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Royal Cornwall Hospitals NHS Trust

Treatment of Acromegaly in Adults with Somatostatin Analogues Clinical Guideline V3.0

November 2018

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of somatostatin analogues (lanreotide / octreotide) when used in acromegaly.

1.2. Data Protection Act 2018 (Also Known as General Data Protection Regulations – GDPR) Legislation

All identifiable information will be contained within the patient medical record and will therefore comply with GDPR regulations

Introduction

1.3. Acromegaly is a rare growth disorder (yearly incidence of 4-6 patients per million) characterised by a clinical syndrome resulting primarily from the effects of excess growth hormone and insulin-like growth factor-1 (IGF-1) on various organ systems. Acromegaly is almost always caused by a pituitary tumour.
There are three therapeutic options for confirmed acromegaly - surgery, radiotherapy and pharmacological therapy. Octreotide and Lanreotide are pharmacological options. They appear to be effective in 55-70% of patients. Somatostatin analogues exert potent inhibitory effects on the secretion of growth hormone and on various peptides of the gastroenteropancreatic endocrine system.
The drug formulations commonly used in acromegaly treatment are biodegradable polymer microspheres that contain and release the drug slowly over a 14-28 day period. Dose adjustments are based on clinical symptoms, suppression of GH & normalisation of IGF-1.

1.4. Indications for the purpose of this guideline - Treatment of patients with acromegaly who are adequately controlled on treatment with octreotide or lanreotide: in whom surgery, radiotherapy or dopamine agonist treatment is inappropriate or ineffective, or in the interim period until radiotherapy becomes fully effective.

1.5. Note: NHS England is the commissioner responsible for use in gastro-enteropancreatic tumors and this NHS England indication falls outside of this guidance.

1.6. This shared care guideline sets out details for the sharing of care of adults with acromegaly prescribed a **somatostatin analogue**. These guidelines provide additional limited information necessary to aid in the treatment of these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, summary of product characteristics and ***do not*** replace them.

2. The Guidance

2.1. Preparations and Dosage

Choice of agent is usually governed by patient preference (subcutaneous vs IM administration), dose required, dose titration options, and cost.

2.1.1. Initiation:

- Octreotide - Sandostatin Lar: Administered by deep intragluteal injection once every four weeks. The usual starting dose is 20mg every four weeks for three months.

- Lanreotide - Somatuline LA as powder for suspension for injection: Administered by intramuscular injection of 30mg every 14 days initially. Subsequently the frequency of injection may be increased to every 7-10 days based upon the clinical and biochemical response.

- Lanreotide - Somatuline Autogel prefilled syringe: Administered by deep subcutaneous injection (into the gluteal region) of 60mg every 28 days initially.

2.1.2. Maintenance

The maintenance dose may be reduced if:

- GH concentrations are consistently below 1µg/L (2mU/L) after an oral glucose load test.
- IGF-1 serum concentrations have normalised.

2.1.2.3. Occasionally higher doses are used in resistant cases, which will require more frequent review in secondary care. Individual doses will be advised by the Endocrine team based on the patient's response to treatment.

2.1.2.4. The site of repeat intragluteal injections should be alternated between the left and right gluteal muscle.

2.1.2.5. Products available are:
Sandostatin (octreotide) Lar 10-mg, 20-mg and 30-mg vial
Somatuline (lanreotide) LA 30mg, Autogel: 60mg, 90mg, 120mg

2.2. Contraindications:

- Hypersensitivity to lanreotide or octreotide, Lactide-glycolide copolymer, Lactic-glycolic copolymer, Mannitol, Carmellose or Polysorbate 80.

- Experience with lanreotide or octreotide in pregnancy or breastfeeding is not available and thus not recommended. BNF reports possible effects on foetal growth in second and third trimesters.

2.3. Precautions:

- Impaired insulin and/or glucagon secretion is known with somatostatin analogues. In patients with concomitant diabetes mellitus; monitoring of glucose tolerance and any antidiabetic treatment is recommended.

- Patients with liver or kidney dysfunction are recommended to have organ function tested and dose adjustments made according to the results.

2.4. Monitoring

Specialist Team:

- Evidence of disease control should be based on normalisation of IGF-1 and reduction of growth hormone on oral glucose testing.

- IGF-1 should be assessed every 6 months.

- Annual growth hormone monitoring.

- Baseline ultrasonic examination of the gallbladder and biliary system according to SPC or local protocol.

- To decide on a 6-monthly basis whether to perform ultrasonic examination of the gallbladder and biliary system during somatostatin analogue therapy (local variation on the SPC).

- Annual thyroid function tests for patients receiving therapy over 1 year in duration.

- In patients whose condition is stable annual review may be recommended.

2.5. General Practice:

There are no specific biochemical monitoring requirements for the GP to undertake other than refer to specialist team if an adverse effect of the drug is noted.

2.6. Side Effects

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

2.6.1. Very common/Common:

Injection site reactions (local pain and, rarely, swelling and rash); GI side effects [≈ 30%] (anorexia, nausea, vomiting, cramping abdominal pain, abdominal bloating, flatulence, loose stools, diarrhoea and steatorrhoea); gallstone formation, altered glucose regulation (both hyperglycaemia [≈15%] and more rarely hypoglycaemia have been reported).

2.6.2. Uncommon/Rare:

Symptoms resembling acute intestinal obstruction; acute pancreatitis has been reported within the first hours or days; cholelithiasis-induced pancreatitis; acute hepatitis without cholestasis (normalised on withdrawal of s/c Octreotide); slow development of hyperbilirubinaemia, transient hair loss.
Development of gallstones has been reported in 10 to 20% of long-term recipients of s/c Sandostatin though 1% of all patients appear symptomatic. Steatorrhoea may respond to pancreatic enzyme treatment. Advice may be sought from the Endocrine department.

2.7. Common/Significant Drug Interactions

May require change in antidiabetic medicine doses: (metformin, sulphonylureas, 'glitazones', 'glinides' and insulins) as somatostatin analogues can alter drug requirements due to inhibitory effects on the secretion of insulin and glucagon.
Possible reduced intestinal absorption of ciclosporin leading to lower plasma levels.
Possible delayed absorption of cimetidine.
Concomitant administration of somatostatin analogue and bromocriptine may increase the bioavailability of bromocriptine.
Caution should be exercised during coadministration of octreotide and drugs mainly metabolised by CYP3A4, which have a low therapeutic index (e.g. carbamazepine, digoxin, warfarin and terfenadine).

2.8. Notes:

Somatuline LA and Sandostatin LAR must be made up in the supplied solution immediately before injection, by shaking the vial, gently, 20 to 30 times, in order to obtain a homogenous suspension with a milky appearance.
The Pituitary Foundation Web resource:
http://www.pituitary.org.uk
links to support groups, patient information and general information relevant to pituitary diseases.

2.9. References:

Summary of Product Characteristics.
Royal College of Physicians of London, Pituitary Tumours 1997 (Recommendations for Service Provision & Guidelines for Management of Patients), 1-39.

2.10. Areas Of Responsibility For The Sharing Of Care

These are suggested ways in which the responsibilities for the management of adult patients with acromegaly who are prescribed a somatostatin analogue (octreotide or lanreotide) can be shared between the specialist and the general practitioners. GPs are invited to participate. 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**.** If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.
In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.10.1. Specialist responsibilities:

- Initiation of drug treatment, provide the first prescription and ensure stabilisation of patient's condition.

- Provide the patient or patient's parents/guardians/carers with suitable written and verbal information about the drug prior to starting medication and discuss the benefits and side effects of treatment.

- Baseline monitoring of Insulin Growth Factor-1 and Growth hormone levels with appropriate monitoring review. Ultrasound of gallbladder at start of treatment and review at 6 month interval thereafter.

- Communicate relevant treatment and education issues with the patient
- Ask the GP whether they are willing to participate in shared care using the shared care agreement letter.

- Provide first prescription(s) of the drug for the patient's condition ensuring that the condition is stabilized and the GP agrees to take over responsibility for prescribing.

- Specify review dates at clinically relevant time intervals for both the GP and the consultant.

- Prompt communication with GP of any changes in treatment or dose requirements, results of monitoring undertaken and assessment of adverse events.

- Advice to GPs on when to stop treatment or alter dose.

- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.

- Reporting adverse events to the MHRA.

2.10.2. General Practitioner responsibilities:

- If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter.

- Take on prescribing of the **Somatostatin analogue** from the second prescription after communication from the specialist that the patient is stabilised.

- Prescribe 1 month of **Somatostatin analogue** at a time.

- Keep a record of test results in the patient's notes.

- Prompt referral to a specialist if there is a change in the patient's health status.

- Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.

- Reporting adverse events to the specialist and MHRA.

- Stopping treatment in the case of a severe adverse event or as per shared care guideline.

2.10.3. Patient and Parent / Carer Responsibilities:

- Sign the shared care agreement letter
- Report any adverse effects to their GP and/or specialist regarding their treatment.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as per shared care guideline.
- Aware that treatment will be stopped if patient does not attend for monitoring.
- Take prescriptions to the pharmacy / dispensing surgery as soon as possible so that they have adequate time to obtain supplies of the medicine.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM

Shared Care Agreement Letter – Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

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

I request your agreement to continue the care of this patient according to the Shared Care Guideline for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Guideline.
The results of any baseline tests and any additional supportive information (target range, date of last blood test etc.) are below:

Patient agreement **I understand and agree to my responsibilities as described above.,** **Signed: ……** **Date: ……..** **Name:**

Principles:
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are no obligation to do so**. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient, the intention should be explained to the patient and accepted by them,
Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequence of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number:**	
Email:			

……..

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP response **I agree/do not agree *to share the care of this patient in accordance with the Shared Care Guideline.** **Signed: …… Date: ……** **Name: ……** *delete as appropriate

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Diversity & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Treatment of Acromegaly in Adults with Somatostatin Analogues Clinical Guideline V3.0		
Date Issued/Approved:	September 2018		
Date Valid From:	November 2018		
Date Valid To:	November 2021		
Directorate / Department responsible (author/owner):	Endocrine Team / Pharmacy - Head of Prescribing Support Unit		
Contact details:	01872 253548		
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists		
Suggested Keywords:	Acromegaly, Octreotide, lanreotide		
Target Audience	RCHT	CFT	KCCG
	✓		✓
Executive Director responsible for Policy:			
Date revised:	Sept'18		
This document replaces (exact title of previous version):	Shared care guideline for treatment of acromegaly (persistent GH excess) in adults with somatostatin analogues: octreotide (Sandostatin LAR), lanreotide (Somatuline LA and Somatuline Autogel)		
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee		
Divisional Manager confirming approval processes	Karen Jarvill		
Name and Post Title of additional signatories	Not required		
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}		
	Name: Kevin Wright		
Signature of Executive Director giving approval	{Original Copy Signed}		

Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only	
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards				
Related Documents:	**2.11. Summary of Product Characteristics.** Royal College of Physicians of London, Pituitary Tumours 1997 (Recommendations for Service Provision & Guidelines for Management of Patients), 1-39.			
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
19 Sept 12	V1.0		M Wilcock, Head of Prescribing Support Unit
23 Sept 2015	V 2.0	New style Appendix and minor text alterations	M Wilcock, Head of Prescribing Support Unit
Sept 2018	V3	Inclusion of share care agreement letter and new format	M Wilcock, Head of Prescribing Support Unit

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document
This document has been created following the Royal Cornwall Hospitals NHS Trust Policy on Document Production. It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Initial Equality Impact Assessment Form

This assessment will need to be completed in stages to allow for adequate consultation with the relevant groups.

<table>
<tr><td colspan="6">Shared care guideline for treatment of acromegaly (persistent gh excess) in adults with somatostatin analogues:
Treatment of Acromegaly in Adults with Somatostatin Analogues Clinical Guideline V3.0</td></tr>
<tr><td colspan="3">Directorate and service area:
Pharmacy</td><td colspan="3">Is this a new or existing Policy?
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="3">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="5">To provide information on prescribing of octreotide or lanreotide to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="5">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="5">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="5">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="5">General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td>Other</td></tr>
<tr><td>X</td><td></td><td></td><td>X</td><td></td></tr>
<tr><td colspan="5">Please record specific names of groups

Cornwall Area Prescribing Committee</td></tr>
</table>

c). What was the outcome of the consultation?	No full impact assessment required

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:

Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No X**	
9. If you are **not** recommending a Full Impact assessment please explain why.				
Not required				
Signature of policy developer / lead manager / director M Wilcock		Date of completion and submission 19Sept18		
Names and signatures of members carrying out the Screening Assessment	1. M Wilcock 2. Human Rights, Equality & Inclusion Lead			

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead
c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

This EIA will not be uploaded to the Trust website without the signature of the Human Rights, Equality & Inclusion Lead.

A summary of the results will be published on the Trust's web site.

Signed __ __M Wilcock_____

Date ___19/09/18_____