HAUTE AUTORITÉ DE SANTÉ

UROLOGY
New medicinal product
January 2018

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ELMIRON (pentosan polysulfate sodium or PPS)

Low actual benefit in bladder pain syndrome in adults but no clinical benefit demonstrated in the management of this syndrome

Main points

- ELMIRON has Marketing Authorisation in the treatment of bladder pain syndrome characterized by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition. It is a rare chronic disease, with symptoms that can affect activities of daily living and impair patient's quality of life.
- Clinical efficacy data, by comparison with placebo, have a low level of evidence, with a duration between 3 and 6 months of treatment. The quantity of effect is modest at best in terms of overall improvement of the symptoms in about one-third of patients. The effect on each of the symptoms (namely pain, pollakiuria, urgency and nocturia) is not properly established.
- Given these limitations, the impact on the quality of life has not been established to date.

Therapeutic use

- The aim of therapeutic management is to reduce the severity of symptoms and their impact on patients' quality of life. There is no cure or unequivocal treatment for all patients.
- Behavioural, physical and psychological approaches can be proposed as first-line therapies. Oral treatments are considered as second-line therapies and, in case of failure, local or more invasive treatments.
- Among oral treatments, apart from pentosan polysulfate sodium, amitriptyline (LAROXYL, ELAVIL), an antidepressant and anxiolytic, is used without Marketing Authorisation. Local treatments include dimethyl sulfoxide (DMSO: RIMSO, solution for intravesical instillation) and botulinum toxin A in case of overactive bladder. Use of local treatments is limited by patients' difficulty tolerating these repeated local procedures and by the risk of infection in case of instillations and of dysuria in case of botulinum toxin A injections. Moreover, bladder hydrodistention requires general anaesthesia.
- **Role of the medicinal product in the therapeutic strategy**
  ELMIRON is a second-line therapy after failure of behavioural, physical and psychological approaches. Its use should be considered in patients with pain of at least moderate intensity, urgent and frequent urination, and when histological lesions (glomerulations, Hunner's lesions) were observed in the cystoscopy. If no improvement occurs after 6 months of treatment, it is recommended that the treatment be discontinued. Its therapeutic benefit, in combination with other therapeutic approaches, has not been assessed.

Clinical data

- The results of four comparative, placebo-controlled, randomised studies are available. The dosage of PPS was between 400 mg/day (not in accordance with Marketing Authorisation [off-label], 1 study) to 300 mg/day (3 studies), for a duration of 3 (3 studies) to 6 months (1 study). The 441 patients included, mainly women with an average age of 40 to 45 years, had pollakiuria, moderate to severe pain, and glomerulations and/or Hunner's lesions in the cystoscopy.
- In the first study, a larger proportion of patients in the PPS group than in the placebo group had an improvement of at least 50% for each of the four symptoms (pain, urgency, pollakiuria and nocturia) compared to baseline. The effect size was slight. The data of each patient for each criterion are not always available and the analysis of the

results was not done according to the dose received, knowing that the 200 mg x2/day dose is not in accordance with the Marketing Authorisation (off-label). In the other three studies, the proportion of patients who reported a moderate overall improvement (≥ 50%) on the overall improvement of symptoms scale was higher in the PPS group than in the placebo group after 3 months of treatment.

- The most common adverse events with PPS were thinning hair, hair loss or alopecia and gastrointestinal disorders (diarrhoea, abdominal cramps, nausea, dyspepsia).

Special prescribing conditions

- Initial prescription restricted to urology specialists.

Benefit of the medicinal product

- The actual benefit* of ELMIRON is low.
- ELMIRON does not provide clinical added value** (CAV V, non-existent) in terms of the management of bladder pain syndrome.
- 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 31 January 2018 (CT-16342) 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”.