WORKING IN PARTNERSHIP WITH

Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath) North East Hampshire & Farnham CCG and Crawley, Horsham & Mid-Sussex CCG

SHARED CARE PRESCRIBING GUIDELINE

Growth hormone for the Treatment of growth hormone deficiency in adult patients

Prescribing Clinical Network classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this guideline & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the GP

Amber drugs: Prescribing to be initiated by a hospital specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs.

The questions below will help you confirm this:
- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of page 4 to the requesting consultant at the Acute Trust. Until the requesting consultant at the Acute Trust has received a signed copy of page 4 indicating that shared care has been agreed all care (including prescribing) remains with the consultant at the Acute Trust.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your practice support pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber’s professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient’s best interests are always paramount

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant.
Information:
Growth hormone deficiency in adults results from decreased production of somatropin (growth hormone (GH)) from the anterior pituitary gland. It usually occurs as a consequence of a structural pituitary disease or peripituitary lesion (e.g. pituitary adenoma), or as a result of the treatment (e.g. cranial irradiation or surgery). The prevalence of adult-onset GH deficiency is approximately 1 in 10,000 of the adult UK population. Growth hormone replacement is initiated in the following circumstances as per NICE guidelines: (NICE TA 64 [www.nice.org.uk/TA064

Human growth hormone (somatropin) in adults with growth hormone deficiency.
Which states that treatment is recommended for the treatment of adults with growth hormone deficiency only if they fulfil all three of the following criteria?

1. Patient has severe GH deficiency, defined as a peak GH response of less than 9mU/litre (3ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test.
2. Patient has a perceived impairment of quality of life 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. Patient is already receiving treatment for any other pituitary hormone deficiencies as required.

Nine months after initiation of therapy and ongoing monitoring, patients are reassessed and GH is only continued in those patients who demonstrate a QOL improvement of more than 7 points in the AGHDA score.

This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

Link to the relevant SPC website: [www.medicines.org.uk/emc

Dose
The dose range is 150 micrograms to 300 micrograms daily, gradually increased if required to a maximum of 1mg daily; minimum effective dose should be used (requirements may decrease with age).

Patients should be taught how to administer by the initiating specialist service. Physiological GH release peaks during sleep therefore the injection should be given in the evening before bedtime.

A recognised technique for monitoring the GH dose is to take regular measurements of serum insulin-like growth factor 1 (IGF-1). IGF-1 levels should increase during therapy.

The aim is to find the dose of GH which maintains IGF-1 levels within the normal range.

The patient will require one or two monthly IGF-1 blood tests until the optimum maintenance dose is reached and six-monthly/annual assessment thereafter.

As well as IGF-1 levels, side effects should be used as guidance for dose titration. The minimum effective dose should be used and dose requirements may decrease with age.

Cautions
Diabetes, papilloedema and relative deficiencies of other pituitary hormones

Contraindications
Active tumour activity, critically ill patients, patients with known hypersensitivity to GH or to any excipients of the product. It is also contraindicated during pregnancy and lactation
Side 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 growth hormone action. This tends to decrease as therapy continues but may occasionally require dose reduction.

Joint and muscle aches (“growing pains”), carpal tunnel syndrome and headache have been among reported side effects. These effects, if they occur, are usually mild and self-limiting. A reduction in the GH dose may be required if they persist. GH therapy has also been shown to reduce insulin sensitivity in these patients by antagonising the action of insulin and may therefore increase the risk of diabetes.

A severe and persistent headache should be reported immediately to the endocrinology department.

There is no evidence to suggest that GH therapy will increase the risk of abnormal or neoplastic growth, either a new growth or a resurgence of an old tumour.

There is no clinical experience of use of GH during pregnancy.

Interactions
Corticosteroids: growth-promoting effect of somatropin may be inhibited by corticosteroids
Oestrogens: increased doses of somatropin may be needed when given with oestrogens (when used as oral replacement therapy)

For information:
Guidelines for initiating new patients or switching existing patients receiving branded growth hormone to Omnitrope®

Following a review at the NHS Surrey Area Prescribing Committee in April 2010 the committee made the following decision: Omnitrope® was approved as the first line growth hormone for adult patients
• All adult patients new to growth hormone should be initiated on Omnitrope® as the brand of growth hormone treatment
• Adult patients currently receiving other brands will be reviewed by the consultant endocrinologists and switched to Omnitrope® where appropriate.

Exceptions
There may be patients who cannot be switched to omnitrope® or who have had a trial of Omnitrope® however did not find treatment acceptable. This could include:
• Needle phobic patients
• Patients suffering an injection site reaction etc.
Options for needle phobic patients include Saizen Easypod (autoinjector device).

There may also be a few patients who are accustomed to receiving Genotropin® Miniquicks for holiday or business travel due to the flexibility provided by these. These arrangements will continue due to the short term nature of these requests.

Products available below

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
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</thead>
<tbody>
<tr>
<td>Omnitrope®</td>
<td>Sandoz</td>
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<tr>
<td>Humatrope®</td>
<td>Lilly</td>
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<tr>
<td>Saizen Easypod®</td>
<td>Merck Serono</td>
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<tr>
<td>NutropinAq®</td>
<td>Ipsen</td>
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<tr>
<td>Norditropin®</td>
<td>Novo Nordisk</td>
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<tr>
<td>Genotropin®</td>
<td>Pharmacia</td>
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<tr>
<td>Zomacton®</td>
<td>Ferring</td>
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</table>
### Criteria for Use

#### RESPONSIBILITIES and ROLES

<table>
<thead>
<tr>
<th>Specialist responsibilities</th>
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<tbody>
<tr>
<td>1. Diagnosis of growth hormone deficiency and assessment of suitability for growth hormone treatment</td>
</tr>
<tr>
<td>2. Discuss the aims, benefits and side effects of treatment with the patient as well as their role. Advise patient to report a severe and persistent headache immediately to the endocrinology department at the initiating trust</td>
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<tr>
<td>3. Explain to the patient their treatment plan including the dosing schedule</td>
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<tr>
<td>4. Perform hospital baseline medical and biomedical assessments as follows:</td>
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<tr>
<td>- Pituitary imaging (MRI or CT scan as appropriate) depending on type of pituitary pathology</td>
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<tr>
<td>- Serum IGF-1</td>
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<tr>
<td>- Body composition measurement</td>
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<tr>
<td>- Visual field measurement (if appropriate)</td>
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<tr>
<td>- Height, weight and body mass index</td>
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<tr>
<td>- Waist : hip ratio</td>
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<tr>
<td>- Lipid profile</td>
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<tr>
<td>- Blood pressure</td>
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<tr>
<td>- ‘AGHDA’ questionnaire (QoL questionnaire)</td>
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<td>- Bone density yearly (only when treating to adult bone mass)</td>
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<tr>
<td>- Thyroid function and serum biochemistry</td>
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<td>- Glucose and HbA1c</td>
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<tr>
<td>5. Initiates therapy of growth hormone in the hospital and prescribe for at least 3 months. <em>(Omnitrope is the most cost effective treatment option available currently and is the 1st line treatment choice for adult patients, unless the patient is needle phobic or has injection site reactions (see notes above)). Genotropin is also comparable in cost to Omnitrope currently</em></td>
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<tr>
<td>6. 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 above monitoring.</td>
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<tr>
<td>7. Monitor and evaluate response to growth hormone treatment, including adverse drug reactions, with the patient and continue/discontinue treatment in line with agreed treatment plan</td>
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<tr>
<td>8. Adjust doses according to biochemical criteria</td>
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<tr>
<td>9. Discuss the possibility of shared care with the patient and ensure they understand the plan for their subsequent treatment</td>
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<tr>
<td>10. Supply GP with summary of patient review (including anticipated length of treatment) and a copy of the shared care guidelines recommending that a shared care arrangement is initiated</td>
</tr>
<tr>
<td>11. Advise GP on dose changes, if treatment is to discontinue at any point and after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated</td>
</tr>
<tr>
<td>12. Monitor the patient regarding self-administration and compliance in conjunction with GP</td>
</tr>
<tr>
<td>13. Inform GP if patient does not attend planned follow-up appointment</td>
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<tr>
<td>14. Ensure provision of initial injection devices or appropriate injections aids and materials, for the entire duration of treatment, even when shared care is confirmed</td>
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<table>
<thead>
<tr>
<th>General Practitioner responsibilities</th>
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<tbody>
<tr>
<td>1. Monitors patient’s overall health and well-being</td>
</tr>
<tr>
<td>2. Subsequent prescribing of Growth Hormone <em>(by brand)</em> at the dose recommended by the initiating consultant. <em>(Delivery of Growth Hormone will be via Homecare)</em></td>
</tr>
<tr>
<td>3. Monitoring of self-administration and compliance in conjunction with specialist nurses at the initiating trust</td>
</tr>
<tr>
<td>4. Liaison with patient’s consultant to discuss any dose adjustments required according to results from regular specialist monitoring of patient response to growth hormone</td>
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<tr>
<td>5. Reports any adverse events to the consultant, where appropriate</td>
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<tr>
<td>6. Reports any adverse events to the CSM, where appropriate</td>
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<tr>
<th>Patient’s / Carer’s role</th>
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<tbody>
<tr>
<td>1. Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment</td>
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<tr>
<td>2. Share any concerns in relation to treatment with Growth Hormone</td>
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<tr>
<td>3. Tell the specialist or GP of any other medication being taken, including over-the-counter products</td>
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<tr>
<td>4. Be aware of and report a severe and persistent headache immediately to the endocrinology department at the initiating trust</td>
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<tr>
<td>5. Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP</td>
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</table>
**BACK-UP ADVICE AND SUPPORT**

<table>
<thead>
<tr>
<th>Contact details</th>
<th>Specialist</th>
<th>Telephone No.</th>
<th>Email address:</th>
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<tbody>
<tr>
<td>Specialist:</td>
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<tr>
<td>Hospital Pharmacy:</td>
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**References:**
NICE guidelines on the use of human growth hormone in adults with growth hormone deficiency: August 2003 [www.nice.org.uk/ta064](http://www.nice.org.uk/ta064)

**AUDIT / SURVEY** (to be carried out by specialist clinic)
**Growth Hormone** for the treatment of **growth hormone deficiency**

### Agreement for transfer of prescribing to GP

**Patient details / addressograph:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>DOB</th>
<th>Hospital No</th>
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**Drug name and dose:**

The following tests, investigations have been carried out:

**List any relevant tests:**

**Date initiated:**

At the last patient review the drug appeared to be effectively controlling symptoms/ providing benefit: Yes / No

The patients has now been stabilised on a dose of: ........................................

I will arrange to review this patient regularly. Date of next clinic appointment: .........................

### Consultant:

<table>
<thead>
<tr>
<th>Address</th>
<th>Contact Number</th>
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### GP:

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<th>Contact Number</th>
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### Main Carer:

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### Key worker if appropriate:

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<th>Contact Number</th>
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### Agreement to shared care, to be signed by GP and Consultant.

<table>
<thead>
<tr>
<th>Consultant Signature:</th>
<th>Date:</th>
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**GP Signature:**

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If shared care is agreed and GP has signed above please return a copy of this page to the requesting consultant or alternatively fax to:  
**Acute Trust please insert appropriate Fax Number:**
Supplementary Information on Growth hormone deficiency and treatment (provided by Prof. Russell Jones from Royal Surrey County Hospital Guildford)

Information
Growth hormone deficiency has long been recognised as a condition in children. It is only since the late 1980s that it has been realised that adults are also physically and psychologically disadvantaged as a result of GH-deficiency and can benefit from replacement therapy\(^1\).

Over the last decade adult patients with GH-deficiency have been treated in clinical trials with replacement biosynthetic growth hormone. The treatment has shown positive benefits for both short-term and long-term health. Replacement therapy has improved quality of life, bringing energy and vigour back to these patients, enabling them to lead a more normal life\(^2\).

There is now overwhelming evidence to support GH replacement therapy (as reviewed \(^3\)). Growth hormone has received licences for treating adults by the FDA, European authorities and most countries in the world.

In the future an increased awareness of this endocrine deficiency and a consequent increase in diagnosis will lead to a growth in this treatment area. With an estimated incidence of 1:10,000, growth hormone deficiency in adults is a condition which general practitioners will now come into contact with in the course of their work\(^5\).

**ACTIONS OF GROWTH HORMONE**

Growth hormone (GH) is released from the pituitary gland with secretion rates peaking during the night. Although production of this hormone does decline after the growth spurt of adolescence, growth hormone continues to be produced and play a key metabolic role throughout adult life.

**Key Effects of Growth Hormone**

Growth hormone has an important role in the regulation of metabolism and body composition in the adult.\(^3\)

Growth hormone has widespread effects including:

- Stimulating bone and cartilage growth
- A lipolytic action which leads to a decrease in body fat
- An anabolic action which leads to an increase in cell mass
- An antinatriuretic action which leads to an increase in extra-cellular water
- Direct and indirect effects on mental function and quality of life

**Causes of Growth Hormone Deficiency**

Adult GH-deficiency is a relatively rare condition, affecting about 1 in 10,000 of the total population\(^5\). The majority of cases are in patients with pituitary or peripituitary tumours, or those who have been treated for such a tumour in the past.

GH-deficiency is a side effect of cranial radiotherapy for other cancers affecting pituitary function. Approximately one third of children with idiopathic growth hormone deficiency will be GHD as adults.
SIGNS AND SYMPTOMS OF GROWTH HORMONE DEFICIENCY

Growth hormone has an important role in the control of metabolism, consequently its deficiency results in a number of physical and psychological signs 1, 3, 6, 7.

Perhaps the most obvious effect is the reduction in psychological well-being and the most prominent of these indicators are outlined below.

**Psychological Symptoms**
- Low energy levels
- Social isolation
- Lack of positive well-being
- Depressed mood
- Increased anxiety

While quality of life indicators are difficult to quantify, the symptom severity of each individual patient needs to be assessed together with the overall degree of dysfunction. Evidence does exist for the benefits of growth hormone replacement on quality of life over a baseline assessment.

In addition, there is growing evidence to suggest that some of the changes associated with Adult GHD may be responsible for the increased morbidity and mortality from cardiovascular disease seen in these patients.

**Physical Signs**
- Increase in body fat
- Reduction in muscle mass
- Reduction in bone density
- Reduced exercise capacity
- Poor physical performance
- Raised serum cholesterol
- Reduction in cardiac muscle
- Impaired cardiac function

THE BENEFITS OF REPLACEMENT THERAPY

The majority of adults with GH-deficiency will find that many of the psychological and physical features of the deficiency are improved by replacement therapy. Clinical trials have shown the following improvements in these patients 3, 4, 6, 8, 9.

- Improved lipid profile
- Cardiac structure and function improved
- Increase in exercise capacity
- Improvement in bone mineralisation
Normalisation in body cell mass and extra-cellular water
• Reduction in body fat (particularly intra-abdominal fat)
• Improved renal function
• Improved well-being and quality of life
• Increased vitality

While GH replacement therapy also improves a range of cardiovascular markers, further studies are required to confirm the effects of therapy on cardiovascular related morbidity and mortality.

DIAGNOSIS OF GH-DEFICIENCY

This condition is diagnosed at hospital level by initial clinical suspicion of those patients likely to have a deficiency of this hormone. The level of growth hormone is then measured using appropriate provocation tests, for example an insulin tolerance test (ITT), consistent with the product licence recommendation.

An accepted definition of pronounced growth hormone deficiency is defined as a peak response less than 3ng/L (9mU/L).

Patients Under Clinical Suspicion 3, 4, 10

• Patients with known or suspected hypothalamic or pituitary disease
• Patients who have received cranial irradiation
• Patients with a deficiency of one or more of the other pituitary hormones
• Patients who have undergone hypophysectomy
• Adults who received growth hormone in childhood for GHD

When To Test

• Diagnostic test after stabilised treatment of other pituitary deficiencies
• Diagnostic test at least one month after pituitary surgery
• Childhood treatment should be interrupted for an appropriate period before retesting of growth hormone level status

HOSPITAL BASELINE ASSESSMENT

On diagnosis each patient should have a series of tests to produce a comprehensive baseline from which any subsequent change can be monitored.

Clinical Assessment

• Current medical history
• Full history of hypothalamic-pituitary disease
• Surgical and radiological history
• Number of pituitary hormone deficiencies
- Current replacement regimen
- Previous growth hormone treatment
- Quality of life assessment using the Nottingham health profile and a disease specific questionnaire

**Medical and Biochemical Assessment**

- Height, weight and body mass index
- Blood pressure
- HbA1c (blood glucose)
- Lipid profile
- IGF-I (insulin-like growth factor-I)
- Body composition
- Waist/hip ratio
- Recent pituitary imaging (MRI or CT scan)
- Visual field measurement, where relevant

**INITIATION OF TREATMENT**

The initial assessment period will allow for adjustment and stabilisation of the dose of growth hormone*.

Most patients are likely to become stabilised within two months of commencing growth hormone therapy.

**Dose**

Growth hormone replacement therapy is usually started as a low dose which is gradually increased. Sensitivity of growth hormone treatment varies with age, weight and possibly gender. The dose required tends to decrease with age, mirroring the physiological production of growth hormone.

The dose will be calculated by the GP and hospital clinician in accordance with recommendations given in the summary of Product Characteristics, attached.

**DELIVERY**

Growth hormone is given by subcutaneous injection which the patient would be expected to self-administer. Physiological growth hormone release peaks during sleep therefore the injection is given in the evening before bedtime.

Training facilities for the patients to self-inject will be established.

The hospital will also be responsible for provision of initial injection devices or appropriate injection aids and materials, for the entire duration of therapy even under general practitioner management.
MONITORING THE DOSE

A recognised technique for monitoring the dose is to take regular measurements of insulin-like growth factor I (IGF-I). IGF-I levels should increase during therapy. IGF-I levels should normally be maintained within the normal range during therapy. The aim is to find the dose of GH which moves IGF-I levels into the normal range.

The patient will require one or two monthly IGF-I blood tests until the optimum maintenance dose is reached.

These tests will be undertaken by the hospital and the result discussed between the hospital endocrinologist and GP. The dose of growth hormone should be adjusted as necessary.

SIDE EFFECTS

Fluid retention is the most commonly reported “side effect” of GH replacement therapy. Fluid retention, with occasional mild ankle oedema, are a normal part of growth hormone action. This tends to decrease as therapy continues but may occasionally require dose reduction.

Joint and muscle aches (“growing pains”), carpal tunnel syndrome and headache have been among reported side effects. These effects, if they occur, are usually mild and self-limiting. A reduction in the GH dose may be required while they persist.

GH therapy has also been shown to reduce insulin sensitivity in these patients by antagonising the action of insulin - this could increase the risk of diabetes.

There is no evidence to suggest that GH therapy will increase the risk of abnormal or neoplastic growth, either a new growth or a resurgence of an old tumour.

RE-ASSESSMENT

On completion of an initial assessment period, the patient should be re-evaluated repeating the baseline clinical, medical and biochemical tests. The decision to continue therapy should be taken after a further discussion between the patient, the GP and the endocrinologist.

The decision will be based on a number of factors. The improvement noted in quality of life and any return to a more normal body composition should be taken into account.

In addition, the long term effects of cardiovascular risk factors will be considered since epidemiological evidence suggests that GH-deficiency in adults increases the risk of cardiovascular disease.

Further long term observations are required to confirm what effects growth hormone replacement therapy may have on the life expectancy of adult patients with a deficiency of GH.
CONTINUING THERAPY

The optimal management of patients continuing with their GH replacement therapy after the assessment period will depend on the shared care co-operation between hospital and general practice.

The Hospital’s Role

An annual medical assessment comprising:

- Height, weight and body mass index
- Blood pressure
- HbA₁c
- Lipid profile
- Serum IGF-I
- Body composition measurement
- Waist/hip ratio
- Pituitary imaging (MRI or CT scan) (as appropriate)
- Visual field measurement, where relevant
- Assessment of quality of life

PLUS

- Monitoring patients overall health and well-being
- Liaison with the GP on patient’s progress
- Adjustment of the dose where appropriate
- Discussion with the patient of any adverse effects
- Monitoring of self-administration and compliance

THE ROLE OF GENERAL PRACTICE

- Monitoring overall patient health and well-being
- Observation and report of any unexpected side-effects to the hospital endocrinologist (*severe headaches to be reported immediately*).
- Monitoring of self-administration and compliance in consultation with specialist nurse (*checking that prescribed dose is being used*).
- Liaison with hospital endocrinologist to reach joint decision about further treatment.

The transfer procedure from hospital to general practice should include recognised lines of communication between the GP and the hospital department.
REFERENCES


