SKYTROFA® (lonapegsomatropin-tcgd) Medicaid Public Comment

SKYTROFA (lonapegsomatropin-tcgd), is a long-acting prodrug of somatropin, approved by the FDA for once-weekly subcutaneous (SC) treatment of growth failure due to inadequate secretion of endogenous growth hormone in children ≥1 year old who weigh ≥11.5 kg. It is the only once-weekly rhGH product to be approved in the US for treatment of PGHD.[1]

Growth hormone deficiency (GHD) due to inadequate secretion of endogenous growth hormone is a rare condition that causes short stature, with an estimated prevalence of 1:3500 in the US.[2] Treatment with daily injections of somatropin has been indicated for children with GHD for over 35 years, with the goal of achieving mid-parental height.[3] Studies have reported nonadherence as high as 66% among patients receiving daily injections of growth hormone, leading to significant decreases in height velocity standard deviation scores when compared to adherent patients.[4]

Lonapegsomatropin is a long-acting prodrug consisting of somatropin conjugated to an inert methoxypolyethylene glycol (mPEG) carrier and linker. The mPEG carrier minimizes renal excretion and receptor-mediated clearance of the drug. The apparent half-life of the somatropin after release from the linker is 25 hours. Once dosed via sub-cutaneous injection, somatropin is released continuously over a week following first-order kinetics.[5]

FDA approval of lonapegsomatropin was based on the results of an open-label trial (heiGHt) in 161 treatment-naive prepubertal children with GHD. Children were randomized to receive lonapegsomatropin once weekly or the equivalent dose of daily somatropin.[1] After 52 weeks, lonapegsomatropin met the prespecified criteria for both noninferiority and superiority compared to daily somatropin for the primary endpoint of annualized height velocity. Medication adherence was greater than 99% for both arms.[6]

In a second phase 3 trial, patients were switched from a mean (SD) 0.29 mg/kg/week (0.05) somatropin dose to 0.24 mg/kg/week lonapegsomatropin. Treatment-emergent adverse events (AEs) reported were similar to the published AE profile of daily somatropin therapies. After switching to lonapegsomatropin, the least-squares mean (LSM) AHV was 8.7 cm/year (95% CI: 8.2, 9.2) at Week 26 and LSM height SDS change from baseline to Week 26 of +0.25 (95% CI: 0.21, 0.29). Patient reported outcomes indicated a preference for weekly lonapegsomatropin among both children and their parents.[7] An open label extension study evaluating patients from the lonapegsomatropin phase 3 clinical trials will be completed by the end of 2026.[8]

SKYTROFA is a lyophilized powder available in single-dose, dual-chamber, prefilled cartridges containing lonapegsomatropin-tcgd and diluent available. Cartridges are available in 9 strengths and used with a SKYTROFA rechargeable Auto-Injector. The contents of the entire cartridge is injected using the auto-injector, reducing the potential for wastage. Refrigeration is not required by the patient for up to 6 months. Drug reconstitution and mixing is aided by the Auto-injector both visually and auditorily. Injections are achieved with a shielded 30-gauge needle. The recommended dosage for treatment-naive patients and for those switching from daily somatropin therapy is 0.24 mg hGH/kg injected SC into the abdomen, buttock, or thigh once weekly. Injection sites should be rotated to prevent lipoatrophy. In patients switching from daily somatropin, at least 8 hours should elapse between the last dose of somatropin and the first dose of SKYTROFA. If a dose is missed, it should be given as soon as possible; the next dose can be given on the previously scheduled dosing day. If more than 2 days have passed since the missed dose, the dose should be skipped. At least 5 days should elapse between doses. If refrigerated, cartridges should be kept at room temperature for 15 minutes before use.[1]

The following is a summary of important safety information

- *Skytrofa* is contraindicated in patients with:
  - Acute critical illness
  - Hypersensitivity to somatropin or any of the excipients in SKYTROFA
  - Children with closed epiphyses
  - Active malignancy
  - Active proliferative or severe non-proliferative diabetic retinopathy
  - Children with Prader-Willi syndrome who are severely obese or have
  - Severe respiratory impairment due to risk of sudden death
- The most common adverse reactions (≥5%) in patients treated with *Skytrofa* were: viral infection (15%), pyrexia (15%), cough (11%), nausea and vomiting (11%), hemorrhage (7%), diarrhea (6%), abdominal pain (6%), and arthralgia and arthritis (6%).
- *Skytrofa* can interact with the following drugs:
  - Glucocorticoids
  - Oral Estrogen
  - Insulin and/or Other Hypoglycemic Agents.
  - Cytochrome P450-Metabolized Drugs
- Complete safety information is available in the SKYTROFA (lonapegsomatropin-tcgd) prescribing information available at www.skytrofa.com.

You are encouraged to report side effects to FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Ascendis Pharma at 1-844-442-7236.[1]

For more information, please see full Prescribing Information for *Skytrofa*.

References

[1] SKYTROFA® (lonapegsomatropin-tcgd) prescribing information, Ascendis Pharma.
[2] Lindsay R, Feldkamp M, Harris D, et al. Utah Growth Study: growth standards and the prevalence of growth hormone deficiency. *J Pediatr*. 1994;125:29–35.
[3] Genotropin® (somatropin) prescribing information, Pfizer Inc.
[4] Cutfield WS, Derraik JG, Gunn AJ, et al. Non-compliance with growth hormone treatment in children is common and impairs linear growth. *PLoS One*. 2011;6(1):e16223.
[5] Gilfoyle D, Mortensen E, Christoffersen ED, Leff JA, Beckert M. A first-in-man phase 1 trial for long-acting TransCon Growth Hormone. *Growth Horm IGF Res*. 2018;39:34-39.
[6] Thornton PS, Maniatis AK, Aghajanova E, et al. Weekly Lonapegsomatropin in Treatment-Naïve Children With Growth Hormone Deficiency: The Phase 3 heiGHt Trial. *J Clin Endocrinol Metab*. 2021;106(11):3184-3195.
[7] Maniatis AK, Nadgir U, Saenger P, et al. Switching to Weekly Lonapegsomatropin from Daily Somatropin in Children with Growth Hormone Deficiency: The fliGHt Trial [published online ahead of print, 2022 Mar 9]. Horm Res Paediatr. 2022;10.1159/000524003. doi:10.1159/000524003.
[8] ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03344458. Accessed April 8. 2022.