09-J4000-16

Original Effective Date: 04/01/22

Reviewed: 12/13/23

Revised: 01/15/24

Subject: Vosoritide (Voxzogo)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Achondroplasia is a genetic disorder that results in impaired endochondral bone formation, growth restriction, bone shortening and distinct craniofacial features. Disproportionate short stature with an average adult height of 4 ft 4 in is characteristic of the condition. Complications such as spinal stenosis, recurrent otitis media, obstructive sleep apnea, leg bowing, or obesity may occur. Life expectancy is normal if there is no compression of the brainstem or upper spinal cord. A genetic mutation in the fibroblast growth factor receptor 3 gene (FGFR3) is responsible which may occur spontaneously in up to 80% of cases.

Vosoritide (Voxzogo) is FDA-approved to increase linear growth in pediatric patients with achondroplasia with open epiphyses. This indication was approved based on an improvement in annualized growth velocity and continued approval is contingent upon verification and description of clinical benefit in confirmatory trials. Vosoritide is a C-type natriuretic peptide that antagonizes FGFR3 signaling in patients with achondroplasia. It is a positive regulator of bone growth which promotes chondrocyte proliferation and differentiation.

The efficacy of vosoritide was compared to placebo in a 52-week randomized trial in 121 patients with genetically-confirmed achondroplasia. Prior to randomization, baseline standing height, weight Z-score, body mass index (BMI) Z-score, and upper to lower body ratio were collected for at least 6 months prior to randomization. Patients had a mean baseline height standard deviation score (SDS) of -5.13. Patients with limb-lengthening surgery in the prior 18 months were excluded. The primary endpoint was the change from baseline in annualized growth velocity (AGV) at Week 52 compared with placebo. The change from baseline in AGV was 1.4 cm/year for vosoritide and -0.17 for placebo. The difference in the change of annualized growth velocity (cm/year) at week 52 was 1.57 cm/year (95% CI, 1.22, 1.93; $p<0.0001$). In an open label extension study, the patients maintained improvement in AGV at 2 years of follow-up. The most common adverse reactions in patients receiving vosoritide included erythema,

swelling, and urticaria of the injection site, vomiting, arthralgia, decreased blood pressure, and gastroenteritis.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of vosoritide (Voxzogo) **meets the definition of medical necessity** when **ALL** of the indication-specific criteria are met:

1. Achondroplasia
    a. The member is diagnosed with achondroplasia confirmed by a genetic mutation in the FGFR3 gene– documentation must be submitted:
    b. Vosoritide will be used to treat linear growth in pediatrics
    c. The member has open epiphyses – documentation of an x-ray from the previous 6 months must be submitted for children over 10 years of age only
    d. Vosoritide is prescribed by or in consultation with a specialist in the treatment of achondroplasia (e.g. geneticist, skeletal dysplasia specialist, endocrinologist)
    e. Assessment of member's baseline annualized growth velocity (AGV) – documentation must be submitted
    f. The member has an eGFR greater than or equal to 60 ml/min/1.73 m^2
    g. The member will not receive concomitant medication to increase linear growth (e.g., somatropin, lonapegsomatropin, mecasermin) or have limb-lengthening surgery during treatment
    h. The dose will not exceed the weight-based dosing in Table 1 and will not exceed the use of one vial per day

Approval duration: 12 months

Continuation of vosoritide (Voxzogo) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for vosoritide has been previously approved by Florida Blue in the past 2 years for the treatment of achondroplasia, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member has open epiphyses – documentation of an x-ray from the previous 6 months must be submitted for children over 10 years of age only
3. Vosoritide is prescribed by or in consultation with a specialist in the treatment of achondroplasia (e.g. geneticist, skeletal dysplasia specialist, endocrinologist)

4. The member has demonstrated a beneficial response to therapy as evidenced by improvement in annualized growth velocity of at least 1.5 cm/year compared to baseline– documentation must be submitted
5. The member has an eGFR greater than or equal to 60 ml/min/1.73 m^2
6. The member will not receive concomitant medication to increase linear growth (e.g., somatropin, lonapegsomatropin, mecasermin) or have limb-lengthening surgery during treatment
7. The dose will not exceed the weight-based dosing in Table 1 and will not exceed the use of one vial per day

Approval duration: 12 months

Table 1: Dosing of Vosoritide

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

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- To increase linear growth in pediatric patients with achondroplasia with open epiphyses.
- Dose based on patient's weight
- Administer subcutaneously once daily
- Monitor growth and adjust dosage according to body weight. Permanently discontinue upon closure of epiphyses.

Actual Body Weight	Vial Strength for Reconstitution*	Dose	Injection Volume
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60-89 kg	1.2 mg	0.7 mg	0.35 mL
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*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.

- If a dose 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.
- Monitor and assess patient body weight, growth and physical development regularly every 3 to 6 months. Adjust the dosage according to the patient's actual body weight.
- Permanently discontinue upon confirmation of no further growth potential, indicated by closure of epiphyses.

Dose Adjustments

- Not recommended in patients with eGFR <60 mL/min/1.73 m^2

Drug Availability

- 0.4 mg, 0.56 mg, or 1.2 mg lyophilized powder in a single-dose vial

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Risk of Low Blood Pressure: Transient decreases in blood pressure have been reported.

BILLING/CODING INFORMATION:

HCPCS Coding

J3490	Unclassified drugs

ICD-10 Diagnosis Codes That Support Medical Necessity

Q77.4	Achondroplasia

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc. Accessed Feb 24, 2023.
2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Accessed Feb 24, 2023.
3. National Organization of Rare Diseases. https://rarediseases.org/rare-diseases/achondroplasia/.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [cited Feb 24, 2023]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Voxzogo Prescribing Information. BioMarin Pharmaceutical Inc. October 2023.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/13/23.

GUIDELINE UPDATE INFORMATION:

04/01/22	New Medical Coverage Guideline.
06/15/22	Review and revision to policy; consisting of updating the position statement.
04/15/23	Review and revision to policy; consisting of updating the references.
12/15/23	Revision to policy to update the position statement to update the age and dosing table.
01/15/24	Revision to policy; consisting of updating the position statement to update documentation requirement.