SHARED CARE PRESCRIBING GUIDELINE
SOMATROPIN (recombinant growth hormone - rGH) for the treatment of Growth hormone deficiency, Turner syndrome, Chronic renal insufficiency, Prader-Willi syndrome, Small for gestational age and Short stature homeobox-containing gene (*SHOX*) deficiency in PAEDIATRICS

SOMATROPIN (rGH)
for the treatment of Growth hormone deficiency, Turner syndrome, Chronic renal insufficiency, Prader-Willi syndrome, Small for gestational age and Short stature homeobox-containing gene (*SHOX*) deficiency in PAEDIATRICS
NOTES to the GP

The information in the shared care guideline has been developed in consultation with CCGs in South East London and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing SOMATROPIN (rGH) for the treatment of Growth hormone deficiency, Turner syndrome, Children with Chronic renal insufficiency, Prader-Willi syndrome, Small for gestational age and Short stature homeobox-containing gene (*SHOX*) deficiency

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local CCG Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email the requesting clinician if you are in agreement to participate in shared care.

GP DECISION FORM

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of **SOMATROPIN (rGH) for the treatment of** Growth hormone deficiency, Turner syndrome, Children with chronic renal insufficiency, Prader-Willi syndrome, Small for gestational age and Short stature homeobox-containing gene (*SHOX*) deficiency can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request within two weeks (see page 4 under GP responsibilities) and complete the form below.

AGREEMENT TO PARTICIPATE IN SHARED CARE

SOMATROPIN (recombinant growth hormone - rGH)
for the treatment of Growth hormone deficiency, Turner syndrome, Children with chronic renal insufficiency, Prader-Willi syndrome, Small for gestational age and Short stature homeobox-containing gene (*SHOX*) deficiency

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**

The brand of somatropin that this patient has been started on is:
(Trust clinicians should refer to the guideline for offering choice of somatropin for details on choice of product.)

The indication for treatment with somatropin for this patient is:

- Children with growth hormone deficiency (GHD) ☐
- Children with Turner Syndrome (TS) ☐
- Children with chronic renal insufficiency (CRI) ☐
- Children with Prader-Willi syndrome (PWS) ☐
- Small for Gestational Age Children (SGA) ☐
- Short stature homeobox-containing gene (*SHOX*) deficiency ☐

Date completed:	**Patient Agreement:** Patient agrees to shared care ☐
Hospital requesting shared care:	Patient does not agree to shared care ☐
GP Name:	**Agree** ☐ **Disagree** ☐

This is to confirm that I **AGREE / DISAGREE (please delete as appropriate)** to participate in shared care for SOMATROPIN this patient as outlined in this shared care document.

GP Signature: **Date signed:**

ACTION

1. HOSPITAL CONSULTANT

Tick to confirm

- Explain shared care to patient and obtain agreement Date obtained:_____ ☐
- Indicate requesting hospital ☐
- Complete and sign agreement ☐
- Email full shared care guideline (including signed agreement to GP) ☐
- Place original in patient's notes ☐

2. GP PRACTICE

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) the GP decision form **(this page)**. This should be sent back to the specialist **within 2 weeks** of receipt of request.
- Refer to section 3 for secondary care consultant and pharmacy contact details.
- If you **do not agree** to participate in shared care, contact consultant and local CCG medicines management team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local CCG medicines management team should be informed.
- Once decision reached file a copy in the patient's medical notes.

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CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the Consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with **1 month's** supply of therapy

1. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Establish or confirm diagnosis and assess patient suitability for treatment in line with NICE guidance.
- Baseline monitoring and assessment: growth parameters, thyroid function, bone age.
- To initiate and supply treatment for the **first month.**
- To inform GP that they are expected to take on prescribing after the first month.
- To inform GP of the brand of somatropin the patient is on. **Note:** Somatropin must be prescribed by the **brand name** (BNF).
- To inform patients of practical issues related to the use of somatropin such as administration, storage and maximum dose – see "Information provided to patient" section on page 7.
- Discuss treatment with patient and ensure they have a clear understanding of it. A specialist nurse carries out training for the administration of the GH. The carer/child is involved with the choice of administration device. The specialist nurse provides ongoing telephone support for any problems with treatment. The consultant makes all decisions about the GH treatment e.g. dose, continuing and stopping treatment and managing side effects.
- Email a signed shared care guideline with patient details completed to GP for consideration of shared care treatment.
- To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk.
- Somatropin supplied via the homecare company must be prescribed by the hospital trust.
- Where prescribing of somatropin is transferred to the GP, the community pharmacy will be dispensing (should not be via homecare as this must be retained by the hospital) and the hospital must ensure that the patient is supplied with the pens where required as they are not prescribable on the NHS. Where BD needles are compatible with the pen, these are prescribable on the NHS.

After agreement to shared care

- Inform GP that they are expected to take on prescribing from one month onwards
- Inform GP of monitoring results and any changes in therapy
- Evaluate adverse events reported by GP or patient
- Recommend the prescribed brand, dose and monitor treatment as below:
    - Regular assessment of growth response by a specialist in child growth at intervals: usually every 3-4 months during the first year.
    - If the response to treatment is satisfactory, the interval between assessments may be extended to six months.
    - Thyroid function annually or when indicated.
    - Bone age assessment annually or when indicated.
    - Assessment of pituitary status as other deficiencies may evolve.
    - Sex hormone replacement to induce puberty at the normal timing if indicated.
    - Examining patients with GHD secondary to an intracranial lesion for evidence of progression or recurrence of underlying disease.
- Regular communication with the GP to update about response, developments and any change in treatment.

General Practitioner responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline, confirmation to the requesting Consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on page 2.
- If do not agree to shared care, discuss with requesting Consultant or local CCG medicines management team within 2 weeks of receipt of shared care request.

After agreement to shared care

- Prescribe the recommended brand of Somatropin. **Note:** Somatropin must be prescribed by the **brand name** (BNF).
- Prescribe dose as recommended
- Inform specialist consultant or nurse specialist of suspected adverse effects and also report via yellow card scheme if necessary: **https://yellowcard.mhra.gov.uk/**
- Stop treatment on advice of specialist or immediately if urgent need arises (and contact specialist in this case).
- Carry out monitoring and follow up according to shared care guideline.
- To advise the specialist if non-compliance is suspected
- Only ask specialist to take back prescribing should unmanageable problems arise.

Monitoring

- Report to the specialist centre any adverse events or significant medical conditions presented by the patient.
- Prescribe on-going somatropin therapy (by brand name) for a minimum one month at a time, and ideally longer (3 months).
- Reporting of changes or additions to patient's other medication (if any).
- The principal method for determining the success or otherwise of GH treatment is by careful and accurate monitoring of the child's growth. This will be carried out at the specialist centre 3-6 monthly and GP will be kept informed by clinic letter.

Patient's / Carer's responsibilities

- Take medicines as agreed.
- Report any adverse events to GP, hospital doctor, pharmacist or Endocrine nurse specialist
- Do not share medicines.
- Attend booked appointments for review. If you miss an appointment the hospital will reschedule according to unit policy.
- Share any concerns you may have about your treatment with your Consultant, GP, Pharmacist or Endocrine nurse specialist.
- To inform GP and hospital of any changes in addresses or telephone contact numbers.

2. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for **Somatropin (the brand prescribed for your patient will be detailed in the hospital letter)** prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Indication(s)

- Children with growth hormone deficiency (GHD)
- Children with Turner Syndrome (TS)
- Children with chronic renal insufficiency (CRI)
- Children with Prader-Willi syndrome (PWS)
- Small for Gestational Age Children (SGA)
- Short stature homeobox-containing gene (*SHOX*) deficiency

Place in Therapy

- Growth Hormone Deficiency - Somatropin should be started as clinically indicated
- Turner Syndrome - Somatropin should be considered from 2 years of age
- Chronic Renal Impairment - nutritional support and metabolic abnormalities have to be optimised and steroid therapy has to be reduced to minimum before starting somatropin.
- Prader-Willi Syndrome - Somatropin should be considered from 18 months onwards until bones fused, in combination with an energy restricted diet.
- Small for Gestational Age - Short children with growth disturbance who were born Small for their gestational age, whose growth has not caught up by the age of 4 years or later.
- Short stature homeobox-containing gene (SHOX) - Somatropin should be prescribed for patients who have growth failure associated with SHOX deficiency, as confirmed by DNA analysis

Dose & route of administration

Growth Hormone is usually given as a subcutaneous injection at night to mimic the child's natural fluctuations in growth hormone.

- Growth Hormone Deficiency
  23-39 micrograms/kg daily, or 0.7-1.0 mg/m^2 daily
- Turner Syndrome
  45-50 micrograms/kg daily, or 1.4 mg/m^2 daily
- Chronic Renal Impairment
  45-50 micrograms/kg daily, or 1.4 mg/m^2 daily
- Prader-Willi Syndrome
  35 micrograms/kg daily or 1.0 mg/m^2 daily; max 2.7 mg daily
- Small for Gestational Age
  33 micrograms/kg to 67mcg/kg daily or 1.0mg/m^2 to 2.0mg/m^2 daily (unlicensed). Note: the GP is asked to take on unlicensed prescribing supported by evidence from references 6 and 7.
- Short stature homeobox-containing gene (SHOX)
  45microgram/kg to 50 microgram/kg daily; 1.4 mg/m^2 daily

Licensing information regarding different brands of Growth Hormone (Somatropin)

The product licence for each manufacturer is as follows:

Product – Manufacturer	Cost per mg (excl VAT)*	GHD	TS	CRI	PWS	SGA	SHOX
Omnitrope® (Sandoz)	£14.75	√	√	√	√	√	
Genotropin® (Pharmacia)	£17.39	√	√	√	√	√	
Norditropin®(Novo Nordisk)	£21.27-£23.18	√	√	√		√	
Humatrope® (Lilly)	£18.00	√	√	√		√	√
Zomacton® (Ferring)	£19.92	√	√				
NutropinAq® (Ipsen)	£20.30	√	√	√			
Saizen® (MerckSerono)	£23.18	√	√	√		√	

*Basic price to primary care[1]
√ denotes that this product is licensed for the stated condition

Somatropin must be prescribed by the brand name (BNF).

Occasionally, GPs may be requested to take on prescribing of Zomacton® for unlicensed indication due to needle phobia with the licensed products.

Duration of treatment

- Growth Hormone therapy should be discontinued in children with Turner Syndrome, SHOX, SGA and PWS when the consultant and the family agree to stop treatment, giving due consideration to likely final height and other clinical issues. The consultant will make the final decision to stop therapy, and will inform the GP.
- Patients with Childhood onset growth hormone deficiency can continue GH treatment in accordance with NICE technology appraisal.
- In children with PWS, evaluation of response to therapy should also consider body composition (NICE).
- In children with CRI, GH treatment should be stopped after renal transplantation, subject to restoration of normal renal function.

Criteria for stopping treatment

- In patients with Turner syndrome, SHOX, SGA or idiopathic isolated GH deficiency treatment should be reviewed after the first year.
- If there is a poor response, i.e. <50% increase in growth rate, or if compliance or growth rate remains poor despite optimisation of GH treatment dose, then GH should be discontinued in line with NICE guidance.
- Treatment can otherwise continue until height velocity is <2cm/year, assessed over 6-12 months, or once final height has been achieved. The Consultant will make this decision.

Monitoring Requirements including frequency

Consultant

Recommend the prescribed dose and monitor treatment as below:

- Regular assessment of growth response by a specialist in child growth at intervals: usually every 3-4 months during the first year.
- If the response to treatment is satisfactory, the interval between assessments may be extended to six months.
- Thyroid function annually or when indicated.
- Bone age assessment when indicated.
- Assessment of pituitary status as other deficiencies may evolve.
- Sex hormone replacement to induce puberty at the normal timing if indicated.
- Examining patients with GHD secondary to an intracranial lesion for evidence of progression or recurrence of underlying disease.
- Regular communication with the GP to update about response, developments and any change in treatment.

GP

Monitoring:

- Report to the specialist centre any adverse events or significant medical conditions presented by the patient.
- Reporting of changes or additions to patient's other medication (if any).

Follow up arrangements

Regular assessment of growth response by a specialist in child growth at intervals: usually every 3-4 months during the first year.
If the response to treatment is satisfactory, the interval between assessments may be extended to six months.

Practical issues including other relevant advice/information

Reminder: this list is not exhaustive - for full details of adverse effects and all potential drug interactions refer to latest Summary of Product Characteristics (SPC) for the drug, available via www.medicines.org.uk.

Adverse Effects

GH therapy is safe and adverse effects are uncommon with recommended dosages, but include these listed below.

1. Local discomfort at the site of injection has been reported and frequent subcutaneous injection into the same site may result in tissue atrophy. This can be avoided by varying the injection site.

2. Headache may be noted transiently in some patients on higher dosage regimens. Rarely benign intracranial hypertension has been reported but this can be detected by fundoscopy.

3. Oedema may be exacerbated in Turner's syndrome but is rare in other patients.

Other associations have been described but are not encountered in routine practice.

Hypothyroidism has been reported in 5-10% of patients undergoing treatment with GH. This may be a result of the natural history of hypopituitarism due to the associated deficiency of TSH. It is essential to correct any deficiency with levothyroxine if the optimal response to GH treatment is to be achieved.

Diabetes mellitus GH exerts effects on both carbohydrate and lipid metabolism. It is both anabolic and diabetogenic and, in theory, hyperglycaemia and ketosis may occur but is rarely seen in practice. In children with existing diabetes mellitus, glycaemic control and insulin therapy may need readjustment; the induction of insulin resistance is also a rare occurrence.

Antibody development has been observed in some patients. It rarely affects the clinical response to treatment.

Acute leukaemia has been reported both in untreated GHD children and GH treated children. Studies show that there is no increased incidence over standard population data so these reports are chance associations. The incidence in treated children is not higher even in children who have had leukaemia previously or a bone marrow transplant.

Interaction with other medications

Corticosteroids in supraphysiological doses may interfere with the growth promoting actions of GH. Children with co-existing ACTH deficiency should have their glucocorticoid replacement dose carefully adjusted to avoid an inhibitory effect on growth. Titration of doses should be managed by a specialist Consultant.
Oral hypoglycaemics and insulin therapy. Diabetic patients may require their glycaemic control measures reviewed to take account of the hyperglycaemic effects of GH.

Information provided to the patient

National Institute for Clinical Excellence (NICE) Technology Appraisal
No 188 (2010) Human Growth Hormone (somatropin) for the treatment of growth failure in children (review)
http://www.nice.org.uk/guidance/TA188/informationforpublic

Evidence Base for treatment and key references

1. British National Formulary for Children (BNFC), June 2016
2. National Institute for Clinical Excellence (NICE) Technology Appraisal No.42 (2002) Full guidance on the use of human growth hormone (somatropin) in children with growth failure. http://www.nice.org.uk/pdf/inChild-42-ALS.pdf.
3. British Society for Paediatric Endocrinology and Diabetes (BSPED). Shared Care Guidelines 2006. Treatment of Children with Recombinant Human Growth Hormone (r-hGH) http://www.emc.medicines.org.uk/
4. National Institute for Clinical Excellence (NICE) Technology Appraisal No 188 (2010) Human Growth Hormone (somatropin) for the treatment of growth failure in children (review) http://guidance.nice.org.uk/TA188
5. UKMi, London New Drugs Group, Comparison of Growth Hormone Products and Devices, October 2013 http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Comparison%20of%20growth%20hormone%20products%20and%20devices.pdf
6. Van Pareren 2003 Journal of Clinical Endocrinology & Metabolism 88:3584–3590.
7. De Zegher 2000 Journal of Clinical Endocrinology & Metabolism 85:2816–2821.

3. COMMUNICATION AND SUPPORT

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
King's College Hospital contacts: **Consultant Paediatric Endocrinologists** **Dr Charles Buchanan** **Dr Ritika Kapoor** Kings College Hospital Denmark Hill, London, SE5 9RS **Tel :0203-299-9000 ext 33431**	**Tel: Tel :0203-299-9000 ext 33431** **Email: ritikakapoor@nhs.net or charles.buchanan@nhs.net**
Medication – Prescribing advice, interactions, availability of medicines **Aileen Parke** W&C Pharmacy Team Leader King's College Hospital Denmark Hill, London, SE5 9RS	**Tel : 0203-299-9000 ext 35723** **Email: aileen.parke@nhs.net**
Guy's and St. Thomas' Hospital switchboard: 0207 188 7188	
Evelina Hospital contacts: **Consultant Paediatric Endocrinologist** **Dr Tony Hulse** **Dr Michal Ajzensztejn** **Dr Moira Cheung** Evelina Children's Hospital, St Thomas's Hospital Westminster Bridge Road, London, SE1 7EH	**Tel: 0207 1884674** **Email: Tony.Hulse@gstt.nhs.uk** **Email: Michal.Ajzensztejn@gstt.nhs.uk** **Email: Moira.Cheung@gstt.nhs.uk**
Medication – Prescribing advice, interactions, availability of medicines **Steve Tomlin (Consultant Paediatric Pharmacist)** Evelina Children's Hospital, St Thomas' Hospital Westminster Bridge Road, London SE1 7EH	**Tel: 02071889202** **Email: Stephen.Tomlin@gstt.nhs.uk**
Lewisham and Greenwich Hospitals switchboard	
Consultant/specialist team N/A	N/A
Medication – Prescribing advice, interactions, availability of medicines N/A	N/A
South London and Maudsley (SLAM): switchboard	
Consultant/specialist team N/A	N/A
Medication – Prescribing advice, interactions, availability of medicines N/A	N/A
Oxleas NHS Trust switchboard	
Consultant/specialist team N/A	N/A
Medication – Prescribing advice, interactions, availability of medicines N/A	N/A