NICE National Institute for Health and Care Excellence

HST routing criteria (refined April 2025)

Vosoritide for treating achondroplasia in people aged 4 months and over [ID6488]

Introduction

1. The NICE HST routing assessment checklist highlights when a technology meets or does not meet the criteria for routing it to the HST Programme. All 4 criteria need to be met for a technology to be routed to HST.

2. Marketing Authorisation (MA) wording:

   company: anticipated MA wording (note: MA not granted but intended wording not confidential): indicated for the treatment of achondroplasia in patients 4 months of age and older whose epiphyses are not closed.

3. **Prioritisation Board routing discussion:** 07/07/2025

4. **Description of the HST Programme's vision**

   Criterion 1 - The rarer a disease is, the more challenging it is to do research and generate an evidence base that is robust enough to bring an effective technology to market. The HST Programme's vision aims to encourage research when it is most challenging.

   Not all ultra-rare diseases are debilitating. The vision focuses on ultra-rare diseases that cause ongoing debilitating symptoms and have an exceptional burden on the people with them, and on their carers and families. This is to justify prioritising access to HST technologies over overall population health.

Criteria	Descriptions of how the criteria are met or not met through assessing the definitions
Criterion 1 **The disease is ultra-rare, that is,** • **1A: it is defined as having a point prevalence of 1:50,000 or less in England (NICE strategic principles for rare disease).** **....and debilitating, that is,** • **1B: it is lifelong after diagnosis with current treatment, and has an exceptional negative impact and burden on people with the ultra-rare disease, and their carers and families.**	The exact number of people living with achondroplasia in England is unknown. Estimates of prevalence vary across regions, and birth prevalence figures based on specialised care settings have been reported to be higher than those from other settings (Foreman et al., 2020) • **Worldwide Incidence**: was reported to be 1/25,000, using ONS Live births in England and Wales in 2023: 563,561, this translates to about **22.5 new cases per year** in England. . Orphanet reports birth prevalence as 3.62/100,000 births in Europe with a birth prevalence of 4.73/100,000 births worldwide. • **Total prevalence of achondroplasia based on worldwide incidence in England**, approximately about **1,800** (22.5 * average UK population life expectancy of 80 years) people living with achondroplasia in England (see details below) **Using live birth prevalence data** ▪ **Live birth prevalence in 4 regions of England**: based on an European population based registry study (Coi A et al. 2019), live birth prevalence of achondroplasia in 4 regions of England ranged between 1.94 /100,000 in Thames Valley to 1.07/100,000 in Wales over the time period between year 1991 and year 2015, averaged around 3.13/100,000 (by NICE technical team), which is 1 in 32,960. If using this estimate as a proxy for incidence, there are **17.6 new cases each year** in England (using ONS 2023 live births estimate 563,561). However, it must be noted that, strictly speaking, these are neither incidence or prevalence estimates, may be close to an average incidence estimate over a period of time. Please see details below. • **Total prevalence of achondroplasia based on live birth prevalence data in England**, approximately **about 1,412 people** (17.6 * average UK population life expectancy of 80 years) people living with achondroplasia in England (see details below) **For information**:

	• Live birth prevalence was estimated to be 3.05/100,000 in Europe (95% confidence interval (CI): 2.63-3.55), 3.72/100,000 birth worldwide (Coi A et al. 2019)
	  • *Live birth prevalence was estimated by: number of cases over a time period/total births over a time period*
	  • *Time period included in the study: year 1991 to 2015*
	• This same study included 4 registries from England (see breakdown below).
	  • Wessex (1994 to 2015): 4.07/100,000 [95% confidence interval (CI): 2.63–6.00)
	  • South-West England (2005 to 2015): 3.12 (95%CI:1.82–4.99)
	  • Northern England (1991 to 2015): 3.03 (95%CI:1.96–4.47)
	  • Thames Valley (1991 to 2015): 1.94 (95%CI: 0.84–3.83)
	Based on the registry data above:
	Average of the 4 regions (using the range): 12.13/4=3.03 per 100,000 births, about 1 in 33,000;
	When taking into account the total cases in the 4 regions:
	Total births (4 England registries): 2,396,975
	Total achondroplasia cases: 75
	  • Live birth prevalence between year 1991 and 2015 = 3.13 per 100,000 births or approximately 1 in 31,960 births

	Has this definition been met or not met? Yes ☐ No ☒
	Notes and rationales:

	Exact number of people living with achondroplasia in England is unknown but estimated to be approximately 1,400 to 1,800 using the reported incidence or live birth prevalence estimate reported in the literature. This assumes same mortality risk as general population.
	A published review on the clinical management of achondroplasia (Pauli R M, 2019) reported that: • Most people with achondroplasia will have a normal or near normal life expectancy. • But several complications including growth, developmental, and neurological complications all impact quality of life. • Psychosocial impact: • On average people with achondroplasia are around 25% shorter than people of average height (Biomarin, accessed online April 17, 2025) **During the scoping workshop, it was also noted that:** • There may be sudden infant death, but from an adult perspective the life expectancy is similar to the general population because of close monitoring, no big difference in children either. Evidence (Pauli 2019) also showed normal life expectancy in achondroplasia, no significant number of people die earlier. • Achondroplasia is a lifelong condition but some people do not consider it a condition that requires cure or treatment, although it can cause complications that may need treatment (Managing and treating achondroplasia, accessed, March 2025). • Different views on whether achondroplasia needs medical treatment: Some felt strongly that people should be supported to live well without intervention. They explained people having vosoritide may be socially excluded and they may not qualify for Paralympian sports. Others believed families deserved the choice of a treatment that could reduce health burden.
	Has this definition been met or not met?

	Yes ☐ No ☒
	Notes and rationales: most people with achondroplasia will have a normal or near normal life expectancy, exact number of people living with achondroplasia in England unknown but estimates higher than 1/50,000.

5. Description of the HST Programme's vision

Criterion 2 - This criterion is designed to uphold the HST Programme's vision to encourage innovation and research into ultra-rare and debilitating diseases for which there is poor service provision within the NHS (for example, delay in diagnosis, no treatment options beyond supportive care). Without these incentives from the HST Programme, the technology may not be available either after launch, or during development or testing of the technology in England. The availability of the innovation can also reshape NHS services and advance awareness.

Criteria	**Descriptions of how the criteria are met or not met through assessing the definitions**
Criterion 2 **The technology is an innovation for the ultra-rare disease.**	Vosoritide is a new molecular entity that targets the signalling pathway responsible for achondroplasia (fibroblast growth factor receptor 3, FGFR3). This promotes bone growth and is a novel approach with no existing licensed alternatives in the NHS. Vosoritide is not a genetic treatment and does not change the underlying genetic mutation that causes (in 95% of people) achondroplasia.
	Has this definition been met or not met? Yes ☒

	No ☐
	Notes and rationales: please see above.

6. Description of the HST Programme's vision

Criterion 3 - This criterion is designed to establish the acceptability of the technology as an effective use of NHS resources, considering the significantly higher ICER threshold. So, the eligible population needs to be small. This is to strike a balance between the desirability of supporting access to treatments for ultra-rare diseases and the inevitable reduction in overall health gain across the NHS because of a higher ICER threshold. A small subpopulation within a population with a common disease would not be suitable for the HST Programme.

Criteria	Descriptions of how the criteria are met or not met through assessing the definitions
Criterion 3 **No more than 300 people in England are eligible for the technology in its licensed indication, and the technology is not an individualised medicine**	Vosoritide is intended for people with achondroplasia 4 months and over whose epiphyses are not closed (assuming around 18 years). Although some studies have suggested epiphyseal closure beyond the age of 18 (O'Connor et al. 2008; Alzyoud et al. 2024). Consensus during the scoping workshop that age 18 is more appropriate for estimating the eligible population, reflecting the variation in epiphyseal closure **Estimation of population eligible for treatment:** 1. Using incidence estimate 1 in 25,0000 (GOSH, Orphanet) suggested a crude estimate of • **Number of all people with achondroplasia in England**: 22.5 new case per year * 80 (average life expectancy) = **1,800** • **405** for people 18 years and under eligible for treatment; and

	• **361** for people 16 years and under eligible for treatment' • These were estimated by multiplying new case each year (22.5) and duration (18 years) or (16 years) 2. Using 1 in 32,960 (Coi et al. 2019): although defined as live birth prevalence, this may approximate incidence • **Number of all people with achondroplasia in England**: 17.6 new case per year * 80 (average life expectancy) = **1,412** • **317** for people 18 years and under eligible for treatment; and • **282** for people 16 years and under eligible for treatment' • These were estimated by multiplying new case each year (22.5) and duration (18 years) or (16 years) During the scoping workshop, stakeholders questioned the company's eligibility estimate of 160 to 272 people (based on age 16 for epiphyseal closure), noting they seemed low. Some queried whether England-specific prevalence/incidence figures (e.g. from EUROCAT or ONS) were most appropriate for decision-making. There was a consensus (clinical experts and patient organisations) that there would be more than 300 potential eligible people with achondroplasia that are 18 or under.
	Has this definition been met or not met? Yes ☐ No ☒
	Notes and rationales: Criterion not met as all methods described result in an eligible population of >300 in England.

7. Description of the HST Programme's vision

Criterion 4 - This criterion is designed to address the lack of effective treatment and access to NHS services for some ultra-rare diseases. To justify prioritising treatment access for ultra-rare diseases over overall population health, the technology under consideration should be anticipated to provide substantial health benefits to people with the disease over existing clinical management and supportive care.

Criteria	Descriptions of how the criteria are met or not met through assessing the definitions
Criterion 4 **The technology is likely to offer substantial additional benefit for people with the ultra-rare disease over existing established clinical management, and the existing established clinical management is considered inadequate.**	• Current treatments for achondroplasia include surgery and managing the symptoms of the condition. During the scoping workshop, it was confirmed that achondroplasia is currently managed by MDT in the NHS, growth hormone generally is not used. • Vosoritide, a C-type natriuretic peptide (CNP) analogue (Legare, 2023), targets the signalling pathway responsible for achondroplasia (Managing and treating achondroplasia, accessed, March 2025). • Evidence from a phase 3 trial reported that vosoritide, when compared with placebo, increased height in children and young people < 18 years with achondroplasia by about 1.57 cm/year until the growth plate closes (Savarirayan et al 2020), but the trial had a 5-year follow up • In the pivotal study for vosoritide (Savarirayan et al 2020), no clinically meaningful difference in quality of life was observed between people having placebo and people having vosoritide. Quality of life was assessed using Paediatric Quality of Life Inventory (PedsQL), and the Quality of Life of Short Statured Youth (QoLISSY). • Concerns have been noted by the short-statured community that a treatment which only increases height without improving long and short term health is not a priority (Savarirayan et al 2020). • As also noted above, some consider that achondroplasia in itself does not require treatment, but complications such as sleep apnoea, middle ear dysfunction, and curvature of the spine may require treatment (Managing and treating achondroplasia, accessed, March 2025).

	Has this definition been met or not met? Yes ☐ No ☒
	Notes and rationales:

Routing decision	**Overall routing decision:** HST☐ STA☒ **Other comments:**

References:

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