Human Growth Hormone (Somatropin)
Prescribing Support Information

What is Growth Hormone?

Growth Hormone (GH) is available as a biosynthetic and biosimilar growth hormone with a sequence identical to human pituitary GH. Since the withdrawal of cadaveric (pituitary) GH in 1985 after the association with a slow virus infection was appreciated (Jacob Creutzfeld Disease), biosynthetic and biosimilar GHs are the only preparations available in the United Kingdom. Biosynthetic GHs are made from either E.Coli bacteria (Eli Lilly, Ferring, Ipsen, Novo Nordisk and Pfizer) or a mammalian cell line (Serono), which act as hosts to recombinant plasmids containing the human GH gene. Biosimilar GHs (Sandoz) are made with similar processes and in general should show similar physicochemical properties, along with bio equivalence, to the established biosynthetic preparations.

NICE Guidance - Children

NICE TA188: Human Growth Hormone (Somatropin) for treatment of growth failure in children

Somatropin is recommended as a treatment option for children with growth failure associated with any of the following conditions:

Growth hormone deficiency (GHD)

Turner syndrome (TS)

Prader–Willi syndrome (PWS)

Chronic renal insufficiency (CRI)

Born small for gestational age with subsequent growth failure at four years of age or later (SGA)

Short stature homeobox-containing gene deficiency (SHOXD).

Treatment with somatropin should always be initiated and monitored by a paediatrician with specialist expertise in managing growth hormone disorders in children. 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.

NICE Guidance - Adults

NICE TA64: Human growth hormone (somatropin) in adults with growth hormone deficiency

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

• 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.

• 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.

• They are already receiving treatment for any other pituitary hormone deficiencies as required.

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 tumors 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.

Prescribing

Prescribing may be via homecare provider or GPs may be asked to prescribe.

When will GPs be asked to prescribe?

Funding approval process - Clinicians will seek funding approval before commencing treatment using the prior approval proforma via Bluteq.

Initiation of GH treatment, including choice of preparation, dose titration and assessment of response during trial periods should be undertaken by a consultant endocrinologist or paediatrician with a special interest in the management of GH disorders. Thereafter, if maintenance treatment is to be prescribed it may be transferred to GP prescribing with the initiating specialist ensuring the patient or their carer has been trained to administer the injections and ongoing support is provided by the specialist.

As per The East Of England Priority Advisory Committee ‘PAC’ guidance statement, for any paediatric patient who chooses to use Norditropin SimpleXx or Nordiflex the growth hormone prescriptions will be provided via secondary care.

Preparations available

Genotropin	- Genotropin Pen 5.3mg and 12mg
	- Go Quick pen 5.3mg and 12mg
	- MiniQuick In increments of 0.2mg
Norditropin	-.Norditropin SimpleXx 5mg, 10mg and 15mg pens
	- Nordiflex
Omnitrope	- SurePal 5mg, 10mg and 15mg pens

Humatrope	- 6mg, 12mg and 24mg pens
Zomacton	- Zomaject 2 vision 4mg
	- Zomaject Vision X 10mg
Saizen	- 6mg, 12mgand 20mg cartridges for use with the Easy Pod
Nutropin Aq	- 10mg

Recommended Growth Hormone Preparations <u>for children</u> as per 'PAC' guidance statement

The East of England Priorities Advisory Committee (PAC) have worked with clinical leads in the East of England to agree a list of recommended products for use in the majority of patients whilst still providing patient choice, and criteria for where the use of more expensive products can be justified.

Group 1 products: Preferred products for use in the majority of patients

These products provide a range of core features, are cost effective, and are the preferred products for use in the majority of patients. The rationale for product selection is outlined below:

- **Omnitrope products** (SurePal, Omnitrope Pen): Currently the least costly products.
- **Genotropin products** (Genotropin pen, GoQuick, Miniquick): These provide a range of devices including a pre-filled pen and a disposable device for travelling. The Miniquick can be stored out of the fridge for up to 6 months.
- **Norditropin SimpleXx and Nordiflex pre-filled pen**: Does not require fridge storage once in use and therefore is useful for children whose care is split between homes or whose lifestyle makes fridge storage difficult. Device has an auto needle inserter which helps to facilitate self-injection. This product is currently significantly more expensive in primary care and therefore, if chosen, prescribing should be retained in secondary care.
- **Humatrope** (HumatroPen) (for SHOX deficiency)

Group 2 products: Products for use in patients with specific needs

The following products are more costly options but have features that provide significant benefits to a cohort of patients: The rationale for product selection is outlined below:

- **Zomacton VisionX needle free**: Needle free device for use in patients with a confirmed needle phobia.
- **Saizen Easypod 3**: This is a larger device which may benefit patients who may have difficulty in handling the smaller devices. It allows monitoring of compliance and is

lockable to prevent dose tampering so may be useful for patients where there are concerns around compliance and safety. The device has a hidden needle and auto inserter making the whole process invisible and which may be necessary to aid compliance in some patients. The Easypod can be kept out of the fridge for up to 7 days.

Group 3 products: not for routine use:

The following products are more costly options and do not offer significant advantages over preferred products in groups 1 & 2. The clinician should offer reasons for choosing group 3 products over products in groups 1 & 2.

NutropinAq pen

Stopping Criteria – Children

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 2cm total growth in one year.
- There are insurmountable problems with adherence.
- Final height is attained.
- Treatment should not be discontinued by default.

The decision to stop treatment should be made in consultation with the patient and/or carers either by:

- A paediatrician with specialist expertise in managing growth hormone disorders in children, or
- An adult endocrinologist, if care of the patient has been transferred from paediatric to adult services.

INFORMATION FOR PRESCRIBING

Contraindications

- avoid injections containing benzyl alcohol in neonates
- evidence of tumor activity (complete antitumor therapy and ensure intracranial lesions inactive before starting)
- not to be used after renal transplantation
- not to be used for growth promotion in children with closed epiphyses (or near closure in Prader-Willi syndrome)
- severe obesity in Prader-Willi syndrome
- severe respiratory impairment in Prader-Willi syndrome
- Critically ill patients (heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions).
- Patients with known hypersensitivity to GH or to any of the excipients.
- Pregnancy or lactation.

Cautions

- Diabetes mellitus (adjusting of antidiabetic therapy may be necessary)
- Disorders of the epiphysis of the hip (monitor of limping)
- History of malignant disease
- Hypothyroidism
- initiation of treatment close to puberty not recommended in child born small for corrected gestational age;
- Papilloedema
- Resolved intracranial hypertension (monitor closely)
- Silver-Russell syndrome

What are the main side-effects?

- Growth hormone deficient patients are characterised by extracellular volume deficit. When treatment with somatropin is initiated, this deficit is corrected. Fluid retention with peripheral oedema may occur.
- In case of severe or recurrent headache, visual problems, nausea and/or vomiting, a funduscopy for papilloedema is recommended. If papilloedema is confirmed, a diagnosis of benign intracranial hypertension should be considered and, if appropriate, the growth hormone treatment should be discontinued.
- Carpal tunnel syndrome is uncommon but may be seen in adults. The symptoms are usually transient, dose dependent and may require transient dose reduction.
- Other mild side effects include headache, myalgia, mild hypertension, visual problems, and nausea/vomiting.
- The safety record is excellent. No serious side effects have been recognised to date. There is no possibility of contamination with a slow virus as occurred with preparations of pituitary-derived growth hormone.
- Antibody formation can be detected but is rarely, if ever, of physiological relevance.
- Local injection site reactions are unusual and are generally due to unnecessary use of a spirit-based skin cleanser.
- GH is potentially diabetogenic (insulin resistance, hyperglycaemia, hypoglycaemia) but international studies have shown that the incidence of permanent diabetes is not increased with treatment.
- Extensive surveys have failed to demonstrate an increase in any form of malignant disease. Some children selected to receive GH will have had cancer and may be at risk of primary tumour recurrence or a secondary tumour; no increased risk of such events has been demonstrated with growth hormone treatment.

Drug Interactions

- Growth promoting effect may be inhibited when combined with corticosteroids.

- Increased doses of GH may be required if on oestrogen replacement therapy. Conversely the dose of GH may need to be reduced if oestrogen is stopped.
- Anti-diabetic therapy may require adjustment.

Monitoring

Biosynthetic human growth hormone has a good safety record and frequent monitoring is not required**. Monitoring is performed in secondary care only.**

Monitoring during therapy Children	
Growth and general condition	Every three to six months. Accurate monitoring of height and weight
Bone age assessment	Every 12 months
Hormone measurement	As indicated; dose to be reviewed if necessary.
Dose Adjustment	Dose to be reviewed if necessary based on surface area

Adults will be reviewed in hospital at least annually, growth hormone requirements may decrease with age.

References

NICE technology appraisal guidance [TA188]. Published date: May 2010. Human growth hormone

(somatropin) for the treatment of growth failure in children. https://www.nice.org.uk/guidance/ta188

BNF online www.medicinescomplete.com

The East of England Priorities Advisory Committee Guidance statement, Recommendations on the use of growth hormone devices in children. Approval date 11th January 2016

Adapted from Cambridge and Peterborough CCG