North and East Devon Shared Care Guideline ~ Somatropin for the treatment of growth hormone deficiency in adults

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to the BNF and individual product SPCs for full prescribing data.

Specialist: Please complete letter at the end of this document and send together with the shared care guideline to the GP.

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then they are 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.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

This prescribing guideline sets out details for the sharing of care of **adult patients** with growth hormone deficiency prescribed somatropin in line with NICE TA64; the use of somatropin other than in line with NICE TA64 is outside the scope of this guidance.

The treatment of **children** with growth hormone deficiency falls within the specialised services commissioned by NHS England. CCGs are not the responsible commissioners for these treatments; the use of somatropin in these patients is outside the scope of this guidance.

The Society for Endocrinology estimates that the prevalence of adult-onset growth hormone (GH) deficiency is approximately 1 in 10,000 of the adult UK population. GH is produced by the anterior pituitary gland. It has a role in the regulation of protein, lipid and carbohydrate metabolism, as well as promoting growth in children.

The clinical features of some adult growth hormone deficiency are different to those seen in children and include:

- Abnormal body composition including increased body fat; poor general health including decreased exercise tolerance
- Impaired psychological well being
- Reduced bone mineral density
- Impaired lipid metabolism
- Increased cardiovascular mortality.

Growth hormone replacement therapy in such patients produces modest, though significant improvements in these clinical features. Somatropin is human growth hormone produced by recombinant DNA technology in *E.coli*. Its amino acid sequence is identical to that of natural human GH.

Recombinant human growth hormone (somatropin) treatment is recommended for the treatment of adults with GH deficiency only if they fulfil all three of the following criteria:

1. They have severe GH deficiency, defined as a peak GH response of less than 9 mU/litre (3 ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test (e.g. Glucagon stimulation test) or have pituitary lesion and 3 or more other pituitary hormone deficiencies
2. They have a perceived impairment of quality of life (QoL), as demonstrated by a reported score of at least 11 in the disease- specific 'Quality of life assessment of growth hormone deficiency in adults' (QoL-AGHDA) questionnaire
3. They are already receiving treatment for any other pituitary hormone deficiencies as required and these therapies have been optimised. Patients who develop GH deficiency in early adulthood, after linear growth is completed but before the age of 25 years, should be given GH treatment until adult peak bone mass has been achieved, provided they satisfy the biochemical criteria for severe GH deficiency (defined as a peak GH response of less than 9 mU/litre (3 ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test).

When adult peak bone mass has been achieved, the decision to continue GH treatment should be reassessed based on the three criteria.

Where an insulin stress test is contraindicated (e.g. Epilepsy, Ischaemic Heart Disease) the use of a glucagon (or arginine) test alone will be appropriate.

Specialist responsibilities

- Adrenal deficiency should be assessed in the initial investigation and replacement therapy should be initiated before somatropin is considered
- Confirm that GH treatment is appropriate and select the appropriate preparation. **Prescribe by brand.**
- Provide the patient or patient's carer with suitable written and verbal information about the drug prior to starting medication and discuss the benefits and side effects of treatment.
- Ensure that training on reconstitution, administration and storage of GH is provided for the patient or carer.
- For female patients of child-bearing age, exclude pregnancy prior to initiating treatment
- Discuss with the patient (and/or carer) the need to immediately consult their physician if there is a possibility of pregnancy
- Initiate drug treatment and undertake period of dose stabilisation over 3 months (this includes prescribing somatropin) – adjust somatropin dose according to clinical response
- Undertake initial and ongoing assessment of the patient (including monitoring section below)
- **After the stabilisation period**, ask the GP whether they are willing to participate in shared care. Specialist to specify brand to be prescribed.
- A decision on continuing therapy will be taken by the consultant after a further 6 months of prescribing in primary care (GH treatment should be discontinued for those people who demonstrate a QoL improvement of less than 7 points in QoL-AGHDA score at this time)
- Specify review dates at clinically relevant time intervals. The first review should be at 6 months after dose stabilisation and thereafter at 12 monthly intervals for continued therapy.
- Promptly communicate with GP any changes in treatment, results of monitoring undertaken and assessment of adverse events
- Provide advice to GPs on when to stop treatment
- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug

- Report adverse events to the to MHRA via the yellow card scheme
- Insulin treated diabetic patients may require adjustment of their insulin dose on initiation of therapy. If necessary insulin dosage alteration will be the responsibility of the consultant based on the results of monitoring.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for shared care.

If GP has agreed to share care:

- **Continue prescribing somatropin by brand** following period of dose stabilisation for a further 6 months after dose stabilisation. At this point the consultant will review the patient to assess whether there is any benefit from continued treatment
- Promptly refer to a specialist if there is symptomatic change in the patient's expected response to treatment
- Refer to the endocrine specialist nurse where education needs are identified
- Report to, and seek advice from, a specialist on any aspect of patient care which is of concern to the GP and may affect treatment
- Report adverse events to specialist and to MHRA via the yellow card scheme
- Stop treatment in the case of a severe adverse event, or if the patient becomes pregnant.

Monitoring

Baseline assessment & ongoing monitoring to be completed by the specialist service provider:

- QoL-AGHDA at baseline and 9 months after initiation of therapy (an initial 3-month period of GH dose titration, followed by a 6-month therapeutic trial period)
- Insulin-like Growth Hormone (IGH-1) at baseline, monthly during titration period; and 3 monthly thereafter
- HbA1c and blood glucose at baseline and every 3 months
- Thyroid function tests at baseline, 6 months, 9 months and then annually.

Monitoring during treatment to be completed by the GP:

- Symptoms/response to treatment, and/or adverse effects, at every contact.

Patient responsibilities

- Ensure they attend specialist appointments and/ or GP/nurse appointments
- Understand that treatment may be stopped if they do not attend for monitoring & treatment review
- Ensure they have a clear understanding of the treatment, expected benefits and potential side effects
- Administer (or support administration of) medication as directed by the prescriber
- Report any adverse effects regarding their treatment to the GP and/or specialist
- Advise the GP immediately if pregnancy is suspected
- Store their medicines safely and securely.

Supporting Information

Somatropin is a biosimilar medicine; it is a biological medicine that is highly similar and clinically equivalent (in terms of quality, safety, and efficacy) to an existing biological medicine however they cannot be considered generic equivalents of the originator biological medicine. Because they are not identical, **biological medicines must be prescribed by brand**.

The decision which brand to prescribe rests with the specialist in consultation with the patient. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines.

Dosage and administration

Refer to the current BNF or individual product SPC for available brands and formulations.

Treatment is self-administered by a daily subcutaneous injection; the initial dose is 150 micrograms – 300micrograms daily (typically 270 micrograms daily).

Note: Somatropin 1mg ≡ 3 units (dose formerly expressed as units)

For the first 2–3 months the consultant and endocrine specialist nurse makes dosage adjustments based on monthly assessments of serum levels of IGF-I and to the appearance of adverse effects, until maintenance dose is achieved. The currently used median maintenance dose is 400 micrograms daily (women higher than men). GH requirements may decrease with age.

Contraindications and precautions

Refer to individual product SPCs and BNF.

Pregnancy and lactation

Refer to individual product SPCs and BNF.

Somatropin containing products are not recommended during pregnancy and in women of childbearing potential not using contraception.

It is not known whether somatropin is excreted in human milk, but absorption of intact protein from the gastrointestinal tract of the infant is extremely unlikely. Therefore caution should be exercised when somatropin containing products are administered to breast-feeding women.

Adverse effects

Refer to individual product SPCs and BNF.

Most common adverse effects reported are oedema, arthralgia and carpal tunnel syndrome. These effects are dose-related and transient, usually subsiding if the dose is reduced. Overtreatment with somatropin results in acromegaly.

Drug interactions

This list is not exhaustive, for additional information, and further interactions, consult the BNF and individual product SPCs.

- The growth-promoting effect of somatropin may be inhibited by **corticosteroids** (interactions do not generally apply to corticosteroids used for topical action (including inhalation)

- Increased doses of somatropin may be needed when given with **oral oestrogens** (when used as replacement therapy). Consideration of oestrogen patch may be appropriate.
- Somatropin may reduce **insulin** sensitivity. For patients with diabetes mellitus, the insulin dose may require adjustment after somatropin therapy is instituted. Patients with diabetes, glucose intolerance, or additional risk factors for diabetes should be monitored closely during somatropin therapy
- Somatropin may increase clearance of **anticonvulsants** and **ciclosporin**, resulting in reduced plasma concentrations of these drugs.

Support

The following prescribers cover the Royal Devon and Exeter NHS Foundation Trust and Northern Devon Healthcare NHS Trust:

Contact details		
Name	**Phone number**	**E-mail address**
Dr A Brooke	01392 403828	antonia.brooke@nhs.net
Dr B Vaidya	01392 402772	Bijay.Vaidya@nhs.net
Dr J Prague	01392 403838	juliaprague@nhs.net
Endocrine Nurses		rduh.exeterendocrinenurses@nhs.net

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Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

I recommend treatment with the following drug: ……

At the following dosage: ……..……

Important: Somatropin must be prescribed by brand.

I request your agreement to continue the care of this patient according to the shared care guideline for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate guideline.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Principles:
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:		**Date:**	
Consultant name:			
Telephone number:		**Fax number**	
Email address			

Continued overleaf

GP please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the shared care guideline.

Signed: …….. Date: …….

GP name: …… *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: …….. Date: …….

Name: