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ORIGINAL RESEARCH

Patient-Centric Design of the Lonapegsomatropin Auto-Injector for Growth Hormone Deficiency: Usability Validation of Safe and Effective Use

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Purpose: Treatment of pediatric growth hormone deficiency (pGHD) with daily somatropin (human growth hormone [hGH]) injections is associated with challenges including needle anxiety, which may lead to poor adherence and ultimately result in suboptimal growth outcomes. The lonapegsomatropin (TransCon hGH, SKYTROFA®) Auto-Injector, designed to deliver once-weekly lonapegsomatropin for the treatment of pGHD while minimizing injection challenges, was validated in usability studies in pGHD.

Patients and Methods: The Auto-Injector was evaluated in a usability validation study conducted under simulated-use conditions in accordance with FDA guidance, involving simulated injections performed by injection-naive or injection-experienced patients with pGHD or proxy medical conditions, caregivers, and health care providers (HCPs) responsible for injections or training patients/caregivers. Half of the patient and caregiver participants received training by a Nurse Trainer.

Results: All participants (60 children, 60 caregivers, and 15 HCPs) were able to complete an injection successfully. All participants reported that they could follow the instructions as written, and 98% felt they could use the device as intended on their own or, for pediatric patients, with supervision. Use deviations observed for injection tasks for all participant groups were low: patients (3.2% of tasks), caregivers (2.4%), and HCPs (2.8%).

Conclusion: The user-centric design of the lonapegsomatropin Auto-Injector enables successful and confident use to deliver an injection as intended, with the potential to overcome known barriers associated with GH injections and facilitate adherence, which may improve treatment outcomes.

Keywords: pediatric growth hormone deficiency, lonapegsomatropin, once-weekly growth hormone therapy, auto-injector, human factors validation, human factors engineering

Introduction

Daily somatropin (human growth hormone, hGH) injections had, until recently, been the standard of care for pediatric GH deficiency (GHD) over the last several decades,[1] yet this approach presents a challenge in terms of treatment adherence.[2] Systematic reviews and qualitative studies have identified injection device related factors—including difficulty in using injection devices or lack of capability to deliver an injection, pain and/or bruising with the injection, or fear of the needle—that contribute to non-adherence to daily pediatric GHD treatment.[3–5] Real-world studies have shown that these adherence and compliance issues with daily somatropin are associated with suboptimal growth outcomes.[6–9]

The burden associated with daily injection requirements, as reported by both pediatric patients and their caregivers, has been linked to nonadherence rates ranging from 5 to 82%.[10,11] As such, a consensus statement from the Growth Hormone Research Society suggests that long-acting growth hormone (LAGH) products have the potential to improve adherence to pediatric GHD treatment through increased convenience of less frequent injections.[2] Lonapegsomatropin, a prodrug of somatropin administered once weekly and approved in 2021 by the Food and Drug Administration (FDA)

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and in 2022 by the European Commission (EC) for the treatment of pediatric GHD, is designed to achieve sustained release of active, unmodified somatropin under physiologic conditions. Safety and efficacy of lonapegsomatropin have been demonstrated in three phase 3 trials in pediatric GHD: the heiGHt trial in treatment-naive participants, the fliGHt trial in participants previously treated with daily somatropin, and the enliGHten open-label extension trial.[12–15]

To maximize convenience and usability of this novel therapeutic for the pediatric population, a dedicated lonapegsomatropin Auto-Injector device was developed to overcome device-related barriers to injection. Patient surveys indicate that the most important device attributes for pediatric patients and their caregivers are reliability, ease-of-use, and lack of pain during injection.[16,17] Auto-injector devices have been shown to improve patient satisfaction and are associated with high treatment adherence, and short, thin needles are more favorably perceived by patients.[18–23] The lonapegsomatropin Auto-Injector was designed to address both injection-related pain and anxiety, and features a small, hidden needle in an easy-to-use device.

The lonapegsomatropin Auto-Injector was developed through iterative formative usability studies to incorporate patient feedback. In the enliGHten trial, participants who switched to the lonapegsomatropin Auto-Injector from vial and syringe preferred the Auto-Injector and reported increased convenience and satisfaction over time (assessed at week 6 and week 13 after switch to the Auto-Injector), as well as lower injection site and local tolerability reactions.[12,15]

While these findings from the enliGHten trial provide insight into user preference and patient-reported experience, they do not constitute a formal regulatory usability validation. The Auto-Injector and associated materials were therefore evaluated through a formal regulatory usability validation study under simulated use conditions and in compliance with FDA guidance.[24] The goal of this study was to demonstrate that the system user interface can be used safely and effectively by intended users to deliver a dose of medication without serious use errors or problems.

Materials and Methods

Participants

Participants in the validation study were intended users of the Auto-Injector and included pediatric or adolescent patients with GHD, their caregivers, and treating health care providers (HCPs). Pediatric patients with GHD and their caregivers are a relatively rare population; therefore, proxy participants with other chronic conditions that require injections or non-injected daily medication were included in this study in addition to patients with diagnosed pediatric GHD. A concerted effort was made to recruit pediatric patients with GHD and their caregivers; however, to ensure adequate representation of relevant user characteristics and to meet sample size expectations consistent with human factors guidance, proxy participants were enrolled as needed. The majority of the proxy participants were pediatric patients with diabetes and/or their caregivers, whose injection-related experience is broadly comparable to those of patients with GHD. In addition, pediatric participants and caregivers with limited or no prior injection experience were included to represent newly diagnosed patients who must learn injection administration for the first time. The patient and caregiver populations comprised half injection-experienced and half injection-naive participants, with the intent that participants with limited or no experience preparing and delivering injections would approximate a scenario of patients recently diagnosed with GHD and learning to inject for the first time. HCPs were nurses, preferably in endocrinology, with experience giving injections and/or instructing patients and caregivers on giving injections.

Auto-Injector Device

The lonapegsomatropin Auto-Injector, intended for four years (210 injections) of use, is supplied with the Instructions for Use (IFU) and Quick Reference Guide (QRG) (Figure 1A). Single-use 0.25 mm x 4 mm (31G x 5/32") needles and dual-chamber cartridges (DCCs) containing lonapegsomatropin (lyophilized drug product) for each injection are supplied for use for four weeks of doses (4 DCCs and 6 needles) (Figure 1B). For the simulated use studies, the DCCs contained a placebo product.

The Auto-Injector user interface was developed through an iterative formative process that included an initial concept preference study evaluating early device concept models, followed by 9 simulated actual use studies of prototypes with increasing functionality. Findings from these studies informed refinements to the Auto-Injector, including control design,

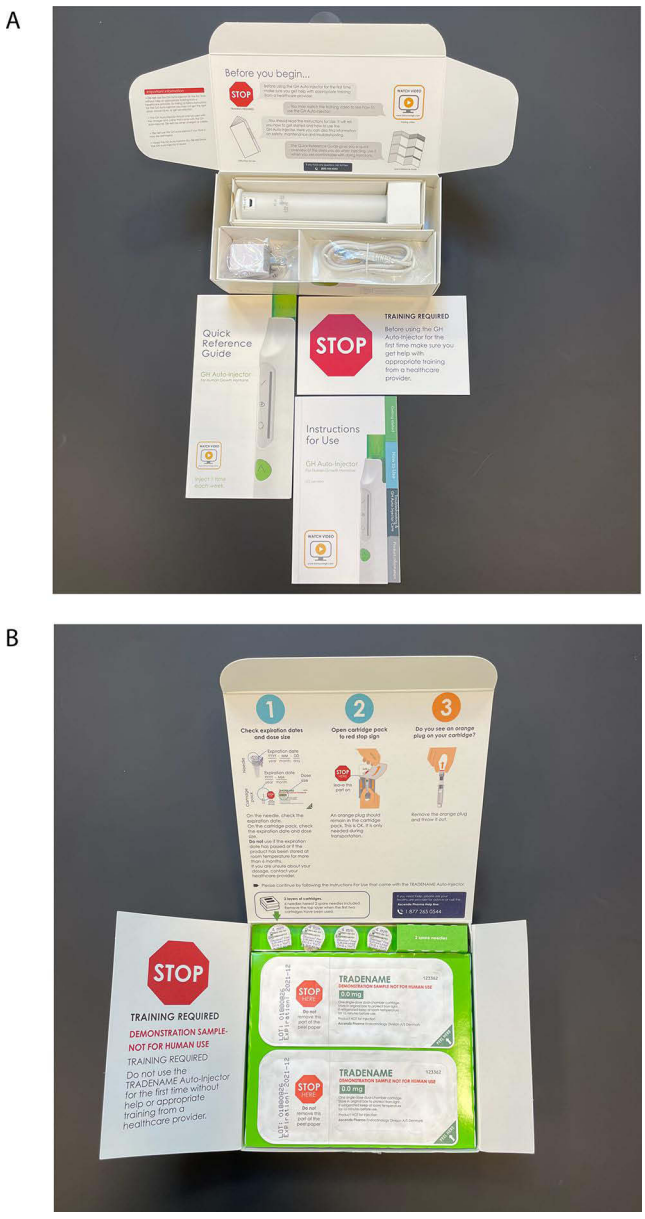

Figure 1 Components Supplied for the Usability Validation Study. (**A**) Auto-Injector and packaging applied in the usability study (minor changes such as deleting the STOP signs were implemented in the marketed version). (**B**) DCC and Needles and packaging.
Abbreviation: DCC, dual-chamber cartridges.

visual and auditory feedback, and instructional materials culminating in the final product (Figure 2). The Auto-Injector guides reconstitution, mixing, and injection through a combination of visual cues and sound signals. The Auto-Injector use steps were evaluated in 3 key tasks for the validation study: Task A, Simulated Injection Assessment; Task B, Charging Performance Assessment; and Task C, IFU Comprehension. Task A, Simulated Injection Assessment, was further subdivided into multiple steps in the process of completing the injection. These steps were: inspect expiration date and dose, screw a new needle on to a new DCC, power on the Auto-Injector and check the battery icon for level of charge remaining, and then press the DCC into the green top of the Auto-Injector to lock the DCC into place. After 4–8 minutes of controlled automatic reconstitution, the Auto-Injector guides the user with beeps and lighted icons to proceed to the next step, which is to manually invert the device 5–10 times to mix the drug, then return the device to upright on a flat surface. Excess air is then automatically removed from the DCC by the Auto-Injector (air shot step), and the user is prompted to inspect the mixture before pressing the Auto-Injector against the skin to automatically complete

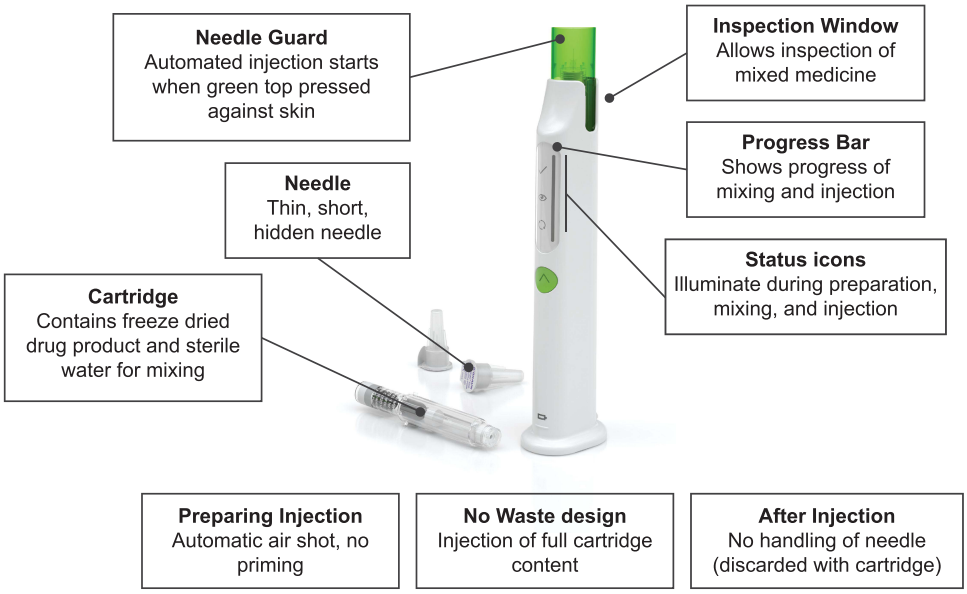

Figure 2 Design and Features of the Lonapegsomatropin Auto-Injector.

the injection. Following injection, the user removes the DCC (together with needle) using the needle cap and disposes of it in a sharps disposal container. The Auto-Injector then powers off.

Validation Study Design

The study design is outlined in a flow chart (Figure 3). The Auto-Injector, DCCs, needles, packaging, IFU, QRG, access to a live Help Line phone number and training video were provided to participants to simulate market-release conditions. Half of the pediatric patients and caregivers were trained by a Nurse Trainer. Training included an introduction to the purpose of the product, delivery route of treatment, product components, and the available instructional materials. The training also included a video demonstration of use of the Auto-Injector followed by hands-on practice with supervision by the Nurse Trainer, including correction and answering questions. After training, a waiting period of 60 minutes occurred to simulate the effects of a delay between training and first use that would occur in a real-world setting. Participants who did not have the training were given a short verbal-only introduction to the product by a moderator and then allowed time to familiarize themselves with the materials on their own as they would do at home, without oversight from a moderator or trainer, but were told not to open any packaging or begin to prepare an injection until they felt ready to give an injection.

Injections were given within the context of a simulated use scenario into a skin pad strapped to the target area of the body for injection (patients) or to a mannequin (caregivers and HCPs). Participants were permitted to find and use the IFU and QRG at their own discretion. The available Help Line was staffed by a study team member who was not able to observe the session and who followed a Help Line script to simulate the interaction that would occur between an actual user and a Help Line representative.

Prior to the summative study, tasks and subtasks were reviewed using a use-related risk assessment to classify them as critical or non-critical. Critical tasks were those that, if performed incorrectly or omitted, could result in patient or user harm, including compromised medical care, or were associated with a high severity rating. Non-critical tasks were important to overall device use but unlikely to cause serious harm if performed incorrectly. For this study, tasks were selected from the use-related risk assessment to be evaluated in simulated-use scenarios, with non-observable tasks evaluated as knowledge-based questions to test comprehension of critical information such as warnings and instructions.

The usability validation study assessed participants over the 3 main tasks in use of the Auto-Injector, each broken down into subtasks which could have multiple steps. Task A, the Simulated Injection Assessment, consisted of 4 subtasks that included 29 steps: preparing the device for injection, mixing the product, injecting the dose, and post-injection tasks.

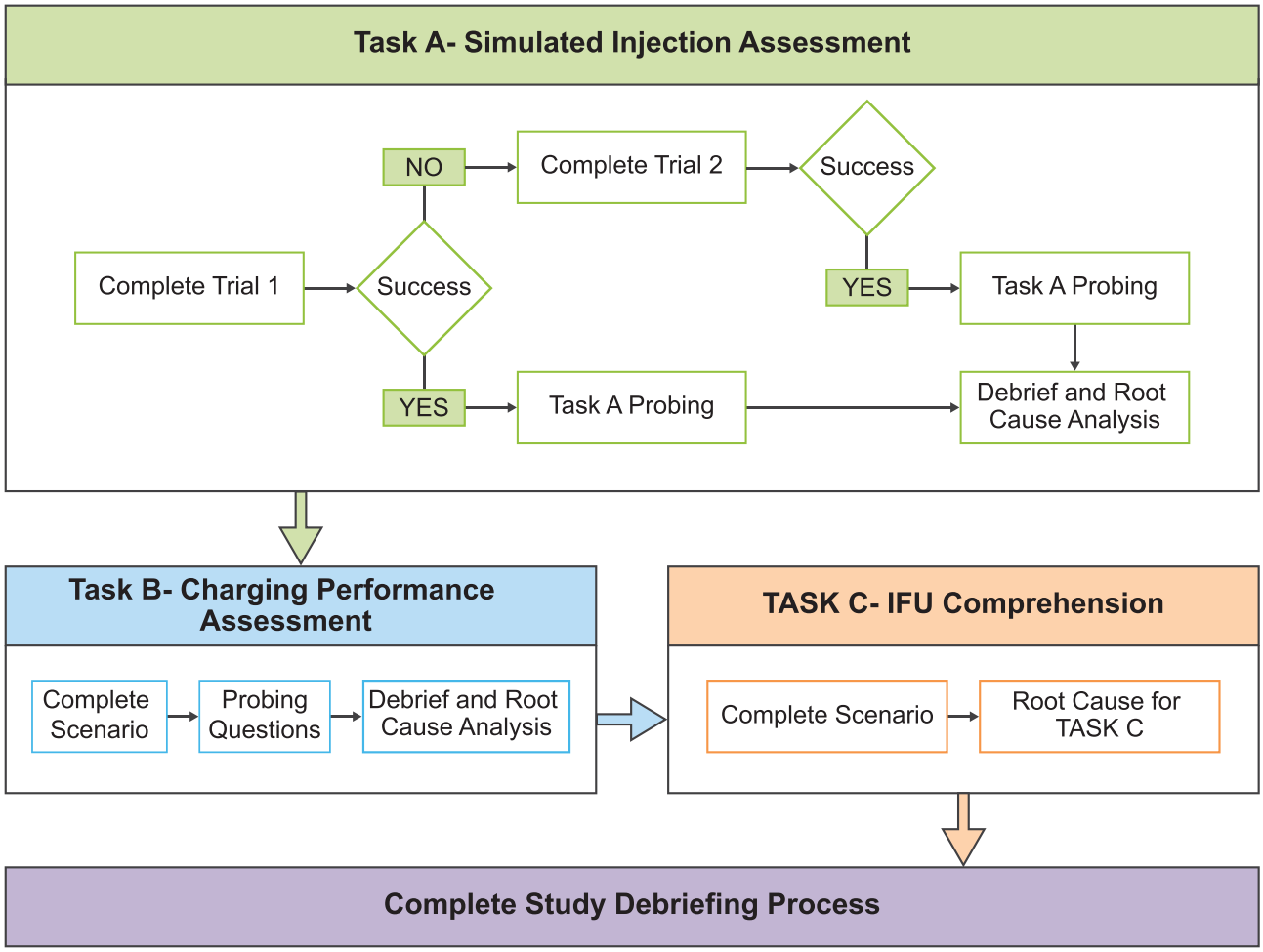

Figure 3 Design of the Usability Validation Study.

Task B, the Charging Performance Assessment, comprised 2 steps in charging the device. Task C, IFU Comprehension, included 5 hypothetical scenarios to evaluate understanding of the IFU content: proper charging, cleaning, sharing the device, safe use prior to injection, and storing the device.

Some use deviations may be attributable to study artifacts, defined as deviations arising from limitations of the simulated-use environment rather than the device design (eg, inability to fully replicate real-world conditions or user assumptions influenced by the testing scenario). All use deviations were evaluated through root cause analysis and debriefing to distinguish study artifacts from product-related use errors.

An additional supplemental usability study with 31 participants (patients and caregivers, half injection-naive, with no training), which included two minor updates to the IFU, was carried out after this validation study.

Results

Participant Demographics

The usability validation study assessed performance with the lonapegsomatropin Auto-Injector in children with GHD. Because pediatric GHD is uncommon and recruiting children for usability studies is challenging, the validation study allowed for a proxy population. The study included 60 pediatric and adolescent patients with GHD or another medical condition requiring regular injections and/or management similar to that of GHD treatment, 60 caregivers for these patient populations, and 15 HCPs who give injections. The injection-experienced cohort included 15 patients with pediatric GHD, and proxy pediatric patient participants with diabetes mellitus (n = 15; one participant had GHD and

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diabetes mellitus) or Crohn's disease (n = 1). The injection-naive proxy pediatric patient population had asthma or allergies (n = 6), cystic fibrosis (n = 1), or no medical condition (n = 23). The pediatric patient participants were well-distributed for age and sex and the majority of injection-experienced patients and caregivers gave ≥1 injection per week (Table 1). The majority of HCPs inject daily and teach how to give injections weekly, with 20% having previously used an auto-injector device. Participants in the usability validation study were in 9 categories: 4 patient groups and 4 caregiver groups (injection-experienced or injection-naive, each split into trained or not trained), and one HCP group (Table 2).

Table 1 Patient and Caregiver Summary in Usability Validation Study

Criteria	Responses	Occurrence
Patients (n = 60)		
Gender	Female	33 (55%)
	Male	27 (45%)
Age (years)	6–12	27 (45%)
	13–17	33 (55%)
Medical condition[a]	Growth hormone deficiency	15 (25%)
	Other	23 (38%)
	None (naive group)	23 (38%)
Caregivers (n = 60)		
Gender	Female	44 (73%)
	Male	16 (27%)
Age (years)[b]	18–29	4 (7%)
	30–49	43 (72%)
	50–69	12 (20%)
Injection experience	Experienced	30 (50%)
	Naive	30 (50%)

Notes: [a]One participant had growth hormone deficiency and diabetes causing an occurrence total greater than 100%. [b]One participant age not recorded, causing total to not equal 100%.

Table 2 Usability Validation Study Participant Overview

		Patient		Caregiver		HCP	Total
		Naive	Experienced	Naive	Experienced	Experienced	
User validation study	Trained	15	15	15	15	0	60
	Untrained	15	15	15	15	15	75
	Total	30	30	30	30	15	135

Abbreviation: HCP, healthcare provider.

Task Performance

All participants successfully completed an injection, and 97% of participants (131/135) did so on their first try without needing the optional second injection attempt.

The validation study assessed performance of 3 tasks: Task A, Simulated Injection Assessment, broken down into 4 subtasks: preparing the device for injection, mixing the product, injecting the dose, and post-injection (safely removing and disposing of the cartridge with needle, putting on the protective cover, and writing down date of injection); Task B, Charging Performance Assessment; and Task C, IFU Comprehension. Observed steps in each task were defined as either completed successfully or having a use deviation. Use deviations were defined in 3 categories as (1) Use difficulties: step performed correctly with effort or apparent struggle, including frustration or confusion, call for help, or multiple attempts, (2) Close calls: a self-corrected deviation from instructions that, if left uncorrected, could result in harm, or (3) Use errors: a deviation from instructions that was not self-corrected and could result in harm.

The mean number of successes across the 29 use steps in Task A, Simulated Injection Assessment, was high for both trained and untrained participants, while treatment-experienced participants had a slightly higher mean number of successes compared with treatment-naive participants (Table 3). The mean number of successes was high and similar between patient, caregiver, and HCP groups in Task A (Table 3). Participants were able to complete an injection with use deviations in only 2.8% of 3921 total observed use steps across all participant groups in Task A. Similarly high rates of success with low use deviation in Task A were observed regardless of injection experience and nurse training (Table 3).

The majority of observed use deviations in Task A occurred in the Prepare and After Injection subtasks, unrelated to Auto-Injector handling and the injection itself. Of the 3921 observed steps across Task A, there were 8 observations of use errors for the "check cartridge expiration date" step, 18 for the "check cartridge dose" step, and 15 for the "check needle expiration date" step. In the Mix subtask, 6 use errors occurred during the "air shot" step. In the Inject subtask, 7 use errors occurred in the "inject" steps, and in the After Injection subtask, 5 use errors were observed in the "remount device cover" step. Use difficulties, close calls, and use errors in the 4 subtasks of Task A are summarized in Figure 4. The root cause description of the use errors in Task A were mainly attributed to study artifacts and causes included lapse (3 observations), negative transfer (2), inattention (3), not real life/simulation limitation (11), and user interface (UI) design (1) (Table 4).

In Task B, Charging Performance Assessment, only 2 use deviations occurred for 673 tasks observed, with one attributed to human fallibility (negative transfer–user made an assumption based on experience with other electronic devices) and one to trainer error (trainer did not specify the difference between different colored flashing battery icons). For Task C, IFU Comprehension, only 1 knowledge task error occurred among 809 tasks, with one participant stating

Table 3 Device Use Deviations by Participant Category in Task A

	Patient				Caregiver				HCP
	Injection-Experienced		Injection-Naive		Injection-Experienced		Injection-Naive		
	Trained	Untrained	Trained	Untrained	Trained	Untrained	Trained	Untrained	
Success	98.2%	97.7%	96.1%	95.2%	98.8%	98.4%	98.2%	94.9%	97.2%
Total Deviations	1.8%	2.3%	3.9%	4.8%	1.2%	1.6%	1.8%	5.1%	2.8%
Difficulty	0.2%	0.7%	0.5%	1.6%	0.5%	0.0%	0.5%	1.8%	0.7%
Corrected use error	0.2%	0.2%	0.2%	0.2%	0.0%	0.5%	0.0%	0.2%	0.2%
Uncorrected use error	1.4%	1.4%	3.2%	3.0%	0.7%	1.1%	1.4%	3.0%	1.8%
Total number of steps observed, n	435	435	435	435	434	435	435	434	435

Abbreviation: HCP, healthcare provider.

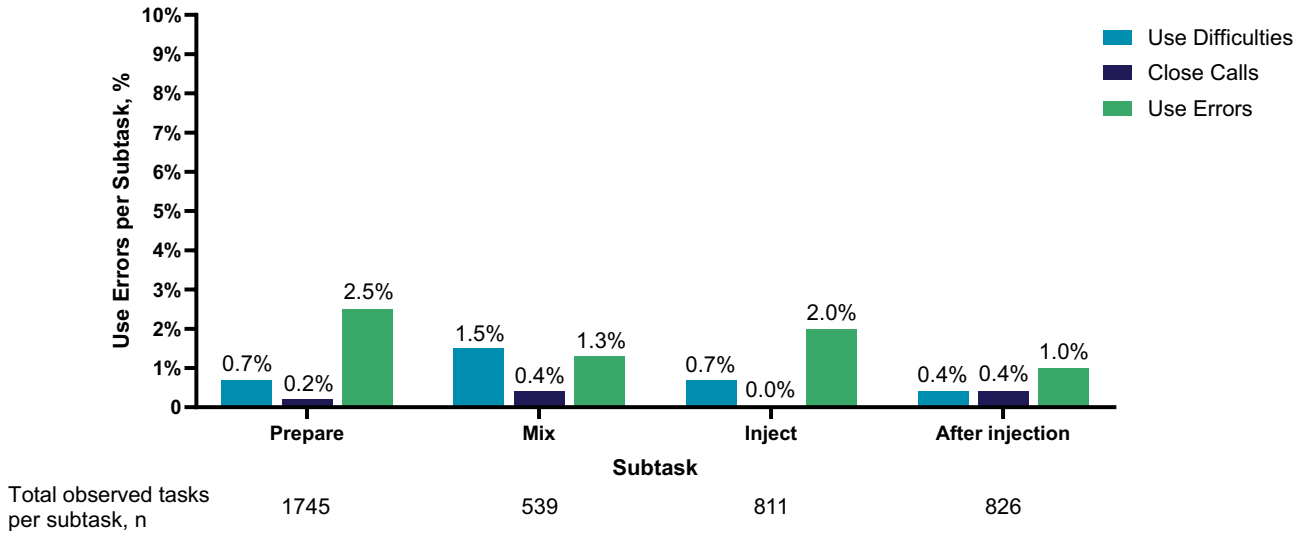

Figure 4 Use Deviations by Subtask in Task A. Use Difficulties: step performed correctly with effort or apparent struggle, including frustration or confusion, call for help, or multiple attempts. Close calls: a self-corrected deviation from instructions that, if left uncorrected, could result in harm. Use errors: a deviation from instructions that was not self-corrected that could result in harm.

they would use any charger despite instructions to only use the charger that is supplied with the Auto-injector device. In the supplemental usability study, 30 of 31 participants performed successful injections without receiving prior training. The success rate for simulated injection tasks (similar to Task A in the present study) was at least 98.4% across all user groups.

Participant Device Design Feedback

Overall, participant feedback indicated a positive impression of the safety and usability of the Auto-Injector and associated material. All participants felt they could follow the instructions, and 94% of participants had an overall impression of the Auto-Injector that was positive or neutral. For overall device safety, 98% of participants reported that they felt they could use the Auto-Injector safely on their own or, for pediatric participants, with the supervision of a parent. Subjective feedback indicated that participants generally reported the QRG as their favorite instructional medium available with the Auto-Injector, and 73% of participants reported no difficulties in using the IFU (Table 5).

Discussion

Daily somatropin injections with pen devices or needle and syringe have been an important mainstay of treatment for pediatric GHD for decades. However, patient and caregiver surveys and real-world evidence indicate there are opportunities to improve upon both frequency of injections and delivery devices in the pediatric population, with these changes having the potential to improve adherence and growth outcomes.[4,6,9,16–18] Although once-weekly treatment can help reduce some of the treatment burden in pediatric GHD, dosing frequency alone is only one factor; other challenges such as storage, reconstitution, needle anxiety, and the need for a reliable and easy to use device must also be addressed.

Lonapegsomatropin is supplied as a stable, preservative-free lyophilized drug product in prefilled single-use cartridges, which facilitates transportation, permits room temperature storage for up to 6 months, and eliminates manual dose setting prior to administration. The lonapegsomatropin Auto-Injector, which is reusable for up to 4 years or 210 injections, was purposefully designed and developed to deliver lonapegsomatropin with an easy-to-use administration device. The Auto-Injector enables simple and well-controlled preparation of the drug before injection, combining an automated reconstitution step with guidance for manual mixing, which is verified by electronic visual and auditory progress indicators. Patient feedback and testing and the usability validation studies demonstrated that participants were

Table 4 Root Cause Analysis of Use Errors in Task A

Step	Use Error Description	Severity	Root Cause Identity	Sub-Root Cause	Number of Observations	Root Cause Description
Check cartridge	User did not check the cartridge expiration date.	S3	Human Fallibility	Lapse	2	User forgot to check the expiration date.
				Negative Transfer	2	User does not check expiration dates at home.
				Inattention	1	User missed step in the instructions.
			Study Artifact	Not Real Life	2	User did not check the expiration dates because patient was not real.
				Simulation Limitation	1	User would've relied on pharmacy/doctor.
	User did not check the cartridge drug volume.	S3	Human Fallibility	Inattention	1	User did not see the step in the instructions.
				Lapse	2	User was not following instructions and forgot.
				Negative Transfer	9	User does not normally check medication at home.
			Study Artifact	Simulation Limitation	3	User believed that a health care provider would have checked for them.
				Not Real Life	1	User did not think it was important to check for a mannequin.
				Simulation Limitation, Not Real Life	1	User's practice has a different prescription and dosage setup than the scenario.
			Study Artifact, Training	Simulation Limitation, Missing Content	1	User believed that the health care provider would have checked for them, and it was not emphasized during training.
Check needle expiration date	User does not check needle expiration date.	S3	Study Artifact	Simulation Limitation	3	User believed the needle expiration date was the same as the training version.
Hold device on skin until 2 loud beeps.	User injected after the device turned off.	S1	Study Artifact, Instructions	Simulation Limitation, Poor Organization	1	User injected with a timed-out device because they took too long strapping on the injection pad.
			Study Artifact, User Interface	Simulation Limitation, UI Design	1	User injected with a timed-out device because they took too long strapping on the injection pad.
			User Interface, Instructions	UI Design, Missing Content	1	User took too long to prepare and the device timed-out; user was unable to troubleshoot using the instructions.

(*Continued*)

Table 4 (Continued).

Step	Use Error Description	Severity	Root Cause Identity	Sub-Root Cause	Number of Observations	Root Cause Description
	User pushed too hard into the injection pad.	S1	Study Artifact	Simulation Limitation	6	The injection pad was not representative of a real person and did not provide feedback on how hard to press.
	User slipped while giving the injection.	S3	Study Artifact	Study Confound	1	The mannequin was placed in a swivel chair which rotated during the injection; chair was replaced after this.
	User did not recognize she had completed the injection.	S1	Human Fallibility	Inattention	1	User did not think the two confirmation beeps were the same.
	User did not push hard enough during the injection.	S1	Instructions, Study Artifact	Instructions, Study Artifact	1	User was unsure how hard to press the device onto the skin and was unable to find it in the instructions.
Put protective cover on device.	User did not replace the cover on the auto-injector.	S1	Study Artifact	Not Real Life	4	The study environment lacked a dedicated place to put things away.
				Study Confound	1	
			Human Fallibility	Lapse	1	User forgot to replace the cover on the auto-injector.

Abbreviation: UI, user interface.

Table 5 Summary of Participant Debriefing

Question Category	Response
Overall impression	94% positive or neutral
Overall system safety	98% of the participants reported that they felt they could use the device safely on their own
Overall instructions feedback	100% of participants felt they could follow the instructions as they are written today
IFU subjective feedback	73% of participants reported no difficulties using the IFU

Abbreviation: IFU, Instructions for Use.

able to deliver a simulated injection successfully and safely with the Auto-Injector. These studies supported the FDA and EC approval of the Auto-injector as a medical device for use with lonapegsomatropin.

In the study described here, ease of use was demonstrated as participants were able to use the lonapegsomatropin Auto-Injector with no uncorrected use errors. For use errors observed during the study, participants were able to correct the error during the root cause analysis by identifying and correctly interpreting the relevant information in the support materials provided with the Auto-Injector. The supplemental usability study of patients and caregivers with no training provided additional evidence that in the highest risk scenario where participants received no training and had no supervision by an HCP, participants were able to use the Auto-Injector effectively and safely.

Minimizing device use errors in the real-world setting is critical, and the Auto-injector device was easy enough to use that training with a Nurse Trainer did not significantly impact the ability of participants to use the Auto-Injector. As

shown by the low number of use errors and high mean number of task successes across all participant groups, users of the Auto-Injector do not need support from a highly trained HCP or to have prior injection experience to successfully use the Auto-Injector. Although there is a robust training program and available assistance for use of the lonapegsomatropin Auto-Injector, the non-ideal scenario of a patient using a device without training is a real-world possibility. A survey of patients with GHD indicated that approximately 9% of participants had not received training from healthcare personnel on their injection device.[25] Materials including the device instructional video and the Help Line, assessed as part of the usability validation study and also made available to patients in routine clinical practice, provide further support for patients using the Auto-Injector.

The lonapegsomatropin Auto-injector design addresses well-known challenges associated with injection anxiety and pain.[7] User feedback indicated that key features of the Auto-Injector, such as the small, hidden needle, were desirable to patients. Additionally, the Auto-injector uses electronic visual cues and audible sound signals to confirm delivery of the medication and the end of the injection sequence, so that users can be confident the full dose of medication was delivered.

Although the usability study was done in the context of a simulated injection into a skin pad, findings from the enliGHten trial support these results.[12,15] The child and parent questionnaires from the enliGHten trial showed that both parents and children considered decreased injection frequency and mode of delivery device in their preference for pediatric GHD treatment.[12] Within the enliGHten trial, early experience after 13 weeks of Auto-Injector use, as reported by 115 participants who completed the device questionnaire, demonstrated that the majority of participants noted that the Auto-Injector did not cause a lot of pain or discomfort (82.6%) and left few to no marks on the skin (95.7%), and the medicine could be injected without difficulty or making a mistake (94.0%) in a short amount of time (94.0%).[12] Importantly, these positive user experiences were supported by the long-term safety outcomes, which showed lower exposure-adjusted injection site reaction rates with the Auto-Injector (1.3%) compared to vial/syringe (7.1%).[15] Furthermore, the ongoing SkybriGHt registry (NCT05820672) is designed to collect real-world evidence on lonapegsomatropin, which may further inform understanding of Auto-Injector use, adherence, and long-term experience in routine clinical practice.

Easy-to-use devices can improve adherence to injection treatments, as has been shown in other chronic medical conditions requiring injected treatment such as diabetes where patients switched from vial/syringe to a pen device.[26,27] Patients with GHD also had higher rates of adherence to daily somatropin therapy when using an electronic injection device than what has been reported with vial/syringe.[28] Reduced injection frequency of GH is also anticipated to improve adherence and outcomes in patients with GHD.[2] Even small changes in injection frequency can have an impact, as data collected from a daily somatropin electronic injection device show that patients prescribed a 6-days-per-week dosing regimen had significantly higher adherence compared with those prescribed a 7-days-per-week dosing regimen.[28] Once-weekly lonapegsomatropin further reduces injection burden to only 52 injections per year, as opposed to up to 365 injections for a daily therapy. Together with the Auto-Injector, this reduction in injection frequency may provide meaningful improvements for users and potentially contribute to treatment adherence.

The lonapegsomatropin Auto-Injector has received FDA clearance and CE-marking and has thus met the expectations for marketability in the US and Europe. Awards in patient-centric design and innovation highlight the value of the lonapegsomatropin Auto-Injector in addressing patient needs for a more convenient and user-friendly GH therapy and support the success of human factors–driven device design. The Auto-Injector was developed specifically to complement once-weekly lonapegsomatropin and meet the particular needs of children with GHD and their caregivers, including developing a device that children are able to safely use on their own with supervision. Future comparative and real-world studies, such as the ongoing SkybriGHt registry (NCT05820672), may further clarify how device design features influence usability and adherence across long-acting growth hormone therapies.

Conclusion

The user-centered lonapegsomatropin Auto-Injector was developed with frequent touch points for users to provide feedback and input. The study shows that the device is safe and effective for its intended use to deliver once-weekly lonapegsomatropin. Adherence in pediatric GHD is influenced by multiple patient-, treatment-, and caregiver/external-

related factors, including patient beliefs, involvement in treatment decisions, communication between physicians and patients, injection training, and duration on therapy. Successful and confident device use may support greater independence for children with GHD, promoting their participation in managing their own health and contributing to a positive user experience, thereby addressing one potential barrier to consistent therapy. Beyond pediatric GHD, the Auto-Injector is expected to be applicable across other patient populations receiving lonapegsomatropin, with the potential to provide similar benefits in usability, adherence, and treatment experience.

Abbreviations

DCC, dual-chamber cartridges; EC, European Commission; FDA, Food and Drug Administration; GHD, growth hormone deficiency; HCP, healthcare provider; hGH, human growth hormone; IFU, Instructions for Use; LAGH, long-acting growth hormone; pGHD, pediatric growth hormone deficiency; QRG, Quick Reference Guide.

Ethics Approval and Informed Consent

The study protocol, its associated Informed Consent Form (ICF), and relevant supporting information was approved by Advarra IRB prior to study initiation. In addition, any participant recruitment materials were approved by the IRB prior to being used. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements. The study was conducted in accordance with all applicable laws and the applicable provisions within the United States Food and Drug Administration (FDA) regulations, including but not limited to 21 CFR 50 and 21 CFR 56, regarding informed consent and IRB procedures. Written informed consent or assent was obtained from all participants. For participants who were not of age to provide consent, consent was obtained from their legal guardian.

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Disclosure

M.L. is an employee of Insight by Nemera; P.E.F. is an employee of Phillips-Medisize A/S; N.B.M. and J.J. are employees of Ascendis Pharma A/S; H.E. is a consultant of Ascendis Pharma A/S.

In addition, H.E. reports a patent US 11,957,880 B2 issued to Ascendis Pharma A/S, a patent US 2024/082494 A1 pending to Ascendis Pharma A/S, a patent US 2024/374827 A1 pending to Ascendis Pharma A/S, a patent US 11,406,760 B2 issued to Ascendis Pharma A/S, a patent US 11,738,147 B2 issued to Ascendis Pharma A/S, a patent US 12,383,676 B2 issued to Ascendis Pharma A/S, a patent US 2025/235618 A1 pending to Ascendis Pharma A/S, a patent US 11,351,305 B2 issued to Ascendis Pharma A/S, a patent US 11,607,496 B2 issued to Ascendis Pharma A/S, a patent US 12,290,663 B2 issued to Ascendis Pharma A/S, a patent US 12,296,148 B2 issued to Ascendis Pharma A/S, a patent US 2025/235620 A1 pending to Ascendis Pharma A/S, a patent US 2025/256031 A1 pending to Ascendis Pharma A/S, a patent US 11,524,115 B2 issued to Ascendis Pharma A/S, a patent US 10,835,677 B2 issued to Ascendis Pharma A/S, a patent US 2023/072178 A1 pending to Ascendis Pharma A/S, a patent US D1,090,824 S pending to Ascendis Pharma A/S, a patent US D907,765 S pending to Ascendis Pharma A/S, a patent US 11,684,724 B2 issued to Ascendis Pharma A/S, a patent US 12,251,541 B2 issued to Ascendis Pharma A/S, a patent US 2025/177656 A1 pending to Ascendis Pharma A/S, a patent US 11,517,673 B2 issued to Ascendis Pharma A/S, a patent US 11,969,581 B2 issued to Ascendis Pharma A/S, a patent US 12,226,616 B2 issued to Ascendis Pharma A/S, a patent US 2025/152831 A1 pending to Ascendis Pharma A/S, a patent US 11,179,524 B2 issued to Ascendis Pharma A/S, a patent US 12,005,241 B2 issued to Ascendis Pharma A/S, a patent US 2024/277944 A1 pending to Ascendis Pharma A/S.

The authors report no other conflicts of interest in this work.

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