Oxford University Hospital NHS Trust, Oxfordshire NHS,
Shared Care Protocol and Information for GPs

This leaflet provides the necessary information and guidance for the shared care of adult patients requiring somatostatin analogue therapy for acromegaly therapy

Summary
Acromegaly is a rare disorder. Primary treatment is by surgery. This is successful in around 90% of patients with microadenomas, but only 30-40% of those with macroadenaoms. Since the majority of patients present with macroadenomas, the overall cure rate is in around 50% of cases. Uncontrolled acromegaly decreases life expectancy. Therefore, treatment after unsuccessful surgery is necessary to render growth hormone and IGF values 'normal'. Current guidelines suggest we should aim for a random GH of <1.5 μg/L and a normal age- and sex-adjusted IGF1. The most frequently effective treatment is by long-acting somatostatin analogues.

Background
Incidence: 4 to 5 new cases per million population per year
Prevalence: 40 to 50 per million population

Acromegaly is a rare growth disorder characterised by a clinical syndrome resulting primarily from the effects of excess growth hormone and insulin-like growth factor-1 on various organ systems. It is almost always caused by a pituitary tumour. Characteristic clinical features include visual disturbances, coarsening of facial features, separation of teeth, bony proliferation, soft tissue overgrowth, spade-like hands and feet and thick greasy skin. Multi-organ involvement is characterised by cardiomyopathy and heart failure, hypertension, headache, respiratory complications, goitre, glucose intolerance and arthralgia.

Untreated acromegaly results in markedly reduced quality of life and life expectancy. It has been estimated that patients with acromegaly have a two fold greater mortality than the general population and that approximately 50% of patients die prematurely mainly as a result of cardiorespiratory disease. In terms of malignancy, it is generally agreed that there is an increased rate of colon cancer, and less certainly of other cancers. ,.

The average age at which patients are diagnosed is 40 to 45 years, but because symptoms develop slowly, the diagnosis is often missed for 5 to 15 years. Treatment is therefore imperative in all patients, except the very elderly or those with minimal abnormalities.

Treatment of acromegaly is aimed at normalising growth hormone secretion, decreasing tumour size and maintaining normal pituitary function, thereby ameliorating clinical effects and reducing mortality from the disease. Evidence of disease control should be based on normalisation of insulin-like growth factor-1 and reduction in growth hormone levels to <1.5 ug/L Three therapeutic options are available for the treatment of acromegaly; surgery, radiotherapy and pharmacological therapy.

SURGERY
Surgery is currently by excision of the pituitary tumour and is considered the first-line treatment in eligible patients. The prognosis after surgery depends upon many factors such as the size and staging of the tumour, the extent of extra-sellar involvement (local invasion) and pre-operative levels of growth hormone and insulin-like growth factor-1.

RADIOTHERAPY
Radiotherapy is usually reserved for patients in whom surgery is contraindicated or not successful at reducing growth hormone to safe levels, or for those with evidence of an invasive tumour. However, it may take 5 to 10 years before radiotherapy reduces growth hormone levels to less than 1.5ug/L . This slow rate of decline means that patients often require supplemental pharmacological therapy. Hypopituitarism also occurs in 40 to 50% of patients after this period.

PHARMACOLOGICAL THERAPY
Medical therapy is usually reserved for patients in whom surgery is contraindicated or not successful at reducing growth hormone to safe levels and for patients in whom the full effects of radiotherapy have yet to

occur. The somatostatin analogues lanreotide and octreotide are accepted as the treatment in these patients, and are more effective than bromocriptine or other dopamine agonists. There are two long-acting formulations, Lanreotide (Somatuline) Autogel (Ipsen)or Octreotide (Sandostatin) LAR (Novartis) Comparative studies suggest that both formulations are equally effective, but lanreotide may have an advantage in that it may be administered by the patient or their carer/partner. **Currently, used at equipotent doses lanreotide is cheaper at NHS prices and is the preferred first choice.**

Prescribing Information

LANREOTIDE (SOMATULINE) AUTOGEL/OCTREOTIDE LAR

Lanreotide/Octreotide

Lanreotide Autogel and Octreotide LAR are analogues of the naturally occurring hormone somatostatin,which exert potent inhibitory effects on the secretion of growth hormone and on various peptides of the gastroenteropancreatic endocrine system, principally via somatostatin receptor subtype 2.. They have become a pharmacological treatments of first choice, either when used alone or as an adjunct to surgery or radiotherapy, which are often ineffective alone. Previously, octreotide was administered as a subcutaneous injection. However, its short duration of action necessitated administration three times a day, which has obvious compliance, morbidity and quality of life implications.

Long-acting release Lanreotide (Somatuline Autogel) and Octreotide LAR (Sandostatin LAR) have therefore recently been developed. Lanreotide is an aqueous solution and is administered by deep subcutaneous injection once every 28 days. The usual starting dose of Lanreotide is 90mg every 28 days for three months. Dose adjustments are based on clinical symptoms, suppression of growth hormone and normalisation of insulin-like growth factor-1.

Octreotide LAR is a long-acting release formulation of octreotide which has been developed by incorporating the drug in microspheres of biodegradable polymer. This is administered by intramuscular injection once every 28 days. The usual starting dose is 20mg every 28 days for three months. Dose adjustments are based on clinical symptoms, suppression of growth hormone and normalisation of IGF1.

When adequately controlled, dose intervals may be increased to 6 or sometimes 8 weeks in appropriate patients, increasing patient convenience and decreasing costs. Recent data suggest that in a small proportion of patients such analogues may be withdrawn entirely after a number of years, even without radiotherapy.

Dosage

Lanreotide
The starting dose is 90mg IM every 28 days and the dose may be increased to 120mg IM every 21 days if there is insufficient suppression of growth hormone.

Octreotide – as above

Who initiates therapy

Churchill Hospital – based on clinical and biochemical parameters demonstrating active disease. The endocrine nurse will give the first single injection.

Who continues therapy

General Practitioner

Management of therapy

Clinical symptoms, mean growth hormone from a day curve and IGF-1 will be monitored by the hospital. The aim of treatment is normalisation of these parameters. In addition, liver biochemistry and possible development of gallstones will be monitored by the hospital. Any dose alterations will be communicated to the general practitioner.

After one year a random GH and IGF1 level will be taken 4 weeks after the last dose, and if normal the dose interval will be reduced to 6 weeks and then, if control is maintained, at 8 weeks. After one one year's control with 8-weekly injections, the drug will be withdrawn to assess for cure.

Adverse effects
Increased risk of gallstone development and gastrointestinal upset. Most patients with gastrointestinal upset find that there is a gradual reduction of these over time. The development of gallstones will be monitored by ultra sound of the gallbladder arranged by the Churchill Hospital at appropriate intervals. Rarely, alopecia may develop.

Dose reduction in diabetic medication may be necessary.

Action if side effects occur

Please liaise with the Endocrine Unit at the Department of Endocrinology, OCDEM , Oxford.

Contra-indications/Cautions
NONE

Pregnancy and lactation (if appropriate)
To be discussed with the hospital on an individual basis.

Drug interactions (refer also to BNF or SPC; include significance of interaction)
NONE

Monitoring
GH & IGF1

Shared Care Responsibilities
Shared care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients should be under regular follow-up which provides an opportunity to discuss drug therapy.

a) Aspects of care for which the Hospital Consultant is responsible:
- Clinical assessment of the suitability of the patient for octreotide/lanreotide therapy
- Initiation and provision of patient training in administration of subcutaneous octreotide /lanreotide
- Provide 1st dose and administer octreotide/lanreotide
- Write to the GP requesting shared care and outline shared care protocol criteria.
- Ongoing medical and biochemical assessment of response to therapy, including pituitary function tests, pituitary imaging and visual field measurement, where relevant
- Ultrasound investigation to detect possible gallstone formation
- Monitor IGF1 and GH
- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments.
- Ensure clinical supervision of the patient is done by follow-up as appropriate.
- Ensure the patient understands the nature and complications of drug therapy and their role in reporting adverse effects promptly.
- Provide clear instruction to GP on when therapy needs to be referred back to specialist.
- Be available to give advice to GP and patient.
- Training by endocrine specialist nurses of practice nurses to administer the somatostatin locally. Responsibility for prescribing is only appropriate for transfer to primary care once sufficient training has been provided to the practice staff

b) Aspects of care for which the GP is responsible:
- Prescription and administration of octreotide / lanreotide therapy once initiated and stabilised in hospital, Providing sufficient training has been given to practice team as above.
- Advise the Hospital Consultant of any clinical changes or adverse effects where appropriate.
- Monitor for adverse effects as detailed above.

c) Aspects of care for which the Patient is responsible:
- Report any adverse effects to their GP and/or consultant
- Attend for regular monitoring as outlined in patient information leaflet.

For further information about your patient's clinical condition, please contact:

Professor Ashley Grossman (Endocrine Consultant) Sec. Tel 01865 857308
Dr. Niki Karavitaki (Endocrine Consultant)
Mrs Viv Thornton-Jones (Endocrine Specialist Nurse) Tel 01865 857337

For further drug information, please contact: Novartis Pharmaceuticals UK Ltd
Tel. 01276 698370

Ms Sarah Poole (Endocrine Pharmacist) Tel 01865 225900

PATIENT SUPPORT GROUP

Provides information leaflets, information on medical developments, contacts with other patients through regional support groups

The Pituitary Foundation
PO Box 1944
Bristol
BS99 2UB.
Tel: 0117 923 8070.

Patient information leaflet
Patients should be supplied with an information leaflet from the manufacturer and/or the hospital team.

Contact Details
Consider including consultant details, pharmacist details, nurse specialist details if relevant etc.