BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (APC)

July 2023

Review Date: July 2024

Bulletin 7 : Information on Somatostatin analogues and Integrated Care Board / NHS England (NHSE) Commissioning Arrangements per indication

The current commissioning arrangements are complex as a result of the planned transfer of commissioning of services from NHS England to Integrated Care Boards. The Prescribed Specialised Services Manual (published 22 March 2023) advises that paediatric and adult specialised endocrinology and cancer services are now commissioned by ICBs but for 2023/24, NHS England is still managing and funding these services and including somatostatin analogues for acromegaly and cancer indications as per the NHSE excluded high cost drugs list[8,13]. In the table below, the term 'responsible commissioner, with respect to NHSE' reflects the transitional arrangements. It is anticipated that these arrangements will change in April 2024 and at that point, the ICB will take over commissioning and funding of many of these indications from NHS England.

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(Original document, approved by the Bedfordshire and Luton Joint Prescribing committee (JPC), Bulletin 217, April 2015, revised and updated June 2020).

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Table 1 - Summary of Indications, Commissioning and Formulary Status (See Table 2 for more detailed information)

Please refer to the Summary of Product Characteristics (SPC) for full prescribing information. Individual SPC's available at http://www.medicines.org.uk/emc/

Drug	Indication	Responsible Commissioner (Commissioned unless otherwise stated)	Agreed Formulary Status
Octreotide	Acromegaly	NHSE	SpIS
	Symptoms associated with carcinoid tumours with features of carcinoid syndrome, VIPomas, glucagonomas	NHSE	
	Inoperable bowel obstruction (Palliative Care)	ICB	
	Intractable diarrhoea (including that caused by chemotherapy and radiotherapy)	NHSE ICB for Palliative Care or non-Cancer indications	
	Bronchorrhoea	ICB for non cancer causes	
	Ascites	ICB for non cancer causes	
	Tumour-antisecretory effect	NHSE	
	Hypertropic pulmonary osteo-arthropathy	ICB for non cancer causes	
	Prevention of complications following pancreatic surgery	ICB	Red
	Emergency management to stop bleeding to gastro-oesophageal varices in patients with cirrhosis. To be used in association with specific treatment such as endoscopic sclerotherapy.	ICB	

Lanreotide	**Acromegaly**	NHSE	**SpIS**
	Symptoms associated with Neuroendocrine (particularly carcinoid tumours)	NHSE	
	Treatment of grade 1 and a subset of grade 2 gastroeterohepatic neuroendocrine tumours of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease.	NHSE	
Pasireotide	**Adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed.**	NHSE	**Red**
	Acromegaly [when surgery has failed or is inappropriate, and control with another somatostatin analogue is inadequate]	NHSE – not routinely commissioned	

Table 2
Please refer to the Summary of Product Characteristics (SPC) for full prescribing information. Individual SPC's available at http://www.medicines.org.uk/emc/

OCTREOTIDE (Octreotide solution for injection (ampoules, vials and pre-filled disposable syringes) Injection (Non-proprietary);Sandostatin®; Sandostatin LAR® and Olatuton® Prolonged–release powder and suspension for Injection {Long-acting depot preparations}) (1)			
Licensed/ unlicensed	**Indication and Responsible Commissioner** (8)(9)(10)	**Dose (NB – all doses stated are for Adults)**	**Comments**
Licensed indications	**Acromegaly** short-term treatment before pituitary surgery *or* long-term treatment in those inadequately controlled by other treatment *or* until radiotherapy becomes fully effective (1). **Responsible Commissioner:-** **NHSE - commissioned** Suitable for shared care with primary care (i.e. Specialist to initiate prescribing and GP to continue).	*Subcutaneous (S/C) administration:* 100-200 micrograms 3 times daily; (1). The product manufacturers state initially 0.05mg (50 micrograms) to 0.1mg (100 micrograms) every 8 or 12 hours. In most patients, the optimal daily dose will be 0.3 mg (300 micrograms). A maximum dose of 1.5 mg per day should not be exceeded (2). Sandostatin LAR®/ Olatuton® Prolonged Release: Start treatment with the administration of 20 mg Sandostatin LAR®/ Olatuton® Prolonged Release by deep intramuscular injection into the gluteal muscle at 4-week intervals for 3 months then adjust according to response (see SPC for further details).Patients on treatment with S/C Octreotide can start treatment with Sandostatin LAR/ Olatuton® Prolonged Release the day after the last dose of subcutaneous Octreotide. (3)(4) (Test dose by S/C injection 50–100 micrograms if S/C octreotide not previously given is recommended by the BNF but not the manufacturer) (1)(3)(4).	Dosage adjustment should be based on monthly assessment of serum growth hormone (GH) and insulin-like growth factor 1/somatomedin C (IGF-1) levels (target: GH <2.5 ng/mL; IGF-1 within normal range), clinical symptoms, and on tolerability. If no relevant reduction in GH levels and no improvement in clinical symptoms have been achieved within 3 months of starting treatment with octreotide, therapy should be discontinued (2). For patients on a stable dose of S/C Octreotide assessment of GH and IGHF-1 should be made every 6 months. (2). For Sandostatin LAR®/ Olatuton® Prolonged Release, dosages are adjusted according to response (GH/IGF-1 concentrations and clinical symptoms) - see SPCs for full details (3,4). For patients on a stable dose of Sandostatin LAR®/ Olatuton® Prolonged Release, assessment of GH and IGF-1 should be made every 6 months. (3)(4). Higher ('off-label') doses may be given by continuous subcutaneous infusion (CSCI). (6)

	Prevention of complications following pancreatic surgery **Responsible Commissioner:-** **ICB – commissioned**	100 micrograms three times daily by S/C injection for 7 consecutive days (2)	Starting on the day of surgery at least 1 hour before laparotomy. (2)
	Symptoms associated with carcinoid tumours with features of carcinoid syndrome, VIPomas, glucagonomas **Responsible Commissioner:–** **NHSE - commissioned** Suitable for shared care with primary care (i.e. Specialist to initiate prescribing and GP to continue).	*Subcutaneous (S/C) administration:* Initially 50 micrograms once or twice daily, gradually increased according to response to 200 micrograms 3 times daily. If rapid response required, initial dose by intravenous injection (with ECG monitoring after dilution) (1) (2). Sandostatin LAR®/ Olatuton® Prolonged Release: ***Treatment of patients with symptoms associated with functional gastro-entero-pancreatic neuroendocrine tumours****:* It is recommended to start treatment with the administration of 20 mg Sandostatin LAR®/ Olatuton® Prolonged Release by deep intramuscular injection into the gluteal muscle at 4-week intervals. Patients on treatment with subcutaneous Octreotide should continue at the previously effective dosage for 2 weeks after the first injection of Sandostatin LAR®/ Olatuton® Prolonged Release (3)(4) ***Treatment of patients with advanced neuroendocrine tumours of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded:*** The recommended dose of Sandostatin LAR®/ Olatuton® Prolonged Release is 30 mg administered by deep intramuscular injection into the gluteal muscle every 4 weeks. Treatment with Sandostatin LAR®/	*Subcutaneous (S/C) administration* Under exceptional circumstances, higher doses may be required. Maintenance doses are variable. In carcinoid tumours discontinue after 1 week, at the maximum tolerated dose, if no effect. (1)(2). Higher ('off-label') doses may be given by continuous subcutaneous infusion (CSCI). (6) Sandostatin LAR®/ Olatuton® Prolonged Release: ***Treatment of patients with symptoms associated with functional gastro-entero-pancreatic neuroendocrine tumours****:* For patients in whom symptoms and biological markers are well controlled after 3 months of treatment, the dose may be reduced to 10 mg Sandostatin LAR®/ Olatuton® Prolonged Release every 4 weeks. For patients in whom symptoms are only partially controlled after 3 months of treatment, the dose may be increased to 30 mg Sandostatin LAR®/ Olatuton® Prolonged Release every 4 weeks. For days when symptoms associated with gastro-entero-pancreatic tumours may increase during treatment with Sandostatin LAR®/ Olatuton® Prolonged Release, additional administration of S/C Octreotide is recommended at the dose used prior

		Olatuton® Prolonged Release for tumour control should be continued in the absence of tumour progression (3)(4)	to the Sandostatin LAR®/ Olatuton® Prolonged Release treatment. This may occur mainly in the first 2 months of treatment until therapeutic concentrations of octreotide are reached (3) (4).
	Emergency management to stop bleeding to gastro-oesophageal varices in patients with cirrhosis. To be used in association with specific treatment such as endoscopic sclerotherapy. **Responsible Commissioner:-** **ICB- commissioned**	*Continuous intravenous infusion:* 25micrograms/hour for 5 days. Octreotide can be used in dilution with physiological saline. In cirrhotic patients with bleeding gastro-oesophageal varices, Octreotide® has been well tolerated at continuous intravenous doses of up to 50 micrograms/hour for 5 days (2).	
	Treatment of TSH-secreting pituitary adenomas **Responsible Commissioner :–** **ICB for non cancerous tumours - commissioned.**	*Subcutaneous (S/C) administration:* The dosage most generally effective is 100 micrograms three times a day by subcutaneous injection (2). Sandostatin LAR® /Olatuton® Prolonged Release: Started at a dose of 20mg by deep intramuscular injection into the gluteal muscle at 4-weekly intervals for three months before considering dose adjustment. (3)(4)	The dose can be adjusted according to the responses of TSH and thyroid hormones. At least 5 days of treatment will be needed to judge the efficacy (2). Sandostatin LAR®/ Olatuton® Prolonged Release: The dose is then adjusted on the basis of the TSH and thyroid hormone response (3)(4).
	Inoperable bowel obstruction (Palliative Care) **Responsible Commissioner:–** **ICB – commissioned.**	250-500 micrograms/24 hours via CSCI administration to 750 micrograms/24 hours via CSCI administration, occasionally higher doses are used.(6)	
Unlicensed Indications	**Intractable diarrhoea (including that caused by chemotherapy and radiotherapy)**	Starting dose 250-500micrograms/24 hours via CSCI administration with a maximum dose of	

	Responsible Commissione :- NHSE **ICB for Palliative Care or non-Cancer indications – commissioned.**	1,500microgram/24hours via CSCI administration, occasionally higher doses are required (6).	
	Bronchorrhoea **Responsible Commissioner :-** **ICB for non cancer causes - commissioned**	Starting dose of 250-500micrograms/24 hours via CSCI administration (6).	
	Ascites **Responsible Commissioner:-** **ICB for non cancer causes – commissioned**	Starting dose 250-500micrograms/24 hours via CSCI administration with a maximum dose of 600microgram/24hours via CSCI administration (6).	
	Tumour-antisecretory effect **Responsible Commissioner:–** **NHSE - commissioned**	Starting dose 50-100micrograms twice daily via S/C injection with a maximum dose of 600microgram/24hours via CSCI administration(6).	
	Hypertropic pulmonary osteo-arthropathy **Responsible Commissioner:-** **ICB for non cancer causes – commissioned**	100micrograms twice daily by s/c injection (6).	

LANREOTIDE (Somatuline® Autogel®)			
Licensed/ unlicensed	**Indication and Responsible Commissioner (8)(9)(10)**	**Dose**	**Comments**
Licensed Indications	**Acromegaly** **Responsible Commissioner:–** **NHSE - commissioned** Suitable for shared care with primary care (i.e. Specialist to initiate prescribing and GP to continue).	Somatuline® Autogel (Deep subcutaneous administration in the gluteal region) - If somatostatin analogue not given previously, initially 60mg every 28 days, adjusted according to response. For patients treated previously with a somatostatin analogue, consult product literature for initial dose (1)(5).	Patient's response measured by reduction in symptoms and/or a reduction in GH and/or IGF-1 levels.(5)(6)
	Symptoms associated with Neuroendocrine (particularly carcinoid tumours) **Responsible Commissioner:–** **NHSE- commissioned** Suitable for shared care with primary care (i.e. Specialist to initiate prescribing and GP to continue).	Somatuline® Autogel® (Deep subcutaneous administration in the gluteal region): Initially 60-120mg every 28 days, adjusted according to response (1)(5).	The dose should be adjusted according to the degree of symptomatic relief obtained.(5)
	Treatment of grade 1 and a subset of grade 2 gastroeterohepatic neuroendocrine tumours of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in	Somatuline® Autogel® (Deep subcutaneous administration): The recommended dose is one injection of Somatuline Autogel 120 mg administered every 28 days.(5)	The treatment with Somatuline Autogel should be continued for as long as needed for tumour control.(5)

	adult patients with unresectable locally advanced or metastatic disease. **Responsible Commissioner:–** **NHSE - commissioned** Suitable for shared care with primary care (i.e. Specialist to initiate prescribing and GP to continue).		
Pasireotide (Signifor®) – Solution for Injection (0.3mg/mL, 0.6mg/mL, 0.9mg/mL); Powder + solvent for suspension for injection (10mg, 20mg, 30mg, 40mg, 60mg)			
Licensed/ unlicensed	**Indication and Responsible Commissioner (8)(9)(10).**	**Dose**	**Comments**
Licensed indications	**Adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed.** **Responsible Commissioner :–** **NHSE – Commissioned in line with NHSE Clinical Commissioning Policy 16052P(8)**	By deep intramuscular injection (Pasireotide pamoate) Initially 10 mg every 4 weeks, increased if necessary up to 40 mg every 4 weeks, dose may be titrated every 2–4 months based on response and tolerability, consider discontinuation if no clinical benefit observed, for dose adjustment due to side-effects—consult product literature. (1)(11) Hepatic impairment - Manufacturer advises initial dose of 10mg every 4 weeks in moderate impairment, (max dose of 20 mg every four weeks) avoid in severe impairment. (1)(11) By subcutaneous injection (Pasireotide disapartate) Initially 600 micrograms twice daily for 2 months, then increased if necessary to 900 micrograms twice daily, consider discontinuation if no response after 2	**Specialist centres only. No GP Prescribing.**

		months of treatment, for dose adjustment due to side-effects—consult product literature. (1) (12) Hepatic impairment - initial dose 300 micrograms twice daily (increased if necessary after 2 months to max. 600 micrograms twice daily) in moderate impairment; avoid in severe impairment. (1)(12).	
	Acromegaly [when surgery has failed or is inappropriate, and control with another somatostatin analogue is inadequate] **Responsible Commissioner:–** **NHSE** **(Not routinely commissioned) (8)**	<u>By deep intramuscular injection (Pasireotide pamoate)</u> Initially 40 mg every 4 weeks, increased if necessary up to 60 mg every 4 weeks, dose may be increased if levels of growth hormone and/or insulin-like growth factor-1 are not fully controlled after 3 months of initial dosing, for dose adjustment due to side-effects—consult product literature. Hepatic impairment - Manufacturer advises reduce initial dose to 20 mg every four weeks (max. dose 40 mg every four weeks) in moderate impairment, avoid in severe impairment. (1)(11)	**Specialist centres only. No GP Prescribing**

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