NORTH AND EAST DEVON HEALTHCARE COMMUNITY SHARED CARE PRESCRIBING GUIDELINE

http://www.devonpct.nhs.uk/Treatments/NE_Devon_Shared_Care_Guidelines.aspx#S

USE OF GROWTH HORMONE (SOMATROPIN) IN CHILDREN (GENOTROPIN®, HUMATROPE®, NORDITROPIN® SAIZEN®, ZOMACTON®, NUTROPINAQ®)

This shared care guideline sets out details for the sharing of care of **CHILDREN / ADOLESCENTS** treated with **SOMATROPIN** and gives limited extra information to help in treatment. **It highlights significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and *does not* replace it.**

INTRODUCTION/BACKGROUND INFORMATION

Growth hormone (GH) is produced by the anterior pituitary gland. As well as increasing growth in children, GH helps regulate protein, lipid and carbohydrate metabolism.

Somatropin is human growth hormone produced by recombinant DNA technology in *E.coli.* Its amino acid sequence is identical to that of natural human GH.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

Human GH (somatropin) treatment is indicated only in the following conditions:

CONDITIONS

- Proven growth hormone deficiency. Diagnosis is made by documentation of slow growth, clinical features, delayed bone maturation and appropriate specialist investigations.
- Turner syndrome. Ideally this is diagnosed early (even at birth) and GH treatment initiated at 2-3 years of age to maximise final height.
- Chronic renal failure. Before GH treatment is given the child's nutrition and metabolism should be optimised and steroid dose as low as possible.
- Prader-Willi syndrome

N.B. Idiopathic short stature is not an indication for GH treatment.

EFFECTIVE PRACTICE COMMITTEE RECOMMENDATION

As per NICE guidance.

DOSAGE AND ADMINISTRATION

The injection should be given subcutaneously and the site varied to prevent lipoatrophy.

- GH deficiency in children: 25–35 micrograms/kg daily or 0.7–1 mg/m^2 daily.
- Turner's syndrome: 45–50 micrograms/kg daily or 1.4 mg/m^2 daily.
- Chronic renal insufficiency (renal function decreased to less than 50%): 45–50 micrograms/kg daily or 1.4 mg/m^2 daily (higher doses may be needed) adjusted if necessary after 6 months.
- Prader-Willi syndrome: in children with growth velocity > 1 cm/year, in combination with energy-restricted diet, 35 micrograms/kg daily or 1 mg/m^2 daily; max. 2.7 mg daily.

CONTRAINDICATIONS

- Evidence of tumour activity (complete antitumour therapy and ensure intracranial lesions are inactive before starting).
- Within one year of renal transplant.
- Severe respiratory impairment in patients with Prader-Willi syndrome.
  - Closed epiphyses mean that linear growth is complete. Attempts to promote further growth with GH would be futile.
  - Pregnancy (interrupt treatment if pregnancy occurs).
  - Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions should not be treated with somatropin.

PRECAUTIONS

- Diabetes mellitus (adjustment of antidiabetic therapy may be necessary). Somatropin may induce a state of insulin resistance and hypoglycaemia in some patients.
- Papilloedema.
- Deficiencies of other pituitary hormones (ACTH deficiency – treatment with steroid replacement should precede other hormone replacement; hypothyroidism - manufacturers recommend periodic thyroid function tests).
- History of malignant disease – (There is no evidence of increased risk of relapse **or** of secondary tumour formation but these possibilities must be considered).
- Disorders of the hip epiphysis (monitor for limping).
- Resolved intracranial hypertension (monitor closely).

QUICK REFERENCE GUIDE:

1. Stabilisation: The dose is calculated by the specialist from body weight or surface area and will not change unless i) there is inadequate response or ii) substantial growth (see Monitoring).
2. Normal response: On starting GH it is common to see a growth spurt for several months. Abnormal response is indicated in the Monitoring and Refer sections.
3. Administration: Training for injecting GH is provided by secondary care nurses to patients and/or carer.
4. Ease of use: Products are multichamber injection devices allowing safe and accurate mixing of drug and excipients in solution (included in training)
5. Monitoring by Consultant Paediatrician: Growth, pituitary hormones, thyroid function (see Monitoring)

SIDE EFFECTS

Very Common: [>1 in 10]; Common: [1 in 10 – 100]; Uncommon: 1 in 100 – 1000; Rare: [1 in 1,000 - 10,000]; Very rare: [<1 in 10,000]

Common

- Transient local skin reactions / pain at the injection site.
- Antibody formation (though binding capacity is low and not thought clinically significant).
- Hypothyroidism.

Uncommon

- Paraesthesia.
- Stiffness in the extremities.
- Arthralgia.
- Myalgia.
- Peripheral oedema.

Rare

- Benign intracranial hypertension, Headache(fundoscopy for papilloedema recommended).
- Gynaecomastia.
- Diabetes mellitus type 2

Very rare

Leukaemia in children with growth hormone deficiency also reported*

Overtreatment with Somatropin results in acromegaly.

MONITORING

- Hospital paediatrician should monitor all children receiving GH. Treatment should be re-evaluated and usually stopped if there is a poor response (less than 50% increase in growth velocity from baseline in the first year of therapy).
- Hospital paediatrician will monitor pituitary hormones. This includes monitoring thyroid function annually and after any dose change.
- Response should be evaluated using standard growth charts. Therapy is normally stopped when final height is approached (height increment <2cm / year).
- Monitoring compliance of injections should be considered when 'response to treatment' is poor.
- In Prader-Willi syndrome it is important to monitor changes in body composition as part of evaluation.
- Hospital paediatrician should monitor until growth is complete, when treatment will be stopped. Decisions must then be made about reassessing for GH deficiency (GH treatment in adulthood may be appropriate) and transfer to the adult services.
- GH is an insulin antagonist; GH administration could therefore unmask latent diabetes and would be expected to increase the insulin requirement in patients with established type 1 diabetes.

REFER TO SPECIALIST TEAM

- Hip pain/limp may signify slipped epiphysis and requires urgent orthopaedic assessment.
- Upper airways obstruction including onset of, or increased snoring in obese patients or those with Prader-Willi syndrome.

COMMON/SIGNIFICANT DRUG INTERACTIONS

- **Corticosteroids** - Inhibit growth-promoting effect of GH. This is unlikely to apply to corticosteroids used for topical action (including inhalations).
- **Oestrogens** - Higher doses of somatropin may be needed with oral oestrogen replacement therapy. Interaction with combined oral contraceptives may also apply to combined contraceptive patches. In the case of hormone replacement therapy low doses are unlikely to induce interactions.
- **Anticonvulsants and ciclosporin** – levels of these agents may be reduced by GH.

NOTES

- There is a separate shared care guideline for adults requiring growth hormone.
- Somatropin is a CD Schedule 4 drug (no handwriting or special storage requirements)
- Somatropin 1mg ≡ 3 units (dose formerly expressed as units).

PRODUCT INFORMATION

- Store at +2°C to+ 8°C (in a refrigerator). Keep the container in the outer carton. Storage by the patient should follow information provided in the product insert.
- The two most commonly prescribed products locally are (Genotropin® and Humatrope®).

Genotropin® (Pharmacia)

- 5.3 mg (£122.87), 12 mg (£278.20) injection for reconstitution.
- Miniquick (dual chamber single dose syringe) doses available 0.2mg to 2mg in 0.2mg steps (£4.637 per 0.2mg)

Humatrope® (Lilly)

- 1.33mg (£30.50), 6mg (£137.25), 12mg (£274.50), 24mg (£549.00) injection for reconstitution

Prices are correct at the time of preparation

Also available are Norditropin®, Saizen®, Zomacton®, NutropinAq®

REFERENCES:

- Summary of Product Characteristics: accessed at http://emc.medicines.org.uk/January 2008
- BNF 55 March 2008
- Stockley Drug Interactions – 7th Edition
- NICE guidelines May 2002 http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11458

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AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggestions about how responsibilities for managing **children / adolescents** prescribed **somatropin** can be shared between specialist and general practitioner. GPs are **invited** to participate- any not confident to take part is not obliged to do so, in which case full clinical responsibility for the GH treatment remains with the specialist. **It is usual practice, and more cost effective, for the GP to prescribe the GH; if a specialist requests this, the GP should reply as soon as practical.**

Sharing of care assumes communication between the specialist, GP and patient; it should be explained to the patient and be accepted by them.

The doctor who prescribes the medication has the clinical and legal responsibility.

Specialist responsibilities:

- ❑ Confirm that GH treatment is appropriate. t
- ❑ Invite the GP to participate in shared care.
- ❑ Select appropriate preparation.
- ❑ Provide the patient or carers with written and verbal information about the drug and discuss the benefits and potential side effects of treatment before treatment is started.
- ❑ Ensure that training on reconstitution, administration and storage of GH is provided.
- ❑ Initiate treatment at appropriate dose, giving the initial prescription on FP10 (HNC).
- ❑ Monitor growth and pituitary hormone and thyroid levels (see monitoring section).
- ❑ Specify review dates at appropriate intervals.
- ❑ Communicate to GP any changes in treatment / monitoring results / adverse events.
- ❑ Advise GPs on when to stop treatment.
- ❑ Give GPs clear arrangements for back-up advice if required.
- ❑ Report adverse events to the CSM.

General Practitioner responsibilities:

- ❑ Reply to the request for shared care as soon as practical.
- ❑ Prescribe somatropin **BY BRAND** after communication with specialist.
- ❑ Seek specialist advice on any aspect that causes concern and may affect treatment.
- ❑ Ensure that a full list of medication for the patient is available to the specialist at a patient review.
- ❑ Report adverse events to the specialist and CSM.
- ❑ Stop treatment in the case of a severe adverse event or refer as per shared care guideline.

Patient / Carer responsibilities:

- ❑ Report any adverse effects to GP and/or specialist.
- ❑ Ensure that they have a clear understanding of their treatment.
- ❑ Ensure they attend for monitoring as per shared care guideline.
- ❑ Be aware that treatment will be stopped if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No:	E-mail address
Dr C Moudiotis	01392 406148	Christopher.moudiotis@nhs.net
Dr J Cox	01271 322397	Julian.Cox@ndevon.swest.nhs.uk

Please note: Specialist endocrinology and diabetes services for children are not commissioned by CCGs. NHS England commissions services complex growth problems including Turner syndrome and growth hormone deficiency; puberty disorders including precocious, delayed or absent puberty. Guidance should be provided to GPs by specialist services if requests are made to share care. This shared care guideline has been archived.

Shared Care Agreement Letter - Consultant Request

To: Dr.....

Practice Address: .....

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Patient Name:
Hospital number:
Date of birth:
Address:

DIAGNOSED CONDITION:
.....

I recommend treatment with the following drug:
.....

I am requesting your agreement to sharing the care of this patient according to the Devon Primary Care Trust North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

Signed:	
Consultant name:	
Department:	
Contact telephone number:	
Date:	

GP RESPONSE

I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: ..... Date: .....

GP name: ..... *Delete as appropriate