AWMSG Secretariat Assessment Report – Limited submission

Lanreotide (Somatuline® Autogel®) 120 mg solution for injection in a prefilled syringe

Company: Ipsen Ltd

Licensed indication under consideration: Treatment of grade 1 and a subset of grade 2 (Ki67 index up to 10%) gastroenteropancreatic neuroendocrine tumours (GEP-NETs) of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease.

Date of licence extension: 27 February 2015

Comparator(s)

- The comparator included in the company submission is octreotide (Sandostatin® LAR®).

Limited submission details

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

Clinical effectiveness

- Lanreotide (Somatuline® Autogel®) was licensed for the indication under consideration in 2015. The company and AWTTC-sought clinical expert opinion have confirmed that despite no health technology appraisal recommendation for somatostatin analogues (SSAs), lanreotide autogel and octreotide (Sandostatin® LAR®) 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 lanreotide autogel and octreotide LAR as first-line systemic therapy to control tumour growth in midgut NETs with advanced locoregional disease and/or distant metastases. The guidelines also advise that SSAs can be considered for pancreatic NETs (Ki67 index up to 10%), with a preference for lanreotide autogel due to greater evidence of lanreotide autogel use in this type of tumour. This difference is reflected in the wider licensed indication for lanreotide autogel compared with octreotide LAR. Clinical expert opinion sought by AWTTC suggests both of these SSAs are used in clinical practice.
- The phase III, double-blind, randomised CLARINET study provides the key clinical effectiveness evidence, comparing lanreotide autogel versus placebo. Patients included in the study had inoperable locally advanced or metastatic NETs of pancreatic, midgut, hindgut or unknown origin; most patients were treatment-naïve. The primary endpoint was progression-free survival. Median progression-free survival was significantly longer in the lanreotide autogel arm versus placebo (not reached [> 24.0 months] versus 18.0 months). A literature-

based analysis of clinical trials indicated that progression free survival is an acceptable surrogate for overall survival for neuroendocrine neoplasms. Change in global quality of life (assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30) from baseline to last visit was not significantly different between the lanreotide autogel and placebo groups. CLARINET also included an open-label extension to assess long-term safety; all patients who continued the study received lanreotide autogel. Median progression-free survival at final analysis was 38.5 months for patients who had received lanreotide autogel during both the core study and the open-label extension.

- Comparisons between the pivotal studies for lanreotide autogel (CLARINET) and octreotide LAR (PROMID) would not be robust due to differences in study design and populations.
- No new safety signals were identified for the indication under consideration at the time of licensing and no additional safety concerns were identified by the long-term CLARINET open-label extension study.
- Lanreotide autogel is administered by deep subcutaneous injection and, with appropriate training, can be self-administered.

Budget impact

- The company estimates that there are approximately 195 people in Wales with NETs treatable under the lanreotide autogel licence. This is based on published prevalence and incidence data for NETs, and unpublished mortality data.
- The company assumes that 95% of people with NETs treatable under the lanreotide autogel licence would be eligible to receive SSAs (with 5% of people on a 'watching and waiting' plan); of these, 50% would receive lanreotide autogel and the remaining 50% would receive octreotide LAR. These assumptions are supported by clinical expert opinion sought by AWTTC. After allowing for discontinuations, the company estimates that 90 people will receive lanreotide autogel in Year 1, rising to 163 people in Year 5.
- The company estimates that the net budget impact is zero, given that lanreotide autogel is already part of standard clinical practice, and lanreotide autogel 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 lanreotide autogel in Wales is 401. This is the sum of the estimated prevalence of the indications for which octreotide is licensed: NET control (185 people), NET symptoms (116) and acromegaly (100). AWTTC consider lanreotide autogel 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 lanreotide autogel 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 lanreotide autogel and octreotide LAR are already considered standard of care for systemic first-line treatment of NETs despite no health technology appraisal recommendation. Lanreotide autogel is the only SSA licensed for the treatment of pancreatic NETs.
Whether the medicine can reverse or cure, rather than stabilise the condition	There is no evidence that lanreotide autogel 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 lanreotide autogel bridges the gap to a "definitive" therapy.
The innovative nature of the medicine	Due to the pre-filled syringe design, lanreotide may be administered by the patients themselves or by their partner, relative or friend. This may benefit NHS resources in terms of outpatient time, and may benefit patients in terms of costs associated with travel and flexibility (being able to administer at home or on holiday). The long-acting formulation also 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)	Lanreotide autogel may give patients more control over their own treatment, e.g. administering at a preferred time during the day, being able to administer at home or whilst away from home. Change in global quality of life was not significantly different between the lanreotide autogel and placebo groups in the CLARINET study.
Added value to the patient's family (e.g. impact on a carer or family life)	As lanreotide autogel can be administered by patients, trained partners, family or friends, treatment can lessen the burden on the family of travelling to hospital visits and having to schedule their holidays around injection times. Symptoms associated with NETs can impact on a patient's ability to carry out activities of daily living and to work, which in turn can impact on the family. Lanreotide autogel can be used to alleviate these symptoms in addition to inhibiting tumour growth.
AWMSG: All Wales Medicines Strategy Group; NET: neuroendocrine tumour; NMG: New Medicines Group; SSA: somatostatin analogue.	

Additional information

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

Evidence search

Date of evidence search: 4 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. Lanreotide (Somatuline® Autogel®) 120 mg solution for injection in a prefilled syringe. Reference number: 1988. July 2018.