Consider A Once-Weekly Growth Hormone That Fits Your Pediatric Patient's Needs

You may see pediatric patients with GHD who would benefit from:

- A medication with the same active ingredient as daily growth hormone
- A formulation without additives
- A prefilled, single-dose cartridge
- A device with a permanent needle guard
- A long-term storage option for overnight trips between parental homes, sleepovers, or summer camp

SKYTROFA® may be the right choice for your pediatric GHD patients

GHD = growth hormone deficiency.

INDICATION

SKYTROFA® is a human growth hormone (GH) indicated for the treatment of pediatric patients aged ≥ 1 years weighing ≥ 11.5 kg with growth failure due to inadequate secretion of endogenous GH.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS

SKYTROFA is contraindicated in patients with:

- **Acute critical illness** after open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure due to risk of increased mortality with use of pharmacologic doses of somatropin
- **Hypersensitivity** to somatropin or any of the excipients in SKYTROFA. Systemic hypersensitivity reactions have been reported with post-marketing use of somatropin products
- **Closed epiphyses**
- **Active malignancy**
- Active proliferative/severe non-proliferative **diabetic retinopathy**
- **Prader-Willi syndrome** who are severely obese, have a history of upper airway obstruction or sleep apnea or have severe respiratory impairment due to the risk of sudden death

Please see Important Safety Information throughout and accompanying full Prescribing Information for SKYTROFA.

Once-weekly Skytrofa® lonapegsomatropin-tcgd

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Why Choose SKYTROFA®

Drug and device features

- Predictable release of **unmodified somatropin over the course of one week**[1,2]
- A **preservative-free** formulation[1]
- An award-winning Auto-Injector designed to **deliver the full dose** and minimize the potential for wasted medication[1]
  - Equipped with an **integrated needle guard** that covers the needle during injection[3]
- **Room temperature storage** for up to 6 months[1]

Help your pediatric GHD patients experience the SKYTROFA difference

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS

- Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with pharmacologic doses of somatropin. The safety of continuing SKYTROFA treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established
- Serious systemic hypersensitivity reactions including anaphylaxis and angioedema have been reported with post-marketing use of somatropin products. Inform patients and caregivers that such reactions are possible and that prompt medical attention should be sought if an allergic reaction occurs. Do not use SKYTROFA in patients with known hypersensitivity to SKYTROFA or any of its excipients
- Patients with active malignancy have an increased risk of progression with somatropin treatment. Any preexisting malignancy should be inactive and treatment complete before instituting therapy with SKYTROFA. In childhood cancer survivors treated with radiation to the brain/head for their first neoplasm who developed subsequent GHD treated with somatropin, an increased risk for a second neoplasm has been reported. Monitor patients with a history of GHD secondary to an intracranial neoplasm routinely for progression/recurrence of the tumor. Monitor patients carefully for development of neoplasms and/or increased growth/potential malignant changes of preexisting nevi
- Treatment with somatropin may decrease insulin sensitivity, and new onset type 2 diabetes mellitus has been reported. Previously undiagnosed impaired glucose tolerance and overt diabetes mellitus may be unmasked. Patients with type 1 and 2 diabetes mellitus or impaired glucose tolerance should be monitored closely, and antihyperglycemic drugs may require adjustment

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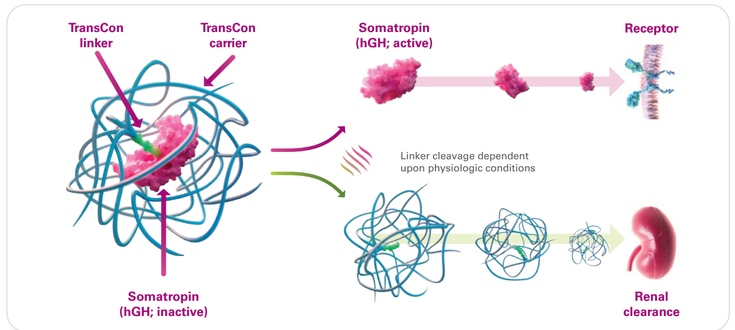
Proprietary TransCon® Technology

TransCon, or "transient conjugation," is an innovative, drug-delivery platform

- Designed to transiently link an inert carrier to a parent drug with known biology to achieve sustained release[2]

SKYTROFA® is a prodrug that releases active unmodified somatropin with the same molecular weight and amino acid sequence as endogenous GH[1,2]

- Once released, the unmodified somatropin is expected to have a similar distribution pattern to daily somatropin in the body[1]



GH = growth hormone; hGH = human growth hormone.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea, and/or vomiting has been reported in a small number of patients treated with somatropin. Symptoms resolved rapidly after cessation of therapy/reduction of the dose. Perform fundoscopic examination routinely before initiating treatment with SKYTROFA to exclude preexisting papilledema, and periodically thereafter. If papilledema is observed, stop the treatment. If somatropin-induced IH is diagnosed, restart treatment at a lower dose after IH-associated signs and symptoms have resolved
- Fluid retention during somatropin therapy may occur. Clinical manifestations of fluid retention (eg, edema, arthralgia, myalgia, nerve compression syndromes including carpal tunnel syndrome/paresthesia) are usually transient and dose dependent
- Patients receiving somatropin therapy may be at risk for reduced serum cortisol levels and/or unmasking of central hypoadrenalism. Patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance/stress doses following initiation of SKYTROFA therapy. Monitor patients with known hypoadrenalism for reduced serum cortisol levels and/or need for glucocorticoid dose increases
- Undiagnosed or untreated hypothyroidism may prevent response to SKYTROFA. Central hypothyroidism may first become evident or worsen with treatment. Perform periodic thyroid function tests and initiate/properly adjust thyroid hormone replacement therapy when indicated

Please see Important Safety Information throughout and accompanying full Prescribing Information for SKYTROFA.

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It's Time to Write the Script

For once-weekly SKYTROFA®

Our dedicated team is here to help.
Scan for easy enrollment into the Ascendis Signature Access Program™ and support navigating coverage, including prompt benefits verification

Visit StartSKYTROFA.com

More than **8500** patients and counting[4]*

*Numbers are based on enrollment data as of February 7, 2024.[4]

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS

- **Glucocorticoids:** SKYTROFA may reduce serum cortisol concentrations, which may require an increase in the dose of glucocorticoids
- **Cytochrome P450-metabolized drugs:** Somatropin may increase cytochrome P450 (CYP450)-mediated antipyrine clearance. Carefully monitor patients using drugs metabolized by CYP450 liver enzymes in combination with SKYTROFA
- **Oral estrogen:** May reduce the response to SKYTROFA. Higher doses of SKYTROFA may be required
- **Insulin and/or other hypoglycemic agents:** SKYTROFA may decrease insulin sensitivity. Patients with diabetes mellitus may require adjustment of insulin or hypoglycemic agents

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.

Please see accompanying full Prescribing Information for SKYTROFA.

References: 1. SKYTROFA. Prescribing information. Ascendis Pharma, Inc.; 2022. **2.** 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. doi:10.1210/clinem/dgab529 **3.** SKYTROFA. Instructions for use. Ascendis Pharma, Inc.; 2021. **4.** Ascendis Pharma, Inc. Data on file. 2024. **5.** Maniatis AK, Nadgir U, Saenger P, et al. Switching to weekly lonapegsomatropin from daily somatropin in children with growth hormone deficiency: the fliGHt trial. *Horm Res Paediatr.* 2022;95(3):233-243. doi:10.1159/000524003 **6.** Vlachopapadopoulou E, Thornton P, Hofman P, et al. The majority of children with pediatric growth hormone deficiency treated with lonapegsomatropin for up to 6 years met or exceeded average parental height SDS: final results of enliGHten [abstract]. *ESPE Abstracts.* 2023;97(LB17). Accessed January 31, 2024. https://abstracts.eurospe.org/hrp/0097/hrp0097lb17 **7.** Maniatis AK, Casella SJ, Nadgir UM, et al. Safety and efficacy of lonapegsomatropin in children with growth hormone deficiency: enliGHten trial 2-year results. *J Clin Endocrinol Metab.* 2022;107:e2680-e2689. doi:10.1210/clinem/dgac217

ascendis pharma

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Improved Growth vs a Daily Somatropin

In heiGHt

SKYTROFA® demonstrated improved growth in a phase 3 clinical trial of 161 treatment-naïve pediatric patients with GHD[1,2]

Higher AHV, a treatment difference of 0.9cm/year (95% CI: 0.2 to 1.5) at 52 weeks compared with daily somatropin[1,2]*

*In the phase 3 heiGHt trial comparing once-weekly SKYTROFA with a daily somatropin in 161 treatment-naïve children with GHD. The primary endpoint was mean AHV at week 52.[1,2]

In fliGHt

Continued growth was observed in a phase 3 clinical trial of pediatric patients with GHD who switched from a daily GH treatment to SKYTROFA[5]

Height SDS increased by 0.25 from baseline through week 26[5†]

† In the fliGHt trial, once-weekly SKYTROFA was studied in a multicenter, phase 3, open-label, 26-week trial investigating the safety, tolerability, and efficacy of SKYTROFA administered once weekly in children with GHD. The trial included 3 treatment-naïve and 143 treatment-experienced patients previously treated with daily somatropin for ≤ 130 weeks. The mean daily somatropin dose was 0.29 mg/kg/week upon entering the trial. Safety and tolerability were the primary endpoints.[5]

In enliGHten

Patients continued to an open-label, long-term follow up‡

59% of those who completed their SKYTROFA treatment (n=81)[5§] achieved or exceeded average parental height[6]

‡ SKYTROFA was studied in an open-label extension study of pediatric patients with GHD who had previously participated in phase 3 SKYTROFA trials. The study enrolled a total of 298 patients: 103 patients on SKYTROFA and 55 patients on daily somatropin from the heiGHt trial, and 140 patients on SKYTROFA from the fliGHt trial. Long-term safety was the primary endpoint. Mean duration of treatment was 4.1 years (maximum 6 years).[6,7]

§ Patients completed SKYTROFA treatment (mean duration 3.2 years) because physician deemed that treatment for pediatric GHD was no longer necessary.[6]

AHV = annualized height velocity; CI = confidence interval; GH = growth hormone; GHD = growth hormone deficiency; SDS = standard deviation score.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- Slipped capital femoral epiphysis may occur more frequently in patients undergoing rapid growth. Evaluate pediatric patients with the onset of a limp or complaints of persistent hip or knee pain
- Monitor patients for progression of preexisting scoliosis
- Cases of pancreatitis have been reported in pediatric patients receiving somatropin. Consider pancreatitis in patients with persistent severe abdominal pain
- Lipoatrophy may result when somatropin is administered at the same site over a long period of time. Rotate injection sites to reduce this risk

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Long-term Safety

Treatment-naïve patients: AEs reported in ≥ 5% of SKYTROFA®-treated pediatric patients and more frequently than in daily-somatropin-treated pediatric patients (52 weeks of treatment)[1]

AEs	SKYTROFA (n = 105), n (%)	Daily Somatropin (n = 56), n (%)
Viral infection	16 (15%)	6 (11%)
Pyrexia	16 (15%)	5 (9%)
Cough	11 (11%)	4 (7%)
Nausea and vomiting	11 (11%)	4 (7%)
Hemorrhage*	7 (7%)	1 (2%)
Diarrhea	6 (6%)	3 (5%)
Abdominal pain	6 (6%)	2 (4%)
Arthralgia and arthritis†	6 (6%)	1 (2%)

*The etiology of hemorrhage in the SKYTROFA treatment group included epistaxis (n = 3), contusion (n = 2), petechiae (n = 1), and eye hemorrhage (n = 1).[1]
†The etiology of arthralgia and arthritis in the SKYTROFA treatment group included arthralgia (n = 5) and reactive arthritis (n = 1).[1]

SKYTROFA demonstrated low immunogenicity, with no neutralizing antibodies detected[1]

Only **6.3%** (19 of 304) of patients showed detectable binding antibodies through week 104[1,7]

Patients switching from a daily somatropin to once-weekly SKYTROFA demonstrated a safety profile consistent with treatment-naïve patients[5‡]

The majority of patients **>95%** did not experience bruising, swelling, or itching at the injection site[5]

Follow up for up to 6 years‡ demonstrated a safety profile consistent with prior observations and no new signals[6]

‡Mean duration of treatment was 4.1 years (maximum 6 years).[6]
AE = adverse event.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- There have been reports of fatalities after initiating therapy with somatropin in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnea, or unidentified respiratory infection. Male patients with one or more of these factors may be at greater risk than females. SKYTROFA is not indicated for the treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome
- Serum levels of inorganic phosphorus, alkaline phosphatase, and parathyroid hormone may increase after somatropin treatment. Monitor abnormal laboratory tests as appropriate

ADVERSE REACTIONS

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%).

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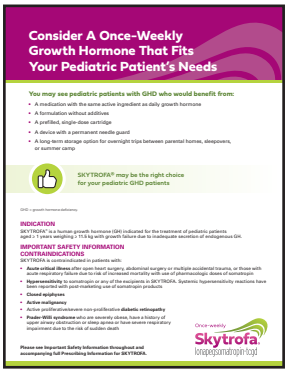
Cover



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Front Cover

Back Cover