Technology Guidance

Ciclosporin 0.1% eye drops

for treating severe vernal keratoconjunctivitis

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing ciclosporin (CsA) 0.1% eye drops on the MOH List of Subsidised Drugs for treating severe vernal keratoconjunctivitis due to the uncertain clinical and cost effectiveness compared with current standard of care.

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Factors considered to inform the recommendations for funding

Technology evaluation

1.1. The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of ciclosporin (CsA) 0.1% eye drops for treating severe vernal keratoconjunctivitis (VKC). The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Local patient and voluntary organisations were also invited to provide their lived experiences to inform the evaluation, however, no submissions were received. Published clinical and economic evidence for CsA 0.1% eye drops was considered in line with its registered indications.

1.2. Tacrolimus eye preparations and other formulations and strengths of CsA eye drops were excluded from the evaluation as they were not registered in Singapore at the time of evaluation.

1.3. The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.4. Additional factors, including social and value judgments, may also inform the Committee's funding considerations.

Clinical need

2.1. Vernal keratoconjunctivitis, an ocular allergic disease, typically occurs in school-age children and often resolves after puberty. When the disease is severe, VKC negatively affects the patients' quality of life (QOL) and may result in corneal ulcers and even vision loss.

2.2. Ciclosporin 0.1% eye drops are the only formulation of CsA registered with the Health Sciences Authority (HSA), Singapore for severe VKC in children and adolescents between four to 18 years old. The Committee heard that in local clinical practice, CsA 0.1% eye drops plus as-needed ophthalmic corticosteroids were used for people with severe VKC who did not achieve adequate symptom control with a dual-acting mast cell stabiliser/antihistamine eye drops and required frequent doses of corticosteroids.

Clinical effectiveness and safety

3.1. The Committee reviewed the available evidence from a phase III randomised, controlled trial (VEKTIS) which compared CsA 0.1% eye drops (four times daily or twice daily) with cationic emulsion vehicle for treating severe VKC among 169 patients. Between-group comparisons showed a statistically significant difference in the primary outcome (penalty-adjusted composite efficacy score) and QOL measure, favouring CsA over vehicle.

3.2. The Committee noted that although CsA 0.1% eye drops appeared to improve the symptoms associated with VKC, the clinical relevance of the observed changes was unknown. The use of a primary composite outcome with no established validity and absence of a minimal clinically important difference (MCID) limited the interpretability and assessment of the clinical relevance of the results.

3.3. The Committee noted that treatment-emergent adverse events were similar in incidence across treatment groups, except for instillation site pain and irritation which occurred at a higher rate in the CsA group. The Committee heard that these events were mostly mild to moderate in severity and transient in nature.

3.4. Due to limitations of the evidence, the Committee concluded that the comparative clinical efficacy and safety for CsA 0.1% eye drops versus current standard of care was uncertain.

Cost effectiveness

4.1. In the absence of a local cost-effectiveness analysis, the Committee reviewed the evaluation from CADTH (Canada), the only overseas reference HTA agency that had reviewed CsA 0.1% eye drops for the treatment of severe VKC. The Committee noted that CADTH only supported funding when a price reduction condition was met, and that an 81% reduction was required for CsA 0.1% eye drops to be considered cost effective versus standard of care.

4.2. The company of CsA 0.1% eye drops was invited to submit a value-based pricing (VBP) proposal for their product for funding consideration. The Committee heard that the treatment cost of CsA 0.1% eye drops for severe VKC could be up to four times the cost for its other licensed indication (severe keratitis in dry eye disease).

4.3. In view of the uncertain comparative clinical benefit and high monthly treatment cost, the Committee considered that CsA 0.1% eye drops were unlikely to represent a cost-effective use of healthcare resources for treating severe VKC in Singapore at the price proposed by the company.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system in the first year of listing CsA 0.1% eye drops on the Medication Assistance Fund (MAF) for treating severe VKC was estimated to be less than SG$1 million.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing CsA eye drops on the MOH List of Subsidised Drugs for treating severe VKC in children and adolescents between four to 18 years old in view of uncertain clinical and cost effectiveness compared with current standard of care.