HAUTE AUTORITÉ DE SANTÉ

RARE DISEASE
New medicinal product
April 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

SIGNIFOR (pasireotide), somatostatin analogue

No clinical benefit demonstrated in acromegaly

Main points

- These new forms of SIGNIFOR, administered by intramuscular injection and at high dosages (20 mg, 40 mg and 60 mg) have Marketing Authorisation in the treatment of acromegaly in adult patients in whom surgery is not conceivable or who did not respond to surgery and who exhibit inadequate control with other somatostatin analogues.
- At the end of 6 months of treatment, 20% of patients treated with SIGNIFOR at a dose of 60 mg obtained control of the laboratory parameters (GH < 2.5 µg/l and normalisation of the level of IGF-1)
- Its safety profile is similar to that of other somatostatin analogues, with the exception of events linked to the carbohydrate metabolism, particularly diabetes, which are more frequent and more serious on SIGNIFOR.

Pre-existing indications

Two pharmaceutical forms of SIGNIFOR currently have Marketing Authorisation in two distinct indications. The pharmaceutical forms for subcutaneous injection, SIGNIFOR 0.3 mg/ml, 0.6 mg/ml and 0.9 mg/ml, have Marketing Authorisation in the treatment of Cushing's disease.
This summary does not cover this indication.

Therapeutic use

- Surgical excision is the first-line treatment for acromegaly. If GH and IGF-1 levels are not under control after surgery, or if surgery is impossible or contraindicated (patient refusal, invasive tumour), treatment with somatostatin analogues is indicated.
- In the event of failure of or intolerance to somatostatin analogues, a treatment with the growth hormone antagonist pegvisomant is suggested before considering radiation therapy.
- In case of adenoma that continues to progress despite surgery and somatostatin analogue treatment, radiotherapy is indicated.

Role of the medicinal product in the therapeutic strategy

SIGNIFOR is an alternative to SOMAVERT (pegvisomant) in patients in whom surgery is not conceivable or was not curative and who exhibit inadequate control with other somostatin analogues (lanreotide or octreotide).

Clinical data

- A study compared SIGNIFOR 40 and 60 mg with continuation of treatment with lanreotide PR or octreotide PR in 198 patients not under control on one of these two somatostatin analogues.
  At the end of 6 months of treatment, 15.4% of patients treated with pasireotide at a dose of 40 mg obtained control of the laboratory parameters (GH < 2.5 µg/l and normalisation of the level of IGF-1), as did 20% of patients receiving 60 mg.
  Normalisation of IGF-1 alone was obtained in about 25% of patients treated with pasireotide, irrespective of the dose.

Among the patients in whom the tumour volume could be evaluated in accordance with the protocol (115/198), a reduction or stabilisation was observed at 6 months in more than 70% of patients treated with pasireotide and in half of those in the active control group.
No significant improvement in quality of life was observed after 6 months of treatment with pasireotide.

- The most common adverse effects on SIGNIFOR in the course of the clinical studies were hyperglycaemia, diabetes, diarrhoea and gallstones.
  The safety profile of SIGNIFOR is generally similar to that of other somatostatin analogues, with the exception of events linked to the carbohydrate metabolism, which are more frequent and more serious on SIGNIFOR. In the above study, the incidence of hyperglycaemia in the groups treated with pasireotide was 33.3% or 30.6%, depending on the dose, versus 13.6% in the group treated with another somatostatin analogue, and that of diabetes was 20.6% and 25.8% respectively, versus 7.6%. No grade 3 or 4 adverse effects were reported in the active control group, whereas their incidence was about 13% in the pasireotide groups, almost exclusively cases of hyperglycaemia and diabetes.
  The hyperglycaemias were reversible upon discontinuation of treatment.
- Marketing Authorisation has not been granted to SIGNIFOR for the treatment of patients naïve to medicinal treatment because of the increased risk of the development of hyperglycaemia or diabetes compared with other somatostatin analogues and in view of the similar efficacy.
- SIGNIFOR has not been compared with SOMAVERT (GH antagonist), the only medicinal product with Marketing Authorisation in patients who did not respond to surgery and who exhibit inadequate control on octreotide or lanreotide.

Special prescribing conditions

- Prescription reserved for specialists in endocrinology, diabetes and metabolic disorders, or internal medicine.
- Medicine requiring special monitoring during treatment

Benefit of the medicinal product

- The actual benefit* of SIGNIFOR is moderate.
- SIGNIFOR does not provide clinical added value** (CAV V) in the management strategy for adult patients with acromegaly in whom surgery is not conceivable or was not curative and who exhibit inadequate control with another somostatin analogue.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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[i] * The actual benefit (AB) of a proprietary 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 AB, 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 means "no clinical added value".