

Practical Management of Pediatric Growth Hormone Deficiency With Lona pegsomatropin-tcgd

Terri Lipman,¹ Mako Sather,² Joseph Permuy,³ Donna Campbell²

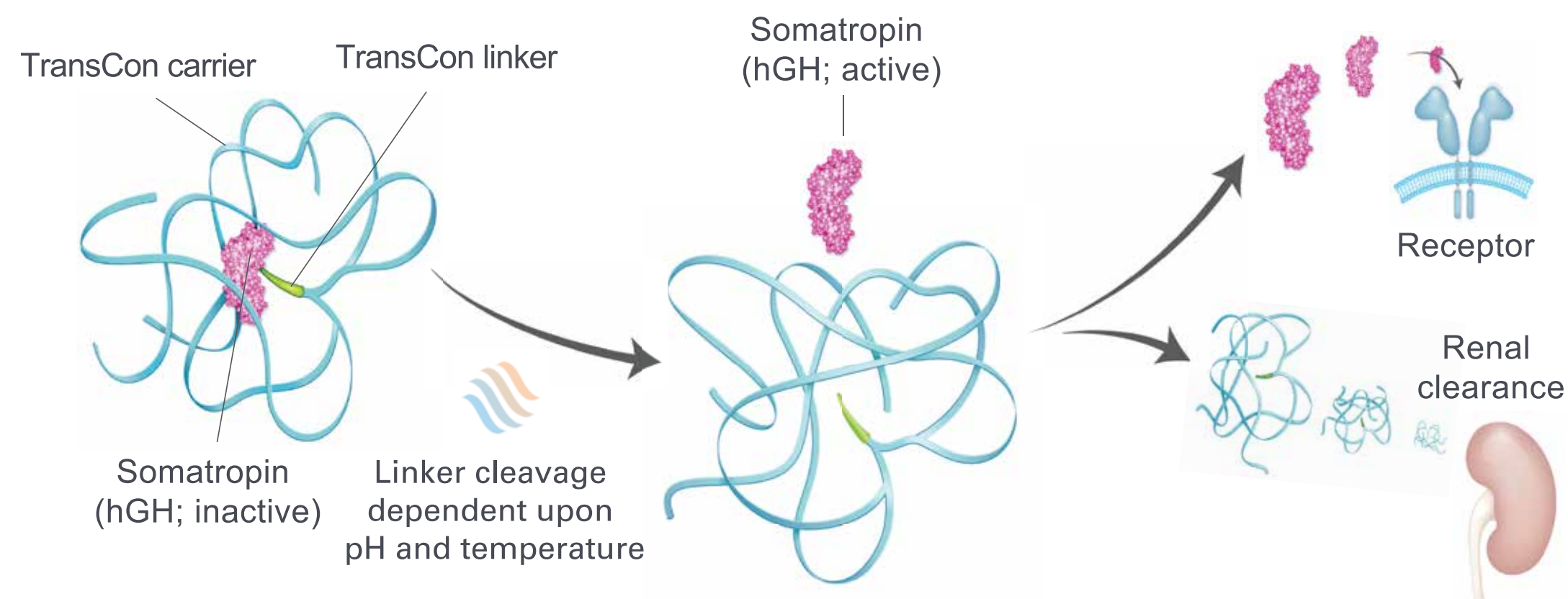
¹University of Pennsylvania School of Nursing, Philadelphia, PA; ²Rocky Mountain Pediatric Endocrinology, Centennial, CO; ³Nemours Children's Health, Jacksonville, FL



BACKGROUND

- Lona pegsomatropin-tcgd (SKYTROFA[®]; TransCon[®] human growth hormone [hGH]), a prodrug of somatropin, is the first FDA-approved once-weekly treatment indicated for children ≥ 1 year of age who weigh ≥ 11.5 kg with growth hormone deficiency (GHD; **Figure 1**)¹
- Efficacy and safety evaluated in three phase 3 clinical trials: heiGHt trial in treatment-naïve participants, fliGHt trial in participants previously treated with daily somatropin, and enliGHten open-label extension trial²⁻⁴
 - Pivotal phase 3 heiGHt trial: Lona pegsomatropin-tcgd was noninferior to daily somatropin
 - Annualized height velocity (least squares mean): 11.2 (lona pegsomatropin-tcgd) vs 10.3 (daily somatropin) cm/year; $P = 0.009$
 - Demonstrated a comparable safety profile⁴
 - Lona pegsomatropin-tcgd adverse event (AE) profile, similar to daily somatropin:²⁻⁴
 - Consistent across phase 3 studies and the majority were categorized as mild or moderate and unrelated to study drug
 - No serious treatment-emergent AEs (TEAEs) related to study drug
 - Low rates of injection site reactions and immunogenicity
 - Most common TEAEs (enliGHten through week 104): upper respiratory tract infection (21.1%), nasopharyngitis (11.1%), cough (8.7%), and pyrexia (8.4%)²

Figure 1. Lona pegsomatropin-tcgd (TransCon[®] hGH) Design^{4,5}



- Lona pegsomatropin is a prodrug of somatropin with once-weekly administration and designed to provide sustained release of active, unmodified somatropin
- The unmodified, unbound somatropin released from lona pegsomatropin has the identical 191 amino-acid sequence and size (22 kDa) as endogenous growth hormone

Table 1. Top Reason for Preference of Once-Weekly Lona pegsomatropin-tcgd vs Daily Somatropin in the fliGHt Trial³

Top 3 Reasons for Preference (most important in bold):

Child (n = 99)

- How often I need to get injections**
- Less annoyed by the injections
- Less interference with my activities

Parent / Caregiver (n = 142)

- How often my child needs to get injections**
- Less interference with my child's activities
- Less interference with my activities

Participants ≥ 9 years old at the time of enrollment and their parents completed the Preference Questionnaire-Child and the Preference Questionnaire-Parent, respectively, at Weeks 6 and 13. Treatment preference (PD-C and PD-P) at week 13 are shown here.

- Once-weekly lona pegsomatropin-tcgd was preferred vs daily somatropin injection (84% of children and 90% of caregivers in the fliGHt trial; **Table 1**)³
- 94% of participants rated the lona pegsomatropin-tcgd Auto-Injector device as easy to use in the enliGHten trial²

UNMET NEEDS IN PEDIATRIC GHD TREATMENT

- Daily somatropin has been the standard of care for decades, but poor adherence is associated with suboptimal growth outcomes⁷
- Burdens of daily injections in pediatric GHD include:^{8,9}
 - Difficulty using injection devices
 - Pain and/or bruising with injection
 - Child's aversion to injection
 - Interference with daily life

PURPOSE

- Discuss practical techniques and clinical pearls for pediatric endocrinology nurses working with lona pegsomatropin-tcgd for the treatment of pediatric GHD

RESULTS

AUTO-INJECTOR USE

- Lona pegsomatropin-tcgd auto-injector provides a fully automated reconstitution of the lyophilized drug¹
- Practice the auto-injector with the patient and caregiver in the clinic¹¹
- Once the green top is pressed against the skin, the auto-injector will inject automatically¹¹
- We recommend waiting 10 minutes after injection before checking for local reactions

IGF-1 MONITORING AND ESTIMATION

- Because lona pegsomatropin-tcgd is administered once-weekly, the IGF-1 profile differs from that of daily somatropin¹²
- To estimate average weekly IGF-1 with lona pegsomatropin-tcgd on any day following a prior dose, a predication curve and calculation has been developed (**Figure 2, 3**)¹²
 - Based on a single blood draw at any time after steady state (> 5 th dose)^{10,12}
 - We recommend scheduling a blood draw with enough time to make dose changes before next medication shipment
 - Calculate the average IGF-1 SDS using the time since last dose administration (to the nearest $\frac{1}{2}$ day)¹²

$$\text{Average IGF-1 SDS} = \text{measured IGF-1 SDS} - \text{correction factor}$$

Figure 2. Average Weekly IGF-1 SDS Prediction Curve¹²

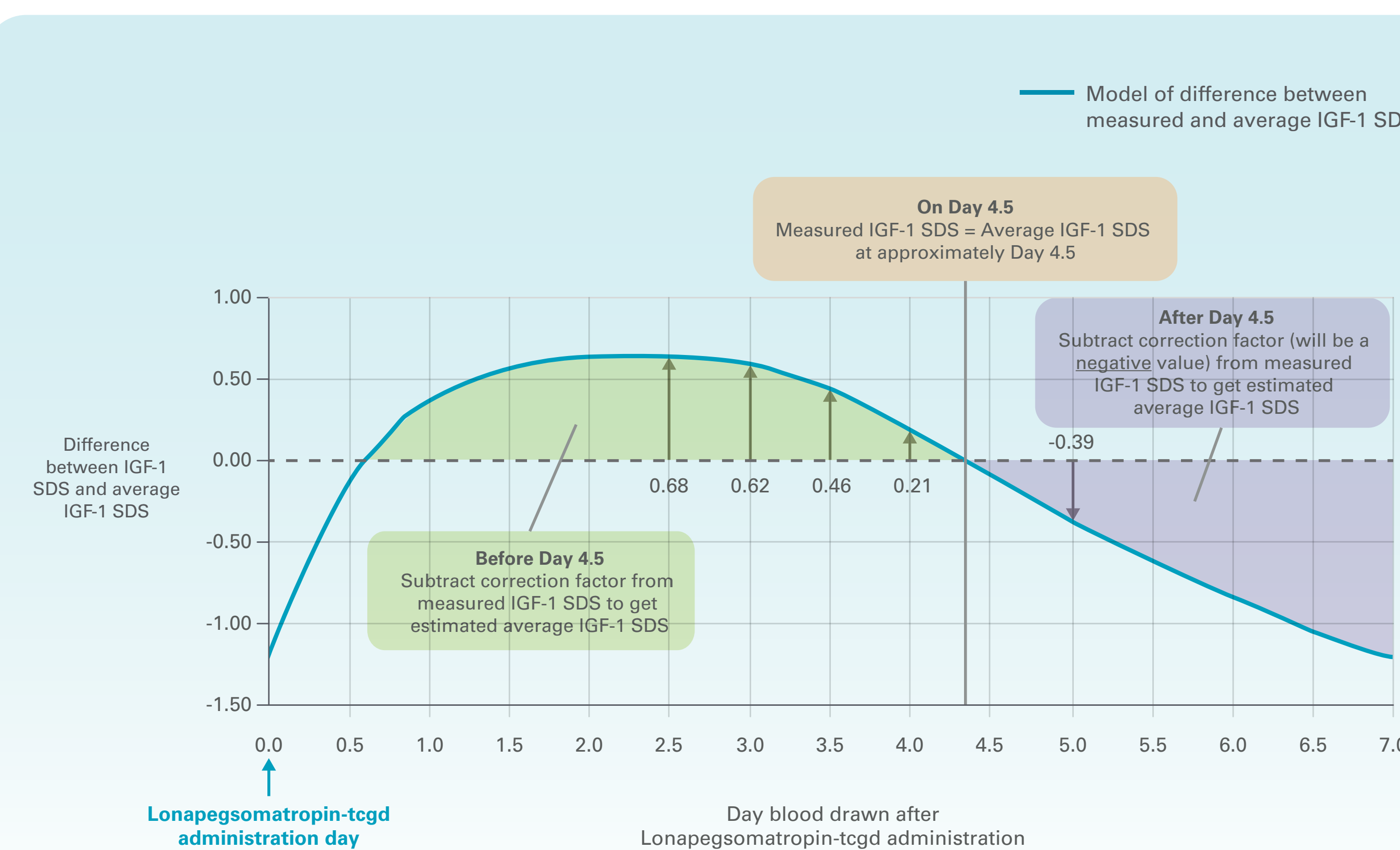


Figure 3. Average IGF-1 SDS Correction Factors¹² and Case Studies

Day	Correction Factor*	90% Prediction Interval†
0	-1.22	-1.80, -0.65
0.5	-0.12	-0.46, 0.22
1.0	0.39	-0.07, 0.86
1.5	0.60	0.16, 1.04
2.0	0.67	0.32, 1.02
2.5	0.68	0.43, 0.93
3.0	0.62	0.45, 0.78
3.5	0.46	0.33, 0.59
4.0	0.21	0.06, 0.36
4.5	-0.09	-0.31, 0.13
5.0	-0.39	-0.68, -0.09
5.5	-0.64	-1.01, -0.26
6.0	-0.85	-1.29, -0.42
6.5	-1.07	-1.57, -0.57
7.0	-1.22	-1.77, -0.68

*Correction factor represents the predicted difference between actual IGF-1 SDS and average IGF-1 SDS by time between dosing and blood draw. Predictions are most accurate between Days 2.5 and 5. Correction factors for average IGF-1 concentration are also available.¹²
†The 90% Prediction interval is the confidence interval for the correction factor.

Average IGF-1 SDS Calculation Case Study #1

- Patient injects on Sunday PM (Day 0)
- Blood is drawn on Wednesday AM (Day 2.5)
- Measured IGF-1 SDS is 2.0
- Correction factor at Day 2.5 is 0.68

$$1.32 = 2.0 - 0.68$$

average IGF-1 SDS = measured IGF-1 SDS - correction factor

Average IGF-1 SDS Calculation Case Study #2

- Patient injects on Wednesday PM (Day 0)
- Blood is drawn on Monday PM (Day 5.0)
- Measured IGF-1 SDS is 0.9
- Correction factor at Day 5.0 is -0.39

$$1.29 = 0.9 - (-0.39)$$

average IGF-1 SDS = measured IGF-1 SDS - correction factor

LONA PEGSOMATROPIN-TCGD DOSING

- Recommended initial dose: 0.24 mg hGH/kg body weight, once-weekly¹
- Weight-based dosing brackets determine cartridge (**Table 2**)¹
 - Initial dose calculation is the same for treatment-naïve patients and those switching from daily somatropin¹
 - Wait at least 8 hours between the final dose of daily somatropin and the first dose of once-weekly lona pegsomatropin-tcgd¹
 - Lona pegsomatropin-tcgd demonstrated a predictable linear dose-response with average IGF-1 SDS^{2,10}
 - Moving up or down one dose bracket corresponds to an average IGF-1 change of 0.3 SDS²
- To avoid missed doses, lona pegsomatropin-tcgd can be taken 2 days before or 2 days after the scheduled dosing day. Resume once-weekly dosing for the next dose at the previously scheduled dosing day¹

Table 2. Weight-based Dosing Brackets¹

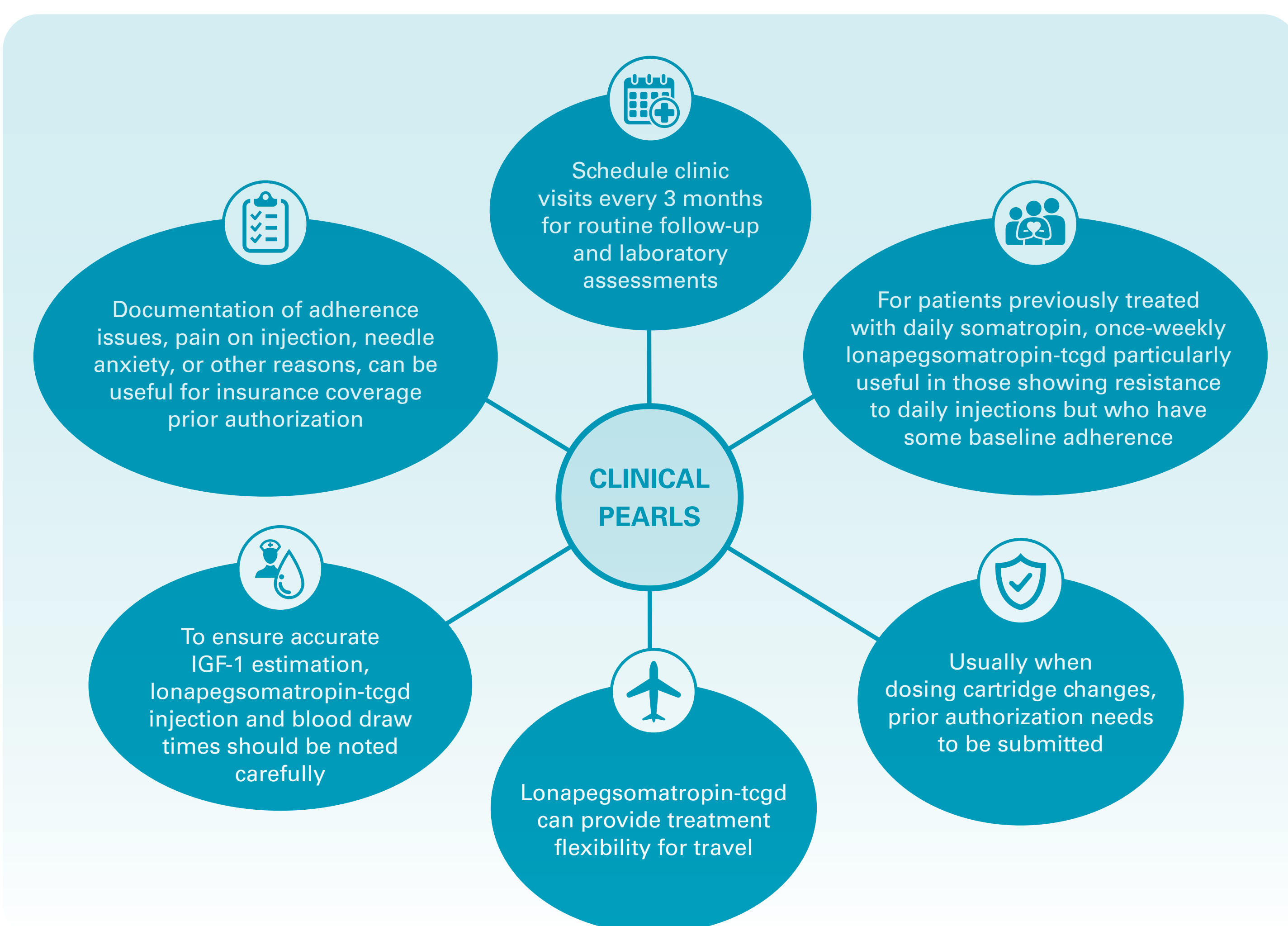
Weight (kg)	Cartridge(s) (mg hGH)	Weight (kg)	Cartridge(s) (mg hGH)
11.5 – 13.9	3.0	35.0 – 41.9	9.1
14.0 – 16.4	3.6	42.0 – 50.9	11.0
16.5 – 19.9	4.3	51.0 – 60.4	13.3
20.0 – 23.9	5.2	60.5 – 69.9 [†]	7.6 x 2
24.0 – 28.9	6.3	70.0 – 84.9 [†]	9.1 x 2
29.0 – 34.9	7.6	85.0 – 100 [†]	11.0 x 2

Every cartridge dose corresponds to a unique color.

[†]Patients requiring a dose greater than the 13.3-mg cartridge will need to inject 2 cartridges per weekly dose. The same dose strength must be used for both doses in those patients requiring a double dose.¹

CLINICAL IMPLICATIONS

Figure 4. Pediatric Endocrinology Nurses and Advanced Practitioners Play a Critical Role in the Multidisciplinary Management With Once-Weekly Lona pegsomatropin-tcgd Treatment



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