Voxzogo (vosoritide)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

Voxzogo (vosoritide), a CNP analog, binds to natriuretic peptide receptor-B (NPR-B) and antagonizes FGFR3 downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway. Voxzogo acts as a positive regulator of endochondral bone growth and promotes chondrocyte proliferation and differentiation, which may lead to widening of the growth plate and subsequent increase in skeletal growth if growth plates remain open.

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Voxzogo (vosoritide) is indicated to increase linear growth in pediatric patients 5 years of age and older who have achondroplasia with open epiphyses.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Chart notes or documentation of symptoms (i.e., short stature with marked shortening of extremities due to rhizomelia, a characteristic facial configuration, trident hand) AND X-ray findings consistent with achondroplasia; OR laboratory test reports of genetic testing for FGFR3 mutation
2. Growth chart showing annualized growth velocity (centimeters per year)

Prescriber Specialties

This medication must be prescribed by or in consultation with an endocrinologist, pediatric endocrinologist, geneticist, or neurologist.

Criteria for Initial Approval

Achondroplasia

Authorization of 12 months may be granted for treatment of achondroplasia in members 5 years of age and older when ALL of the following criteria are met:

1. The diagnosis of achondroplasia was confirmed by EITHER of the following:
   a. Symptoms (i.e., short stature with marked shortening of extremities due to rhizomelia, a characteristic facial configuration, trident hand) AND X-ray findings consistent with achondroplasia
   b. Genetic testing for FGFR3 mutation
2. Epiphyses are open

Continuation of Therapy

Authorization of 12 months may be granted for continuation of therapy in members 5 years of age and older when all of the following criteria are met:

A. All criteria for initial approval are met
B. The member's improvement or stabilization of annualized growth velocity (centimeters per year) from baseline

Voxzogo is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits:

Medication	Standard Limit	FDA-recommended dosing			
Voxzogo single-dose vial 0.4mg	30 per 30 days	Subcutaneous injection once daily based on patient's actual body weight:			
Voxzogo single-dose vial 0.56 mg	30 per 30 days	Actual Body weight	Vial strength for reconstitution	Dose	Injection Volume
Voxzogo single-dose vial 1.2 mg	30 per 30 days	10- 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

CLINICAL RATIONALE

Background

Achondroplasia is the most common bone dysplasia in humans which prevents the changing of cartilage to bone and is characterized by disproportionate short stature. The skeletal dysplasia is caused by heterozygous mutations in the fibroblast growth factor receptor 3 (FGFR3) gene. More than 250,000

individuals are estimated to be affected with achondroplasia worldwide with an estimated birth incidence of one in every 10,000 to 30,000 births. Approximately 80% of cases are de novo mutations, and the remaining are inherited. These mutations result in the suppression of chondrocyte differentiation and cartilage production and proliferation. Endochondral ossification is impaired, resulting in poor extension of the long bones. Individuals with achondroplasia reach an average adult height of approximately 120 cm to 135 cm. Common complications include delayed motor milestones, otitis media, bowing of the lower legs, chronic pain, sleep apnea, kyphosis, and spinal stenosis. Overall mortality was shown to be increased in individuals with achondroplasia, with an overall reduction of life expectancy of approximately 10 years.

There are no standard guidelines for the management of achondroplasia and treatment is currently targeted towards the management of clinical manifestations. Surgical extended limb lengthening is an option to treat short stature that can result in a height increase of up to 30 cm to 35 cm, but it is associated with frequent complications. In addition, growth hormone therapy has been assessed as a possible treatment that has shown an initial acceleration of growth with lessening effect over time. Growth hormone therapy is not FDA approved for achondroplasia, and there is little evidence for its use. Pharmacological therapies addressing the underlying pathophysiology of achondroplasia are limited, although there are several agents currently in clinical studies.

Voxzogo (vosoritide) was approved by the FDA in November 2021 to increase linear growth in pediatric patients 5 years of age and older who have achondroplasia with open epiphyses. Voxzogo binds to natriuretic peptide receptor-B (NPR-B) and antagonizes *FGFR3* downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway. Voxzogo acts as a positive regulator of endochondral bone growth and promotes chondrocyte proliferation and differentiation, which may lead to widening of the growth plate and subsequent increase in skeletal growth. Voxzogo is available as 0.4 mg, 0.56 mg and 1.2 mg vials for subcutaneous administration. The recommended dose is 15 mcg/kg based on actual body weight subcutaneously once daily.

Efficacy

Voxzogo (vosoritide) was studied in a phase III, multinational, double-blind, randomized, placebo-controlled trial (study 111-301) which had a primary end point of change in average growth velocity and secondary endpoints of change in height Z-score and change in upper to lower body segment ratio. The trial enrolled 121 patients between 5 and 18 years of age with a diagnosis of achondroplasia confirmed by genetic testing who completed a six-month lead-in, observational growth study. Patients were excluded if they had closed growth plates, planned bone surgery, untreated OSA, or other conditions that are known to affect growth. At 52 weeks, Voxzogo demonstrated significantly increased growth velocity ($p=<0.0001$) and height Z-scores ($p=<0.0001$) compared with placebo. It did not meet on the secondary endpoint of change in upper to lower body segment ratio.

An ongoing, open-label, phase III extension study is currently being conducted in the same patients (N=119) from study 111-301 and the 2-year Voxzogo treatment duration results have been published. The extension study demonstrated improvement in the annualized growth velocity in children who continued treatment with Voxzogo with an annualized growth velocity of 5.75 cm per year at week 78 and 5.52 cm per year at week 104. Annualized growth velocity also increased to 5.97 cm per year at week 78 and 5.43 cm per year at week 104 for children who crossed over from placebo to Voxzogo in the open-label extension study. Height Z-scores and upper to lower body segment ratios also demonstrated improvement at week 104. No new adverse effects were detected after 2 years of treatment.

Safety

Treatment-related adverse events occurred in almost all patients (Voxzogo 98% vs. placebo 98%), but most were mild, the most common reactions being injection site erythema, injection site swelling, vomiting, and injection site urticaria. No grade 3 or higher reactions were reported. Transient decreases in

blood pressure were noted in clinical studies and patients are instructed to hydrate and have adequate food intake before receiving Voxzogo.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Not applicable (N/A)

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POLICY HISTORY

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