HAUTE AUTORITÉ DE SANTÉ

CARDIOVASCULAR
New indication
April 2018

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

FLUCORTAC (fludrocortisone), corticosteroid

Low clinical benefit for the treatment of neurogenic orthostatic hypotension, with no proven clinical added value for the treatment of this disease.

Main points

- FLUCORTAC has been granted a marketing authorisation for the treatment of neurogenic orthostatic hypotension in the event of failure of and to supplement non-medicinal measures.
- The data available, which have a low level of evidence, suggest a modest improvement in blood pressure on standing.
- No comparative data are available to date documenting the efficacy and safety of fludrocortisone compared to midodrine.
- The use of fludrocortisone is well-established in cases of failure of non-medicinal measures.

Pre-existing indication*

FLUCORTAC has been granted a marketing authorisation for mineralocorticoid replacement treatment for cases of primary, regardless of aetiology, or secondary corticoadrenal insufficiency, in combination with a glucocorticoid.

Therapeutic strategy

- The management of neurogenic orthostatic hypotension starts with non-medicinal measures such as patient education (training on recovery measures), lifestyle and dietary advice and daytime venous support of the lower limbs
- Pharmacological treatment will only be envisaged for cases of symptomatic neurogenic orthostatic hypotension as a supplement to non-medicinal measures, the aim being to reduce the intensity and/or frequency of postural symptoms associated with reducing the fall in blood pressure on standing.
  The main recommended treatments target 3 major areas: vasoconstriction (midodrine), salt sparing (fludrocortisone, hitherto off-label) or the use of recombinant erythropoietin (off-label).
- Failing a direct comparison between midodrine and fludrocortisone, the position of one in relation to the other is not known. The choice between the two substances is frequently dependent on their respective contraindications and may in some cases, particularly in cases of resistant orthostatic hypotension, be associated.
- **Role of the medicinal product in the therapeutic strategy**

  Despite efficacy data with a low level of evidence, FLUCORTAC is among the recommended first-line treatments for the treatment of neurogenic orthostatic hypotension, in the event of the failure of and to supplement non-medicinal measures.

* This summary does not concern this indication.

Clinical data

- The new data are essentially based on 5 studies, generally having a low level of evidence, obtained from a review of the literature:
  - two clinical studies: one comparative versus placebo, the other non-comparative,
  - three observational studies: two retrospective cohorts and one prospective paediatric cohort in children (aged 13 on average).

  It was not specified in these studies whether non-medicinal measures had failed for these patients. In total, blood pressure data were available in 4 of the 5 studies and suggested, without robust evidence, a modest increase in blood pressure on standing.
  The 5th study examined the improvement of postural syndromes versus atenolol in children. Although the data per treatment group are not available in the study, the authors concluded that there was no difference between the two treatment groups. This study does not provide robust data on the use of fludrocortisone in children.
- No impact on morbidity-mortality and on quality of life is demonstrated.
- The safety profile observed in the literature and the pharmacovigliance data is similar to that already known for fludrocortisone. It is marked particularly by swelling of the ankles, hypertension, nausea, headaches, vertigo and dizziness.

Benefit of the medicinal product

- The actual clinical benefit* of FLUCORTAC is low.
- FLUCORTAC does not provide any clinical added value** (CAV V) for the treatment of neurogenic orthostatic hypotension.
- 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 18 April 2018 (CT-16117) 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".