HAUTE AUTORITÉ DE SANTÉ

PAEDIATRICS
New medicinal product
October 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

SIANALAR (glycopyrronium bromide), anticholinergic

Moderate clinical benefit but no demonstrated clinical improvement in the treatment of severe sialorrhoea in children (3 to 18 years) in cases in which rehabilitation treatment has failed or is not possible

Main points

- SIANALAR has MA for the symptomatic treatment of severe sialorrhoea in children aged 3 years and over and adolescents suffering from chronic neurological disorders.
- Its period of use should be short term and intermittent.
- The efficacy data, which are solely bibliographic, are limited and concern another medicinal product based on the same active ingredient. No clinical study specifically assessing efficacy, safety and/or quality of life is available for SIANALAR.
- The anticholinergic adverse effects of glycopyrronium were relatively frequent in the clinical studies. The medium- and long-term safety data are very limited.

Therapeutic strategy

- Sialorrhoea treatment is intended to: reduce salivary flow, improve social interactions, self-esteem and hygiene. Early treatment is recommended; it includes, as a first-line approach, rehabilitation treatment followed by, in the event of failure or insufficient response, medicinal product-based treatment currently off-label (scopolamine patch, botulinum toxin injections).
- After the failure, intolerance or insufficient response in respect of these non-surgical treatments, the surgical option may be envisaged (submaxillary and sublingual gland ablation or Wharton or Stensen duct ligation/bypass). However, it involves a risk of complications.
- **Role of the medicinal product in the therapeutic strategy**
  SIANALAR has a role as a second-line approach after the failure of appropriate and sufficiently long rehabilitation treatment for the treatment of severe sialorrhoea in children from 3 years and adolescents.
  As limited long-term data are available , the period of use should be short term and intermittent. SIANALAR should not be administered to children with minor to moderate sialorrhoea.

Clinical data

- SIANALAR has been granted European MA for paediatric use based on bibliographic data on other medicinal products containing the same active ingredient (CUPVOSA and ROBINUL). No clinical study specifically assessing the efficacy and safety of SIANALAR has been made available. The superiority of CUPVOSA compared to the placebo was demonstrated primarily in a double-blind, randomised study in terms of the rate of responder patients (primary endpoint). The response was defined as an improvement of at least 3 points in a 9-point scale. The responder rate at 8 weeks was 74% with CUPVOSA versus 18% with the placebo.
- Numerous methodological limitations are observed: multiplicity of analyses with no alpha risk inflation management, brief study duration, and difficulty transposing the findings to clinical practice.
- The safety data are very limited; only short-term data on small samples are available. The anticholinergic adverse effects of glycopyrronium bromide were relatively frequent in the clinical studies.
- No data assessing quality of life in patients treated with glycopyrronium bromide are available.

Special prescription requirements

- Prescription reserved for paediatrics or neurology specialists

Benefit of the medicinal product

- The actual clinical benefit* of SIANALAR is moderate.
- SIANALAR does not provide an improvement in actual clinical benefit** (IACB V) in the treatment of severe sialorrhoea in children from 3 years and adolescents.
- 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 3 October 2018 (CT-16916) 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"