Original Effective Date: 01/26/2022
Current Effective Date: 09/01/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C22221-A

Voxzogo (vosoritide)

PRODUCTS AFFECTED

Voxzogo (vosoritide)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Achondroplasia

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ACHONDROPLASIA:
   1. Documentation of achondroplasia confirmed by genetic testing for variants in the fibroblast growth factor receptor 3 (FGFR3) gene [DOCUMENTATION REQUIRED]

AND

2. Documentation of member's baseline annualized growth velocity
   AND
3. Documentation of member's open epiphyses (x-ray of proximal tibia, distal femur) [DOCUMENTATION REQUIRED]
   AND
4. Prescriber attests that there are no plans for the member to have limb-lengthening surgery and the member has not had limb-lengthening surgery in the past 18 months

CONTINUATION OF THERAPY:

A. ACHONDROPLASIA:
   1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
      AND
   2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   3. Documentation of member's positive clinical response as demonstrated by improvement in annualized growth velocity
      AND
   4. Documentation of member's open epiphyses (x-ray of proximal tibia, distal femur) [DOCUMENTATION REQUIRED]
      AND
   5. Prescriber attests that there are no plans for the member to have limb-lengthening surgery

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified geneticist, endocrinologist, neurologist, orthopedic surgeon, or specialist with experience in treating achondroplasia. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
Up to 18 years of age

QUANTITY:
3 boxes of 10-day supply per 30 days

The recommended dose and vial strength are based on the patient's actual body weight as follows administered once daily.

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

33-43 kg	1.2 mg	0.5 mg	0.25 mL
44-59 kg	1.2 mg	0.6 mg	0.3 mL
60-89 kg	1.2 mg	0.7 mg	0.35 mL
≥90 kg	1.2 mg	0.8 mg	0.4 mL

*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.
Intermediate body weights that fall within these weight bands should be rounded to the nearest whole number.

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Natriuretic Peptides

FDA-APPROVED USES:
Indicated to increase linear growth in pediatric patients 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).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Achondroplasia is a bone dysplasia that is caused by mutations in the fibroblast growth factor receptor 3 (FGFR3) gene. The condition is commonly characterized by disproportionate short stature, macrocephaly, long-bone shortening in the arms and legs (rhizomelic shortening) and shortening of the fingers and toes (brachydactyly). About 1 in 20,000 live births in North America are impacted by achondroplasia.

The clinical management of achondroplasia concentrates on treating complications and maximizing functional capacity. Typical treatments include physical therapy, occupational therapy, and proper nutrition. The use of growth hormone is not recommended as it is possible to worsen the disproportion in achondroplasia patients.

Voxzogo (vosoritide) is a C-natriuretic peptide (CNP) analog which targets FGFR3 downstream signaling by binding to natriuretic peptide receptor-B (NPR-B). It functions as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation. Voxzogo is currently the only FDA approved therapy indicated to increase the linear growth in patients 5 years of age and older with

achondroplasia with open epiphyses.

Voxzogo received accelerated approval from the FDA based on a Phase 3 clinical trial and the open-label extension period. The study was a randomized, multi-center, double-blind, placebo- controlled trial. Patients age 5-18 years old with genetically confirmed achondroplasia were randomized 1:1 to receive daily subcutaneous injections of Voxzogo (n=60) or placebo (n=61). Patients were excluded if there was evidence of closed growth plates, planned limb-lengthening surgery, severe untreated sleep apnea, or other treatments or conditions known to impact bone growth. The change from baseline in annualized growth velocity (AGV) at week 52 was significantly different in the treatment group compared to placebo (1.40 cm/year vs. -0.17 cm/year; 95% CI 1.22, 1.93; P< 0.0001). The open-label extension demonstrated that the AGV improvement can be maintained over time (4.26 cm/year at baseline; 5.39 cm/year at week 52; 5.52 cm/year at week 104).

Overall, patients treated with Voxzogo had a similar safety profile to the placebo group. The most common adverse reactions that were greater in the treatment group were injection site erythema, swelling, and urticaria; arthralgia; vomiting; decreased blood pressure; gastroenteritis; diarrhea; dizziness; ear pain; and influenza. The drug label includes a warning for decreased blood pressure and encourages patients to have adequate food and water before Voxzogo administration.

In October 2023, the FDA approved a supplemental NDA for Voxzogo to increase linear growth in all pediatric patients with open epiphyses. It was previously labeled for 5 years and older with open epiphyses only. The approval was supported by a randomized, double-blind, placebo-controlled Phase 2 clinical trial evaluating the safety and efficacy of VOXZOGO in children aged 5 and under that demonstrated VOXZOGO has a similar efficacy and safety profile in the younger and older patient subpopulations.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Voxzogo (vosoritide) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Voxzogo (vosoritide) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:
If a dose of Voxzogo is missed, it can be administered within 12 hours of the scheduled time of administration. Beyond 12 hours, skip the missed dose and administer the next daily dose according to the usual dosing schedule.
Permanently discontinue Voxzogo upon confirmation of no further growth potential, indicated by closure of epiphyses.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Voxzogo SOLR 0.4MG single-dose vial
Voxzogo SOLR 0.56MG single-dose vial
Voxzogo SOLR 1.2MG single-dose vial

REFERENCES

1. Voxzogo (vosoritide) [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc; October 2023.
2. Savarirayan, R., Tofts, L., Irving, M., Wilcox, W., Bacino, C., & Hoover-Fong, J. et al. (2021). Safe and persistent growth-promoting effects of vosoritide in children with achondroplasia: 2- year results from an open-label, phase 3 extension study. *Genetics In Medicine*, *23*(12), 2443- 2447. doi: 10.1038/s41436-021-01287-7
3. Savarirayan, R., Tofts, L., Irving, M., Wilcox, W., Bacino, C., & Hoover-Fong, J. et al. (2020). Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. *The Lancet*, *396*(10252), 684-692. doi: 10.1016/s0140-6736(20)31541-5
4. Savarirayan, R., Irving, M., Bacino, C., Bostwick, B., Charrow, J., & Cormier-Daire, V. et al. (2019). C-Type Natriuretic Peptide Analogue Therapy in Children with Achondroplasia. *New England Journal Of Medicine*, *381*(1), 25-35. doi: 10.1056/nejmoa1813446

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Quantity	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Age Restrictions Quantity FDA-Approved Uses Background Available Dosage Forms References	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy FDA-Approved Uses Other Special Considerations Available Dosage Forms	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file