THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

For

The Treatment of Children with Recombinant Human Growth Hormone

Shared Care Protocol developed by:

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Sheffield Place Shared Care Protocol for the Treatment of Children with Recombinant Human Growth Hormone (r-hGH)

Statement of Purpose

This Shared Care Protocol (SCP) has been written to enable the continuation of care by primary care clinicians of patients initiated on recombinant human growth hormone (somatropin and somatrogon) by specialist paediatric endocrinologists at Sheffield Children's NHS Foundation Trust. Primary care will only be requested to take over prescribing of growth hormone therapy within its licensed indication unless specifically detailed otherwise below.

Responsibilities of specialist clinician

- Undertake necessary testing to confirm diagnosis and prescribe in line with NICE TA188 for somatropin (daily growth hormone therapy) and adhere to guidance for somatrogon as per NICE TA863 and the product information.
- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent. This is particularly important for unlicensed / off label products.
- Provide written information to patients and their carers about their condition and treatment.
- To initiate somatropin or somatrogon in appropriate patients.
- Discuss preparations available in line with appendix 1, and if more than one suitable, use the most cost effective preparation.
- To discontinue therapy if side effects pose a clinical risk to the patient.
- To train patients and families to self administer r-hGH injections.
- To monitor the patient as described above.
- To prescribe the first three month's supply or until patient stable.
- To prescribe / supply sharp bin for safe disposal of needles / devices or arrange for homecare delivery depending on the agreement with the manufacturer.
- To contact patient's GP to request prescribing in line with this shared care protocol and send a link to or copy of the protocol.
- To advise the GP regarding continuation of treatment, including the length of treatment
- To discuss any concerns with the GP regarding the patient's therapy.
- The patient to remain under the consultants care whilst ever the patient is being prescribed somatropin or somatrogon.

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment.
- To agree to prescribe for patients in line with the shared care protocol.
- To report any adverse reaction to the MHRA and the referring consultant.
- To continue to prescribe for the patient as advised by the consultant.
- To prescribe sharps bin for safe disposal of needles / devices as requested by the specialist.
- To inform the consultant if the patient discontinues treatment for any reason.
- To seek the advice of the consultant if any concerns with the patient's therapy.
- To conduct an annual medication review or more frequent if required.
- In the event that the GP is not able to prescribe, or where the share care is agreed but the consultant is still prescribing certain items e.g. Hospital only product; the GP will

provide the consultant with full details of existing therapy promptly by a secure method on request.
For medication supplied from another provider GPs are advised to follow recommendations for Recording Specialist initiated Drugs on Clinical Practice Systems.

Patient/Carer Responsibilities

- To ensure they have clear understanding of the prescribed treatment.
- To administer the r-hGH as directed by the supervising Consultant; attend clinic reviews as requested.
- To share any concerns in relation to treatment with the supervising Consultant and/or GP.
- To report any adverse effects to the supervising Consultant and/or GP whilst taking r-hGH.

1. Prescribing information for somatropin

1.1 Indication

Somatropin (recombinant human growth hormone) is recommended as a treatment option for children with growth failure associated with any of the following conditions:

- growth hormone deficiency
- Turner syndrome
- Prader–Willi syndrome
- chronic renal insufficiency
- born small for gestational age with subsequent growth failure at 4 years of age or later
- short stature homeobox-containing gene (*SHOX*) deficiency (Lilly product only)

Somatropin is a potent metabolic hormone of importance for the metabolism of lipids, carbohydrates and proteins. In children with inadequate endogenous growth hormone, somatropin stimulates linear growth and increases growth rate.

NICE technology appraisal TA188 Human growth hormone (somatropin) for the treatment of growth failure in children can be found using the following link:
https://www.nice.org.uk/guidance/ta188

1.2 Selection of patients

Specialist paediatric endocrinologists at Sheffield Children's Hospital will assess patients as per NICE guidance (TA188) and start treatment as appropriate for patients with the conditions listed above.

1.3 Dosage and dose titration

The dosage varies according to the condition being treated:

Indication	Dose
Turner syndrome	45–50 microgram/kg daily or 1.4 mg/m² daily
Growth hormone deficiency	23–39 microgram/kg daily or 0.7–1mg/m² daily
Prader–Willi syndrome	35 microgram/kg daily or 1mg/m² daily (with a maximum of 2.7 mg daily)
Chronic renal insufficiency	45–50 microgram/kg daily or 1.4 mg/m² daily
Growth disturbance in children born small for gestational age	35 microgram/kg daily or 1mg/m² daily
SHOX deficiency	45–50 microgram/kg daily

Somatropin is a daily injection either self-administered or given to the child by an adult, at home, usually as a subcutaneous injection.
Doses may be adjusted as necessary by the Consultant Paediatric Endocrinologist.

1.4 Contra-indications

Hypersensitivity to the active substance or to any of the excipients.
Somatropin must not be used when there is any evidence of an active tumour. Intracranial tumours must be inactive and anti-tumour therapy must be completed prior to starting growth hormone therapy. Treatment should be discontinued if there is evidence of tumour growth.
Somatropin should not be used for growth promotion in children with closed epiphyses.
Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions should not be treated with somatropin

1.5 Side–effects

The summary of product characteristics (SPC) for somatropin states that side effects include headache, visual problems, nausea and vomiting, fluid retention (peripheral oedema), arthralgia, myalgia, carpal tunnel syndrome, paraesthesia, antibody formation, hypothyroidism and reactions at injection site. Paediatricians should pay particular attention when giving somatropin to children with diabetes mellitus or its risk factors, slipped capital femoral epiphyses, idiopathic intracranial hypertension, or malignancies.

The above details are not a complete list and the BNFC and the SPC remain authoritative.

1.6 Monitoring

The Specialist Paediatric Endocrinology team will be responsible for the monitoring of r-hGH therapy.
The principal method for determining the success or otherwise of r-hGH treatment is by careful and accurate measurement of the child's growth.

- Regular assessment of growth response by a specialist in child growth at intervals - usually three to four months during the first year.
- If the response to treatment is satisfactory, the interval between assessments may be extended to six months.
- Insulin – like Growth Factor (IGF-1) monitoring three to four monthly for the first year then 6 monthly.
- Assessment of pituitary status as other deficiencies may be unmasked by treatment with r-hGH if indicated.

1.7 Stopping treatment

The decision to stop treatment should be made in consultation with the patient and/or carers and by the Consultant Paediatric Endocrinologist

Treatment with somatropin should be discontinued if any of the following apply:

- growth velocity increases less than 50% from baseline in the first year of treatment
- final height is approached and growth velocity is less than 2 cm total growth in 1 year
- there are insurmountable problems with adherence
- final height is attained.

In Prader–Willi syndrome evaluation of response to therapy should also consider body composition.

1.8 Interactions

Corticosteroids – growth promoting effect may be inhibited.
Oestrogens – increased doses of somatropin may be required.
Insulin and hypoglycaemic medicinal products - In patients with diabetes mellitus requiring somatropin, the dose of insulin and/or oral/injectable hypoglycaemic medicinal products may require adjustment when somatropin therapy is initiated.
Thyroid medicinal products - Treatment with daily growth hormone may unmask previously undiagnosed or subclinical central hypothyroidism. Thyroxine replacement therapy may need to be initiated or adjusted.

The above details are not a complete list and the current BNFC and the SPC remain authoritative.

2. Prescribing information for somatrogon (Ngenla®)

2.1 Indication

Somatrogon (Ngenla®) is indicated for the treatment of growth hormone deficiency (GHD) in children aged three years and over. It is a long-acting recombinant human growth hormone (r-hGH) that provides sustained and prolonged release of growth hormone.

Somatrogon is administered through subcutaneous injection and is administered once a week. This extended dosing interval offers convenience and may improve adherence to treatment compared to daily or multiple weekly injections of conventional growth hormone therapies.

The efficacy and safety of somatrogon have been evaluated in clinical trials involving pediatric patients with GHD. These studies have demonstrated that somatrogon effectively promotes growth and improves height outcomes in children with growth hormone deficiency. Doses may be adjusted as necessary by the Consultant Paediatric Endocrinologist.

NICE have produced evidence-based recommendations on somatrogon for treating growth disturbance in children and young people aged 3 years and over (NICE TA863). Evidence from clinical trials shows that somatrogon is as effective as one preparation of somatropin (Genotropin®). The cost modelling used a range of dosages of somatropin (0.023 to 0.039 mg/kg per day), using this range of dosages, a cost comparison suggests the costs of somatrogon are similar to those of the somatropin preparations.

2.2 Selection of patients

Specialist paediatric endocrinologists at Sheffield Children's Hospital will assess patients as per NICE TA863 and start treatment as appropriate for patients with growth hormone deficiency.

2.3 Dosage and dose titration

The recommended dose is 0.66 mg/kg body weight administered once weekly by subcutaneous injection. When doses higher than 30 mg are needed (i.e. body weight >45 kg), two injections have to be administered.

For patients switching from daily r-hGH medicinal products, the weekly therapy with somatrogon maybe initiated at a dose of 0.66 mg/kg/week on the day following their last daily injection.

The somatrogon dose may be adjusted as necessary by the specialist, based on growth velocity, adverse reactions, body weight and serum IGF-1 concentrations. When monitoring for IGF-1, samples should always be drawn 4 days after the prior dose. Dose adjustments should be targeted to achieve average IGF-1 standard deviation score (SDS) levels in the normal range, i.e. between –2 and +2 (preferably close to 0 SDS). In patients whose serum IGF-1 concentrations exceed the mean reference value for their age and sex by more than 2 SDS, the dose of somatrogon should be reduced by 15%. More than one dose reduction may be required in some patients.

2.4 Contra-indications

Hypersensitivity to somatrogon or to any of the excipients.
Somatrogon must not be used when there is any evidence of an active tumour. Intracranial tumours must be inactive and anti-tumour therapy must be completed prior to starting growth hormone therapy.
Somatrogon should not be used for growth promotion in children with close epiphyses.
Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions should not be treated with somatrogon

2.5 Side-effects

It is noted that somatrogon (Ngenla®) is currently a black triangle medication. The summary of product characteristics for somatrogon states that side effects include injection site reactions, headache and pyrexia. There are other possible side effects not seen with Ngenla® but which have been reported with other growth hormones. See section above.

The above details are not a complete list and the BNFC and the SPC remain authoritative.

2.6 Monitoring

The Specialist Paediatric Endocrinology team will be responsible for the monitoring of somatrogon therapy.
The principal method for determining the success or otherwise of r-hGH treatment is by careful and accurate measurement of the child's growth.

- Regular assessment of growth response by a specialist in child growth at intervals - usually three to four months during the first year.
- Interim monthly telephone follow-up monthly for 12 months to ensure safety.
- IGF-1 monitoring three monthly.
- Assessment of pituitary status as other deficiencies may be unmasked by treatment with r-hGH if indicated.

2.7 Stopping treatment

The decision to stop treatment should be made in consultation with the patient and/or carers and the Consultant Paediatric Endocrinologist.

Treatment with somatrogon should be discontinued if any of the following apply:

- growth velocity increases less than 50% from baseline in the first year of treatment
- final height is approached and growth velocity is less than 2 cm total growth in 1 year
- there are insurmountable problems with adherence
- final height is attained.

2.8 Interactions

Corticosteroids – growth promoting effect may be inhibited.
Oestrogens – increased doses of somatrogon may be required.
Insulin and hypoglycaemic medicinal products - In patients with diabetes mellitus requiring somatrogon, the dose of insulin and/or oral/injectable hypoglycaemic medicinal products may require adjustment when somatrogon therapy is initiated.
Thyroid medicinal products - Treatment with daily growth hormone may unmask previously undiagnosed or subclinical central hypothyroidism. Thyroxine replacement therapy may need to be initiated or adjusted.

The above details are not a complete list and the current BNFC and the SPC remain authoritative.

Additional information

The choice of product should be made on an individual basis after informed discussion between the responsible clinician and the patient and/or their carer about the advantages and disadvantages of the products available, taking into consideration therapeutic need and the likelihood of adherence to treatment. If, after that discussion, more than one product is suitable, the least costly product should be chosen. For SHOX deficiency Lilly hold the only licence for the use of somatropin to treat this condition (Humatrope®).

It should be noted that both somatropin and somatrogon are both classed as Controlled Drugs in line with The Misuse of Drugs Regulations 2001 under Schedule 4 part II. The Department of Health have issued strong recommendations that the maximum quantity prescribed should not exceed 30 days. This is not a legal restriction, but prescribers should be able to justify the quantity requested (on a clinical basis) if more than 30 days' supply is prescribed. There may be genuine circumstances for which medicines need to be prescribed in this way.

Re-Referral guidelines

Contact the Endocrinology Team if there are any concerns about patient compliance (e.g. prescriptions not being requested or collected).

Financial implications

The cost of treatment with somatropin or somatrogon depends on the dose, which is determined by the weight or body surface area of the child as well as by the indication for growth hormone treatment. The costs of the different growth hormone products are listed in appendix 1:

Ordering information

The eleven licensed products are available to order from pharmaceutical wholesalers:

Humatrope® (Lilly)
Zomacton® (Ferring)
NutropinAq® (Ipsen)
Norditropin® (Novo Nordisk)
Genotropin® (Pfizer)
Omnitrope® (Sandoz)
Saizen® (Merck)
Somatrogon/Ngenla® (Pfizer)

Support, education and information

Endocrinology Team at Sheffield Children's Hospital:

Dr N P Wright, Consultant Endocrinologist
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Child Growth Foundation: www.childgrowthfoundation.org

References

Paediatric Formulary Committee. BNFc (online) London: BMJ Group, Pharmaceutical Press and RCPCH Publications http://bnfc.nice.org.uk

SPC Genotropin - https://www.medicines.org.uk/emc/search?q=somatropin

NICE TA188, Human growth hormone (somatropin) for the treatment of growth failure in children - https://www.nice.org.uk/guidance/ta188

Shared Care Guidelines: Paediatric use of Recombinant human Growth Hormone (r-hGH, Somatropin), BSPED.
https://www.bsped.org.uk/media/1377/sharedcaregh_july2015.pdf

The East of England Priorities Advisory Committee – Recommendations on the use of growth hormone devices in children. 2018

NICE Technology appraisal guidance [TA863]; Somatrogon for treating growth disturbance in children and young people aged 3 years and over https://www.nice.org.uk/guidance/ta863

Pfizer Ltd. NGENLA Summary of Product Characteristics for Great Britain. Available at: GB SPC: https://www.medicines.org.uk/emc/search?q=Ngenla.

Zelinska N, Iotova V, Skorodok J et al. Long-acting C-terminal peptide modified hGH (MOD-4023): results of a safety and dose-finding study in GHD children. J Clin Endocrinol Metab 2017;102:1578-87.

Maniatis AK, et al. Treatment Burden of Weekly Somatrogon vs Daily Somatropin in Children With Growth Hormone Deficiency: A Randomized Study. J Endocr Soc 2022;6:1–10.

Pfizer Ltd. NGENLA instructions for use for Great Britain. Available at: GB Instructions for use: https://www.medicines.org.uk/emc/product/13486/pil and https://www.medicines.org.uk/emc/product/13476/pil.

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Drug Tariff July 2023 NHS Business Services Authority

MIMS online Norditropin NordiFlex

Version History

This SCP is an update of the original SCP produced by:

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Appendix 1 Growth Hormones Products

There are eleven different devices currently available that deliver growth hormone. The table below lists the products available in different groups. The choice of product will be individualised for the patient; the majority of patients needs should be able to be met by a device in group 1.

Group	Product Name	Available Strengths	Formulation	Additional Information	Cost per mg in primary care
1 Preferred products for the **majority** of patients	**Omnitrope®**	5mg/1.5mL 10mg/1.5mL 15mg/1.5mL	Cartridge	**Most cost effective preparation** Preset dose preparation available. To be used with Omnitrope SurePal 5, 10 or 15. Pens are non-NHS but available free of charge from clinics.	**£14.75**
	Genotropin Miniquick®	200mcg, 400mcg, 600mcg, 800mcg, 1mg, 1.2mg, 1.4mg, 1.6mg 1.8mg, 2mg	Pre-filled pen	Prefilled unit dose preparation Can be kept at room temperature	£17.39
	Humatrope®	6mg, 12mg, 24mg	Powder and solvent	Requires reconstitution. Only preparation licensed SHOX deficiency	£18.00
	Norditropin Flexpro®	5mg/5mL 10mg/5mL 15mg/5mL	Pre-filled pen	Can be stored at room temperature (for <3 weeks after first use). Autoinjector to aid administration. Larger doses and more increments available for dosing than Nordiflex.	£23.18
	Saizen®	5.83mg/mL 8mg/mL	Cartridge	Pre-set dose available Monitors compliance (Easypod®3) Can be kept at room temperature for 7 days.	£23.18 (although costs variable depending on prescribing volume)
	Zomacton®	4mg	Powder and solvent	Requires reconstitution.	£17.07
	Somatrogon (Ngenla®)	24mg, 60mg	Pre-filled pen	Once weekly injection	£7.90 (note dose not equivalent)
2	Genotropin®	5.3mg, 12mg	Powder and solvent	Requires reconstitution	£17.39

Products for use in patients with specific needs	Genotropin GoQuick®	5.3mg, 12mg	Pre-filled pen	Fewer strengths available than MiniQuick®	£17.39
3 Not for routine use	Norditropin Nordiflex®	5mg/1.5mL, 10mg/1.5mL, 15mg/1.5mL	Pre-filled pen	No added benefits	£23.18
	Nutropin Aq®	10mg/2mL	Multi-dose cartridge	To be use with Nutropin Aq® pen	£20.30