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Our reference
2023028301

Date 19 July 2023
Re: GVS advice potassium citrate/potassium hydrogen carbonate (Sibnayal®)

Dear Mr Kuipers,

In your letter of 31 October 2022 (ref. CIBG-22-04609), you asked the National Health Care Institute to assess whether potassium citrate/potassium hydrogen carbonate (Sibnayal®) is interchangeable with a product that is included in the Medicine Reimbursement System (GVS). If this were not the case, you asked for the therapeutic value to be assessed. Finally, you requested a per-patient cost assessment for the standard therapy and for the new therapy (i.e. Sibnayal®), as far as the costs covered by the outpatient pharmaceutical budget are concerned, and where relevant supplemented by costs covered by the Healthcare Budget Framework.

Sibnayal® (potassium citrate/potassium hydrogen carbonate) is registered for the treatment of distal renal tubular acidosis (dRTA) in adults, adolescents and children aged one year and older.
The marketing authorisation holder requests the inclusion of Sibnayal® on List 1B of the Health Insurance Regulation on the basis of a claim of added value compared to the non-registered treatment alternatives.

The National Health Care Institute, advised by the Scientific Advisory Board for Medicinal Products (WAR-CG), has now completed this assessment. The outcomes of this assessment can be found in the enclosed GVS report and the underlying attachments.

Outcome of the substantive assessment
Review of interchangeability
- Sibnayal® (modified-release granules) is a combination preparation containing potassium citrate and potassium hydrogen carbonate (KCHC). No registered medicinal product is included in the GVS for the indication dRTA.

Standard or usual treatment
- The standard treatment for dRTA is alkali therapy. A European guideline states that there are many different forms of alkali supplements. These can be classified by cation type (sodium (Na^+), potassium (K^+) or sometimes magnesium (Mg^{++})), alkali (citrate or bicarbonate) and formulation (liquid,

tablet, powder or granules). KCHC and the other alkali therapies are based on the same action mechanism, which is to compensate for the acidity in the plasma.
- In the Netherlands, patients are treated with pharmacy preparations such as potassium citrate or magnesium citrate. The use of these pharmacy preparations is based on rational pharmacotherapy.
- A pharmacy preparation with potassium citrate oral solution is available for young children and people with difficulty swallowing. KCHC is not suitable for these patients.
- Potassium hydrogen carbonate as a treatment for dRTA is not common in the Netherlands, nor is a (compounded) pharmacy preparation available. Potassium hydrogen carbonate (also called hydrogen bicarbonate) is available as an over-the-counter 'Warenwetproduct' (Commodities Act product).
- In the assessment of the National Health Care Institute, KCHC is compared with alkali therapies.

Therapeutic value
- The effects of KCHC for dRTA were studied in one multicentre, open-label, pre-post (non-randomised) study involving 37 patients. In this study, an intra-patient comparison was made of the treatment with KCHC with treatments with potassium citrate, potassium bicarbonate, sodium bicarbonate and sodium citrate. The matching study questionnaire indicates that a randomised controlled study is desirable and feasible; this is, however, not available. Due to the absence of a sufficient qualitative comparison between KCHC and current standard alkali therapies, it is unclear whether KCHC has a clinically relevant effect on metabolic control compared to standard therapy.
- An added value of KCHC compared to standard alkali therapy (such as the pharmacy preparation with potassium citrate) has not been demonstrated. The benefit of ease of use (2 times a day instead of 3 times a day, no nightly dosing, better taste) does not translate into more beneficial or less adverse effects.
- KCHC is not better or worse than the potassium citrate preparation provided by compounding pharmacies; both products have an equal value.
- KCHC meets the established medical science and medical practice for dRTA in adults, adolescents and children aged one year and older.

Budget impact analysis (BIA)
Approximately 378 dRTA patients are expected to be eligible for treatment with KCHC. This estimate assumes that 100% of children and adolescents switch to KCHC due to its improved ease of use compared to standard alkali therapy. In addition, 33% of adults are assumed to switch to KCHC This corresponds to the current number of adult dRTA patients who do not achieve adequate metabolic control with standard alkali therapy.

The pharmacy purchase price of one KCHC sachet of potassium citrate (282 mg) and potassium hydrogen carbonate (527 mg) is € 2.30. The cost of a capsule of potassium citrate (500 mg; pharmacy preparation) is € 0.16.
The average annual cost for treatment with KCHC is approximately € 14,000 for adults and adolescents and around € 8,000 for children, depending on the applied dosage.

Taking into account the different assumptions, the addition of KCHC for the treatment of patients with dRTA aged 1 year and older to List 1B of the insured package results in additional costs charged to the pharmaceutical budget of approximately € 4.2 million in the third year after reimbursement. The analysis did not take into account substitution due to the lack of data on the use of standard alkali therapies in dRTA patients in Dutch clinical practice. However, the National Health Care Institute estimates that the impact of substitution on the estimated budget impact would be small, due to the (much) lower cost of pharmacy preparations compared to KCHC.

The BIA assumes that adult patients who currently achieve metabolic control with standard alkali therapy do not switch to KCHC. However, according to the registered indication, adult patients with metabolic control could also switch to KCHC due to its improved ease of use. The extent to which this will actually happen in practice is not clear. Therefore, two hypothetical scenario analyses were performed in which 50% and 100% of adult patients who achieve metabolic control with standard alkali therapies switch to KCHC. The additional costs to the pharmaceutical budget for these scenarios are approximately € 6.6 and € 9 million in the third year after reimbursement, respectively.

Pharmaco-economic analysis
Based on the estimated budget impact, the product is exempt from pharmaco-economic analysis.

Considerations

- KCHC is a fixed combination preparation with potassium citrate/potassium hydrogen carbonate. Due to the presence of two substances, it is not equivalent[1] to the single pharmacy preparation with potassium citrate.
- Based on the substantive assessment, it was concluded that KCHC has a therapeutic equivalent value compared to alkali therapy, including the pharmacy preparation with potassium citrate.
- Adding KCHC to the GVS will involve additional costs.
- The National Health Care Institute takes the view that a medicinal product that does not have any added value for the patient, but entails additional costs, is not eligible for the package.
- Therefore, the National Health Care Institute recommends that KCHC is placed on List 3A of the Health Insurance Regulation. Placement on List 3A means that the authorised medicinal product is not reimbursed, but that the pharmacy preparation containing those active substances is reimbursed in case of rational pharmacotherapy. This allows patients with dRTA to have access to treatment with alkali therapy including potassium citrate.

Recommendations from the National Health Care Institute
The National Health Care Institute has concluded that potassium citrate/potassium hydrogen carbonate (Sibnayal®) meets the established medical science and medical practice, but that there are no differences in clinical effects between potassium citrate/potassium hydrogen carbonate (Sibnayal®) and already available pharmacy preparations containing alkali supplements.

[1] 'Equivalent' as referred to in Article 2.5 - 5 Pharmaceutical care of the Health Insurance Decision.

Due to the unnecessarily high price, and from the point of view of solidarity, which is the basic principle of our healthcare system, the National Health Care Institute advises you not to include potassium citrate/potassium hydrogen carbonate (Sibnayal®) in List 1B of the GVS. To continue to guarantee patient access to alkali therapy through the pharmacy preparations, the National Health Care Institute recommends that potassium citrate/potassium hydrogen carbonate (Sibnayal®) is included in List 3A of the Health Insurance Regulation.

Yours sincerely,

Peter Siebers
Acting Chairperson of the Executive Board

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