Ciclosporin (Ikervis®) for the treatment of severe keratitis in adult patients with the dry eye syndrome

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 18 September 2019

Zorginstituut Nederland carried out an assessment in relation to the medicinal product ciclosporin 0.1% eye drops (Ikervis®) and concluded as follows.

In a letter dated 14 May 2019 (CIBG-19-08160), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* to assess whether the product ciclosporin 0.1% eye drops (Ikervis®) is interchangeable with any other product currently included in the insured standard package. The *Zorginstituut* has completed its assessment.

The manufacturer has asked for inclusion on List 1B of the Health Insurance Decree.

Ciclosporin 0.1% (Ikervis®) is registered for the treatment of severe keratitis in adult patients with dry eye syndrome which has not improved despite treatment with tear substitutes. Ikervis® is available as a cationic emulsion containing 0.1% ciclosporin. Each ml contains 1 mg ciclosporin. The recommended dose is one drop of Ikervis® once daily to be applied to the affected eye(s) at bedtime.

Assessment of interchangeability
Based on the criteria for interchangeability, ciclosporin 0.1% (Ikervis®) is not interchangeable with other products included in the Medicine Reimbursement System (GVS). Based on the above, ciclosporin 0.1% (Ikervis®) cannot be placed on List 1A. What has to be examined is whether ciclosporin 0.1% is eligible for placing on List 1B.

Therapeutic value
Reimbursement has been requested for the treatment of severe keratitis in adult patients with dry eye syndrome which has not improved despite treatment with tear substitutes. For this indication, a large proportion of the patients currently use the pharmacy preparation or re-delivery from compounding pharmacies (AB/DB) of a watery ciclosporin 0.05% eye drop. This AB/DB with 0.05% ciclosporin has been prescribed for these patients for more than 10 years in the Netherlands.

The European Medicine Agency (EMA) also describes, in the summary of product characteristics (SmPC) of Ikervis®, how pharmacy-prepared ciclosporin eye drops have been used for decades for severe forms of dry eye syndrome.

However, the effectiveness of the most frequently used pharmacy-prepared eye drop containing 0.05% ciclosporin has not been examined in clinical studies. We therefore discuss the effectiveness of ciclosporin 0.1% (Ikervis®) versus the baseline measurement (before the start of treatment) in patients with the indication for which reimbursement has been requested.

Zorginstituut Nederland concludes that the treatment of patients with the indication for which reimbursement has been requested, ciclosporin 0.1%

(Ikervis®) has an added value in comparison with the baseline measurement (before the start of treatment). Due to lack of information about the intended and unintended effects of AB/DB ciclosporin 0.05%, no statement can be issued about the value of ciclosporin 0.1% (Ikervis®) in comparison with AB/DB ciclosporin 0.05%. Based on the composition, the product is probably (practically) equivalent.

Budget impact analysis
The use of ciclosporin 0.1% (Ikervis®) for the indication for which reimbursement has been requested will result in estimated costs of at least €810,000 up to at most €1.6 million in the third year after inclusion in the standard package. If the substitution of AB/DB ciclosporin 0.05% is taken into account, the expected savings are estimated to be at least €345.000 and at most €691,000 in the third year after market introduction.

This budget impact analysis assumed that all patients treated with AB/DB ciclosporin 0.05% will switch to Ikervis®. Once the registered product becomes available, the sold-on preparations, which are as good as equivalent, will not (or no longer) be condoned by the Inspectorate for Health and Youth Care (IGJ).

Advice on inclusion in the GVS
Based on the criteria for interchangeability, ciclosporin 0.1% (Ikervis®) is not eligible for inclusion on List 1A. Based on the above-mentioned considerations, the *Zorginstituut* advises the Minister to include ciclosporin 0.1% (Ikervis®) on List 1B of the Health Insurance Decree. Its inclusion on List 1B will reduce costs.

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.