observed in clinical trials.[4] Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[3]
- The phase 2b APPROACH trial evaluated the safety and efficacy of navepegritide in children (n=84) with genetically confirmed achondroplasia.[4] Compared to placebo, once weekly navepegritide resulted in a LSMD in annualized growth velocity of 1.49 centimeters (cm)/year (4.41 vs.5.89 cm/year; 95% confidence interval [CI] 1.05 to 1.93; P<0.0001; moderate-quality evidence) over 52 weeks.[4] Although this difference was statistically significant, the clinical significance of this change is not clear. Evidence to support navepegritide to reduce symptoms, avoid complications, and improve functional outcomes in patients with achondroplasia is insufficient.
    - The most frequently reported adverse events in the trial and subsequent open-label extension study were vomiting, injection site reactions, pain in the extremity, and nausea (see **Table 2**).[3]
    - Evidence specific to demographic characteristics such as race, ethnicity, and comorbidities are insufficient due to underrepresentation in the studies. Study results are most applicable to white patients with achondroplasia ages 2 to 11 years which may limit broader applicability.

Recommendations:

- Create a new drug class on Oregon's Practitioner-Managed Prescription Drug Plan (PMPDP) called "C-Type Natriuretic Peptides" and include vosoritide and navepegritide in this class.
- Designate vosoritide and navepegritide as non-preferred and require prior authorization (PA) to ensure appropriate use (see **Appendix 6**).

Summary of Prior Reviews and Current Policy:
The first drug approved for management bone development in children with achondroplasia was vosoritide, which was reviewed by the Pharmacy and Therapeutic Committee at the April 2022 meeting. The Committee approved the recommendation to implement PA criteria for vosoritide to ensure appropriate use in FDA-approved populations. The PA criteria are presented in **Appendix 6**.

Background:
Achondroplasia, the most common form of short-stature skeletal dysplasia, is caused by a recurrent pathogenic variant in the gene encoding the fibroblast growth factor receptor 3 (FGFR3) protein, which results in impaired conversion of cartilage to bone (ossification).[5,6] Features associated with achondroplasia are short fingers, shortened proximal limb bones, macrocephaly, midface hypoplasia, and a long trunk.[6] The estimated prevalence of achondroplasia is 3.72–4.6 per 100,000 births.[7] About 20% of individuals inherit the disorder in an autosomal dominant pattern.[8] About 75% of individuals with achondroplasia are born to average-stature parents due to a de novo genetic mutation.[8] Advanced paternal age (over 35 years) is a risk factor for de novo genetic mutations, as the mutation is thought to occur during spermatogenesis.[8] There is no recognized ethnic or sex predisposition for this condition.[8] In 2025, there were 55 Oregon Health Plan members with the diagnosis of achondroplasia (ICD 10: Q77.4), of whom 10% were enrolled in the fee-for-service (FFS) program.

Achondroplasia can be diagnosed before birth by fetal ultrasound to identify shortened fetal long bones during late second-trimester or third-trimester imaging.[8] DNA testing is also available before birth to confirm fetal ultrasound findings for parents who are at increased risk of having a child with achondroplasia.[8] After birth, the diagnosis can usually be made on the basis of clinical characteristics and specific features on radiographs, including a square-shaped pelvis with a small sacrosciatic notch, short pedicles of the vertebrae with interpedicular narrowing from the lower thoracic through lumbar region, proximal shortening of the long bones, proximal femoral radiolucency, and a characteristic chevron shape of the distal femoral epiphyses.[8]

Potential medical complications of achondroplasia include kyphosis, hydrocephalus, middle ear dysfunction, sleep apnea, spinal stenosis, and genu varum (bowlegs).[6] The most common complication, occurring in adulthood, is related to lumbosacral spinal stenosis with compression of the spinal cord.[9] Lumbosacral spinal stenosis is usually treatable by surgical decompression, with better outcomes if treated at an early stage.[9] Children diagnosed with achondroplasia commonly have delayed motor milestones, chronic otitis media which can impair hearing, and bowing of the lower legs, which can cause tripping and frequent falls.[9] Less commonly, infants and children may have serious health consequences related to craniocervical junction compression because of a relatively small foramen magnum (the bony hole at the base of the skull through which the brainstem and spinal cord exit the skull), which can result in numbness, weakness, increased irritability, poor feeding, difficulty walking, and loss of bowel and bladder control.[9] Most individuals with achondroplasia have average intelligence and are able to lead independent and productive lives.[9] The mean lifespan in this condition is about 10 years shorter than the general population.[10] The average height of an adult with achondroplasia is about 4 feet.[10]

There is no universally accepted standard of care for the management of patients with achondroplasia, and there is limited evidence-based guidance to assist providers and caregivers. There is no known cure for achondroplasia. The 2020 practice guideline from the American Academy of Pediatrics (AAP) focuses on identification of patients at high risk of developing complications.[8] Monitoring recommendations are stratified by age and include recommendations for diagnostic procedures, genetic counseling, and type of medical evaluation.[8] Most of the AAP recommendations are based on expert opinion. The guideline does not meet criteria for high quality and therefore is not discussed in detail here. There is insufficient comparative evidence to guide recommendations on first-line medical therapy.

Clinical trials in patients with achondroplasia often evaluate outcomes such as improvements in final height, weight, and proportionality.[11] To monitor growth, specialized charts have been created for children with achondroplasia since their height advances considerably below the normal curve area.[12] Deficits in growth in terms of annualized growth velocity from infancy to adolescence are often tracked and compared to population norms.[12] Some studies have used these values and converted measurements to an age- and sex-appropriate score known as a height Z-score which allows a comparison with normal references.[11,12] A negative Z-score value such as -2 is interpreted as 2 standard deviations lower than the mean height for a particular age and sex.[12] Clinically relevant outcomes in patients with achondroplasia include final height, functional improvement, and avoidance of long-term disease complications but no minimal clinically important difference has been established for these outcomes in this population. Research investigating whether there may be a correlation between height Z-score and negative outcomes such as spinal cord compression or stenosis in patients with achondroplasia is ongoing.[13]

All children with achondroplasia should receive regular follow-up by a multidisciplinary team, guided by a health-care provider with expertise in achondroplasia.[14] Close monitoring in the first 2 years of life is important.[14] Treatment for spinal stenosis might include decompression and fusion. Treatment for lower extremity misalignment may include surgery to correct the limbs. Growth hormone therapy has not been shown to be effective in improving final adult height in patients with achondroplasia.[9]

Medical treatments enhancing C-type natriuretic peptide (CNP) activity have recently been approved to promote bone growth in children with achondroplasia. Vosoritide is a recombinant CNP analog that is FDA-approved to promote linear growth in children with achondroplasia and open epiphyses.[1] Approval was based on data demonstrating the efficacy of vosoritide in improving annualized growth velocity and changes in height Z-scores.[1] The effects of vosoritide on final height, proportional growth, or other areas of clinical significance such as reduced symptoms, avoidance of medical complications, or improvements in functionality of people with achondroplasia are unknown. Navepegritide is a prodrug of CNP that is converted in the bloodstream to its active form.[3] Navepegritide recently received accelerated approval by the FDA to promote linear growth in children with achondroplasia aged 2 years and older whose epiphyses have not fused.[3] Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[3] Additional details on the safety and efficacy of this medication are provided in the New Drug Evaluation section of this report.

Methods:
A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 2**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canada's Drug Agency (CDA-AMA), the Oregon Mental Health Clinical Advisory Group (MHCAG), and the Scottish Intercollegiate Guidelines Network (SIGN) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:
No new high-quality systematic reviews were identified. Three systematic reviews were excluded due to poor quality (e.g., indirect network-meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or endpoints studied (e.g., non-clinical).[15-17]

Clinical Practice Guidelines:
No new high-quality guidelines were identified. Current published recommendations are based on expert opinion and consensus of practitioners experienced in managing this condition. Two guidelines were excluded due to poor quality.[18,19]

New Formulations or Indications:
10/2023: The FDA approved the expanded use of vosoritide for all children with achondroplasia and open epiphyses.[1] Prior to this approval, vosoritide was only approved in children aged 5 years and older.[1] The expanded indication was based on results from a 52-week, double-blind, placebo-controlled, phase 2 RCT evaluating the efficacy and safety of vosoritide in 64 children younger than 5 years (range: 4.4 months to 59.8 months).[2] The study was not powered for the efficacy endpoints.[2] The first primary endpoint was safety and tolerability of vosoritide, administered subcutaneously once daily, assessed in all participants who received at least one study dose.[2] The most common adverse events were injection-site reactions (86%) and rash (28%).[1] The second primary endpoint was change in height Z- score from baseline to week 52.[2] The LSMD at 52 weeks in height Z-score between the vosoritide (-0.06) and placebo (-0.31) was 0.25 (95% CI -0.02 to 0.53; low-quality evidence).[2] Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]

New FDA Safety Alerts:
No new FDA Safety Alerts identified.

Randomized Controlled Trials:
A total of 10 citations were manually reviewed from the initial literature search. None of the trials were included because of either wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or endpoints studied (e.g., non-clinical).

NEW DRUG EVALUATION:
See **Appendix 3** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and pharmacokinetic properties are listed in **Appendix 4**.

Clinical Efficacy:

The APPROACH trial contributed the efficacy and safety data used for the approval of navepegritide in children with achondroplasia, which is described and evaluated below in **Table 2**. This was a multi-center, double-blind, placebo-controlled, 52-week, Phase 2b RCT, followed by a single-arm 52-week open-label study period.[4] The trial enrolled 84 pediatric participants aged 2 years and older with genetically confirmed achondroplasia who had never received treatment. Fifty-seven participants received navepegritide 100 mcg/kg administered subcutaneously (SC) once weekly and 27 participants received placebo SC once weekly.[4] Mean age at enrollment was 5.7 years (range, 2–11 years).[4] Forty-five participants (54%) were male and 39 (46%) were female.[4] Participants had a mean baseline Centers for Disease Control and Prevention (CDC)–based height Z-score of −5.0 and mean baseline height of 89 cm (range, 64–120 cm).[4]

The primary efficacy endpoint was annualized growth velocity at week 52.[4] Height Z-scores were calculated using reference data from untreated children with achondroplasia (achondroplasia-specific height Z-score) and using reference data from the general population (CDC–based height Z-score).[4] Compared to placebo, treatment with navepegritide resulted in a LSMD in annualized growth velocity of 1.49 cm/year (5.89 vs. 4.41 cm/yr; 95% CI 1.05 to 1.93; P<0.0001) and

a LSMD increase in achondroplasia-specific height Z-score of 0.3 (95% CI 0.2 to 0.4; P<0.0001) at 52 weeks (see **Table 3**).[4] The clinical significance of these relatively modest differences in height-related outcomes is unclear.

All 57 patients in the phase 2 trial entered a single-arm, open-label follow-up study with navepegritide for another 52 weeks.[4] Annualized growth velocity was maintained among those who had received 2 years of treatment with navepegritide 100 mcg/kg once weekly.[3]

Trial Limitations:

The trial used annualized growth velocity and changes in height Z-scores as primary and secondary endpoints, which are intermediate clinical endpoints. It is unclear if a change of 1.49 cm in annualized growth velocity is clinically significant and whether treatment with navepegritide leads to sustained growth velocity improvements throughout a child's natural growth period. It is also unknown if the study results apply to those with more severe disease as participants were required to be able to stand without assistance and not have a prior bone fracture. The trial did not evaluate the long-term effects of navepegritide on adult height nor how efficacy may differ based on longer treatment duration.[4] The analyses also do not directly evaluate functional improvements, medical complications, or the need for surgical interventions.[4] Investigations are underway to assess the long-term effects of navepegritide, the efficacy and safety in additional age groups (<2 years and 12-18 years), and additional outcomes, including orthopedic outcomes and health-related quality of life.[4]

Clinical Safety:

The most frequently reported adverse events in the navepegritide phase 2B RCT and open-label extension study were vomiting, injection site reactions, pain in the extremity and nausea (**Table 1**).[3]

Table 1. Adverse Events Reported in Clinical Studies of Navepegritide.[3]

Adverse Event	**Navepegritide 0.1 mg/kg/week** (n=68)	**Placebo** (n=42)
Vomiting	21%	14%
Injection-Site Reactions	19%	14%
Pain in Extremity	12%	7%
Nausea	6%	0

Hypotension was not reported with navepegritide, but the manufacturer recommends that providers advise their patients to contact them if they experience symptoms of low blood pressure (dizziness, fatigue, and/or nausea) while being treated with navepegritide.[3] Navepegritide is not recommended for patients with moderate or severe renal impairment (estimated glomerular filtration rate [eGFR] < 60 mL/min).[3]

Look-alike / Sound-alike Error Risk Potential: None identified

Comparative Endpoints:

Clinically Meaningful Endpoints:
1) Final adult height
2) Disease progression and complications (cervicomedullary compression, spinal stenosis, etc.)

Primary Study Endpoint:
1) Annualized growth velocity at 52 weeks

3) Health-related quality of life and function
4) Serious adverse events
5) Study withdrawal due to an adverse event

Table 2. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
Savarirayan, et al.[4] Phase 2B, R, DB, PC, MC	1. Navepegritide 100 mcg/kg SC once a week 2. Placebo SC once a week 52 weeks	Demographics: -Mean age: 5.5 y (range: 2 to 11 y) -Age < 5 y: 37% -Age ≥ 5 y: 63% -Male: 54% -Race: Asian: 9.5% Black: 0% White: 88.1% Other: 24% -Mean Height: 89 cm (range 64 to 120 cm) -Mean baseline AGV: 3.9 cm/y -Mean baseline CDC-based height Z score: -5.0 -Mean baseline ACH-specific height Z score: 0.1 Key Inclusion Criteria: -Aged 2-11 y -Genetically confirmed ACH -Able to stand without assistance Key Exclusion Criteria: -Closed epiphysis -Planned or history of bone surgery -Untreated sleep apnea -Treatment with growth hormone therapies -Bone fracture within 6 months of screening	ITT: 1. 57 2. 27 PP: 1. 55 2. 27 Attrition: 1. 2 (4%) 2. 0	Primary Endpoint: AGV at week 52 1. 5.89 cm/yr 2. 4.41 cm/yr LSMD: 1.49 cm/y (95% CI 1.05 to 1.93; p<0.0001) Secondary Endpoints: Change from baseline in achondroplasia-specific height Z-score at week 52 1. 0.3 2. 0.0 LSMD: 0.3 (95% CI 0.2 to 0.4; p<0.0001) Change from baseline in CDC height Z-score at week 52 1. 0.1 2. -0.2 LSMD: 0.3 (95% CI 0.1 to 0.5; p-value NR, endpoint analyzed outside of prespecified testing strategy)	NA NA NA	TEAEs 1. 52 (91.2%) 2. 26 (96.3%) Serious AEs 1. 3 (5.3%) 2. 3 (11.1%) Pyrexia 1. 20 (35.1%) 2. 6 (22.2%) Vomiting 1. 11 (19.3%) 2. 3 (11.1%) Injection Site Reactions 1. 11 (19.3%) 2. 4 (14.8%) p-values and CIs NR	NA for all	**Risk of Bias (low/high/unclear)**: Selection Bias: Low. Randomized 2:1 to active treatment or placebo and stratified by age and gender (< 5 y, ≥ 5 y and male, ≥ 5 y and female) via interactive web response system. Baseline characteristics similar between groups. Performance Bias: Low. Participants, investigators, and caregivers blinded to treatment assignment. Placebo visually identical to active treatment. Injection site reactions with active treatment may have risked unblinding. Detection Bias: Low. Data assessors blinded to treatment assignment. Attrition Bias: Low. Attrition was less than 5%. Reporting Bias: Low. Protocol published on- line and all prespecified endpoints were reported per protocol. Other Bias: High. Study funded by manufacturer. Investigators received personal fees and grants from manufacturer. **Applicability**: Patient: Recruitment limited by the rare condition. Results most applicable to children with aged 2 to 11 y with achondroplasia. Most participants were white (88%). Intervention: Only the 100 mcg/kg weekly dose improved AGV compared to placebo. Comparator: Placebo is an appropriate comparator to determine efficacy. Comparative trials with vosoritide needed. Outcomes: AGV is a surrogate marker to demonstrate drug efficacy in treatment of disproportional short stature at 52 weeks. The impact on long-term growth velocity, final height upon closed epiphyses, physical symptoms or daily functioning improvement is unknown. Setting: 10 sites in 7 countries: Australia, Canada, Denmark, Ireland, New Zealand, Spain, United States.

Abbreviations: ACH = achondroplasia; AE = adverse events; AGV = annualized growth velocity; ARR = absolute risk reduction; CDC = Centers for Disease Control and Prevention; cm = centimeters; DB = double-blind; CI = confidence interval; ITT = intention to treat; kg = kilograms; LSMD = least-squares mean difference; MC = multi-center; mcg = micrograms; mITT = modified intention to treat; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; PC = placebo-controlled; PP = per protocol; R = randomized; SC = subcutaneous; TEAEs = treatment-emergent adverse effects; y = year(s).

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Appendix 1: Current Preferred Drug List

Generic	Brand	Route	Form	PDL
vosoritide	VOXZOGO	SUBCUT	VIAL	
navepegritide	YUVIWEL	SUBCUT	VIAL	

Appendix 2: Medline Search Strategy

Ovid MEDLINE(R) ALL <1946 to May 13, 2026>

1	exp Achondroplasia/th [Therapy]	110
2	vosoritide.mp. or Natriuretic Peptide, C-Type/	1558
3	navepegritide.mp.	5
4	2 or 3	1560
5	1 and 4	10

Appendix 3: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use YUVIWEL safely and effectively. See full prescribing information for YUVIWEL.

YUVIWEL® (navepegritide) for injection, for subcutaneous use
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------
YUVIWEL is a C-type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric patients 2 years of age and older with achondroplasia with open epiphyses. (1)

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). (1)

----------DOSAGE AND ADMINISTRATION----------
- Administer once-weekly by subcutaneous injection. Dosage is based on body weight. (2.1)
- Periodically monitor growth and adjust dose according to body weight. Discontinue when no further growth potential, as indicated by epiphyseal closure. (2.2)
- See Full Prescribing Information for instructions on preparation and administration. (2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------
For injection: 1.3 mg, 2.8 mg, and 5.5 mg as a lyophilized powder in single-dose vial for reconstitution. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
Risk of Low Blood Pressure: Transient decreases in blood pressure have been reported with a once daily CNP analog. Advise patients to contact their healthcare provider if they experience symptoms of decreased blood pressure while being treated with YUVIWEL. (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥ 5%): vomiting, injection-site reaction, pain in extremity, and nausea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Ascendis Pharma at 1-844-442-7236 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------
Renal Impairment: Not recommended for patients with moderate or severe renal impairment (eGFR < 60 mL/min/1.73 m^2). (8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 2/2026

Appendix 4. Pharmacology and Pharmacokinetic Properties.[3]

Parameter	
Mechanism of Action	Prodrug of C-type natriuretic peptide, which stimulates skeletal bone growth
Oral Bioavailability	Not Applicable
Distribution and Protein Binding	Volume of Distribution: 1.8 Liters Protein Binding: Not Described
Elimination	Clearance = 0.052 Liters/day
Half-Life	6.7 days
Metabolism	Natural degradation pathways for peptides

Appendix 5: Key Inclusion Criteria.

Population	Children with achondroplasia aged 2 years and older
Intervention	100 mcg/kg administered subcutaneously once a week
Comparator	Placebo
Outcomes	Annualized growth velocity, Height Z-Scores
Timing	52 weeks
Setting	Outpatient

Appendix 6: Prior Authorization Criteria.

C-type Natriuretic Peptides

Goal:

- Ensure medically appropriate use of approved agents for the treatment of achondroplasia in pediatric patients

Length of Authorization:

- Up to 12 months

Requires PA:

- Vosoritide and navepegritide (pharmacy claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1: Vosoritide Weight-Based Dosing

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

Actual Body Weight*	Dose	Injection Volume	Vial Strength for Reconstitution**
44-59 kg	0.6 mg	0.3 mL	1.2 mg
60-89 kg	0.7 mg	0.35 mL	1.2 mg
≥90 kg	0.8 mg	0.4 mL	1.2 mg

*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.

Table 2. Navepegritide Weight-Based Dosing

Patient Body Weight	Weekly Dose	Injection Volume	Vial Strength for Reconstitution*
8 to 9.9 kg	0.88 mg	0.4 mL	1.3 mg
10 to 13.4 kg	1.2 mg	0.55 mL	
13.5 to 17.5 kg	1.6 mg	0.35 mL	2.8 mg
17.6 to 23 kg	2.1 mg	0.45 mL	
23.1 to 30.5 kg	2.8 mg	0.6 mL	
30.6 to 41.2 kg	3.6 mg	0.65 mL	5.5 mg
41.3 to 55.9 kg	5 mg	0.9 mL	
56 to 73.5 kg	6.6 mg	1.2 mL (use 2 kits; administer 0.6 mL from each kit)	
73.6 to 90 kg	8.8 mg	1.6 mL (use 2 kits; administer 0.8 mL from each kit)	

*The concentration of navepegritide is 2.2 mg/mL in a reconstituted 1.3 mg vial; 4.6 mg/mL in a 2.8 mg vial; and 5.5 mg/mL in a 5.5 mg vial

Approval Criteria	
1. What diagnosis is being treated?	Record ICD-10 code.

Approval Criteria		
2. Is this an FDA-approved indication based on diagnosis and current age restrictions? *Vosoritide is approved for all pediatric patients and navepegritide is approved for pediatric patients aged 2 years and older	**Yes**: Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
~~2.~~3. Is the prescribed agent being dosed according to actual body weight (ABW) as outlined in Tables 1 and 2?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
~~3.~~4. Is the request for continuation of therapy in a patient previously approved under fee-for-service (FFS) criteria?	**Yes:** Go to Renewal Criteria	**No:** Go to #5
~~4.~~5. Is the agent prescribed by, or in consultation with, a pediatric endocrinologist, neurologist, or other prescriber specialized in the care of patients with achondroplasia or skeletal dysplasia?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
~~5.~~6. Is there documented evidence of a baseline measurement of annualized growth velocity (AGV) within the last 90 days AND (for males ≥15 years or females ≥13 years old) documented non-closure of epiphyseal plates?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
~~6.~~7. Does the patient have a history of bone-related surgery or fracture of long bone or spine within the previous 6 months or planned bone surgery?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Approve for 6 months ~~Go to #8~~
~~7. Does the patient have a diagnosis of recurrent symptomatic hypotension with or without orthostasis?~~	~~**Yes:** Pass to RPh. Deny; medical appropriateness~~	~~**No:** Approve for 6 months~~

Renewal Criteria		
1. Is this FDA-approved for the diagnosis and current age restrictions?	**Yes**: Go to #2	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
~~2. Is there documented evidence that the regimen is well tolerated with no adverse effects or drug toxicity?~~	~~**Yes:** Go to #3~~	~~**No:** Pass to RPh. Deny; medical appropriateness~~
~~6.~~2. Is there documented evidence of ≥ 85% adherence to therapy regimen (verified through claims history and/or provider assessment) OR < 85% adherence with documented temporary interruption due to surgery or infection?	**Yes:** Go to #3~~4~~	**No:** Pass to RPh. Deny; medical appropriateness
~~7.~~3. Is this the first renewal request?	**Yes:** Approve for 6 months	**No:** Go to #4~~5~~
~~8.~~4. Is there documented evidence of an improvement in annualized growth velocity (AGV) ≥ 1.0 cm/year from baseline AND, if male ≥15 years or female ≥13 years old, evidence of non-closure of epiphyseal plates?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: 8/26 (DM); 4/22 (DE)
Implementation: TBD; 5/1/22