

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

**Vosoritide for treating achondroplasia in people 4 months and over**

**Draft scope**

**Draft remit/evaluation objective**

To appraise the clinical and cost effectiveness of vosoritide within its marketing authorisation for treating achondroplasia in people 4 months and over.

**Background**

Achondroplasia is the most common cause of disproportionate short stature, a condition where the bones in the arms and legs do not develop properly and are shorter than normal. In over 95% of cases, achondroplasia results from a mutation of the gene that makes fibroblast growth factor receptor 3 (FGFR3)<sup>1</sup>. The normal functioning of this receptor is to slow down formation of cells that make cartilage<sup>2</sup>. The mutation causes continuous activation of FGFR3, which leads to continuous suppression of cartilage and bone formation in the growth plate. The growth plate (epiphysis) is the area of growing tissue near the end of the long bones in children and adolescents. The growth plate usually closes for most people by age 18 years but some studies report complete closure beyond age 18 years<sup>3</sup>. The FGFR3 mutation may be inherited from one or both parents, although 80% of children with achondroplasia develop the mutation spontaneously<sup>1</sup>.

Achondroplasia is characterised by a short stature, bowed legs, short upper arms and thighs, an enlarged head with a prominent forehead, and an exaggerated inward curvature of the spine. It can also cause other serious complications including build-up of fluid in the brain (hydrocephalus), sleep apnoea, recurrent ear infections, and numbness or weakness in the legs due to spinal cord compression (spinal stenosis)<sup>2,4</sup>. People who have inherited a mutated FGFR3 gene from both parents are the most severely affected and normally die within a few months of birth. People who have one mutated gene may also have a shorter lifespan because of the effects of the condition on the heart<sup>5</sup>. People with achondroplasia live for 10 years less than the general population, on average<sup>2</sup>.

People with achondroplasia face challenges with daily tasks due to their short stature and disproportionately short limbs<sup>6</sup>. They may also encounter bullying, particularly during adolescence, and as adults they may be discriminated against and limited in their ability to work. Studies indicate that mental health may also be negatively impacted by the condition<sup>7,8</sup>.

The incidence of achondroplasia is estimated to be 1 in 25,000 live births<sup>9</sup>. This corresponds to around 24 new cases in England and Wales in 2023<sup>10</sup>. There were 211 hospital episodes with a primary diagnosis of achondroplasia in England in 2023 – 2024<sup>11</sup>.

Current treatment for achondroplasia is aimed at managing the symptoms of the condition and require a multidisciplinary team of clinicians. People may require surgery to lengthen the limb, treat bowed leg or correct abnormal spine<sup>1</sup>. Other treatments include surgical removal of the adenoids and tonsils to address sleep apnoea, speech therapy to address hearing loss and treatment of ear infection (such

as otitis media)<sup>2</sup>. There is some evidence that growth hormones can increase short-term growth, but there is no long-term evidence that they significantly increase final adult stature<sup>2</sup>.

### The technology

Vosoritide (Voxzogo, BioMarin Pharmaceutical) does not currently have a marketing authorisation in the UK for treating achondroplasia. It has been studied in clinical trials for infants, children and young people, and adults with achondroplasia. These studies are either single-arm or compare vosoritide against placebo.

<b>Intervention(s)</b>	Vosoritide
<b>Population(s)</b>	People 4 months and over with achondroplasia
<b>Comparators</b>	Established clinical management without vosoritide
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• change in height and weight</li> <li>• change in annual growth velocity</li> <li>• change in body proportions</li> <li>• change in presence of non-orthopaedic complications associated with achondroplasia (e.g. hydrocephalus, numbness or weakness in legs, sleep apnoea and otitis media)</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<b>Other considerations</b>	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
<b>Related NICE recommendations</b>	<b>Related technology appraisals:</b>

	<p><a href="#">Somatrogen for treating growth disturbance in children and young people aged 3 years and over</a> (2023) NICE technology appraisal guidance 863</p> <p><a href="#">Human growth hormone (somatropin) for the treatment of growth failure in children</a> (2010) NICE technology appraisal guidance 188</p> <p><b>Related technology appraisals in development:</b></p> <p>Somapacitan for treating growth hormone deficiency in children NICE technology appraisal guidance [ID6178]. Publication date to be confirmed.</p> <p><b>Related interventional procedures:</b></p> <p><a href="#">Interspinous distraction procedures for lumbar spinal stenosis causing neurogenic claudication</a> (2010) NICE interventional procedures guidance [IPG365]</p> <p><a href="#">Intramedullary distraction for lower limb lengthening</a> (2006) NICE interventional procedures guidance [IPG197]</p>
--	--

### Questions for consultation

How is achondroplasia in infants and young children identified and diagnosed in the NHS? What are the diagnosis criteria?

Is the population in the draft scope appropriate?

How many people are with achondroplasia in the UK? Among them, how many are seen by the NHS for the treatment of their condition?

Is vosoritide expected to be used by children and young people, and adults in practice?

What is the expected age of growth plates closure (epiphyseal plates closure) in the general population?

Do growth plates close in people with achondroplasia at a similar age to the general population?

- If not, what proportion of people with achondroplasia would have their epiphyses closed at an age earlier or later than that of the general population, respectively?

Have all the relevant comparators for vosoritide been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for achondroplasia in people 4 months and over?

To what extent is human growth hormone (somatropin and somatrogen) used for the treatment of achondroplasia in the NHS?

Where do you consider vosoritide will fit into the existing treatment pathway for achondroplasia?

Are the outcomes listed appropriate?

Are there any other relevant outcomes to consider?

Are there any subgroups of people in whom vosoritide is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

Please select from the following, will vosoritide be:

- A. Prescribed in primary care with routine follow-up in primary care
- B. Prescribed in secondary care with routine follow-up in primary care
- C. Prescribed in secondary care with routine follow-up in secondary care
- D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would vosoritide be a candidate for managed access?

Do you consider that the use of vosoritide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which vosoritide will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

### References

1. Wright M J and Irving M D (2012) Clinical management of achondroplasia. Archives of Disease in Childhood 97(2): 129-34
2. Pauli R M (2019) Achondroplasia: a comprehensive clinical review. Orphanet Journal of Rare Diseases 14: 1
3. O'Connor et al. (2008) A method to establish the relationship between chronological age and stage of union from radiographic assessment of epiphyseal fusion at the knee: an Irish population study. J Anat. 2008 Feb;212(2):198-209.
4. Restricted Growth Association (2025) [Medical information: types of dwarfism](#). Accessed February 2025
5. European Medicines Agency (2013): [EU/3/12/1094](#). Accessed February 2025
6. Gollust S E et al. (2003) Living with Achondroplasia in an Average-Sized World: An Assessment of Quality of Life. American Journal of Medical Genetics 120A: 447-458
7. Witt S et al. (2019) Quality of life of children with achondroplasia and their parents - a German cross-sectional study. Orphanet Journal of Rare Diseases 14(1): 194
8. Coi A et al. (2019) Epidemiology of achondroplasia: A population-based study in Europe. American Journal of Medical Genetics Part A 179(9): 1791-1798
9. [Orphanet \(2019\) Achondroplasia](#). Accessed February 2025
10. Office for National Statistics (2024) [Births in England and Wales: 2023](#). Accessed February 2025.
11. NHS England (2024) [Hospital Admitted Patient Care Activity, 2023-24](#). Accessed September 2024.