# AWMSG Secretariat Assessment Report – Limited submission

## Octreotide (Sandostatin® LAR®) 10 mg, 20 mg and 30 mg powder and solvent for suspension for injection

**Company:** Novartis Pharmaceuticals UK Ltd

**Licensed indication under consideration:** Treatment of patients with advanced neuroendocrine tumours of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded

**Marketing authorisation date:** 13 July 2011

## Comparator(s)

- The comparator included in the company submission is lanreotide (Somatuline® Autogel®).

## Limited submission details

- Anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

## Clinical effectiveness

- Octreotide (Sandostatin® LAR®) was licensed for the indication under consideration in 2011. The company and AWTTC-sought clinical opinion have confirmed that despite no health technology appraisal recommendation for somatostatin analogues (SSAs), octreotide LAR and lanreotide (Somatuline® Autogel®) for the treatment of neuroendocrine tumours (NETs) is considered standard clinical practice in Wales. However, mode of access varies across health boards.
- European Neuroendocrine Tumor Society Consensus Guidelines (2016) recommend the use of octreotide LAR and lanreotide autogel as first-line systemic therapy to control tumour growth in midgut NETs with advanced locoregional disease and/or distant metastases. Despite differences in the licensed indications for octreotide LAR and lanreotide autogel, the guidelines make no distinction between octreotide and lanreotide in the treatment pathway. The company states that although there are differences in the licensed indications, clinicians will use either of these SSAs in clinical practice. This view is supported by clinical guidelines and clinical expert opinion sought by AWTTC.
- The phase III, double-blind, randomised PROMID study provides the key clinical effectiveness evidence, comparing octreotide LAR versus placebo. Patients included in the study had locally inoperable or metastatic, midgut NETs and were treatment-naïve. The primary endpoint was time to tumour progression (or to tumour-related death). Patients in the octreotide LAR arm had significantly longer median time to tumour progression compared to placebo (14.3 months versus 6 months, respectively). A literature-based analysis of clinical trials indicated that progression free survival is an acceptable surrogate for overall survival for

neuroendocrine neoplasms. Global quality of life (assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30) was comparable between the two arms at randomisation and six months.

- There is no direct evidence comparing octreotide LAR with lanreotide autogel for the indication under consideration. The company considers that comparisons of the pivotal studies for octreotide LAR (PROMID) and lanreotide autogel (CLARINET) would not be robust due to differences in study design and populations.
- No new safety signals were identified in the PROMID study; the safety profile is consistent with that observed for patients treated with octreotide for previously licensed indications.
- Octreotide LAR is administered by deep intramuscular injection and should only be administered by a trained healthcare professional.

## Budget impact

- The company estimates that there are approximately 174 people in Wales with advanced midgut NETs. This is calculated using published prevalence and incidence data for NETs.
- The company assumes that 95% of people with advanced midgut NETs would be eligible for SSAs (with 5% of people on a 'watching and waiting' plan); of these, 50% would receive octreotide LAR and the remaining 50% would receive lanreotide autogel. These assumptions are supported by clinical expert opinion sought by AWTTC. Therefore, the company estimates that 82 people would receive octreotide in Year 1, rising to 144 people in Year 5.
- The company estimates that the net budget impact is zero, given that both octreotide LAR and lanreotide autogel are already part of standard clinical practice, and octreotide LAR is not displacing any other treatments.

## Consideration of All Wales Medicines Strategy Group (AWMSG) policy relating to orphan and ultra-orphan medicines and medicines developed specifically for rare diseases

- The company estimates that the maximum total number of people eligible for treatment with octreotide LAR in Wales is 407. This is the sum of the estimated prevalence of the indications for which octreotide is licensed: NET control (141 people), NET symptoms (198), acromegaly (62) and pituitary adenomas (6). AWTTC consider octreotide eligible to be appraised as an orphan-equivalent medicine as the full population of the licensed indications is ≤ 5 in 10,000 persons.
- The New Medicines Group (NMG) and AWMSG will consider additional criteria (see Table 1) if they consider octreotide meets the criteria to be appraised in line with the orphan, ultra-orphan and medicines developed specifically for rare diseases policy.

## Table 1. Evidence considered by NMG/AWMSG

| NMG/AWMSG Considerations | AWTTC Comments |
|---|---|
| The degree of severity of the disease as presently managed, in terms of survival and quality of life impacts on patients and their carers | NETs are slow-growing tumours and symptoms, if and when they develop, may be non-specific. As a result, diagnosis is often delayed for several years. Around 40–50% of people with small intestinal and pancreatic NETs have distant metastases at diagnosis. Where surgical cure is not possible management of the condition aims to prolong time to progression and maintain quality of life for as long as possible. Patients often maintain a good quality of life for a long period despite having metastases. However, when they do develop, symptoms resulting from peptide hormonal hypersecretion, e.g. flushing, diarrhoea, abdominal pain and bronchospasm can impact the patient's activities of daily life, emotional health, finances and ability to work. In some cases these symptoms can be life-threatening. Unpredictable tumour growth also presents psychological and physical challenges which impact on the quality of life for both the patient and their carers. |
| Whether the medicine addresses an unmet need (e.g. no other licensed medicines) | Both octreotide LAR and lanreotide autogel are already considered standard of care for systemic first-line treatment of NETs, despite no health technology appraisal recommendation. |
| Whether the medicine can reverse or cure, rather than stabilise the condition | There is no evidence that octreotide LAR can reverse or cure NETs. |
| Whether the medicine may bridge a gap to a "definitive" therapy (e.g. gene therapy) and that this "definitive" therapy is currently in development | There is no evidence that octreotide bridges the gap to a "definitive" therapy. |
| The innovative nature of the medicine | The long-acting formulation allows for four-weekly dosing. |
| Added value to the patient (e.g. impact on quality of life such as ability to work or continue in education/function, symptoms such as fatigue, pain, psychological distress, convenience of treatment, ability to maintain independence and dignity) | Global quality of life was found to be comparable between octreotide LAR and placebo in the PROMID study. |
| Added value to the patient's family (e.g. impact on a carer or family life) | Symptoms associated with NETs can impact on a patient's ability to work and to carry out activities of daily living, which in turn can impact on their family. Octreotide LAR can be used to alleviate these symptoms in addition to inhibiting tumour growth. |
| AWMSG: All Wales Medicines Strategy Group; NETs: neuroendocrine tumours; NMG: New Medicines Group | |

## Additional information

- AWTTC is of the opinion that, if recommended, octreotide (Sandostatin® LAR®) may be appropriate for prescribing within NHS Wales for the indication under consideration with a shared care agreement.
- The company anticipate that octreotide (Sandostatin® LAR®) may be supplied by a home healthcare provider.

## Evidence search

**Date of evidence search:** 16 and 19 April 2018
**Date of range of evidence search:** No date limits were applied to database searches.

## Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Octreotide (Sandostatin® LAR®) 10 mg, 20 mg and 30 mg powder and solvent for suspension for injection. Reference number: 3732. July 2018.