BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VOXZOGO™ (vosoritide) injection
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Voxzogo (vosoritide) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist or Pediatric Endocrinologist

2. Individual is less than 18 years of age

3. Individual has a confirmed diagnosis of achondroplasia

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

a. Pathogenic gain of function variant in fibroblastic growth factor receptor 3 (*FGFR3*) gene or clinical and radiographic evidence of achondroplasia (see Definitions section)
b. Recent (within the last 12 months) radiographic evidence epiphyses have not closed

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual does not have hypochondroplasia or short stature condition other than achondroplasia

7. Individual is not planning to have limb-lengthening surgery

8. Individual does not have systolic blood pressure (BP) < 70 millimeters of mercury (mm Hg) or recurrent symptomatic hypotension (defined as episodes of low BP generally accompanied by symptoms such as dizziness, fainting) or recurrent symptomatic orthostatic hypotension

9. Estimated glomerular filtration rate is at least 60 mL/min/1.73m^2

10. Individual is not on anabolic steroids

11. Will not be used in combination with or alternating with growth hormone, growth hormone analog, or Increlex (mecasermin)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Voxzogo (vosoritide) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist or Pediatric Endocrinologist

2. Individual's condition has responded while on therapy with response defined as the following:
   a. Growth velocity is at least 1.5 cm/year
   b. No evidence of disease progression
   c. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Recent (within the last 12 months) radiographic evidence epiphyses have not closed

4. Individual has been adherent with the medication

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual does not have hypochondroplasia or short stature condition other than achondroplasia

7. Individual is not planning to have limb-lengthening surgery
8. Individual does not have systolic blood pressure (BP) < 70 millimeters of mercury (mm Hg) or recurrent symptomatic hypotension (defined as episodes of low BP generally accompanied by symptoms such as dizziness, fainting) or recurrent symptomatic orthostatic hypotension
9. Estimated glomerular filtration rate is at least 60 mL/min/1.73m^2
10. Individual is not on anabolic steroids
11. Will not be used in combination with or alternating with growth hormone, growth hormone analog, or Increlex (mecasermin)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Voxzogo (vosoritide) is a C type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older 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).

In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (*FGFR3*). Binding of vosoritide to natriuretic peptide receptor-B (NPR-B) antagonizes *FGFR3* downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, vosoritide, like CNP, acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation.

In animal models with open growth plates, vosoritide administration resulted in the promotion of chondrocyte proliferation and differentiation that led to a widening of the growth plate and subsequent increase in skeletal growth. In models of FGFR3-related chondrodysplasia, a partial or complete normalization of the dwarfism phenotype was observed.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Clinical and radiographic evidence of achondroplasia:

- Clinical manifestations characteristic of achondroplasia (e.g., macrocephaly, frontal bossing, midface retrusion, disproportionate short stature with rhizomelic shortening of the arms and the legs, brachydactyly, trident configuration of the hands, thoracolumbar kyphosis, and accentuated lumbar lordosis)

- Radiographic findings characteristic of achondroplasia (e.g., large calvaria and narrowing of the foramen magnum region, undertubulated, shortened long bones with metaphyseal abnormalities, narrowing of the interpedicular distance of the caudal spine, square ilia and horizontal acetabula, small sacrosciatic notches, proximal scooping of the femoral metaphyses, and short and narrow chest)

Resources:

Voxzogo (vosoritide) subcutaneous injection product information, revised by BioMarin Pharmaceutical Inc. 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 27, 2024.

Bacino CA. Achondroplasia. In: UpToDate, Hahn S, Tehrani N (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated December 08, 2023. Accessed January 09, 2025.

Savarirayan R, Irving M, Bacino CA, et al: C-Type Natriuretic Peptide Analogue Therapy in Children with Achondroplasia. NEJM 2019 July 4; 381:25-35. Accessed February 22, 2022. Re-evaluated January 09, 2025.

Savarirayan R, Tofts L, Irving M, et al.: Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomized, double-blind, phase 3, placebo-controlled, multicenter trial. Lancet 2020 Sept 05; 396: 684–92. Accessed January 09, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03197766. A study to evaluate the efficacy and safety of BMN 111 in children with achondroplasia. Available from: http://clinicaltrials.gov. Last updated May 15, 2020. Last verified May 2020. Accessed February 07, 2022. Re-evaluated January 09, 2025.