

# BSPED recommendations for the use of once-weekly long-acting growth hormone therapy in children with growth hormone deficiency

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## Background

Long-acting growth hormone (LAGH) is now available in the UK and is recommended by NICE (2023) as an option for the treatment of growth hormone deficiency for children and young people aged three years and over.

Currently only one LAGH preparation is licenced (somatrogen) but other preparations are likely to become available. This guidance therefore focuses on somatrogen and will be updated when new LAGH preparations are accessible to patients in the UK.

There are separate BSPED guidance/clinical standards available for:

- Shared care guidelines for GH therapy
- <https://www.bsped.org.uk/media/alxow2wv/gh-shared-care-guidelines-20240206.pdf>
- Standards for GH treatment for GHD  
<https://www.bsped.org.uk/media/iczlv32f/clinical-standards-for-gh-treatment-of-ghd-in-childhood-and-adolescence-v1.pdf>
- Standards for GH treatment for other growth disorders excluding GHD  
<https://www.bsped.org.uk/media/kfnh1unq/clinical-standards-for-gh-treatment-of-growth-disorders-excluding-ghd-19122023.pdf>

## Somatrogen

Somatrogen is currently approved as a once weekly subcutaneous injection for children over the age of three years with growth hormone deficiency (GHD) up until adult height has been reached [1]. Somatrogen has a half-life of 28 hrs compared to 2-3 hrs for somatropin.

In a global phase three study [2], once weekly somatrogen at 0.66mg/week demonstrated non-inferiority to once daily somatropin in children with GHD with dose-dependent increases in height velocity and IGF-I concentrations between three doses (0.25, 0.48 and 0.66 mg/kg/week). This trial included pre-pubertal children diagnosed with GHD (peak GH  $\leq 10$ ng/ml) and excluded patients with a prior history of cancer, treatment with chemotherapy or radiotherapy and syndromes e.g. Prader Willi Syndrome.

We recommend caution if using somatrogen in patient groups not included in the phase three study.

### Recommended dose and timing

- The recommended dose of somatrogen is 0.66mg/kg/week.
- Each pre-filled pen delivers 0.2mg to 12mg in a single injection in 0.2mg increments, or 0.5mg to 30mg in 0.5mg increments.
- If the patient's weight is >45kg, two (or three if >90kg -see point below\*) injections at different anatomical sites are needed. Written plans provided by the company can be helpful for administering doses accurately and minimising wastage.
- \*In overweight or obese patients, the clinician may want to consider using ideal body weight or body surface area rather than actual body weight to calculate the dose as no guidance regarding a maximum dose is available.
- The injection should be administered on the same day each week. However, the need for blood tests to assess IGF-1 levels on day 4 after the injection should be taken into consideration.
- If a dose is missed within three days, it should be given as soon as possible, and the usual weekly dosing resumed on the usual day. If more than three days have passed, the missed dose should be skipped and the next dose given on the usual day.
- If the patient wishes to change the administration day, they should ensure that the time between any two doses is at least three days. Ideally, they should discuss this with their clinician beforehand, to ensure that appropriate timing of blood tests remains.

### Recommended surveillance

- We recommend 4-6 monthly auxology and pubertal status/thyroid function 12 monthly. More frequent evaluation of pubertal status should be considered during puberty.
- Consider bone age assessment every 12-24 months during treatment if there are medical concerns, or if assessing the growth potential in a young person considered to be near final adult height.
- Serum IGF-1 peaks on day 2 following the somatrogen injection and then decreases to low concentrations before the next injection [3]. The IGF-1 concentration on day 4 following the injection reflects the average IGF-1 over the week [3]. There are no validated calculators to generate an average IGF-1 concentration from samples taken at time points other than day 4. The long-term effects of high IGF-1 concentrations on days 2-3 are not known. Therefore, we recommend that day 4 IGF-1 concentrations

are kept in the normal range. For this reason, every effort should be made to ensure that the day of the injection is 4 days before the usual clinic day (and therefore the monitoring blood tests).

- Mean IGF-1 approached 0 SD in the first month in the somatrogen group but with large interindividual variation, and at 12 months the mean IGF-1 was +0.65 SD (range -3.3 to +3.2 SD) compared to a range of -0.69 to -0.16 in the once daily somatropin group at 12 months. Dose reductions were required in 2.2% of patients due to high IGF1 concentrations in the trial [2].
- We recommend the assessment of IGF-1 (4 days after an injection) at 6 to 8 weeks after the initiation of treatment and then 4 to 6 monthly (4 days after an injection) thereafter, as a minimum.
- Dose adjustments should aim to achieve day 4 IGF-1 SDS within the normal range (between -2.0 and +2.0 SDS but ideally close to 0 SD). To achieve this, the somatrogen dose can be reduced by 15% and IGF-1 re-checked after 4-8 weeks. A further dose reduction of 15% may be required.

#### Monitoring of possible adverse events

- The most common adverse events were injection site pain (39.4% of somatrogen-treated *versus* 25.2% somatropin-treated), erythema (8.5% *versus* 0) and pruritus (5.5% *versus* 0)[2]. Clinical assessment should include monitoring for these.
- Currently, there are no data available on incidence of other side effects seen in once daily GH treatment such as intracranial hypertension and slipped upper femoral epiphysis. We recommend reporting any side effects through the Yellow Card Scheme <https://yellowcard.mhra.gov.uk>
- PROGRES is a post marketing surveillance study, and inclusion of patients treated with somatrogen is recommended where possible.

#### References

1. National Institute for Health and Care Excellence. Somatrogen for treating growth disturbance in children and young people aged 3 and over. 1 February 2023; Available from: <https://www.nice.org.uk/guidance/ta863/resources/somatrogen-for-treating-growth-disturbance-in-children-and-young-people-aged-3-years-and-over-pdf-82613611006405>
2. Deal, C.L., et al., Efficacy and Safety of Weekly Somatrogen vs Daily Somatropin in Children With Growth Hormone Deficiency: A Phase 3 Study. *J Clin Endocrinol Metab*, 2022. **107**(7): p. e2717-e2728.
3. Zadik, Z., et al., An open-label extension of a phase 2 dose-finding study of once-weekly somatrogen vs. once-daily Genotropin in children with short stature due to growth hormone deficiency: results following 5 years of treatment. *J Pediatr Endocrinol Metab*, 2023. **36**(3): p. 261-269.

**Appendix** Patient information sheet developed by Dr Rebecca Moon and Prof Justin Davies, Southampton University Hospital.

## **Patient information sheet daily vs long-acting growth hormone**

### **Growth hormone therapy for children**

**We have given you this factsheet because your child has been diagnosed with growth hormone deficiency and is eligible for growth hormone therapy. It explains what growth hormone therapy is and the different types of growth hormone available for children.**

**We hope it will help you to make an informed decision about what is right for your child. You will also have individual discussions with your child's paediatric endocrinologist (a doctor with special expertise in looking after children and young people with hormone disorders). If you have any further questions or concerns, please contact us using the details at the end of this factsheet.**

#### **What is growth hormone deficiency?**

Growth hormone deficiency is a condition where the pituitary gland (a pea-sized gland just below the brain) fails to produce enough of a hormone (a chemical messenger) called 'growth hormone'. Growth hormone is responsible for releasing other hormones in the body that are needed for growth.

If a child does not produce enough growth hormone, their growth may slow down or stop from the age of two or three years onwards. They may also experience puberty later than usual or not at all.

#### **What is growth hormone therapy?**

Growth hormone therapy is the treatment for growth hormone deficiency and other conditions linked with poor growth. It works by replacing the missing growth hormone with a man-made version.

#### **Why does my child need growth hormone therapy?**

Your child's paediatric endocrinologist has recommended that your child would benefit from having growth hormone therapy to treat their growth hormone deficiency. They have suggested that both the daily and long-acting growth hormone are suitable treatment options for your child.

#### **Types of growth hormone therapy**

There are currently two types of growth hormone available for children.

##### **Daily**

This type of growth hormone has been used since 1985. It is given as a daily injection under the skin (subcutaneous), usually in the evening.

##### **Long-acting**

This is a new type of growth hormone. It became available in 2023 for children (aged 3 to 17 years) who have a confirmed diagnosis of growth hormone deficiency. Unlike the daily injection, this long-acting growth hormone only needs to be given once a week as a subcutaneous injection.

**What are the differences between the two types of growth hormone?**

There are differences between the daily growth hormone and the long-acting growth hormone.

To help you decide which option is right for your child, please see the table below for a comparison of the two types of growth hormone.

	Daily	Long-acting
<b>How many injections and how/when are they given?</b>	<p><b>One</b> injection every evening before bed.</p> <p>We will train you on how give this injection.</p>	<p><b>One or more</b> injections on one day each week. You will be trained on how to give the injection/s.</p> <ul style="list-style-type: none"> <li>• If your child weighs <b>45kg (seven stone) or more</b>, they will need to have <b>two</b> injections at the same time on one day each week and <b>three</b> injections if they weigh <b>more than 90 kg</b>.</li> <li>• If your child weighs <b>less than 45kg</b>, the correct dose will usually be <b>one</b> injection. However, please be aware that the last dose of medication in your child’s injection device may not always be a full dose. If this is the case, you may need to give two injections for your child to get their full dose. You will need to inject the amount left in your injection device, then prepare a new pen to inject the rest of the dose on the same day.</li> </ul>
<b>What monitoring and blood tests are required?</b>	<p>Your child will need occasional blood tests to check their growth hormone level, medically known as ‘insulin-like growth factor-1 (IGF-1)’ and to monitor for other hormone deficiencies.</p>	<p>Your child will need a blood test to check their IGF-1 level 6 to 8 weeks after starting growth hormone. After this, they will need at least two blood tests each year.</p> <p>The blood sample must be collected four days after your child has had their usual</p>

	<p>These blood tests are usually not more than once a year and we do them during your child's scheduled clinic appointments.</p> <p>Your child will be seen in the outpatient clinic at least twice a year.</p>	<p>growth hormone injection (this can usually be organised for the same day as their clinic appointment).</p> <p>Your child will be seen in the outpatient clinic at least twice a year.</p>
<p><b>What injection devices are available?</b></p>	<p>There are various options available which your endocrine team will be able to go through with you.</p> <p>We will show you how to use whichever device you choose.</p>	<p>There is currently only one injection device available but newer ones will become available soon.</p> <p>The device is a pre-filled pen. It does not need a cartridge to be inserted or pre-mixing.</p>
<p><b>How are the injections stored?</b></p>	<p>Most devices <b>must</b> be stored in a refrigerator and only taken out 30 minutes before giving the injection. They can be transported in cool bags for short trips (if needed).</p>	<p>The device <b>must</b> be stored in a refrigerator. Each pen can be kept at room temperature for up to four hours at a time (for a maximum of five times).</p>
<p><b>Delivery and support</b></p>	<p>Both types of growth hormone will be delivered to your home by a home care delivery team. You will have access to a dedicated support team.</p>	
<p><b>Are there any side effects?</b></p>	<p>There are similar side effects for both types of growth hormone.</p> <p>Injection site reactions, such as:</p> <ul style="list-style-type: none"> <li>• itchiness</li> <li>• pain</li> <li>• redness</li> <li>• soreness at the injection site</li> </ul> <p>can happen with any growth hormone injection but have been reported more commonly with the long-acting growth hormone.</p> <p>Other rare side effects (e.g. headaches, hip/knee pain), have been reported with daily growth hormone and should be reported to your healthcare team if these occur with either daily or weekly growth hormone.</p>	
<p><b>What is known about the safety of the treatment?</b></p>	<p>Daily growth hormone is licensed and approved by the NHS. It has been used since 1985.</p>	<p>Long-acting growth hormone was licensed and approved for use by the NHS in 2023.</p>

	<p>Evidence-based research since this time has found the long-term use of daily growth hormone to be safe.</p>	<p>The National Institute for Health and Care Excellence (NICE) UK has reviewed long-acting growth hormone to ensure it is as effective and safe as daily growth hormone.</p> <p>Information on the long-term safety of long-acting growth hormone is not yet available. As with any new medication, there might be new side effects that appear as more people start to use it. If you choose long-acting growth hormone, it is important to tell us if your child experiences any unexpected side effects that we have not told you about.</p>
<p><b>Will my child need to continue this medication when they are older?</b></p>	<p>Growth hormone has other benefits as well as growth. For some people, we may recommend that they continue growth hormone therapy in adulthood.</p> <p>Daily growth hormone can be used to treat growth hormone deficiency in childhood and adulthood.</p>	<p>The long-acting growth hormone which is currently available is only licensed for use during growth.</p> <p>If we think that your child will benefit by continuing growth hormone therapy after they have finished growing, they will need to switch to the daily growth hormone, because LAGH is not currently licensed for use in adults. We will discuss this with you if and when appropriate.</p>
<p><b>Where can I find more information?</b></p>	<p>For more information about your specific growth hormone injection device, please read the manufacturer's instructions.</p>	

**What happens next?**

We hope that reading this factsheet has helped answer some of your initial questions about growth hormone therapy treatment for your child.

If you feel that you would like to proceed with growth hormone therapy for your child, please let us know. We will then arrange an appointment to see you in clinic.

You will be able to choose between the daily and long-acting treatment options. If you have a clear preference, please let us know when you contact us. If you are unsure, please let us know when you contact us, and a member of the team will be able to discuss this further with you.

**What follow-up care is needed?**

We will arrange regular follow-up appointments for your child. At each appointment, we will check whether the type of growth hormone your child is taking remains appropriate. If there

are concerns about your child's response to the type of growth hormone you have chosen, it may be necessary to switch to a different type of growth hormone.

Please note that if your child frequently misses growth hormone doses, we may not be able to continue prescribing this for them.

**Useful links:**

[www.nice.org.uk/guidance/ta863/informationforpublic](http://www.nice.org.uk/guidance/ta863/informationforpublic)

*Patient information sheet developed by Dr Rebecca Moon and Prof Justin Davies, Southampton University Hospital. Version 1. Published November 2023. Due for review November 2026. 3667. Modified by BPSSED-SIG, 2024.*