HAUTE AUTORITÉ DE SANTÉ

OPHTHALMOLOGY
New medicinal product
September 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

IKERVIS (ciclosporin), ophthalmic medicinal product

In the treatment of severe keratitis with dry eye disease, no clinical benefit demonstrated compared with eye drops that do not contain ciclosporin.

Main points

- IKERVIS is an eye-drop emulsion based on ciclosporin that is indicated in the treatment of severe keratitis in adult patients with dry eye disease that has not improved despite the instillation of tear substitutes.
- Two studies did not demonstrate the superiority of ciclosporin compared with a reference emulsion in terms of improvement in symptoms of dry eye disease after 6 months of treatment. Exploratory results suggest that IKERVIS has a positive effect on the progression of keratitis and on signs of inflammation on the ocular surface.
- In combination with tear substitutes or treatments that increase tear persistence, IKERVIS is a second-line treatment.

Therapeutic use

- The initial care of dry eye syndrome is based firstly on the correction of some of the factors that contribute to dryness (medicinal products, environmental factors) and secondly on treatment with tear substitutes (artificial tears as eye drops and gels, as well as medical devices employing viscoelastic solutions used after failure of the other two treatments).
- After failure of tear substitutes, several therapeutic options are used, depending on the severity of dry eye, its aetiology and patient characteristics, particularly: anti-inflammatories including ciclosporin, tetracyclines, punctal plugs, moisture chamber glasses, autologous serum, etc.)

Role of the medicinal product in the therapeutic strategy

IKERVIS, in combination with tear substitutes or treatments that increase tear film persistence, is a second-line treatment for severe keratitis in adult patients with dry eye disease, after the failure of tear substitutes.

Clinical data

- The efficacy of ciclosporin 0.1% has been evaluated in two phase III multicentre, randomised, comparative studies carried out in 496 and 246 patients with dry eye disease and moderate to severe keratitis. Their objective was to demonstrate the superiority of ciclosporin 0.1% relative to the vehicle (i.e. the excipients) after 6 months of treatment. This objective was not achieved in none of the two studies.
- Despite these negative results, the Transparency Committee stressed that ciclosporin has a positive effect on the progression of keratitis and the signs of inflammation on ocular surface. However, these are exploratory results that must be interpreted with caution due to the non-significance of the primary endpoint and the multiplicity of secondary tests that limit their methodological acceptability.
- The most commonly reported adverse effects with ciclosporin 0.1% were local pain (16%) and eye irritation (9%) related to instillation. The lack of experience relating to ocular safety should be emphasised, especially given uncertainties associated with the presence of cetalkonium chloride in the formulation of the eye drops.

Benefit of the medicinal product

- The actual benefit* of IKERVIS is low despite an substantial therapeutic need, given:
  - the lack of methodologically acceptable clinical data,
  - and uncertainties regarding safety, in particular due to the presence of cetalkonium chloride in the eye drops,

- IKERVIS does not provide improvement in actual benefit (CAV V) in the treatment strategy for severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

HAUTE AUTORITÉ DE SANTÉ

This document was created on the basis of the Transparency Committee Opinion of 23 September 2015 (CT-14365) and is available at **www.has-sante.fr**

[i]

[i] * 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".