Zorginstituut Nederland

Idebenone (Raxone®) for the treatment of Leber's Hereditary Optic Neuropathy

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 20 October 2017

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

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

Idebenone (Raxone®) is an orphan drug and is indicated for the treatment of vision impairment in adolescent and adult patients with Leber's Hereditary Optic Neuropathy (LHON). LHON is a hereditary disorder characterised by sudden vision impairment in both eyes. Idebenone is available as 150 mg film-coated tablet. The recommended dose is 900 mg idebenone per day, with a dose of two 150-mg tablets three times a day.

Assessment of interchangeability
No medicinal product is included in the GVS for LHON. Idebenone is the only registered medicinal product for the treatment of LHON and it is not interchangeable with other medicinal products that are included in the GVS.

Based on the above, idebenone (Raxone®) cannot be placed on List 1A. Whether idebenone is eligible for placing on List 1B needs to be ascertained.

Therapeutic value
There are indications that treatment with idebenone has a favourable effect on vision, particularly for some LHON-patients. To date, the biggest effect, and which is also clinically relevant, was found in patients with discordant eyes.
European and Dutch guidelines advise starting with idebenone up until 1 year after vision impairment in the second eye. This is in line with the fact that to date the biggest effect has been seen in patients with discordant vision.

Zorginstituut Nederland, advised by the Scientific Advisory Board (WAR), arrived at the final conclusion that idebenone has therapeutic added value in the treatment of Leber's Hereditary Optic Neuropathy (LHON) in comparison with placebo or no treatment. Idebenone should be used according to the Dutch guidelines, i.e., starting up to 1 year after vision impairment in the second eye; furthermore, after 12 months assessment should take place, once per 3 months, of whether the treatment should continue.

Budget impact analysis
In assessing the budget impact of idebenone on the pharmacy budget, assumptions are made about numbers of patients, the average duration of treatment and the market penetration. Including idebenone (Raxone®) on List 1B of the GVS for patients with LHON will be accompanied by additional costs to the pharmacy budget of between €870,000 and €2.3 million in the third year after its inclusion in the GVS. Uncertainty exists about the potential number of patients who are eligible for treatment with idebenone and the average duration of treatment and market penetration. The costs of idebenone per patient, per year, amount to €67,000.
On the grounds of the estimated budget impact, the product has been granted exemption from pharmacoeconomic analysis.

Appropriate use
The Dutch guidelines apply the same start criteria as the European guidelines. The Netherlands Ophthalmological Society (NOG) endorses the importance of starting treatment of patients with recent vision impairment. The Dutch guidelines also include stop criteria, which will promote appropriate use. Additional data on effectiveness over a longer period than 6 months are being collected within the framework of the conditional market registration (under exceptional circumstances). In their response, the medical experts indicate that they feel that for this orphan disorder it is desirable to be able to guarantee continuity of structured follow-up and thus to continue to limit the prescription of idebenone to neuro-ophthalmologists in the three centres of expertise: OZR, UMCG and MUMC.

Monitoring
The orphan drugs monitor was announced in the report on orphan drugs package management dated October 2015. The objective of the monitor is to support the policy of the government and health insurers, and to encourage appropriate use of orphan drugs by medical experts. The first edition of the orphan drugs monitor will be published at the latest in Q1 2018. After this, the monitor will be published annually. This monitor will follow the use and costs of idebenone (Raxone®).

Advice on inclusion in the GVS
Idebenone (Raxone®) is not interchangeable with any product in the GVS. Based on the above-mentioned considerations, *Zorginstituut Nederland* advised the Minister of WVS to include idebenone on List 1B and List 2 of the Health Insurance Decree. Inclusion on List 1B will involve additional costs.

Condition
Only for adolescent and adult patients with Leber's hereditary optic neuropathy (LHON) and who are being treated according to the relevant guidelines that have been accepted in the Netherlands by the professionals involved.

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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.