Voxzogo Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
2/1/2024	7/1/2022

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Voxzogo® (vosoritide) Subcutaneous injection	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)		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Achondroplasia	Achondroplasia is the most commonly occurring abnormality of bone growth (skeletal dysplasia), occurring in approximately 1 in 15,000-35,000 live births and affects both males and females equally. This genetic disorder is caused by a mutation in the fibroblast growth factor receptor 3 (*FGFR3*) gene. Fibroblast growth factor receptors (FGFRs) belong to the tyrosine kinase family and regulate various biological processes including cell proliferation and differentiation during development, as well as tissue repair. Achondroplasia occurs as a result of a spontaneous genetic mutation in approximately 80 percent of patients. In the remaining 20 percent of cases, it is inherited from either parent and follows an autosomal dominant pattern of inheritance. The risk of passing the abnormal gene from an affected parent to an offspring is 50% for each pregnancy.(3) Like some other severe growth disorders, it is also associated with potentially serious medical complications such as foramen magnum and spinal stenosis, both of which cause increased morbidity and mortality.(2) This genetic disorder is characterized by an unusually large head (macrocephaly), short upper arms (rhizomelic dwarfism), and short stature (adult height of approximately 4 feet). Achondroplasia does not typically cause impairment or deficiencies in mental abilities. If the bones that join the head and neck do not compress the brainstem or upper spinal cord (craniocervical junction compression), life expectancy is near normal.(3) Growth hormone treatment has been found to be ineffective in patients with deformities of the lower limbs and to date, it has not been confirmed whether the administration of somatropin negatively affects the severity of foramen narrowing and pressure on the spinal cord, and no symptoms of acromegaly have been observed in the treated patients. A meta-analysis of recombinant human growth hormone treatment in achondroplasia based on an extensive group of patients shows that data about body disproportion in GH treatment are ambiguous.(5)

Efficacy	Voxzogo is a recombinant C-type natriuretic peptide analog that stimulates endochondral ossification, a process that is inhibited in patients with achondroplasia patients. The safety and effectiveness of Voxzogo in 121 genetically confirmed patients with achondroplasia were assessed in one 52-week, multi-center, randomized, double-blind, placebo-controlled, phase 3 study - Study 1 (NCT03197766). The dosage of Voxzogo was 15 mcg/kg administered subcutaneously once daily. 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. Subjects with limb-lengthening surgery in the prior 18 months or who planned to have limb-lengthening surgery during the study period were excluded and patients must have been ambulatory and able to stand to participate.(6) The study included a 52-week placebo-controlled treatment phase followed by an open-label treatment extension study period in which all subjects received Voxzogo. The primary efficacy endpoint was the change from baseline in annualized growth velocity (AGV) at Week 52 compared with placebo. The subjects' ages ranged from 5.1 to 14.9 years with a mean of 8.7 years. Sixty four (53%) subjects were male and 57 (47%) were female. Overall, 86 (71%) subjects were White, 23 (19%) were Asian, 5 (4%) were Black or African American, and 7 (6%) were classified as "multiple" race. The subjects had a mean baseline height standard deviation score (SDS) of -5.13. Patients treated with vosoritide had a greater increase in mean annualized growth velocity from baseline to 52 weeks compared with the placebo group (adjusted mean difference 1.57 cm/year; 95% CI 1.22-1.93). Among the subjects who had 2 years of follow-up since randomization, the improvement in AGV was maintained.(10) Longer-term studies are needed to determine whether vosoritide affects pubertal growth velocity, body segment proportionality, final adult height, or complications associated with achondroplasia.
Safety	Voxzogo does not have any contraindications.(1)

REFERENCES

Number	Reference
1	Voxzogo Prescribing Information. BioMarin Pharmaceutical Inc. November 2021.
2	Hogler, W., Ward, LM. New developments in the management of achondroplasia. Wien Med Wochenschr 170, 104–111 (2020). https://doi.org/10.1007/s10354-020-00741-6
3	Achondroplasia. NORD. https://rarediseases.org/rare-diseases/achondroplasia
4	Kubota T, Adachi M, Kitaoka T, et al. Clinical Practice Guidelines for Achondroplasia. Clin Pediatr Endocrinol. 2020;29(1):25-42. doi:10.1297/cpe.29.25
5	Wrobel W, Pach E, Ben-Skowronek I. Advantages and Disadvantages of Different Treatment Methods in Achondroplasia: A Review. International Journal of Molecular Sciences. 2021; 22(11):5573. https://doi.org/10.3390/ijms22115573
6	A Study to Evaluate the Efficacy and Safety of BMN 111 in Children With Achondroplasia. BioMarin Pharmaceutical. Available at: https://clinicaltrials.gov/ct2/show/NCT03197766

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Voxzogo	vosoritide for subcutaneous inj	0.4 MG ; 0.56 MG ; 1.2 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Voxzogo	vosoritide for subcutaneous inj	0.4 MG ; 0.56 MG ; 1.2 MG	30	Vials	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Voxzogo	vosoritide for subcutaneous inj	0.4 MG ; 0.56 MG ; 1.2 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. ALL of the following: 1. The patient has a diagnosis of achondroplasia as confirmed by ONE of the following (medical records required): A. Genetic testing **OR** B. Radiographic findings **AND** 2. The requested agent will be used to increase linear growth **AND** 3. The patient has open epiphyses **AND** 4. The patient is ambulatory and able to stand without assistance **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with another growth hormone agent for the requested indication **AND**

Module	Clinical Criteria for Approval
	5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has open epiphyses **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient will NOT be using the requested agent in combination with another growth hormone agent for the requested indication **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval:** 12 months