HAUTE AUTORITÉ DE SANTÉ

NEUROLOGY
New medicinal product
September 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

LIKOZAM (clobazam in oral suspension), benzodiazepine

No clinical benefit demonstrated in the treatment of partial or generalised epilepsy in patients over 2 years of age, in case of failure of 2 consecutive monotherapies.

Main points

- LIKOZAM has Marketing Authorisation, in combination with another antiepileptic treatment, in adults or children over 2 years of age, when treatment with one of more antiepileptics is ineffective: treatment of simple or complex partial epilepsies, with or without secondary generalisation and treatment of all types of generalised epilepsy (tonic-clonic seizures, myoclonic seizures, absence seizures).
- Without a comparative study, there was no demonstrable clinical benefit compared with other antiepileptics. The oral suspension form of clobazam has a particular benefit in patients for whom the tablet form is not suitable as well as in patients over 6 years of age.

Therapeutic use

- When prescribing an antiepileptic, the type of epilepsy and especially the type of seizures, comorbidities, associated treatments, and desire for contraception or pregnancy in a woman of childbearing age are taken into account.
- In first line, a monotherapy at progressive doses is recommended to avoid adverse effects at the start of treatment (digestive disorders and drowsiness). If needed, the dose will be increased. In case of failure or intolerance, another medication in monotherapy should be considered in the same conditions.
- Dual therapy should be used only after at least two monotherapies have failed. The use of a triple therapy or quadruple therapy must be reserved strictly for the most severe cases.
- Epilepsy and its treatment should be re-assessed, at a specialist centre, in the event of failure of one or more dual therapies.

- **Role of the medicinal product in the therapeutic strategy**

  Clobazam in oral suspension, in combination with another antiepileptic, is a therapeutic alternative in the treatment of all types of epilepsy in case of failure of two consecutive monotherapies, in adults or children over 2 years of age.

  In the treatment of certain epileptic syndromes in children, such as Dravet syndrome or Lennox-Gastaut syndrome, the use of clobazam as long-term basic treatment should be in a highly specialised setting. The treatment should be re-evaluated after an initial period not exceeding 4 weeks and regularly thereafter.

Clinical data

- The bioequivalence between pharmaceutical forms of clobazam (tablets and oral suspension) was demonstrated in a study that included 24 healthy volunteers.
- Two studies have evaluated the efficacy and safety of clobazam products in Lennox-Gastaut syndrome:
  - In a study of 68 patients aged 2 to 26 years, the mean number of weekly seizures with fall after 4 weeks of treatment decreased from 141 (±188) to 91 (±122) seizures in the group receiving a dose of clobazam of 0.25 mg/kg/day and from 207 (±229) to 32 (±57) in the group receiving a dose of 1 mg/kg/day, in combination with an antiepileptic treatment.
  - In a study of 238 patients with 61% aged 2 to 11 years, the number of weekly seizures with fall decreased linearly with the dose of clobazam after 12 weeks of treatment ($p<0.0001$).
  - The primary adverse events considered to be treatment-related were: drowsiness, lethargy, sedation, hypersialorrhea, constipation, agression, hypomania, insomnia, fever.

Benefit of the medicinal product

- The actual benefit* of LIKOZAM is substantial.
- LIKOZAM, in combination with other antiepileptics, does not provide clinical added value** (CAV V) in the therapeutic strategy for partial or generalised epilepsy in adults or children over 2 years of age, which in particular includes clobazam in the form of tablets in patients over 6 years of age, in case of failure of two consecutive monotherapies.
- Recommends 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 21 September 2016 (CT-15100) and is available at **www.has-sante.fr**

* 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”.