HAUTE AUTORITÉ DE SANTÉ

UROLOGY
New indication
April 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

DITROPAN (oxybutynin), urinary antispasmodic, anticholinergic

Low clinical benefit in the treatment of nocturnal enuresis but no demonstrated clinical advantage in the therapeutic strategy

Main points

- DITROPAN has been granted a marketing authorisation for the treatment, in children over the age of 5 years, of nocturnal enuresis associated with detrusor urinal muscle hyperactivity, whether or not combined with non-medicinal therapy, in the event of failure of another treatment
- Efficacy data are extremely limited and of low level of evidence.
- It is less safe than other anticholinergic agents in adults. In children, in cases of prolonged prescription, it may impair quality of life and compliance.
- Oxybutynin (DITROPAN) should only be prescribed upon specialist advice and its efficacy/adverse effects ratio should be regularly reassessed to determine whether or not the treatment should be continued.

Pre-existing indications*

- DITROPAN already has a marketing authorisation in adults and children over the age of 5 years for urinary incontinence, urinary urgency and pollakiuria in cases of bladder instability potentially resulting from idiopathic overactive bladder or neurogenic bladder impairment.

Therapeutic strategy

- The first-line management of nocturnal enuresis in children relies on a child information and education approach, along with observance of lifestyle and dietary rules (for a period of 1 to 3 months):
  - monitor food intake (quantity and quality), while ensuring that water intake is optimally spread out throughout the day. The recommended liquid intake for an enuretic child remains normal (i.e. 45 to 60 ml/kg), though it should be limited after 5 pm and poorly mineralised drinking water should be preferred. End-of-day access to sweet beverages, sodas and very salty foods should be banned. Evening calcium intake should be limited by moderating dairy intake.
  - promote regular micturitions throughout the day. The patient should go to the toilet five to six times per day (not forgetting when waking up and going to bed), whenever the need is felt and, when urinating, to relax as much as possible and to allow a free stream of urine, without forcing.

  According to the recommendations of a French expert, should non-medicinal management fail, if the child is motivated, then medicinal treatment may be considered. Recommended treatments are determined by the clinical orientation:
  - in the event of nocturia: treatment with desmopressin alone.
  - in the event of small bladder capacity: use of an alarm system alone.
  - otherwise: treatment with desmopressin or alarm system, as the family sees fit (alarm systems are restrictive).
- If no improvement is observed, the desmopressin / alarm system combination is recommended. After 6 months of management, if treatment has failed, treatment is stopped or specialist advice is sought. Specialist advice, imaging or a urodynamic study can be performed after 1 year of management.

* This summary does not concern these indications.

- Oral desmopressin (MINIRINMELT) has been granted a marketing authorisation for the symptomatic treatment of nocturnal enuresis in children over the age of 6 years and in adults, once any underlying organic disease has been eliminated. Treatment duration at the minimum effective dose, determined after dose adaptation, is limited to 3 months, renewable once.
- Outside of oxybutinin, no other anticholinergic agents have been granted an marketing authorisation in France for the treatment of primary nocturnal enuresis in children.

Role of the medicinal product in the therapeutic strategy

DITROPAN, combined with a non-medicinal therapy, is a second-line medicinal product. Efficacy data were obtained primarily in combination with desmopressin.

Clinical data

- Available efficacy data in the treatment of nocturnal enuresis in children are extremely limited and of low level of evidence.
- The safety profile of this anticholinergic agent (less well-tolerated in adults than other anticholinergic agents available in France) is such that it may impair quality of life and compliance in children in the event of prolonged prescription. The clinical data available for children are insufficient to allow the effect of oxybutinin to be quantified, or its therapeutic benefit to be clearly determined, including as second-line medicinal treatment after failure of desmopressin and in the event of low bladder capacity.

Benefit of the medicinal product

- The actual clinical benefit* of DITROPAN is low in this indication.
- DITROPAN does not provide any clinical added value ** (CAV V) in the therapeutic strategy.
- Approved 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 03 April 2019 (CT-17228) 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 may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

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