HAUTE AUTORITÉ DE SANTÉ

NEUROLOGY
New indication
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SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VIMPAT (lacosamide), antiepileptic

High clinical benefit but no proven clinical added value, as monotherapy, for the therapeutic strategy of partial-onset seizures with or without secondary generalisation, for adults and adolescents with epilepsy.

Main points

- VIMPAT has now been granted, in addition to the marketing authorisation for combination therapy, a marketing authorisation for monotherapy treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents (16-18 years) and children over 4 years with epilepsy.
- Its non-inferiority has been demonstrated compared to carbamazepine LP in terms of efficacy, on the rate of seizure-free patients over a 6-month period.
- No robust data are available inferring superior safety of lacosamide compared to other antiepileptic treatments.
- In monotherapy treatment, it is now an alternative first-line option.

Pre-existing indications*

VIMPAT had been granted a marketing authorisation only in combination with other antiepileptics for adults, adolescents (16-18 years).
On the date of this opinion, the laboratory has not applied for the monotherapy to be registered for reimbursement for children over 4 years.

Therapeutic strategy

- In partial-onset epilepsy, monotherapy is recommended as a first-line treatment. The conventional treatments are carbamazepine, levetiracetam or phenytoin. Other substances have also been granted a marketing authorisation for this indication but are considered to be less effective and/or less safe.
- In cases of failure (inadequate response, adverse effects resulting in treatment discontinuation) despite suitable treatment dosage and compliance, replacement monotherapy is set up progressively.

- **Role of the medicinal product in the therapeutic strategy**
- VIMPAT monotherapy is an alternative first-line treatment for the treatment of partial-onset seizures with or without secondary generalisation for adults and adolescents (16-18 years) presenting with epilepsy.
- It must not be used during pregnancy, other than in cases of obvious necessity (i.e. where the benefit for the mother clearly outweighs the potential risk for the foetus). If a woman is planning a pregnancy, the use of this substance must be carefully reviewed.

Clinical data

- A double-blind non-inferiority study assessed lacosamide (400 mg/day) monotherapy versus carbamazepine LP (800 mg/day) in patients presenting with newly or recently diagnosed epilepsy with partial-onset seizures or generalised tonic-clonic seizures.

* This summary does not concern this indication.

It demonstrated the non-inferiority of lacosamide compared to carbamazepine LP on the rate of seizure-free patients over a 6-month period at the last treatment dose assessed (primary endpoint).

- A double-blind comparative prospective study versus a historical control group assessed the change for lacosamide monotherapy, in patients presenting with partial-onset epileptic seizures (with or without secondary generalisation) previously treated with 1 to 2 other antiepileptics (AEs). The rate of patients withdrawn from the study due to lack of efficacy on day 112 was 0.300 (95% CI [0.246; 0.355]) in the lacosamide 400 mg/day group suggesting superiority of the lacosamide 400 mg/day group over the historical control group. Given the heterogeneity of the characteristics of the patients from the historical control group compared to those of the lacosamide 400 mg/day group and the short study assessment period (112 days), not suitable for assessing medium-term efficacy, these data should be interpreted with caution.
- A Bayesian indirect comparison network meta-analysis assessed the efficacy and safety of lacosamide monotherapy compared to 9 other AEs used for monotherapy treatment of partial-onset epileptic seizures. The analyses of the 12 studies selected inferred numerical benefits in respect of the ratio of seizure-free patients for lacosamide compared to other AEs; however, the breadth of the confidence intervals of the comparisons meant that it was not possible to infer a difference between lacosamide and the other treatments.
- A non-comparative, non-interventional retrospective study assessed the efficacy and safety over a 12-month period of a lacosamide monotherapy treatment for partial-onset epileptic seizures with or without secondary generalisation. After 12 months of treatment, data were available for 92.7% of the patients included and the rate of patients continuing to receive lacosamide monotherapy was 60.2% (95% CI: [50.5; 69.9]) in the first-line treatment group and 62.5% (95% CI: [57.3; 67.6]) in the conversion group.
- The SPC reports a higher incidence (difference ≥ 5 %) of falls, diarrhoea and tremors in elderly patients compared to younger adult patients with monotherapy use. The most frequently reported adverse cardiac effect in elderly subjects compared to a younger population was a first-degree AV block.

Benefit of the medicinal product

- The actual clinical benefit* of VIMPAT is high.
- VIMPAT monotherapy does not provide any clinical added value** (CAV V) for the treatment of partial-onset epilepsy with or without secondary generalisation for adults and adolescents (16-18 years) presenting with newly diagnosed epilepsy.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 6 December 2017 (CT-16249)
available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV rating from I, major, to IV, minor. A CAV rating of V (equivalent to "no CAV") denotes a "lack of clinical improvement".