HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
September 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

SANDOSTATINE LP 30 mg (octreotide), somatostatin analogue

Substantial clinical benefit in the treatment of advanced, non-progressive neuroendocrine tumours of the midgut or unknown primary site with a Ki-67 index ≤ 10%, constituting a possible alternative to simple monitoring.

Insufficient clinical benefit for advanced and progressive neuroendocrine tumours of the midgut or unknown primary site.

Main points

- SANDOSTATINE LP 30 mg now has indication in the treatment of advanced neuroendocrine tumours (NETs) of the midgut or of unknown primary origin where non-midgut sites of origin have been excluded.
- Its efficacy compared with placebo has been demonstrated in terms of mean time to progression or tumour-related death. No benefit on overall survival was demonstrated
- No data in patients with this type of progressive tumour is available: its therapeutic value in progressive NETs is not established.

Pre-existing indications*

- SANDOSTATINE LP 30 mg already has Marketing Authorisation in the treatment of acromegaly, TSH-secreting pituitary adenomas and symptoms associated with functional gastro-entero-pancreatic endocrine tumours.

Therapeutic use

- Surgical resection is the only curative treatment for gastro-entero-pancreatic NETs. When this is impossible, the treatment differs according to the characteristics of the tumour:
  - In the case of non-progressive tumour, therapeutic monitoring or treatment with a somatostatin analogue at an anti-tumour dose is recommended.
  - When the tumour is progressive, the therapeutic strategy differs depending on the primary origin of the tumour. The available treatments are chemotherapy, targeted therapies (everolimus or sunitinib), interferon or chemoembolisation.
- In case of functioning tumour, regardless of its origin and its progression, symptomatic treatment with somatostatin analogue must be initiated, whether the tumour is progressive or not.
- **Role of the proprietary medicinal product in the therapeutic strategy**

Octreotide LP at anti-tumour dose can be used first line as an alternative to simple monitoring in the treatment of patients with an advanced, non-progressive NET of the midgut or unknown primary site with a Ki-67 index ≤10 %. Octreotide may allow the implementation of more aggressive treatment to be delayed. On the other hand, when the tumour is progressive, octreotide LP at anti-tumour dose has not proven its efficacy in the therapeutic strategy.
The role of octreotide as a symptomatic treatment for functioning tumours remains well established.

* This summary does not cover these indications

Clinical data

- The assessment of the safety and efficacy of octreotide LP in this new indication relies on a phase III, randomised, double-blind, versus placebo-controlled study of 85 patients with a non-resectable NET of the midgut or unknown primary site, predominantly non-proliferative (Ki-67 index ≤ 5% in 95% of cases) and with hepatic involvement < 10 % (61% of cases).
  - Octreotide LP has demonstrated its superiority versus placebo on the primary endpoint: the median time until tumour progression or death related to the tumour was longer in the octreotide LP group (14.3 months) than in the placebo group (5.9 months): HR = 0.36; 95% CI = [0.21; 0.61].
  - On the other hand, no difference was demonstrated between the two groups in terms of overall survival (HR = 0.78, 95% CI = [0.29; 2.10]).
  - Quality of life was not changed in the octreotide LP group compared to the placebo group (non-significant difference on the EORTC QLQ-C30 scale).
- The most commonly reported adverse reactions were gastrointestinal disorders (diarrhoea, abdominal pain, flatulence), erythema and depression.

Special prescribing conditions

- Initial hospital prescription.

Benefit of the medicinal product

- In advanced, non-progressive NETs of the midgut or unknown primary site with a Ki-67 index ≤ 10% in adults:
  - The actual clinical benefit* of SANDOSTATINE LP 30 mg is **substantial**,
  - SANDOSTATINE LP 30 mg does not have clinical added value** (CAV V, non-existent) in the treatment strategy for advanced, non-progressive NETs of the midgut or unknown primary site with a Ki-67 index ≤ 10%,
  - Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

- In advanced and progressive NETs of the midgut or unknown primary site in adults:
  - The actual clinical benefit* of SANDOSTATINE LP 30 mg is **insufficient**,
  - Does not recommend inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 07 September 2016 (CT-15290) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent of “no CAV”) means “no clinical added value”.