Somatropin for the treatment of growth hormone deficiency in adults (TLS Amber with Shared Care)

Shared Care Guidelines: For the treatment of growth hormone deficiency in adults

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of somatropin (growth hormone) and adults with growth hormone deficiency are 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 as soon as practicable.

Sharing of care assumes communication between the Specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with the condition are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

Introduction

Growth hormone (GH) deficiency has long been recognised and treated as a condition in children. However, since the late 1980's GH deficiency has been recognised as clinical entity in which adults with GH deficiency have impaired quality of life, abnormal body composition, abnormal lipid profile, impaired physical performance and reduced bone mineral density. Some of these patients can benefit from replacement therapy. The most common cause in adults is secondary to pituitary tumours and their treatment. It is estimated that the incidence of deficiency is 1:10,000 and thus a condition, which General Practitioners will now occasionally come in to contact with in the course of their work.

Pharmacology

Somatropin is human growth hormone produced by recombinant DNA technology. GH is normally produced by the anterior pituitary gland. Once released, it binds to specific receptors (expressed mainly in the liver), thereby activating the gene coding for the hormone, insulin-like growth factor-I (IGF-1). It is the IGF-1 that mediates most of the physiological effects of GH.

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Diagnosis of growth hormone deficiency (see Appendix 1). On diagnosis each patient will have a series of tests (indicated in the table) to produce a comprehensive baseline from which any subsequent change can be monitored.
2	Ensure the patient is suitable for treatment according to the NICE guidelines (see Appendix 2).
3	Discuss the benefits and side effects of treatment with the patient.
4	Initiation & supply of growth hormone, adjustment of the dose and assessment of response to therapy during the initial 3 month assessment period will be done by Secondary care.
5	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.
6	To monitor the patient after 9 months and then at least yearly in an endocrinology clinic if they continue on GH after this 9 month initial period.
7	All patients will be taught self-injection technique at the clinic. (Injection devices are available for specific brands of somatropin and are supplied free of charge through the clinic).
8	To provide the GP with written information regarding the treatment plan and test results after each hospital visit.
9	Review the patient's condition every year and monitor response to treatment.
10	To discontinue therapy when appropriate and advise the GP.
11	Report adverse events to the MHRA.
12	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

Monitoring by Secondary care

	Baseline tests	At 3 months	At 9 months	If therapy is to continue: Yearly tests (done in hospital)
Height, weight & body mass index	√	√	√	√
Waist / hip ratio	√	√	√	√
Body composition	√	√	√	√
Blood pressure	√	√	√	√
Lipid profile	√	√	√	√
HbA1c and random blood glucose	√	√	√	√
IGF1	√	At regular intervals during 9 month assessment period, until optimum maintenance dose is reached(the aim is for the dose titration to occur within the first 3 months of therapy) √		
TFTs and T3	√	√	√	√
Quality of life questionnaire	√		√	√

General Practitioner responsibilities	
1	Reply to the request for shared care as soon as practicable.
2	Prescribe brand and dose of somatropin as indicated by the hospital Specialist after the initial 3 month trial assessment period (if the treatment has been successful).
3	Prescribe sharps containers, 1L Sharpsafe® or 1L Sharpsguard®, and advise patient to contact local authority for collection of sharps waste – see additional information at end of SCA.
4	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
5	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6	Stop treatment on the advice of the specialist.
7	Report adverse events to the specialist and MHRA.

Patient's role	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.
4	Store the medication appropriately. Place used syringes, pens and needles in sharps bin provided by GP on prescription and contact local authority to arrange disposal of sharps waste – see additional information at end of SCA.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Email address:
RUH Specialist: Endocrine consultant	Via consultant connect		ruh-tr.endocrinediabetes@nhs.net
RUH Pharmacy Department	01225 825361		ruh-tr.medicines-information@nhs.net

Patient Information Leaflets

These are provided by each individual company that produces GH to accompany the medication. There is also a leaflet produced by NICE on The Use of Human Growth Hormone (somatropin) for Adults with Growth Hormone Deficiency.

SUPPORTING INFORMATION

Summary of condition and licensed indications.

The GH replacement treatments discussed in this document are licensed for use in both children and adults (including GH deficiency; growth disturbance associated with Turner's syndrome or chronic renal disease; small for gestational age – children; replacement therapy in adults with pronounced GH deficiency). Use in the context of this SCA relates to severe GH deficiency in adults. All patients are to be considered for shared care after an initial 3 months of treatment by Secondary care.

Growth Hormone (GH) is released in a pulsatile manner from the pituitary gland with secretion rates peaking during the night. GH release is maximal during the growth spurt of adolescence, after which there is a gradual decline. However in adulthood, GH continues to be produced and play a key metabolic role throughout adult life.

Also see appendices 1 and 2 at the end of this document.

Product Information

Several brands of somatropin currently have licenses for adult administration in the UK.

First line cost effective options include:

- Omnitrope® SurePal (Sandoz) 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution for injection cartridges.
- Humatrope® (Eli Lilly) 6mg, 12mg and 24mg powder with solvent for solution for injection cartridges.
- Genotropin® Injection (Pfizer) 5.3mg and 12mg powder with solvent for solution for injection cartridges.
- Genotropin MiniQuick® Injection** (Pfizer) powder with solvent for solution in pre-filled disposable injection pen. Devices are available in the range 0.2mg/0.25ml – 2mg/0.25ml in increments of 200micrograms.

Other options include:

- Zomacton® (Ferring) 4mg and 10mg powder with solvent for solution for injection vials.
- Norditropin Simplexx (NovoNordisk) 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution for injection cartridges.
- Norditropin Nordiflex (NovoNordisk) 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml solution for injection pre-filled pen.
- Nutropin Aq (Ipsen) 10mg/2ml solution for injection cartridges.
- Saizen (Merck Serono) 6mg/1ml, 12mg/1.5ml and 20mg/2.5ml solution for injection cartridges.

Patients are given a choice of product due to variability in the delivery device however the most cost effective options should be offered first.

Storage Information

Somatropin requires protection from light and storage in a refrigerator (2°C – 8°C). Refer to the correct product SPC on https://www.medicines.org.uk/emc/search?q=somatropin for further information on storage after reconstitution.

MiniQuick syringes are a range of fixed dose, preservative free, disposable devices. These can be stored by the patient before they are reconstituted at temperatures up to 25°C for up to 6 months. They are more expensive than any other brand. **If patients using GH are unable to store their injections in a refrigerator for a short period of time e.g because they are going on holiday, they may temporarily be prescribed MiniQuick syringes. The hospital specialist would normally round the dose up or down to the nearest 200 microgram. The hospital specialist can be contacted for advice on this.

Ancillary products which may need to be prescribed by the GP

Needles and Sharps bins are required for safe delivery of GH therapy. GPs can prescribe a 1L Sharpsafe© or Sharpsguard© bin on FP10s. The patients will use approximately 1 – 2 sharps bins a year and the boxes of needles contain 100 single use needles.

Area	Disposal of cytotoxic waste details	Telephone No.
BANES	Contact Council for sharps waste disposal https://www.bathnes.gov.uk/services/bins-rubbish-and-recycling/recycling-and-rubbish-collections/sharps-collections or https://www.somersetwaste.gov.uk/contact-us/	01225 394041
Wiltshire	Contact Council for sharps waste disposal http://www.wiltshire.gov.uk/rubbishrecycling/householdwaste/sharpsboxesclinicalwaste.htm	0300 456 0102

If GH is set up via the hospital to be delivered via Home Care, then sharps boxes and ancillaries will be included. This service is often available free of charge.

Treatment Schedule (including dosage and administration)
All of these treatments are administered, by the patient, daily by subcutaneous injection in the evening to mimic normal GH release patterns in the body. An initial dose of 0.3mg is prescribed and is then titrated against serum blood levels of insulin like growth factor -1 (IGF-1) by the hospital specialist team, as required.

Contra-indications
Somatropin must not be used when there is evidence of tumour activity (complete antitumour therapy and ensure intracranial lesions inactive before starting); hypersensitivity to the active substance.

Precautions for Use
Diabetes mellitus (adjustment of antidiabetic therapy may be necessary); disorders of the epiphysis of the hip (monitor for limping); history of malignant disease; hypoadrenalism (initiation or adjustment of glucocorticoid replacement therapy may be necessary); hypothyroidism: papilloedema; relative deficiencies of other pituitary hormones; resolved intracranial hypertension (monitor closely); Silver-Russell syndrome.

Pregnancy: There is currently little information on the use of somatropin during pregnancy. If a patient becomes pregnant while using somatropin the hospital Specialist should be informed. Pregnant patients should be managed by Secondary care.

Side-effects
The most commonly reported adverse effects are listed below. Refer to the SPC or BNF for a full list of adverse effects.

- Fluid retention is the most commonly reported side effect of GH replacement therapy. Fluid retention, with occasional mild ankle oedema, is a normal part of GH action. This tends to decrease as therapy continues but if it persists, the Specialist should be informed as it may occasionally require dose reduction.

- Joint and muscle pains, carpal tunnel syndrome and headache have been reported. These effects, if they occur, are usually mild and self-limiting. A reduction in the GH dose may be required while they persist. The Specialist should therefore be informed if the patient is suffering from any of these.

- Rare cases of benign intracranial hypertension have been reported. A severe and persistent headache should be reported immediately to the Specialist.

- Hypothyroidism is a complication, which is not relevant in most patients, who are already receiving thyroxine.

Monitoring
Monitoring is undertaken by Secondary Care (as per the table on P2).

Drug Interactions
In women on oral oestrogen replacement, a higher dose of GH may be required to achieve that treatment goal.

Cost
Based on doses in the range of 200 micrograms to 1mg a day, using the most cost-effective product, Omnitrope® SurePal, the cost of one year's drug treatment is estimated to be between £1110 and £5530.

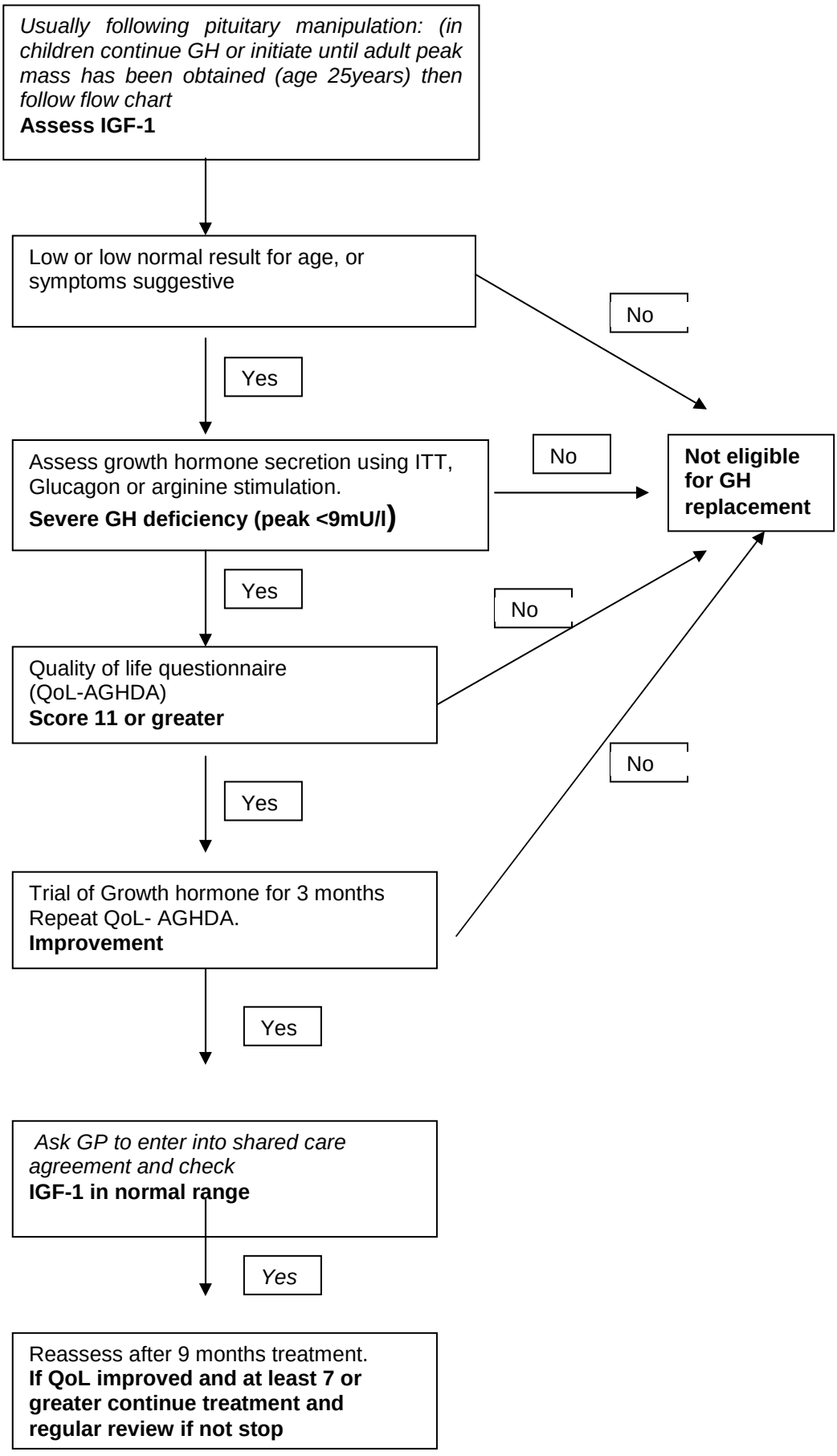
References

1. Electronic BNF accessed online via https://bnf.nice.org.uk/ 13/11/2019
2. SPCs for somatropin accessed online via https://www.medicines.org.uk/emc/search?q=somatropin 13/11/2019
3. NICE Technology Appraisal Guidance [TA64] Human growth hormone (somatropin) in adults with growth hormone deficiency accessed online via https://www.nice.org.uk/guidance/ta64 13/11/2019
4. UKMI Comparison of growth hormone products and devices updated 2016 accessed online via https://www.sps.nhs.uk/articles/comparison-of-growth-hormone-products-and-devices/ on 13/11/2019

Document details

Document review	Date	Whom
First edition	Nov 2009	Dr T Robinson Consultant Endocrinologist and J Reason BCAP interface pharmacist.
Second edition	November 2019	J Forrest BCAP formulary pharmacist – updated to reflect latest licensing positions and include information on sharps disposal.

Appendix 1 – Growth Hormone replacement in adults



Appendix 2

Summary of NICE guidance (NICE TAG 64 August 2003) on human growth hormone (GH) (somatropin) in adults with growth hormone deficiency.

1. NICE recommend GH therapy for the treatment of adults with GH deficiency only if they fulfil all three of the following criteria:
    - a. They have severe GH deficiency, defined as a peak GH response of less than 9mU/litre during an insulin tolerance test or a cross validated GH threshold in an equivalent test.
    - b. They have a perceived impairment of quality of life (QoL), as demonstrated by a reported score of at least 11 in the disease specific 'QoL assessment of GH deficiency in adults questionnaire.'
    - c. They are already receiving treatment for any other pituitary hormone deficiencies as required.

2. NICE state the QoL status of people who are given GH treatment should be reassessed 9 months after initiation of therapy.

OF NOTE: There are, however, two special cases referred to in the NICE guidelines. NICE recommends that:

a. Patients who develop GH deficiency in early adulthood, after linear growth is completed but before the age of 25 years.

b. Patients with childhood onset GH deficiency should have their GH replacement stopped at completion of linear growth for 2 to 3 months, and GH status re-assessed.

Patients falling into either of the two groups listed above (a or b) should receive GH at adult doses if they satisfy the biochemical criteria for severe GH deficiency (section 1 - above) and it should be continued until adult peak bone mass has been achieved (normally around 25 years of age).

In these cases GH will be initiated, and the dose of GH replacement will be adjusted to achieve an IGF-1 level within the appropriate physiological age related range, by the hospital. The hospital specialist will ask the GP to take over the prescribing of GH after a stable dose has been reached until adult peak bone mass has been achieved. The patient will continue to be followed up and monitored at least yearly by the hospital.
Written liaison with the GP will occur after each hospital visit and when there are any changes in therapy.

The hospital specialist will then stop the patient's GH therapy at around the adult peak bone mass acquisition (approximately 25 years of age). The decision to restart GH treatment will be based on the adult criteria (section 1). If eligible, patients will then enter into the ninth month assessment period and efficacy will be assessed according to the adult guidelines.

The monitoring and communication referred to in the rest of these shared care guidelines relates to adult patients fulfilling all the criteria in section 1 (above) and undergoing the 3 month trial assessment period. Shared care will only be considered in this group of patients if this trial is successful.