

## CLINICAL UPDATE

<b>Brand Name</b>	Skytrofa™
<b>Generic Name</b>	lonapegsomatropin-tcgd
<b>Drug Manufacturer</b>	Ascendis Pharma Inc.

### Clinical Update

#### TYPE OF CLINICAL UPDATE

New Formulation

#### FDA APPROVAL DATE

August 25, 2021

#### LAUNCH DATE

4<sup>th</sup> quarter 2021

#### REVIEW DESIGNATION

NA; Orphan

#### TYPE OF REVIEW

Biologic License Application (BLA): 761177

#### DISPENSING RESTRICTIONS

Specialty Pharmacy Required

### Overview

#### INDICATION(S) FOR USE

Skytrofa™ is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).

#### MECHANISMS OF ACTION

Skytrofa™ is a pegylated human growth hormone (somatropin) for once-weekly subcutaneous injection [see Pharmacokinetics. Somatropin binds to the growth hormone (GH) receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. Somatropin has direct tissue and metabolic effects, and indirect effects mediated by insulin-like growth factor-1 (IGF-1), including stimulation of chondrocyte differentiation and proliferation, stimulation of hepatic glucose output, protein synthesis and lipolysis. Somatropin stimulates skeletal growth in pediatric patients with growth hormone deficiency (GHD) as a result of effects on the growth plates (epiphyses) of long bones.

#### DOSAGE FORM(S) AND STRENGTH(S)

Injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg, and 13.3 mg.

#### DOSE & ADMINISTRATION

Skytrofa™ should be administered subcutaneously into the abdomen, buttock, or thigh with regular rotation of the injection sites. The recommended dose is 0.24 mg/kg body weight once weekly.

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### EFFICACY

#### Treatment-Naïve Pediatric Patients with Growth Hormone Deficiency (NCT02781727):

A multi-center randomized, open-label, active-controlled, parallel-group phase 3 study was conducted in 161 treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD); 105 subjects received once-weekly Skytrofa™, and 56 received daily somatotropin. The dose in both arms was 0.24 mg/kg/week. The primary efficacy endpoint was annualized height velocity at Week 52.

**Table: heiGHt Trial (NCT02781727): Study Design Summary**

<b>Study Population (N = 161)</b>	<ul style="list-style-type: none"> <li>• 161 treatment-naïve, prepubertal patients with GHD</li> <li>• Weight: ≤11.5 kg</li> <li>• Mean age: 8.5 years (range, 3.2–13.1 years)</li> <li>• 82% male; 18% female</li> <li>• 94.4% White</li> </ul> <p><b>Key exclusion criteria:</b> Prior exposure to GH or IGF-1 therapies, body weight below 12 kg, past or present intracranial tumor growth, psychosocial dwarfism, idiopathic short stature, history, or presence of malignant disease, closed epiphyses, major medical conditions and/or presence of contraindication to hGH treatment.</p>
<b>Interventions</b>	<p>Study participants were randomized 2:1 to receive:</p> <ul style="list-style-type: none"> <li>• Skytrofa™ 0.24 mg hGH once weekly (n = 105) or</li> <li>• Genotropin (0.034 mg hGH/kg) once daily (n = 56)</li> </ul>
<b>Endpoints</b>	<ul style="list-style-type: none"> <li>• Primary: AHV at Week 52</li> <li>• Secondary: Change from baseline in height SDS</li> </ul>
<b>Efficacy and Safety Results</b>	<ul style="list-style-type: none"> <li>• LS mean (SE) AHV at 52 weeks was 11.2 (0.2) cm/year for Skytrofa™ vs. 10.3 (0.3) cm/year for daily Genotropin (<i>P</i> = 0.009), with Skytrofa™ demonstrating both noninferiority and superiority over daily Genotropin.</li> <li>• LS mean (SE) height SDS increased from baseline to Week 52 by 1.10 (0.04) vs. 0.96 (0.05) in the weekly Skytrofa™ vs. daily Genotropin groups (<i>P</i> = 0.01).</li> <li>• Bone age/chronological age ratio, adverse events, tolerability, and immunogenicity were similar between groups.</li> <li>• The trial met its primary objective of noninferiority in AHV and showed superiority of Skytrofa™ compared to daily Genotropin, with similar safety, in treatment-naïve children with GHD.</li> </ul>

Abbreviations: AHV, annualized height velocity; GHD, growth hormone deficiency; LS, least squares; SDS, standard deviation scores; SE, standard error.