National Institute for Health and Care Excellence

Health Technology Evaluation

Somapacitan for treating growth hormone deficiency in children and young people ID6178
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Novo Nordisk Ltd	Novo Nordisk agrees with the appraisal and with the proposed route of evaluation through a cost comparison.	No action needed.
Wording	Novo Nordisk Ltd	[redacted] The wording of the remit should therefore be amended to:	Thank you for your comment. We have amended the wording to include adolescents.

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		*'To appraise the clinical and cost effectiveness of somapacitan within its marketing authorisation for treating **children and adolescents** with growth hormone deficiency'*	
Additional comments on the draft remit	Novo Nordisk Ltd	This evaluation should be conducted as a priority, since MHRA approval for somapacitan for the relevant population (children and adolescents) is expected in [redacted] We propose the NICE guidance to be published in [redacted] to approximately coincide with the regulatory approval of somapacitan.	Thank you for your comment. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK. NICE has scheduled this topic into its work programme

Section	Stakeholder	Comments [sic]	Action

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Merck Serono	A few additional points for background section: - Clarification that human growth hormone modulates IGF-1 which has a direct impact on growth plates. Suggest to clarify that TAG 188 also states the choice of product should be made on an individual basis after informed discussion between the responsible clinician and the patient and/or their carer about the advantages and disadvantages of the products available, taking into consideration therapeutic need and the likelihood of adherence to treatment.	Thank you for your comment. The scope is intended to provide a brief background to the disease area and not give information on mechanisms of action or directions for prescribing treatment.
	Novo Nordisk Ltd	The background information provides a useful overview of the disease area and the treatment landscape.	No action needed.
	Pfizer	NICE Technology appraisal guidance 863 recommends somatrogon for treating growth disturbance in children and young people aged 3 years and over. This should be included in the background section for completeness.	Thank you for your comment. This has been added to the background section
	Sandoz	No current marketing authorisation in the UK for this potential treatment option	Thank you for your comment. This is included in the section 'The Technology'.

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Population	Novo Nordisk Ltd	Yes, the population is defined appropriately. Our only suggestion is the below minor amend: ***'Children and adolescents from 2.5 years of age diagnosed with growth hormone deficiency'***	Thank you for your comment. This has been amended using NICE style, which uses young people rather than adolescents
Subgroups	Merck Serono	The clinical trial for somapacitan does not include patients up to transition age, only patients between 2.5-11 years. As such, considering the transition of care from paediatric to adult endocrine services of young people whose linear growth is not complete is not aligned with the proposed marketing authorisation for somapacitan and is also beyond the remit/evaluation objective for this appraisal.	Thank you for your comment. This has been removed as a subgroup.
	Novo Nordisk Ltd	Novo Nordisk does not have any comments on this section.	Thank you for your comment.
	Pfizer	It is unclear whether "transition of care from paediatric to adult endocrine services of young people whose linear growth is not complete" is a subgroup that should be considered separately. It is of our opinion that this should be included under 'other considerations'.	Thank you for your comment. This has been removed as a subgroup.

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Comparators	Novo Nordisk Ltd	Novo Nordisk proposes removing *'management strategies without human growth hormone'* from the draft scope, as this is not a relevant comparator. Growth hormone replacement therapy is currently the standard of care for the treatment of growth hormone deficiency, as stated in numerous clinical guidelines (BSPED, 2015, Grimberg, 2016, GH Research Society, 2000) and is the only treatment option recommended by NICE (NICE TA188, 2010, TA10989). In the somatrogon appraisal (TA10989), somatrogon was not compared with management strategies without human growth hormone. In Section 3.2 of the External Assessment Report on this appraisal, the EAG commented as follows: *'The NICE scope states that management strategies without the use of human growth hormone should be considered in this appraisal. The company do not provide direct clinical or narrative evidence for the effectiveness of somatrogon against non-active management of GHD. The EAG accepts that this is reasonable, given that somatrogon is intended as replacement for somatropin, and is not a distinct treatment, and that it is expected that only children with a contraindication to rhGH or who decline treatment will receive non-active management for GHD.'*	Thank you for your comment. The scope is intended to be broad and inclusive. As such, management strategies without human growth hormone remains in scope.

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Outcomes	Merck Serono	The following outcome should also be considered: Height achieved compared to expected height (with mid parenteral height as the marker for expected height).	Thank you for your comment. The outcome list is not intended to be exhaustive and therefore this outcome hasn't been included.
	Novo Nordisk Ltd	Novo Nordisk proposes expanding the list of outcomes, as follows (please see the 'Questions for consultation' section below for details): • annual height velocity • height standard deviation score-height relative to the distribution of height in children of the same chronological age • body composition, and biochemical and metabolic markers. • change in bone maturation • adverse effects of treatment • health-related quality of life. • **injection pain** • **treatment adherence**	Thank you for your comment. Please note that outcomes are defined broadly at the scoping stage. Specific outcomes can be defined in the submission and will be assessed by the appraisal committee during the appraisal.
	Sandoz	The following outcomes should be considered within the scope of this review: Annual height velocity Height standard deviation score-height relative to the distribution of height in children of the same chronological age	Thank you for your comment. Please note that outcomes are defined broadly at the scoping stage. Specific outcomes can be defined in the submission and will be assessed by the appraisal

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		Body composition, and biochemical and metabolic markers. Specifically, IGF-1 levels at days 1-3 and impact of fluctuation on the body. Change in bone maturation Adverse effects of treatment including injection site reactions and anti-drug antibody formation Health-related quality of life **Adherence and compliance**	committee during the appraisal.
Equality	Novo Nordisk Ltd	Novo Nordisk would like to highlight the importance of considering the following when conducting this appraisal: **1) Potential for gender bias** In the UK, a higher frequency of boys than girls has been noted among children with GHD treated with hGH (Shepherd, 2019), an observation that is consistent globally (Ranke, 2017 and Grimberg, 2018). Boys are also over represented among hospital referrals for short stature (Grimberg, 2005 and Grote, 2008). Thus, an awareness of potential gender biases is important for the adequate care of girls with short stature. **2) Socioeconomic factors** Several studies have evaluated the effects of socioeconomic status on adherence to GH therapy in children (Graham, 2020, Hartmann, 2013, Haverkamp 2011). In a 2011 literature review, key factors identified in relation to poor adherence to GH therapy were psychological/emotional problems, socioeconomic/everyday problems, and issues with technical handling of the drug delivery device. The authors emphasised the need for	Thank you for your comment. The appraisal committee will consider the impact of its recommendations on protected characteristics as stated in equality legislation during the appraisal. These issues will be considered in the equalities impact assessment.

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		healthcare professionals to be sensitive to socioeconomic factors that can affect adherence, including poverty, low levels of education, unemployment, unstable living conditions, transport costs, and poor social support networks (Haverkamp 2011). As poor adherence to GH treatment is associated with poorer clinical outcomes compared with compliant patients (Cutfield, 2011, Hughes, 2016, Fisher, 2013), disadvantaged children are at risk of poorer health outcomes than those living in more favourable socioeconomic circumstances.	
Other considerations	Merck Serono	The frequency, method of delivery and injection cartridge size could lead to drug wastage. Economic analyses should account for impact of drug wastage (as well as impact on growth outcomes in the case of a cost-effectiveness analysis): - If doses are missed due to patient tolerability/adherence issues - Any remaining drug in the cartridge after 28 days of opening are discarded	Thank you for your comment. The committee will take these comments into consideration during the course of the appraisal
	Sandoz	- Impact of IGF-1 levels and the sharp rise on days 1-3 - Economic modelling to show an average weight comparison rather than per mg dosage as this adds an element of confusion for HCPs and portrays a misleading message	Thank you for your comment. The committee will take these comments into consideration

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			during the course of the appraisal
Questions for consultation	Novo Nordisk Ltd	**Where do you consider somapacitan will fit into the existing care pathway for children with growth hormone deficiency?** Somapacitan is intended to fit into the current pathway of care for GHD as an alternative to current GH replacement treatment options, with initial administration carried out in hospital under the supervision of an endocrinology expert. Currently available facilities used for initial diagnosis and treatment administration will be appropriate for this new technology; thus no major changes to structure, staffing or training are expected with the introduction of somapacitan. **Do you consider that the use of somapacitan can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Novo Nordisk agrees with a cost comparison approach (please see below), in which QALY calculations will not be needed. We would like to highlight the following benefits provided by somapacitan over the relevant comparators (data to be included in the company submission):	Thank you for your comment. The committee will take these comments into consideration during the course of the appraisal

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		1) Greater treatment adherence and lower disease burden vs once-daily hGH. Somapacitan is expected to reduce treatment burden compared with once-daily hGH, leading to improved adherence. Indeed, results from disease specific patient reported outcomes for children and patients/caregivers (GHD-CTB and GHD-PTB) collected in the phase 3 REAL 4 trial favour somapacitan over somatropin across all domains including treatment interference and emotional well-being. Trial data also demonstrate higher mean adherence among children treated with somapacitan vs somatropin (Miller 2022). **2) Better injection site profile vs once-weekly somatrogon** [redacted] [redacted] **NICE is considering evaluating this technology through its cost comparison evaluation process. Please provide comments on the appropriateness of appraising this topic through this process.** Novo Nordisk agrees that a cost comparison approach is the most appropriate and efficient way to evaluate somapacitan vs the relevant comparators. [redacted]	

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		[redacted]	
Additional comments on the draft scope	Novo Nordisk Ltd	Novo Nordisk requests that the following related national policies are added to the scope: • NHS England (2017). NHS Medicines for Children's Policy • NHS England (2013). E03/S/e 2013/14 NHS standard contract paediatric medicine: endocrinology & diabetes (since paediatric endocrinology is concerned with the diagnosis and management of children and young people with hormonal disorders, including growth and bone problems) **Department of Health and Social Care (2016). NHS outcomes framework 2016 to 2017**	Thank you for your comment. These have been added to the scope.

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The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

- Neonatal and Paediatric Pharmacists Group (NPPG)
- Child Growth Foundation