TRANSPARENCY COMMITTEE OPINION SUMMARY

SAMSCA (tolvaptan), vasopressin antagonist

High clinical benefit in hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion, but no clinical improvement in the therapeutic strategy.

Main points

- SAMSCA has MA for the treatment of adult patients with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Its efficacy has been demonstrated versus placebo only in terms of blood sodium correction, but not on clinically relevant criteria such as hyponatraemia complications, quality of life, duration of hospitalisation or mortality.
- Overly rapid correction of hyponatraemia with tolvaptan should be avoided.

Therapeutic strategy

- The treatment of SIADH includes the etiological treatment and the correction of the hyponatraemia itself, which should be progressive.
- Fluid restriction is the conventional treatment.
- ALKONATREM (formerly LEDERMYCINE) based on demeclocycline no longer has MA in France and is available via imports in exceptional cases. Other treatments such as urea and loop diuretics, not cited in the European guidelines, cannot be proposed in routine practice.
- **Role of the medicinal product in the therapeutic strategy**
  SAMSCA is a second-line treatment for chronic hyponatraemia secondary to SIADH, i.e. in cases of contraindication or failure (essentially due to non-compliance by the patient) of fluid restriction. This treatment should not be initiated in cases of acute hyponatraemia (within the first 24 to 48 hours of treatment). Reassessment of the benefit of continuing treatment and regular monitoring, particularly of liver function, are recommended.

Clinical data

- In addition to the efficacy data analysed in 2010, an interim analysis of a placebo-controlled study on 30 patients with moderate hyponatraemia confirmed the superiority of tolvaptan over the placebo in terms of the rate of patients having had a blood sodium level correction ≥ 136 mmol/L at 14 days: 94% versus 8%, p<0.001. Nevertheless, no statistically significant difference between the two groups was demonstrated on the clinical parameters assessed as secondary endpoints (mental state and duration of hospitalisation).
- The adverse effects most frequently associated with tolvaptan were thirst, dryness of mouth and pollakiuria. Overly rapid correction of hyponatraemia and potential liver toxicity in the case of repeated administration remain a major concern in respect of tolvaptan treatment and should be monitored.

Benefit of the medicinal product

- The actual clinical benefit* of SAMSCA is high
- SAMSCA does not provide an improvement in actual clinical benefit** in the therapeutic strategy for chronic hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion.
- Approved for non-hospital pharmacy reimbursement and for hospital treatment.

HAUTE AUTORITÉ DE SANTÉ

This document was drafted on the basis of the Transparency Committee opinion dated 11 July 2018 (CT-16886) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product 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 improvement in actual clinical benefit (IACB) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the IACB rating from I, major, to IV, minor. An IACB rating of V (equivalent to "no IACB") denotes a "lack of clinical improvement"