New Drug Overview

Yuviwel (navepegritide)

PDL Category: Achondroplasia Treatments

Introduction

Disease Background:

- In humans, the most common bone dysplasia is achondroplasia, which is described as an autosomal dominant disorder due to pathogenic variants in the fibroblast growth factor receptor 3 (*FGFR3*) gene (*Bacino 2026*).
  - The most striking aspects are disproportionate short stature, long-bone shortening that mainly involves the proximal features of the upper and lower extremities (rhizomelic shortening), and lastly macrocephaly. Adult height is about 4 feet.
  - While cognition is normal, patients with this condition may have delayed motor development early on, and there are several medical comorbidities linked to this condition.
  - The approximate incidence in the United States is reported to be 0.36 to 0.6 per 10,000 live births (*Mortimer et al 2026*).
- FGFR-3 is a tyrosine kinase receptor that is involved in control of bone growth. Upon binding of fibroblast growth factors to FGFR-3, signaling pathways are activated, and downstream signaling leads to inhibition of proliferation and differentiation of chondrocytes, and eventually, in slowing of bone growth. Mutated FGFR-3 is always active and results in excess inhibitory signal to growth plate chondrocytes (*Mortimer et al 2026*). This leads to impaired endochondral bone formation, growth restriction, bone shortening, and other skeletal anomalies (*Bacino 2026*).
  - Unbalanced growth of bones and organs causes a variety of complications affecting many body structures and functions, such as narrow craniocervical junction leading to significant cervical cord compression, small chest size, small airway size, hydrocephalus, and reduced diameter of spinal canal, among others (*Mortimer et al 2026*).
  - C-type natriuretic peptide (CNP) activity offsets the FGFR3 inhibitory effects and signifies a therapeutic target for growth promotion in achondroplasia (*Bacino 2026*).
- Complications as well as growth needs to be monitored closely, using disease-specific growth curves (*Bacino 2026*).
  - It is recommended that the linear growth (height) and head circumference be plotted on appropriate disease-specific growth curves to avert unnecessary concern and clinical evaluations.
  - There are treatments that enhance C-type natriuretic peptide (CNP) activity to promote growth in children with achondroplasia.
- Yuviwel was FDA approved in 2026.

Pharmacology/Usage

- Yuviwel (navepegritide) is a C-type natriuretic peptide (CNP) analog. It is a prodrug of active CNP consisting of a CNP moiety transiently conjugated to two branched 20 kDa methoxy polyethylene glycol (mPEG) moieties via a proprietary TransCon Linker.
  - CNP released from navepegritide has the same receptor binding affinity and activity as endogenous CNP. CNP binds to natriuretic peptide receptor-B (NPR-B), which inhibits the mitogen activated protein kinase signaling (MAPK) pathway.
  - Achondroplasia is caused by a gain-of-function variant in the fibroblast growth factor receptor 3 (FGFR3) leading to overactive downstream signaling. The overly active FGFR3 inhibits endochondral ossification leading to short stature and skeletal dysplasia.
    - Like endogenous CNP, CNP released from navepegritide binds to NPR-B, stimulating an increase in cyclic guanosine monophosphate (cGMP) and signaling through protein kinase G, resulting in an inhibition of the MAPK signaling pathway and thus antagonizing the overactive FGFR3 signaling in achondroplasia. CNP promotes chondrocyte differentiation and proliferation, thus stimulating skeletal bone growth in patients with achondroplasia.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Yuviwel (navepegritide)
• To increase linear growth in pediatric patients 2 years of age and older with achondroplasia with open epiphyses. *	✔

***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).**

(Prescribing information: Yuviwel 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Yuviwel (nave-pegritide)	Lyophilized powder in a single-dose vial for reconstitution, for Injection: 1.3mg, 2.8mg, and 5.5mg of CNP	SC	Once weekly SC injection with dose per patient's body weight, given at any time of the day on the dosing day. -Start once weekly Yuviwel on the day after completing the last dose of daily CNP therapy.	• Reconstitute prior to use. The concentration of navepegritide is 2.2mg/ml in a reconstituted 1.3mg vial; 4.6mg/ml in a reconstituted 2.8mg vial; and 5.5mg/ml in a reconstituted 5.5mg vial. • Periodically monitor the patient's growth and adjust the dosage per the actual body weight. Discontinue upon confirmation of no further growth potential, indicated by closure of the epiphyses. • Patients and caregivers who will administer Yuviwel should receive appropriate training by a healthcare provider prior to use.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				• If the product was refrigerated, allow the vial and diluent syringe to reach room temperature (30 minutes) before reconstitution. • Administer SC in the abdominal region (2 inches from the belly button) or thighs. If a caregiver is administering, SC injection in the buttocks or back of the upper arm is also acceptable. Rotate injection sites. • Use is not recommended with moderate or severe renal impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Yuviwel has been established in a clinical trial of navepegritide consisting of a randomized, double-blind, placebo-controlled 52-week period, followed by a single-arm 52-week open-label extension (OLE) period (Trial 1).
  - This trial enrolled treatment-naïve pediatric patients (N=84) with genetically confirmed achondroplasia who were randomized to receive navepegritide 0.1mg/kg (N=57) once weekly or placebo (N=27).
  - The mean age at enrollment was 5.7 years (range 2 to 12), while 54% were male and 88% were White. The patients had a mean baseline CDC-based height Z-score of -5.0 and mean baseline height of 89cm.
  - The primary efficacy endpoint was annualized growth velocity (AGV) at week 52. Height Z-scores 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) were also evaluated.
    - Treatment with once-weekly navepegritide for 52 weeks resulted in a least-squares mean treatment difference in AGV of 1.5cm/year and a least-squares mean increase from baseline in achondroplasia-specific height Z-score of 0.3.
      - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

	Navepegritide (N=57)	Placebo (N=27)	Treatment difference	p-value
Annualized growth velocity (cm/yr)	5.9	4.4	1.5	<0.0001

	Navepegritide (N=57)	Placebo (N=27)	Treatment difference	p-value
Change from baseline				
Achondroplasia-specific height Z-score	0.3	0.0	0.3	<0.0001
CDC height-Z score	0.1	-0.2	0.3	Not Applicable

- Improvements in AGV and height Z-scores were observed in navepegritide-treated patients across all predefined subgroups analyzed, including age group, sex, and region. In patients <5 years of age, the least-squares mean treatment difference for AGV at week 52 was 1.0cm/year. In patients ≥5 years of age, the least-squares mean treatment difference was 1.8cm/year.
- All 57 patients in a 52-week randomized, double-blind, placebo-controlled phase 2 dose-finding trial (Trial 2) entered the single-arm OLE and continued treatment with navepegritide. AGV was maintained among those who had received 2 years of treatment with navepegritide 0.1mg/kg once weekly.

Clinical guidelines

- There are currently no published guidelines addressing the use of Yuviwel.
- **International Consensus Statement on the diagnosis, multidisciplinary management and lifelong care of individuals with achondroplasia** (*Savarirayan et al 2022*).
  - It is important to adopt a multidisciplinary approach to the clinical and psychosocial care of patients with achondroplasia during their lifetime.
    - All children with achondroplasia should receive regular consistent care and follow-up with a multidisciplinary team. In the first two years of life, close monitoring is vital.
  - Specific charts and growth parameters register should be provided to parents for management follow-up.
  - Refer to the guideline for additional information.
- **International consensus guidelines on the implementation and monitoring of vosoritide therapy in individual with achondroplasia** (*Savarirayan et al 2025*).
  - Educate patients and caregivers about achondroplasia and medication usage requirements, as well as adverse events prior to vosoritide treatment.
  - Vosoritide treatment should be discussed with all who are eligible.
    - Educate on the potential benefits and adverse effects of vosoritide, regarding daily injection needs, storage and the important of long-term monitoring.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Transient decreases in blood pressure have been reported with a once daily CNP analog. Subjects with hemodynamically significant cardiovascular disease were excluded from participation in navepegritide clinical trials.
    - Advise patients to contact their healthcare provider if they experience symptoms of decreased blood pressure (eg, dizziness, fatigue, and or/nausea) while being treated with Yuviwel.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (navepegritide 0.1mg/kg/week) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included vomiting (7%), injection-site reaction (5%), pain in extremity (5%), and nausea (6%).

- **Drug interactions:** None.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
  - The safety and efficacy of use in the pediatric population less than 2 years of age have not been established.

Conclusion

- In humans, the most common bone dysplasia is achondroplasia, which is described as an autosomal dominant disorder due to pathogenic variants in the fibroblast growth factor receptor 3 (*FGFR3*) gene (*Bacino 2026*).
  - The most striking aspects are disproportionate short stature, long-bone shortening that mainly involves the proximal features of the upper and lower extremities (rhizomelic shortening), and lastly macrocephaly.
- 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.
  - 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).
- The efficacy of Yuviwel was assessed in a double-blind, placebo-controlled 52-week period, followed by a single-arm 52-week OLE period.
  - The primary efficacy endpoint was annualized growth velocity (AGV) at week 52.
    - Treatment with once-weekly navepegritide for 52 weeks resulted in a least-squares mean treatment difference in AGV of 1.5cm/year, which was statistically significant compared to placebo ($p<0.0001$).
- There are currently no published guidelines addressing the use of Yuviwel. Guidelines do discuss vosoritide (brand name Voxzogo), which was FDA approved in 2021, as a treatment option. Voxzogo is a comparator to Yuviwel that is to be administered once daily as a SC injection while Yuviwel provides an alternative less frequent SC once weekly dosing. As a note that the continued approval of Yuviwel may require additional data to support safety and efficacy of this treatment.

- It is recommended that Yuviwel should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

References

- Bacino CA. Achondroplasia: Clinical features, diagnosis, and management. UpToDate website. Last updated March 16, 2026. Accessed June 15, 2026. https://www.uptodate.com.
- Mortimer E, Valentine S, Jolanda van Zuuren E. Achondroplasia. Dynamed website. Last updated March 19, 2026. Accessed June 15, 2026. www.dynamed.com.
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