BSW APC: BaNES, Swindon & Wiltshire (BSW) CCG, Avon & Wiltshire Mental Health Partnership NHS Trust (AWP), Royal United Hospitals Bath NHS Foundation Trust, Great Western Hospitals NHS Foundation Trust, Salisbury NHS Foundation Trust, Virgin Care, Swindon Community Health Services, Wiltshire Health & Care

SHARED CARE AGREEMENT

Somatropin for the treatment of growth hormone deficiency – Adults

Amber TLS – 3 Months

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and in the patient's best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) concerned and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

Responsibilities of Secondary Care Specialist

Specific to this Shared Care Agreement (SCA)

- Initiate treatment and prescribe for the length of time agreed – this should be a sufficient amount of time to allow optimisation of treatment and demonstrate that the patient's response is consistent. For patients naïve to growth hormone, this takes 9 months to ensure patients fulfil NICE criteria to remain on somatropin therapy.
- Ensure patient is established on appropriate preparation/injection device and that they have been trained to self-inject and assessed as competent.
- Ensure patient aware of arrangements for sharps disposal and collection (see also link to BSW document in section 16)
- Arrange outpatient follow up at clinically appropriate interval. Typically at least annually.
- Arrange for relevant multidose device to be provided and to provide replacement devices if required.

General

- Discuss the benefits and side effects of treatment with the patient.
- Review concurrent medications for potential interactions prior to initiation.
- Undertake the clinical assessment and relevant monitoring at baseline and during the initiation period.
- Communicate details of treatment to GP (in writing or via secure email) within the first month of treatment and ask the GP whether he or she is willing to participate in shared care.
- Discuss shared care arrangements with the patient/carer, obtain their consent and explain their responsibilities.
- Review the patient's condition and monitor response to treatment regularly where indicated.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Supply GP with clinic letter or discharge summary within 14 days of an outpatient review or inpatient admission, and inform GP if patient does not attend scheduled clinic appointments.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Report adverse events to the MHRA.
- Stop treatment where appropriate or provide GP with advice on when to stop.

Responsibilities of GP/Primary Care Prescriber

- Reply to the request as soon as practicable if they are **unable** to support shared care (in writing or via secure email).
- Prescribe medicine at the dose recommended after the initiation period. Issue FP10 prescriptions for appropriate sharps containers and reinforce advice on arrangements for collection of sharps waste collection (see also link to BSW document in section 16)

- Undertake ongoing clinical assessment and relevant monitoring following initiation period. In practice all routine monitoring will be undertaken by specialist at annual review.
- Review any new concurrent medications for potential interactions.
- 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.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Report adverse events to the specialist and MHRA.
- Stop treatment on the advice of the specialist.

Responsibilities of Patient/Carer

- Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
- Share any concerns in relation to treatment with medicine.
- Report any adverse effects to the specialist or GP whilst taking the medicine.
- Attend appointments for clinical review and monitoring.

1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	Growth hormone (GH) is produced by the anterior pituitary gland. It has a role in the regulation of protein, lipid and carbohydrate metabolism, as well as in increasing growth in children. Its secretion is intermittent and occurs predominantly during deep sleep. Secretion reaches maximal levels during adolescence, and then declines with age by approximately 14% per decade. Adult GH deficiency may be of adult onset or childhood onset, and may occur as isolated GH deficiency or as part of multiple pituitary hormone deficiency. In adult onset, GH deficiency is commonly due to pituitary tumours or their treatment, and to cranial irradiation. Childhood-onset GH deficiency is often idiopathic, and may continue into adulthood. Also, iatrogenic GH deficiency may occur in childhood or adulthood in survivors of childhood malignancy, as a result of previous cranial irradiation and/or chemotherapy. The prevalence of adult-onset GH deficiency is approximately 1 in 10,000 of the adult UK population. If adults with childhood-onset GH deficiency are also considered, the prevalence may be as high approximately 12,600 adults with GH deficiency in England and Wales. GH deficiency in adults may be associated with the following adverse features to a variable degree in any individual: reduced quality of life (QoL) especially reduced energy levels; altered body composition (reduced lean mass and increased fat mass, especially in the trunk); osteopenia/osteoporosis (reduced bone mineral density); dry skin (reduced sweating); reduced muscle strength and exercise capacity; lipid abnormalities (especially elevated LDL cholesterol); insulin resistance; increased levels of fibrinogen and plasminogen activator inhibitor; reduced extracellular fluid volume; increased thickness of the intima media of blood vessels; and impaired cardiac function. Several tests are available for the diagnosis of GH deficiency. The Insulin Tolerance Test (ITT) is regarded as the 'gold standard' test for adults. A general definition of severe GH deficiency in adults is a peak concentration of less than 9 mU/litre (3 nanogram/ml) in response to insulin-induced hypoglycaemia. When the ITT is contraindicated other tests such as GH-releasing hormone-arginine test or glucagon stimulation test can be is in used. The clinical management of GH deficiency in adults is centred on replacement therapy with biosynthetic human GH (somatropin).

	See also NICE TA64 Human growth hormone (somatropin) in adults with growth hormone deficiency, via www.nice.org.uk/guidance/ta64, for additional information.
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	Somatropin is a potent metabolic hormone of importance for the metabolism of lipids, carbohydrates and proteins. In children with inadequate endogenous GH, somatropin stimulates linear growth and increases growth rate. In adults, as well as in children, somatropin maintains a normal body composition by increasing nitrogen retention and stimulation of skeletal muscle growth, and by mobilization of body fat. Visceral adipose tissue is particularly responsive to somatropin. In addition to enhanced lipolysis, somatropin decreases the uptake of triglycerides into body fat stores. Serum concentrations of IGF-I, and IGFBP3 (Insulin-like Growth Factor Binding Protein 3) are increased by somatropin. In addition, the following actions have been demonstrated: - Lipid metabolism: Somatropin induces hepatic LDL cholesterol receptors, and affects the profile of serum lipids and lipoproteins. In general, administration of somatropin to GH deficient patients results in reductions in serum LDL and apolipoprotein B. A reduction in serum total cholesterol may also be observed. - Carbohydrate metabolism: Somatropin increases insulin but fasting blood glucose is commonly unchanged. Children with hypopituitarism may experience fasting hypoglycemia. This condition is reversed by somatropin. - Water and mineral metabolism: GH deficiency is associated with decreased plasma and extracellular volumes. Both are rapidly increased after treatment with somatropin. Somatropin induces retention of sodium, potassium and phosphorus. - Bone metabolism: Somatropin stimulates the turnover of skeletal bone. Long-term administration of somatropin to growth hormone deficient patients with osteopenia results in an increase in bone mineral content and density at weight-bearing sites. - Physical capacity: Muscle strength and physical exercise capacity are improved after long-term treatment with somatropin. Somatropin also increases cardiac output, but the mechanism has yet to be clarified. A decrease in peripheral vascular resistance may contribute to this effect. **There are six brands of somatropin available in the UK for the treatment of adults each with a number of presentations.** **Genotropin® (Pfizer)** - 0.2mg, 0.4mg, 0.6mg, 0.8mg, 1mg, 1.2mg, 1.4mg, 1.6mg, 1.8mg & 2mg MiniQuick - 5.3mg & 12mg powder and solvent (for use in prefilled GoQuick multidose device) - 5.3mg & 12mg powder and solvent (for use in Genotropin Pen multidose device) **Humatrope® (Eli Lilly)** - 6mg, 12mg & 24mg powder and solvent (for use in compatible CE marked pen injection systems) **Norditropin® (Novo Nordisk)** - 5mg/1.5ml, 10mg/1.5ml & 15mg/1.5ml FlexPro multidose prefilled device) - 5mg/1.5ml, 10mg/1.5ml & 15mg/1.5ml NordiFlex multidose prefilled device) **NutropinAq® (Ipsen)** - 10mg/2ml (for use in NutropinAqPen) **Omnitrope® (Sandoz)**

<table>
<tr><td></td><td colspan="2">
- 5mg/1.5ml, 10mg/1.5ml & 15mg/1.5ml Surepal cartridges (for use in SurePal multidose devices) *Note different strengths are intended for specific SurePal devices (5, 10 & 15) and not interchangeable*

Saizen® (Merck)
- 6mg/1.03ml, 12mg/1.5ml & 20mg in 2.5ml solution for injection cartridges (for use in EasyPod device. EasyPod uses SeroFine needles which cannot be substituted. Merck funds ongoing supplies of these via the homecare provider. The initiating Specialist/Trust will register patients for homecare. When transferring the drug element for Shared Care, the homecare account is changed to a 'stores only' account. The patient can contact the homecare provider directly for ancillaries (needles/batteries) which are posted via courier and charged to Merck.)

GH generally require refrigerated transport and storage (2 – 8°C). Check individual SPC Storage requirements may be relevant if there is a change in patient requirements, i.e. during periods of travel. In these circumstances, the hospital specialist can be contacted for advice regarding a change in growth hormone preparation that can be administered without need to re-titrate dose or make additional monitoring arrangements.

Choice of product is in part dependent on patient preference/ability to use devices available. The most cost effective option should be offered first.
</td></tr>
<tr><td rowspan="4">3. Pharmaceutical aspects</td><td>Route of administration:</td><td>Subcutaneous injection</td></tr>
<tr><td>Formulation:</td><td>See above</td></tr>
<tr><td>Administration details:</td><td>Subcutaneous injection</td></tr>
<tr><td>Other important information:</td><td>N/A</td></tr>
<tr><td>4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy
Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results.
All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
The duration of treatment will be determined by the specialist, based on clinical response and tolerability.
Termination of treatment will be the responsibility of the specialist.</td><td colspan="2">
Dose titrated and device/preparation established before patient referred for on-going support via Shared Care Agreement.

Administration is once daily by subcutaneous injection in the evening to mimic normal hormone release patterns.

See individual SPC for dosing advice. Typically;
- Adults continuing after childhood Growth Hormone Deficiency (GHD) 0.2 – 0.5 mg (200 – 500 micrograms) per day
- In adults with adult-onset Growth Hormone Deficiency (GHD) 0.15 – 0.4 mg (150 – 400 micrograms) per day
- In adults over 60 years of age 0.1 – 0.2 mg (100 – 200 micrograms) per day

All doses are titrated against serum blood levels of insulin like growth factor-1 (IGF-1). IGF-1 levels decrease with age and there are age related reference ranges specific to the assay used. Therefore as patients age, their somatropin dose requirements may decrease. This will be monitored and adjusted by their specialist.
</td></tr>
</table>

5. Baseline investigations, initial monitoring and annual surveillance to be undertaken by specialist

Baseline investigations and monitoring

- See summary table below. Summary relates to monitoring within secondary care. As per section 6 no routine monitoring required within primary care.

	Baseline	3-6 months	9 months	Annual
Height, weight & body mass index	✓	✓	✓	✓
Waist / hip ratio	✓	✓	✓	✓
Body composition	✓	✓	✓	✓
Blood Pressure	✓	✓	✓	✓
Lipid Profile	✓	✓	✓	✓
HbA1c and random blood glucose	✓	✓	✓	✓
IGF1	✓	See note*		✓
TSH and FT4	✓	✓	✓	✓
Quality of life questionnaire (QoL AGHDA)	✓	-	✓	

* IGF1 assessed at regular intervals during 9 month assessment period and until optimum maintenance dose is reached and with the aim to titrate dose within first 3 months of treatment.

6. Ongoing monitoring requirements to be undertaken by primary care

Monitoring	Frequency
• Nil routine.	• N/A

7. Action(s) to be taken by primary care if abnormal result(s)

- N/A as no routine monitoring within primary care.
- Contact relevant endocrinology service (section 13) if any suspected adverse reactions relating to treatment or any associated clinical concerns.

8. Cautions and contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.

See https://bnf.nice.org.uk/drug/somatropin.html

Cautions

- 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);
- Papilloedema;
- Resolved intracranial hypertension (monitor closely);
- Risk of hypothyroidism—manufacturers recommend periodic thyroid function tests;
- Known hypothyroidism – Levothyroxine demand can change on initiation of somatropin or at times of dose alteration
- Experience in patients with Silver-Russell syndrome is limited.

Contraindications

- Evidence of hypothalamic-pituitary tumour activity (complete antitumour therapy and ensure intracranial lesions inactive before starting);
- Malignancy: somatropin should be discontinued on diagnosis with malignancy
- Not to be used after renal transplantation;
- Severe obesity or severe respiratory impairment in Prader-Willi syndrome

<table>
<tr><td>9. Significant medicine and food interactions and management
For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)</td><td colspan="2">See https://bnf.nice.org.uk/interaction/somatropin-2.html
• Glucocorticoids may reduce effects of somatropin.
• Patients receiving oral oestrogen replacement may require a higher somatropin dose.</td></tr>
<tr><td rowspan="5">10. Adverse effects and management
Include details of incidence, identification, importance and management.</td><td>Adverse Effect</td><td>Action to be taken if detected</td></tr>
<tr><td>• 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.</td><td>• This tends to decrease as therapy continues but if it persists, the Specialist should be informed as it may occasionally require dose reduction.</td></tr>
<tr><td>• Joint and muscle pains, carpal tunnel syndrome and headache have been reported.</td><td>• 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.</td></tr>
<tr><td>• Uncommon cases of benign intracranial hypertension have been reported.</td><td>• A severe and persistent headache, visual problems, nausea/vomiting should be reported immediately to the Specialist. Consider fundoscopy for papilloaedema.</td></tr>
<tr><td>• Hypothyroidism</td><td>• Patients with unknown hypothyroidism developing this after starting somatropin require initiation on Levothyroxine. FT4 levels should be used to guide dosing as TSH can be misleading in pituitary disorders, the Specialist can be consulted for advice. Those with known hypothyroidism may have a drop or rise in their FT4 levels and require Levothyroxine dose adjustments, the Specialist will advise on this.</td></tr>
<tr><td>11. Advice to patients and carers
The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.</td><td colspan="2">• NICE Patient Information Leaflet on treatment is available via https://www.nice.org.uk/guidance/ta64/resources/the-use-of-human-growth-hormone-somatropin-for-adults-with-growth-hormone-deficiency-pdf-371615005</td></tr>
<tr><td>12. Pregnancy and breast feeding
It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.</td><td colspan="2">• Not recommended and limited information available.
• Not eligible for shared care during either pregnancy or breastfeeding.
• Somatropin should be discontinued if patient becomes pregnant until breast feeding complete. Will require specialist advice on restarting.
• Refer to specialist for advice if patient become pregnant or if conception is planned.</td></tr>
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<tr><td>13. Specialist contact information</td><td>Other Specialist Contact Information

<table><tr><td>Contact details</td><td>Telephone No.</td><td>Email address:</td></tr><tr><td>GWH Endocrinology</td><td>-</td><td>Use Cinapsis app</td></tr><tr><td>RUH Endocrinology</td><td>Via consultant connect</td><td>ruh-tr.endocrinediabetes@nhs.net</td></tr></table></td></tr>
<tr><td>14. Additional information
For example, process for when Specialist or GP changes roles; specific issues related to patient age/ capacity/ specific monitoring.</td><td>• Somatropin is a Schedule 4 (CD Anab) Controlled drug. See link in section 16 to BNF advice on prescription requirements.
• See individual product SPCs for storage advice and in use expiries. Generally all somatropin preparations require refrigeration (2 – 8°C) prior to and during use.
•</td></tr>
<tr><td>15. References</td><td>• Summary of Product Characteristics for (accessed June 2021) via https://www.medicines.org.uk/emc
• BNF online (accessed June 2021) via https://bnf.nice.org.uk/
• NICE Technology appraisal guidance [TA64] Human growth hormone (somatropin) in adults with growth hormone deficiency via www.nice.org.uk/guidance/ta64</td></tr>
<tr><td>16. To be read in conjunction with the following documents</td><td>• NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
• BSW Guidance – Sharps Disposal and Prescribing Sharps Bins on FP10. Accessed via: https://prescribing.bswccg.nhs.uk/wpdm-package/bsw-guidance-sharps-disposal-and-prescribing-sharps-bins-on-fp10
• Accessed via: https://bnf.nice.org.uk/guidance/controlled-drugs-and-drug-dependence.html</td></tr>
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Date Last Updated:	May 2022
Date Approved by BSW:	27/05/22
Review Date:	August 2023
Document Version:	V1.1
Document history	Minor update May 2022 to product information

Shared Care Agreement template adapted with agreement from AWP by Rachel Hobson, October 2020. Version 1.0