



## Shared Care Guidelines: Paediatric use of Recombinant human Growth Hormone (r-hGH, Somatropin)

### General Guidance:

Shared care is the mechanism of sharing patient care between primary and secondary care providers. Sharing of care assumes good communication between the patient and all professionals in primary care (GP) & secondary care (hospital consultant, specialist nurses, pharmacist etc). The intention to share care with a GP should be explained to the patient and their carers by the specialist initiating treatment and an outline of responsibilities provided.

**The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. If a GP is invited by a specialist to participate in a shared care arrangement and is not confident to undertake these roles, then he or she is under no obligation to do so, but should discuss this with the specialist as soon as possible.**

### Shared Care Criteria

Treatment with r-hGH should always be initiated and monitored by a specialist (Consultant Paediatric Endocrinologist or Consultant Paediatrician with expertise in growth disorders) as recognised by the British Society for Paediatric Endocrinology and Diabetes (BSPED). Prescribing should be in keeping with guidelines for r-hGH usage in children published by the National Institute for Clinical Excellence (NICE).

### General Guidelines for Shared Care Strategy:

1. Patients started on r-hGH therapy require specialist supervision and review in a growth/endocrine clinic 2-3 times a year.
2. r-hGH has a good safety record and is licensed for use in children fulfilling criteria laid down by NICE and covered in the supporting document.
3. Dose adjustments will be required intermittently and should be instigated by the supervising Consultant based on changes in height, weight and IGF 1 levels.
4. Updates should be communicated to the GP by the supervising Consultant following every clinic visit.

### Specialist / Consultant Responsibilities:

1. To undertake necessary testing to confirm a diagnosis that requires r-hGH treatment, as indicated by NICE guidance.
2. To provide GP with written information regarding the diagnosis and indication for r-hGH therapy along with dosage and preparation to be used.
3. To supervise training of patients and families with r-hGH injections, liaise with GP about local arrangements necessary for instigation of therapy and identify any possible barriers to treatment.
4. To monitor patient's growth, pubertal development, assessment of any other ongoing or evolving endocrinopathy and general condition at 4-6 monthly intervals following instigation of therapy and to advise about dose and/or preparation changes.
5. Strict adherence to published NICE guidance for initial prescription of r-hGH and monitor ongoing r-hGH therapy.
6. To supervise the timing for cessation of treatment at final height, reassessment and transition to adult endocrine care where necessary.

### General Practitioner Responsibilities:

1. To prescribe r-hGH as advised by the supervising Consultant and, where local practice dictates, discuss with the local Prescribing Advisor; feedback to the consultant any concerns regarding r-hGH prescribing and/or shared care.
2. To monitor patient's overall health and well-being.
3. To report any adverse effects of therapy to the supervising Consultant or deputy.

**Patient/Parent Responsibilities**

1. To ensure they have clear understanding of the prescribed treatment.
2. To administer the r-hGH as directed by the supervising Consultant; attend clinic reviews as requested.
3. To share any concerns in relation to treatment with the supervising Consultant and/or GP.
4. To report any adverse effects to the supervising Consultant and/or GP whilst taking r-hGH.

**GP & Hospital Communication:**

In case of concern regarding any aspect of a patient's care, please contact the supervising Consultant or deputy as soon as possible.

Name	Phone Number	Fax Number	Email address
Consultant:			
Specialist Nurse:			
Other			

## Supporting information for recombinant human Growth Hormone (r-hGH, Somatropin) usage in children.

For full guidance, readers should refer to published guidelines from NICE on use of r-hGH in children <http://guidance.nice.org.uk/TA188/Guidance/pdf/English>. r-hGH is administered by subcutaneous injection or needle free transjection, once daily. Depending on the brand, injections may be prepared from multi-dose ampoules or by using cartridges in a multi-dose pen injection device or other disposable devices. r-hGH has a role in protein, lipid and carbohydrate metabolism, in addition to increasing linear growth in children.

### Licensed Indications for r-hGH therapy, as approved by NICE

1. Growth failure in children with growth hormone insufficiency/deficiency (GHD):
  - Idiopathic isolated GHD
  - Congenital hypopituitarism e.g. anomalies of the pituitary gland such as septo-optic dysplasia.
  - Acquired hypopituitarism e.g. craniopharyngioma, post cranial irradiation, neuro-surgery or traumatic brain injury
2. Growth failure in girls with Turner Syndrome (confirmed by chromosome analysis).
3. Growth failure in children with chronic renal failure (CRF).
4. Poor growth and body composition in children with Prader-Willi Syndrome (confirmed by chromosome analysis).
5. Growth failure in children born Small for Gestational Age (SGA) (defined as birth length SDS <-2 or birth weight SDS <-2) :
  - Growth disturbance (current height SDS <-2.5 and parental adjusted height SDS <-1) in short children born SGA who fail to show catch up growth by 4 years.
6. Growth failure associated with SHOX deficiency (confirmed by DNA analysis).

### Diagnostic Criteria for GHD in Children

The early recognition of growth failure is an essential component of a national strategy leading to rational and effective use of r-hGH. Monitoring of growth (height & weight) should be part of all childhood health surveillance in primary care and in school.

The diagnosis is based on a combination of the following:

1. Short stature that is inappropriate for the parental height.
2. Subnormal growth rate: i.e. height velocity below 25<sup>th</sup> centile.
3. Association with other pituitary hormones deficiency, as in multiple pituitary hormone deficiency.
4. Growth delay confirmed by delayed skeletal maturation (bone age).
5. Clinical and/or imaging evidence of a structural disorder of the hypothalamo-pituitary axis; this includes previous cranial irradiation.
6. Exclusion of other genetic, psychosocial and systemic causes of growth failure.
7. Biochemical evidence of GHD to provocation testing. Consideration should be given to neurosecretory dysfunction of GH release where provocation testing may reveal a normal response but other evidence suggests a diagnosis of GHD.

### Growth Hormone Dosage (calculated in mcg/kg/day or mg/m<sup>2</sup>/day)

Indication	Dose – mcg/kg/day	Dose – mg/m <sup>2</sup> /day
GHD	23–39	0.7-1.0
Turner Syndrome	45-50	1.4
Chronic Renal failure	45-50	1.4
Prader-Willi Syndrome	35	1.0
Small for Gestational Age	35	1.0
SHOX deficiency	45-50	1.4

### Adverse Effects

In general side effects of r-hGH therapy are rare. These include:

1. Transient skin reactions and loss or increase of adipose tissue at injection sites can occur, particularly if the injection sites are not rotated.

2. r-hGH can lead to fluid retention and peripheral oedema in adults, but less common in children. Fluid retention may play a role in the generation of raised intra-cranial pressure (benign intra-cranial hypertension). This may occur at the onset of r-hGH therapy and is associated with severe headache and papilloedema; in such circumstances r-hGH therapy is discontinued for 2–3 weeks and then recommenced at a lower dose and gradually increased to the full dose. If the patient is undergoing major surgery, r-hGH should be stopped as a precaution.
3. Slipped upper femoral epiphysis (SUFE) is anecdotally recognised and hence patients on hGH should be clinically monitored for limping or other hip problems. Xray imaging is indicated if SUFE is suspected to determine if referral to an orthopaedic surgeon is required.
4. r-hGH therapy is associated with insulin insensitivity; there is a rise in serum insulin concentrations but blood glucose & glycated haemoglobin concentrations usually remain within normal limits. Consequently, patients with diabetes mellitus taking r-hGH may need their diabetic therapy adjusted. Consideration also needs to be given to the possible unmasking of diabetes in patient groups with a family history of Type 2 diabetes mellitus, and unmasking of potential ACTH deficiency.
5. r-hGH may cause worsening of scoliosis due to increasing spinal growth, if scoliosis is already present. Spinal curvature will need to be monitored in such cases and if clinically detected, may require referral to a spinal surgeon for further evaluation.

### **Safety record**

In general r-hGH has an excellent safety record; although antibody formation can be detected, this is rarely of physiological relevance.

### **Risk of Neoplasia:**

Extensive surveys have **not** suggested any increased risk of tumours or leukaemia with r-hGH therapy compared with similar patients who have not received therapy when replacement doses are physiological in confirmed GHD. Supra-physiological doses have not been assessed. Concern has been expressed following a report from the UK that young adults treated with human pituitary GH up until 1985 had a higher mortality risk for colon cancer and non Hodgkin lymphoma than the general population (Swerdlow AJ et al, Risk of cancer in patients treated with human pituitary growth hormone in the UK, 1959-85: a cohort study. Lancet 2002; 360: 273-7). However, these data were collected on patients on high doses of human pituitary derived GH which may have also contained other growth factors. Although these data raise concern, **they do not provide firm evidence of an association**. Long-term surveillance of patients receiving r-hGH therapy irrespective of diagnosis is continuing through National Cancer Registries.

**Prader Willi Syndrome (PWS):** PWS is a rare genetic disorder. In the first year of life it is characterised by hypotonia and failure to thrive, but in later years severe obesity may ensue. These children usually have short stature, which is now generally accepted to be associated with GHD. Randomised controlled studies of r-hGH in PWS have demonstrated an increase in short term linear growth analogous to that seen in patients with GHD. The r-hGH dosing schedule is similar to that used in GHD. Data on final heights are now becoming available and are similar to those observed in GHD patients. Although the value of increasing the stature of these individuals can be questioned, the effect of r-hGH treatment on body composition is perhaps of greater importance. r-hGH therapy leads to a decrease in fat mass and an increase in lean body mass. The latter is less obvious in PWS but is in contrast to the reports of increased muscle strength and agility. The observation of improved respiratory muscle function is of particular importance in these individuals. To date the safety profile of growth hormone in PWS is similar to that observed in the GHD child. However, in severely obese patients with PWS and those with sleep apnoea, careful consideration needs to be given to r-hGH as potential risk of sudden death has been reported. Sleep studies and ENT opinions are now recommended prior to commencement of r-hGH therapy in children with PWS.

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