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Our reference
2020017331

Date 19 March 2020
Subject Medication Reimbursement System (GVS) assessment of trientine tetrahydrochloride (Cuprior®)

Dear Mr Bruins,

In your letter of 6 January 2020, you asked the National Health Care Institute (Zorginstituut Nederland) to carry out a substantive review of whether trientine tetrahydrochloride (Cuprior®) is interchangeable with a product that has been included in the Medication Reimbursement System (GVS). The Zorginstituut has now completed the substantive assessment. The considerations are included in the GVS report and budget impact analysis that are attached to this letter.

Cuprior® is indicated for the treatment of Wilson's disease (WD) in adults, adolescents and children aged ≥ 5 who are intolerant to therapy with D-penicillamine. Cuprior® is available as a film-coated tablet containing trientine tetrahydrochloride (trientine 4HCL), equivalent to 150 mg trientine.

The marketing authorisation holder is asking for Cuprior® to be included in Appendix 1B of the Health Insurance Regulation.

Assessment outcome

Conclusions of the GVS report

Cuprior® is not mutually interchangeable with Wilzin® (zinc acetate), the only medicinal product included in the GVS that is intended for treating WD. Any clustering that occurs as a result is thus not relevant.
Given the fact that the use of trientine dihydrochloride (triëntine 2HCL) (Cufence®) has been well-established since the sixties in treating WD, that this medicine is recommended in guidelines, and that the EMA has concluded that no significant limitations (in particular in the pharmacokinetics) have been found for Cuprior® with respect to Cufence®, the National Health Care Institute accepts the applicant's claim that Cuprior® has an equivalent therapeutic value to Cufence® for the requested indication. Because Cufence® is not included in the GVS, the question of clustering is not relevant here. Cuprior® is thus eligible for placement on list 1B.

Budget impact analysis

Including Cuprior® on list 1B of the GVS for Wilson's disease in adults, adolescents and children aged ≥ 5 who cannot tolerate therapy with D-

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penicillamine will mean additional costs estimated at between €2.1 and €7.6 million in the third year after inclusion in the basic health insurance package, if only the costs of Cuprior® are included. If allowance is made for the substitution of Cufence®, the inclusion of Cuprior® will mean cost savings estimated at between €0.6 and €1.8 million in the third year.
There is a risk that Cuprior® will be used off-label as the first line treatment. In the realistic scenario (of 196 diagnosed patients and a daily dose of 4 tablets of Cuprior®), this would involve 108 patients. If Cuprior® were to be used as a substitute for D-penicillamine, the total budget impact of Cuprior® after three years is estimated to be €7.1 million.

Advice on inclusion in the GVS
The National Health Care Institute recommends including trientine tetrahydrochloride (Cuprior®) in Appendix 1B and Appendix 2 of the Health Insurance Regulation and imposing the conditions stated below. Inclusion in Appendix 1B can be associated with cost savings. If Cuprior® is used off-label as the primary treatment, its inclusion could be associated with additional costs.

Reimbursements conditions for trientine
To be used exclusively for insured parties with Wilson's disease for whom therapy with D-penicillamine at the maximum tolerated dose is not sufficient.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board