Western Locality Shared care on prescribing of somatostatin analogues – gastrointestinal neuroendocrine tumours

April 2013

- Somatostatin analogues
- Treatment of: Gastrointestinal neuroendocrine tumours

Aim of Treatment

Gastrointestinal neuroendocrine tumours (GI-NETs) are a genetically diverse group of malignancies. They arise from the secretory cells of the neuroendocrine cell system that produce peptides causing characteristic hormonal syndromes. Carcinoid syndrome may present with flushing, diarrhoea, abdominal pain, telengiectasia or bronchoconstriction in patients with functional GI-NETs. Poor long term control may cause carcinoid heart disease (plaque-like, fibrous thickening of the endocardium, tricuspid and pulmonary valves) which is associated with substantial morbidity and mortality.

The treatment of choice for patients with GI-NETs is curative surgery to remove the primary malignancy and/ or local lymph nodes. However curative surgery is often not feasible due to advanced disease at diagnosis or further progression. Therefore symptom control remains an important part of therapy for many patients.

Somatostatin is an endogenous inhibitor of various hormones secreted from the endocrine system including serotonin, insulin, glucagons and gastrin. Somatostatin itself has limited clinical use due to its short half-life. Somatostatin analogues have a longer duration of action and therefore can be used to relieve symptoms and to suppress tumour growth and spread.

Specialist responsibilities

1. Initiation of drug treatment, provide first prescription(s) of the drug for the patient's condition ensuring that the condition is stabilized.
2. To send a letter to the GP requesting shared care for a particular patient
3. 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.
4. Ultrasound of gallbladder at start of treatment and review at 6 month interval thereafter
5. Communicate relevant treatment and education issues with the patient
6. Specify review dates at clinically relevant time intervals for both the GP and the consultant.
7. Prompt communication with GP of any changes in treatment or dose requirements, results of monitoring undertaken and assessment of adverse events.
8. Advice to GPs on when to stop treatment or alter dose.
9. 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.
10. Report adverse events to the MHRA

General practitioner responsibilities

If GP has agreed to share care:

1. To contact the referring consultant without delay if they do not wish to enter into a shared care agreement.
2. Take on prescribing of the somatostatin analogue from the second prescription after communication from the specialist that the patient is stabilised.
3. Prescribe 1 month of somatostatin analogue at a time.
4. Keep a record of test results in the patient's notes.
5. Prompt referral to a specialist if there is a change in the patient's health status.
6. 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.
7. Report adverse events to the specialist and MHRA.
8. Stopping treatment in the case of a severe adverse event or as per shared care guideline.

Monitoring

Monitoring in secondary care

- Evidence of disease control; assessment of symptoms
- 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 three monthly review in oncology outpatients

Monitoring during treatment – 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.

Back-up advice and support

Oncology

- Dr D Sherriff 0845 1558155
- Dr S Pascoe 0845 1558155
- Oncology outpatients 01752 763959

Derriford Medicines Information: 01752 439976

Medicines Optimisation Teams

- NEW Devon CCG, Western Locality 01752 398800
- Kernow CCG 01726 627953

Supporting Information

Preparations

Sandostatin® (octreotide) Lar 10-mg, 20-mg and 30-mg vial

- Store at 2 to 8°C, protect from light. Can remain at room temperature on the day of injection. However the suspension must only be prepared immediately prior to injection.

Somatuline® (lanreotide) LA 30mg, Autogel: 60mg, 90mg, 120mg

Dose

- **Octreotide - Sandostatin® Lar:**
  Administered by deep intragluteal injection once every four weeks, alternated between the left and right gluteal muscle. The usual starting dose is 20mg every four weeks for three months. Response should be assessed after 3 months of treatment. (Initially, adequate control should be established with octreatide s.c. which is initiated in a secondary care environment).

For patients in whom symptoms are only partially controlled after 3 months of treatment or in patients whose symptoms relapse between injections, the dose may be increased to 20- 30mg

- **Sandostatin LAR** every 3-4 weeks. Occasionally a dose of 60mg every 3-4 weeks may be required. For patients in whom symptoms and biological markers are well controlled after 3 months of treatment, the dose may be reduced to 10mg Sandostatin LAR every 4 weeks.
- **Lanreotide - Somatuline® LA**: Administered by intramuscular injection, 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**: Administered by deep subcutaneous injection (alternated between the left and right gluteal muscle), 60mg every 28 days initially in patients receiving a somatostatin analogue for the first time. For patients considered by the specialist to be stabilised on their treatment with Somatuline Autogel, the injection may be administered by an appropriately trained friend or relative of the patient. Alternatively, such patients may self-administer the product after appropriate training. In this case the injection should be given in the upper, outer thigh.
- If required the dose of Lanreotide Autogel may be increased to 90-120mg every 4 weeks. Occasionally a dose of 240mg every 3-4 weeks may be required.

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.

Cautions

- Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients, although clinical hypothyroidism is rare (<1%). Tests of thyroid function should be done where clinically indicated.
- 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.
- Uncommon cases of bradycardia have been reported. Dose adjustments of drugs such as beta-blockers, calcium channel blockers, or agents to control fluid and electrolyte balance, may be necessary.

Side effects

(Refer to SPCs for further information)

- Injection site reactions (local pain and, rarely, swelling and rash); GI side effects (nausea, vomiting, cramping abdominal pain, abdominal bloating, flatulence, loose stools, diarrhoea and steatorrhoea); gallstone formation.
- 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.
- Steatorrhoea may respond to pancreatic enzyme treatment.

Interactions

(Refer to the BNF for further information)

The following drugs have a potentially serious interaction with somatostatin analogues, and caution must be used when prescribing concurrently:

- 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 co administration of octreotide and drugs mainly metabolised by CYP3A4, which have a low therapeutic index (e.g. carbamazepine, digoxin, warfarin and terfenadine).