Cysteamine (Cystadrops®) for the treatment of cystinosis
Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 4 January 2018

Zorginstituut Nederland carried out an assessment of the medicinal product cysteamine (Cystadrops®), whereby they came to the following conclusion.

In a letter dated 14 August 2017 (CIBG-17-04956), the predecessor of the Minister of Health, Welfare and Sport (WVS) asked *Zorginstituut Nederland* to carry out an assessment of whether Cystadrops® (viscous cysteamine eye drops) is interchangeable with a product that is already included in the Medicine Reimbursement System (GVS). The *Zorginstituut*, advised by the Scientific Advisory Committee (WAR), has now completed this assessment.

Cystadrops® is registered for the treatment of corneal cystine crystal deposits in adults and children from 2 years of age with cystinosis. Cystadrops® is available as viscous cysteamine HCL 0.55% eye drops. Each ml contains mercaptamine hydrochloride equivalent to 3.8 mg mercaptamine (cysteamine). The recommended dose of Cystadrops® is one drop in each eye 4 times a day (during waking hours).

Assessment of interchangeability
No other product is included in the GVS for the indication 'cystinosis for the treatment of corneal cystine crystal deposits'. Cysteamine, the active substance of Cystadrops®, is already included in the GVS for the indication 'proven nephropathic cystinosis'. This is a form of cysteamine with immediate release (Cystagon®) that has been placed on List 1B. Based on the current criteria, Cystadrops® is not interchangeable with Cystagon® due to a different means of administration.

Based on the above, Cystadrops® cannot be placed on List 1A. What needs to be examined is whether Cystadrops® is eligible for placing on List 1B.

Therapeutic value
The *Zorginstituut* decided, based on various arguments, not to compare the therapeutic value of Cystadrops® with the 'Dutch pharmacy preparation', the watery cysteamine 0.5% (as HCL) eye drops that are currently used by most patients. This is because the effectiveness of the most frequently used pharmacy-prepared eye drop (drawn up by the Radboud UMC) has not been researched in clinical studies: the necessary frequency of administration is not usually realised in practice, and there are issues regarding the quality/stability of pharmacy-prepared watery cysteamine HCL eye drops. During the consultation round, these issues relating to the Dutch pharmacy preparation were confirmed by various parties, including the pharmacists involved in preparing this product from the Radboud UMC.

For this reason, the pharmacotherapeutic report only assessed the direct comparative study in which Cystadrops® (cysteamine HCL 0.55% eye drop) was compared with watery cysteamine HCL 0.1% eye drops. The final conclusion is that the therapeutic value of administering 1 drop of Cystadrops® 4 X daily is greater than that of a watery cysteamine HCL 0.1% eye drop 4 X daily.

Budget impact analysis
Taking into account various assumptions, including therapy compliance and market penetration, the inclusion of cysteamine eye drops (Cystadrops®) on List 1B of the GVS will result in a total added burden on the pharmacy budget of approximately €2.2 million in 2020. The costs of Cystadrops® per patient per year amount to €53,300, while the costs of the Dutch pharmacy preparation amount to approximately €1,840.00 per patient per year.
On the grounds of the estimated budget impact, exemption was granted from performing a pharmacoeconomic analysis.

Advice on inclusion in the GVS
The viscous cysteamine HCL 0.55% eye drop (Cystadrops®) is not interchangeable with any product in the GVS. Based on the above-mentioned considerations, we advise that Cystadrops® are included on List 1B. Inclusion on List 1B will involve additional costs amounting to €2.2 million in 2020. We should point out that the costs of Cystadrops® per patient per year amount to €53,300, while the costs of the Dutch pharmacy preparation amount to approximately €1,840 per patient per year.

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