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Newcastle University

Health Technology Briefing
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Somapacitan for treating idiopathic short stature or Noonan syndrome or small for gestational age in people aged 2 to 18 years

Company/Developer	Novo Nordisk Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 37110	NICE ID: Not available	UKPS ID: 674594

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Somapacitan is in clinical development for the treatment of small for gestational age or Noonan syndrome or idiopathic short stature in patients aged 2 to 18 years. Idiopathic short stature is defined as shortness in childhood without a specific cause. This condition may be familial (run in families) or nonfamilial and may be associated with or without delay of puberty. Noonan syndrome is a genetic condition that can cause a wide range of distinctive features and health problems, including short stature. Small for gestational age describes newborn babies with a birth weight and/or length below the normal range for gestational age. Current treatment for growth disturbance in Noonan syndrome or children born small for gestational age whose growth has not caught up by 4 years or later involves daily growth hormone injections that can be burdensome for patients and caregivers. There is no approved growth hormone for idiopathic short stature.

Somapacitan, administered subcutaneously, acts in the same way as human growth hormone. Once injected into the patient, it attaches to a protein in the blood called albumin, which makes it remain in the body for longer. This allows the medicine to be given once a week, compared with other growth hormone replacement therapies which are given daily. If licensed, somapacitan will offer an additional treatment option for idiopathic short stature, Noonan syndrome and small for gestational age in patients aged 2 to 18 years.

Proposed Indication

The treatment of short stature either born small for gestational age or with Turner syndrome, Noonan syndrome, or idiopathic short stature in people aged 2 to 18 years.[1,2]

Technology

Description

Somapacitan (Sogroya), is a long-acting human growth hormone (LAGH) derivative. It works by binding to the growth hormone receptor and induces signals to increase the sensitivity of a hormone called insulin-like growth factor I (IGF-1). This IGF-1 causes growth in bones and muscle tissue.[3,4] Somapacitan is linked to a small non-covalent albumin-binding moiety facilitating reversible binding to endogenous albumin. This delays somapacitan elimination, prolongs half-life, and thereby extends duration of action.[5]

Somapacitan is currently in phase III clinical development for the treatment of small for gestational age or Noonan syndrome or idiopathic short stature in patients aged 2 to 18 years (NCT05330325 (REAL 8), NCT05723835 (REAL 9)).[1,2] In the phase IIII trial REAL 8, somapacitan is administered subcutaneously (SC) at a dose of 0.24 mg/kg/week for a 156-week period.[5] In the phase III trial REAL 9, somapacitan is administered SC at a dose of 0.24 mg/kg/week for a 26-week main phase followed by an 130-week extension phase.[2]

Key Innovation

There is no treatment available for children with familial short stature.[6] The treatments of short stature in children that are small for gestational age and those with restricted growth in Noonan syndrome often involve daily human growth hormone injections that can be burdensome for patients and caregivers.[5,7,8] However, as somapacitan is given weekly, it might provide a less burdensome treatment option for these patients. In addition, somapacitan at a dose of 0.24 mg/kg/week has been found to be very efficacious and provides similar efficacy, safety, and tolerability as daily GH 0.067 mg/kg/day.[5] If licensed, somapacitan will offer an additional treatment option for small for gestational age or Noonan syndrome or idiopathic short stature in patients aged 2 to 18 years.

Regulatory & Development Status

Somapacitan currently has Marketing Authorisation in the UK for growth hormone (GH) deficiency in adults and children from 3 years of age.[9]

Patient Group

Disease Area and Clinical Need

Idiopathic short stature is defined as a condition in which the height of an individual is more than 2 standard deviation scores below the corresponding mean height for a given age, sex, and population group without evidence of systemic, endocrine, nutritional, or chromosomal abnormalities. Children with idiopathic short stature have normal birth weight and are GH sufficient. Idiopathic short stature is experienced by a heterogeneous group of children, for many of whom, the cause of their short stature is unidentified.[10] The majority of children with idiopathic short stature have either familial short stature or constitutional delay in growth and puberty. Children with familial short stature are within their target height range; either one or both parents will have short stature. Their bone age is not delayed, and their rate of growth is normal. Young people with constitutional delay in growth and puberty have delayed growth but most will catch

up, reaching a final adult height within the range expected for their family size. Some, who have a considerably prolonged delay, may not.[6] Noonan syndrome is a clinically and genetically heterogeneous congenital disorder.[11,12] Clinical features include short stature, facial dysmorphism, a wide spectrum of congenital heart defects, pectus deformity, cryptorchidism, and coagulation defect.[13] The diagnosis is clinical, although in 80% of patients a genetic defect can be detected. Inheritance is predominantly autosomal dominant and seldom autosomal recessive. The condition is familial in less than 50% of cases, and in the other cases, a spontaneous mutation has occurred.[11] Small for gestational age describes neonates born with a birth weight and/or length below 2 standard deviation scores for gestational age. Small for gestational age is caused by a complex interaction of maternal, placental, and foetal factors. The risk of small for gestational age is significantly higher among mothers with chronic hypertension, preeclampsia, malnutrition, subclinical hypothyroidism (particularly in iodine-deficient areas), chronic infections, and malaria.[13]

Idiopathic short stature (including constitutional delay of growth and puberty and familial short stature) affects about 23 in 1000 children.[14] It is estimated that between 1 in 1,000 and 1 in 2,500 children are born with Noonan syndrome. It affects both sexes and all ethnic groups equally.[15] The size of the population with small for gestational age could not be estimated from published sources. In England 2022-23, there were 296 finished consultant episodes (FCE) and 278 admissions for congenital malformation syndromes predominantly associated with short stature (ICD-10 code Q87.1) which resulted in 754 FCE bed days and 163 day cases. In England 2022-23, there were 195 FCE and 193 admissions for delayed milestone (ICD-10 code R62.0) which resulted in 39 FCE bed days and 156 day cases. Also in England 2022-23, there were 4,793 FCE and 4,490 admissions for small for gestational age (ICD-10 code P05.1) which resulted in 8,946 FCE bed days and 0-day cases.[16]

Recommended Treatment Options

Somatropin (recombinant human growth hormone) is recommended by NICE as a treatment option for small for gestational age with subsequent growth failure at 4 years of age or later.[8] There is no single treatment for Noonan syndrome, but it's possible to treat many aspects of the condition. If a child's growth rate is thought to be seriously reduced, treatment with human GH may be suggested (somatropin is most often used).[7] Whilst those with constitutional delay in growth and puberty can be given hormonal supplementation to induce puberty, there is no treatment available in the UK for the remaining children and young people with idiopathic short stature as GH is not approved for this population.[6]

Clinical Trial Information

Trial	NCT05330325, EudraCT 2021-005607-13; A Study Comparing the Effect and Safety of Once Weekly Dosing of Somapacitan With Daily Norditropin® as Well as Evaluating Long-term Safety of Somapacitan in a Basket Study Design in Children With Short Stature Either Born Small for Gestational Age or With Turner Syndrome, Noonan Syndrome, or Idiopathic Short Stature **Phase III** – Ongoing **Locations:** 17 EU countries, UK, USA, Canada, and other countries **Primary completion date:** May 2024
Trial Design	Randomised, parallel assignment, open label
Population	N=399; subjects born small and who stay small, or with Turner syndrome, Noonan syndrome, or idiopathic short stature; aged 2 to 10 years old

Intervention(s)	Somapacitan administered SC once weekly for 156 weeks
Comparator(s)	Norditropin® administered SC once daily for 52 weeks (main phase) and somapacitan for 104 weeks (extension phase)
Outcome(s)	Primary outcome: Height velocity reported separately for small for gestational age, Turner syndrome, Noonan syndrome and idiopathic short stature See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	
Trial	NCT05723835, EudraCT 2022-501055-87; A Study Evaluating the Safety and Efficacy of Once-weekly Dosing of Somapacitan in a Basket Study Design in Paediatric Participants With Short Stature Either Born Small for Gestational Age or With Turner Syndrome, Noonan Syndrome or Idiopathic Short Stature **Phase III** – Ongoing **Locations:** 3 EU countries, USA, Republic of Korea, and Malaysia **Primary completion date:** November 2024
Trial Design	Single group assignment, open label
Population	N=48; subjects either born small for gestational age or with Turner syndrome, Noonan syndrome, or idiopathic short stature; aged 10 to 18 years old
Intervention(s)	Somapacitan (0.24 mg/kg/week) will be administered SC for 26 weeks (main phase) followed by 130 weeks (extension phase)
Comparator(s)	No comparator
Outcome(s)	Primary outcome: Number of adverse events (AEs) reported separately for small for gestational age, Turner syndrome, Noonan syndrome, and idiopathic short stature See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of somapacitan is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Human growth hormone (somatropin) for the treatment of growth failure in children (TA188). May 2010.

- NICE guideline. Faltering growth: recognition and management of faltering growth in children (NG75). September 2017.
- NICE quality standard. Faltering growth (QS197). August 2020.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract Paediatric Medicine: Endocrinology & Diabetes. E03/S/e.

Other Guidance

- Hokken-Koelega ACS, van der Steen M, Boguszewski MCS, Cianfarani S, Dahlgren J, Horikawa R, et al. International Consensus Guideline on Small for Gestational Age: Etiology and Management from Infancy to Early Adulthood. 2023.[13]
- BSPED Growth Disorders Special Interest Group (SIG). BSPED recommendations for the initial clinical assessment, investigation and genetic testing of children with growth failure and/or short stature. 2022.[17]
- BSPED Growth Disorders Special Interest Group (SIG). Clinical standards for growth assessment and referral criteria for children with a suspected growth disorder. 2021.[18]
- NHS Wales. Management of the Small for Gestational Age Fetus Guideline. 2017.[19]

Additional Information

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