Health Technology Briefing
January 2026

Lonapegsomatropin for treating growth hormone deficiency in children and adolescents

Company/Developer	Ascendis Pharma

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 20630	NICE ID: 9946	UKPS ID: 675271

Licensing and Market Availability Plans

Lonapegsomatropin is currently licensed in the UK.

Summary

Lonapegsomatropin is currently approved (licensed) for the treatment of growth failure in children and adolescents due to insufficient endogenous (produced in the body) growth hormone secretion (growth hormone deficiency (GHD)). GHD is a condition caused by a severe shortage of growth hormone, sometimes even a complete absence of growth hormone, in the body. Growth hormone is produced by the pituitary gland, a small organ in the brain. A lack of growth hormone will restrict the child's growth, resulting in a height below average. GHD can be present at birth or develop later. Rarely, some types of GHD are inherited. Potential causes of GHD could be the pituitary gland not developing properly during pregnancy, or head injury, tumours, radiotherapy or surgery later on in childhood. Symptoms include short stature, being overweight, and delayed tooth development. Current treatment of GHD is with a daily or weekly injection of growth hormone.

Lonapegsomatropin is a long-acting 'prodrug' (inactive form of a medicine that doesn't start working until after it enters the body) of somatropin, a growth hormone that replaces the missing hormone in the body. It is administered as an injection under the skin once weekly. Now, licensed, lonapegsomatropin will provide an additional treatment option for children and adolescents with GHD.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Indication

Growth failure in children and adolescents aged from 3 years up to 18 years due to insufficient endogenous growth hormone secretion (growth hormone deficiency (GHD)) [1]

Technology

Description

Lonapegsomatropin (Skytrofa, TransCon hGH)[2,3] is a long-acting 'prodrug' of somatropin. It consists of the parent drug, somatropin, that is transiently conjugated to a methoxypolyethylene glycol carrier (mPEG) via a proprietary TransCon Linker. The linker undergoes autohydrolysis to serve as a timer, enabling controlled release of somatropin at body temperature and pH. The carrier has a shielding effect that minimises renal excretion and receptor-mediated clearance of lonapegsomatropin.[3,4]

Somatropin binds to the dimeric human growth hormone (hGH) receptor on the cell membrane of target cells, resulting in intracellular signal transduction and a range of pharmacodynamic effects. Somatropin has direct tissue and metabolic effects and indirect effects mediated by serum insulin-like growth factor-1 (IGF-1), including stimulation of chondrocyte differentiation and proliferation, and stimulation of hepatic glucose output, protein synthesis, and lipolysis. Somatropin stimulates skeletal growth in paediatric patients with GHD by acting on the growth plates (epiphyses) of bones.[3]

Lonapegsomatropin is currently licensed for the treatment of growth failure in children and adolescents aged 3 to 18 years due to insufficient endogenous growth hormone secretion. In the phase III clinical trial (NCT03344458), lonapegsomatropin was administered subcutaneously (SC) at 0.24 mg hGH/kg/week.[2,5]

Key Innovation

The proprietary TransCon™ technology of lonapegsomatropin achieves a longer half-life (~25 hours) and maintains therapeutic levels without altering the hormone's natural structure, which enables once-weekly, sustained, and predictable delivery of unmodified hGH, offering practical and potentially clinical advantages over conventional daily growth hormone therapies.[6,7] The once-weekly formulation significantly reduces the number of injections per year and may improve adherence and quality of life for paediatric patients and their families.[4] Lonapegsomatropin demonstrated non-inferiority and, in some measures, superiority in growth outcomes compared with daily somatropin injections.[6] It has also demonstrated non-inferiority to other long-acting, once-weekly administered growth hormones such as somapacitan and somatrogon.[8]

Now licensed, lonapegsomatropin will offer an additional treatment option for paediatric patients with GHD.

Regulatory & Development Status

Lonapegsomatropin currently has Marketing Authorisation in the UK for the treatment of GHD in children and adolescents aged 3 to 18 years due to insufficient endogenous growth hormone secretion.[1]

Lonapegsomatropin is currently in phase II or III clinical development for:[9]

- Turner syndrome
- Achondroplasia

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Lonapegsomatropin was granted an Orphan Drug Designation by the EMA in 2019, by the FDA in 2020, and the MHRA in 2022 (PLGB 47497/0001-009/OD1) for the treatment of growth hormone deficiency. [10-12]

Patient Group

Disease Area and Clinical Need

GHD is a rare and treatable condition that occurs when the pituitary gland doesn't make enough growth hormone. [13] It causes short height in children. If GHD is acquired later in life, GHD may cause a relative increase in fat mass, along with a decrease in muscle mass, decreased energy levels, anxiety, and/or depression. Lipid levels are also affected, resulting in an increase in LDL-cholesterol and triglyceride levels. [14] Growth hormone is required for normal growth, muscle and bone strength, and the distribution of body fat. There are three main types of GHD. [14]

- Congenital GHD: refers to a condition evident from birth resulting from a genetic mutation or structural abnormalities in the infant's brain
- Acquired GHD: develops later in life due to pituitary gland injury
- Idiopathic GHD: means there's no known cause

The main symptom of GHD is that growth slows or stops from age 2 or 3 years onward. It can be detected through routine monitoring using growth charts, or it may become more obvious when a child starts nursery or school and is much shorter than other children in the class.[15] Other symptoms of GHD include proportionate arms and legs relative to the chest and abdomen, a younger-looking face, a more rounded body build, impaired hair growth, delayed tooth development, and delayed or absent puberty.[15,16]

Around 500 children are diagnosed with GHD every year in the UK.[17] The prevalence of GHD is estimated to be between 1 in 3,500 and 1 in 4,000 children. In about half of the children with GHD (50%), the cause is unknown (idiopathic GHD).[13] In England (2024-25), there were 4823 finished consultant episodes (FCE) for hypofunction and other disorders of the pituitary gland (ICD10 code E23), with 4454 admissions resulting in 3668 day cases and 4230 FCE bed days.[18]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommend the following interventions for children and adolescents with GHD:[13,19,20]

- Somatropin
- Somapacitan
- Somatrogon

Clinical Trial Information

Trial	**enliGHten;** NCT03344458; 2017-003410-20: A multicentre, phase 3, long-term, open-label trial investigating safety and efficacy of TransCon hGH administered once-weekly in children with growth hormone deficiency (GHD) who have completed a prior TransCon hGH clinical trial **Phase III:** Completed **Location(s):** 3 EU countries, USA and other countries **Primary Completion Date:** February 2023
Trial Design	Single group assignment, open label

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Population	N=298 (actual); children aged 1 to 18 years; prior participation in a specific Phase 3 TransCon hGH trial; no permanent discontinuation of study drug in the prior trial
Intervention(s)	Lonapegsomatropin, once weekly SC
Comparator(s)	No comparator
Outcome(s)	Primary outcome measures: Number of Subjects with treatment-emergent adverse events (TEAE) [long-term safety and tolerability] See trial record for other outcomes
Results (efficacy)	Mean (SD) height standard deviation score (SDS) continued to increase over time, approaching 0 SDS, which corresponds to the mean height for children of average stature (adjusted for sex and age). By year 4 (Week 208), the mean (SD) height SDS for participants remaining in the trial at this time point (*n* = 148) was −0.39 (0.90). Weekly average IGF-1 SDS mean levels remained within the protocol-specified target range of 0–2 SDS over time in the trial for the full analysis set.[5]
Results (safety)	75.8% (*n* = 226) of participants experienced treatment-emergent adverse events (TEAEs) at any time during the trial. Most TEAEs were assessed as mild (40.9%) or moderate (31.2%); 11 (3.7%) participants experienced TEAEs assessed as severe, but none of these were assessed as related to the study drug. 25 participants experienced TEAEs assessed as related to study drug by the investigator. The most common were general disorders and administration site conditions (2.7%), musculoskeletal and connective tissue disorders (2.3%), in which 2 participants experienced scoliosis events assessed as mild or moderate. There were no cases of intracranial hypertension or pancreatitis.[5]

Clinical Trial Information

Trial	**FliGHt;** NCT03305016; A multicentre, phase 3, open-label, 26-week trial investigating the safety, tolerability and efficacy of TransCon hGH administered once weekly in children with growth hormone deficiency (GHD) **Phase III:** Completed **Location(s):** USA, Canada, Australia and New Zealand **Primary Completion Date:** March 2019
Trial Design	Single group assignment, open label
Population	N=146 (actual); GHD diagnosis; ages 6 months to 17 years; if 3-17 years old, on hGH ≥ 0.20 mg/kg/week for 13-130 weeks; if 6 months - < 3 years old, hGH treatment-naïve or on hGH ≥ 0.20 mg/kg/week for ≤ 130 weeks; Tanner stage < 5; open epiphyses (bone age ≤14.0 years for females or ≤16.0 years for males)
Intervention(s)	Lonapegsomatropin once weekly SC at a starting dose of 0.24 mg/kg/week
Comparator(s)	No comparator

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Outcome(s)	Primary outcome measures: Number of participants with treatment-emergent adverse events (AE) (safety and tolerability) See trial record for other outcomes
Results (efficacy)	Continued growth was observed across all subgroups; higher growth outcomes were observed among subjects who were younger or of less advanced Tanner stage, those treated with prior daily somatropin for a shorter duration of time (<1 year), and those with lower baseline peak GH stimulation results. Similar growth rates were observed between males and females.[21]
Results (safety)	Over half of the subjects (57%) (83/146) experienced at least 1 adverse event (AE), with only 4% experiencing an AE that was assessed by the investigator as related to study drug. Most patients experienced AEs that were mild (45%) or moderate (12%) in severity. The most common AEs were pyrexia (12%), nasopharyngitis (10%), upper respiratory tract infection (10%), headache (8%), and oropharyngeal pain (5%). No patients discontinued the study drug due to an AE.[21]

Clinical Trial Information	
Trial	**heiGHt;** NCT02781727; 2016-001145-11; A multicentre, phase 3, randomised, open-label, active-controlled, parallel-group trial investigating the safety, tolerability, and efficacy of TransCon hGH administered once a week versus standard daily hGH replacement therapy over 52 weeks in prepubertal children with growth hormone deficiency (GHD) **Phase III**: Completed **Location(s):** 5 EU countries, US, Australia and other countries **Primary Completion Date:** January 2019
Trial Design	Randomised, parallel assignment, open label
Population	N=162 (actual); ages 3-12 for boys and 3-11 for girls; prepubertal children in Tanner Stage 1; GHD, either isolated or part of multiple pituitary hormone deficiency; height at least 2.0 standard deviations below the mean; GHD confirmed by two growth hormone stimulation tests with peak growth hormone ≤10 ng/mL; bone age at least 6 months less than chronological age; IGF-1 level at least 1 standard deviation below the mean.
Intervention(s)	Once weekly SC lonapegsomatropin
Comparator(s)	Once daily SC hGH
Outcome(s)	Primary outcome measures: Annualised height velocity at 52 weeks for weekly Lonapegsomatropin and daily hGH Treatment Groups See trial record for other outcomes

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Results (efficacy)	Lonapegsomatropin was both non-inferior and superior to daily somatropin for the primary endpoint of annualised height velocity (AHV) at 52 weeks, 11.2 cm/year vs. 10.3 cm/year (P=0.009).[6]
Results (safety)	Lonapegsomatropin was well tolerated, with mostly mild or moderate AEs consistent with those observed with daily somatropin.[6]

Estimated Cost

The cost of lonapegsomatropin is currently unknown.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Somapacitan for treating growth hormone deficiency in people 3 to 17 years (TA1066) June 2025
- NICE technology appraisal. Somatrogon for treating growth disturbance in children and young people aged 3 years and over (TA863) February 2023
- NICE technology appraisal. Human growth hormone (somatropin) for the treatment of growth failure in children (TA188) May 2010

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- British Society for Paediatric Endocrinology and Diabetes. Clinical Standards for GH Treatment of GH Deficiency (GHD) in Childhood and Adolescence. 2021[22]

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