HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
15 DECEMBER 2021

The legally binding text is the original French opinion version

potassium (citrate and bicarbonate)
SIBNAYAL
8 mEq prolonged-release granules
24 mEq prolonged-release granules

First assessment

Key points

Favourable opinion for reimbursement in the treatment of distal renal tubular acidosis (dRTA) in adults, adolescents and children aged one year and older.

What therapeutic improvement?

Therapeutic improvement compared to standard alkalising therapy.

Role in the care pathway?

In distal renal tubular acidosis (dRTA), alkalising therapy is required to correct metabolic acidosis. Patients are generally prescribed sodium bicarbonate or sodium citrate. Children require higher doses (4 to 8 mEq/kg/d) than adults (1 to 2 mEq/kg/d).

The products currently available are immediate-release formulations that require repeated daily doses (up to 6 doses per day), sometimes at night, to adequately control metabolic acidosis over a 24-hour period and have a positive impact on growth and renal function. More than 30 different alkalising formulations are available in Europe, and the absence of reimbursement means that the use of pharmacy-compounded preparations is widespread.

In France, three rapid-release medicinal products (excluding pharmacy-compounded preparations) are also available: FONCITRIL 4000 granules in single-dose sachets (containing citric acid monohydrate, anhydrous monopotassium citrate and anhydrous monosodium citrate, i.e. around 22 mEq for one single-dose sachet; medicinal product not reimbursed in the retail sector); ALCAPHOR 250 mL oral solution (containing dipotassium citrate, disodium citrate and trometamol, i.e. 25 mEq per tablespoonful; medicinal product not reimbursed in the retail sector) and UROCIT-K 10 mEq tablets (1,080 mg of potassium citrate/tablet) or 5 mEq tablets (540 mg of potassium citrate/tablet; available as part of a named-patient compassionate use programme (ATU)). In clinical practice, these medicinal products are little used. Potassium replacement (potassium citrate) is also necessary in the event of hypokalaemia.

Role of the medicinal product in the care pathway

SIBNAYAL (potassium citrate/potassium bicarbonate) represents a first-line alternative to alkalising therapy in pharmacy-compounded preparation form, already used in children aged one year and older. In children, in particular, this pharmaceutical product, administered as two doses per day, should make it possible to reduce the number of daily doses compared to alkalising therapy in pharmacy-compounded preparation form, which can require up to 6 doses per day.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Distal renal tubular acidosis (dRTA) is a rare, chronic and severe disease related to a marked deficiency in proton secretion by the distal renal tubule. The disease may be hereditary or acquired. It is expressed biologically by hyperchloraemic metabolic acidosis and plasma bicarbonate levels below the usual normal value and, sometimes, by hypokalaemia. Clinically, it can cause nephrocalcinosis, intrarenal lithiasis, or even chronic kidney disease. Delayed growth may also occur. In the absence of appropriate treatment, it has an impact on morbidity and mortality and leads to a marked deterioration in quality of life. dRTA is chronically incapacitating due to the delay in growth, skeletal deformities, kidney stones and chronic kidney failure and can be life-threatening. Some genetic forms are accompanied by deafness.

◗ SIBNAYAL (potassium citrate/potassium bicarbonate) is a curative medicinal product.

◗ Its efficacy/adverse effects ratio has not been adequately established: the non-inferiority of SIBNAYAL (potassium citrate/potassium bicarbonate) compared to a standard alkalising therapy has not been determined due to the methodology (before/after) used in the study having tested it.

◗ There are therapeutic alternatives: alkalising therapies mainly prescribed in pharmacy-compounded form.

◗ It is a first-line treatment.

Public health impact

Considering:

- the seriousness of distal renal tubular acidosis (dRTA) and its relative rarity,
- the already partially met medical need,
- the inadequately established response to the identified need, with:
    - the administration conditions for SIBNAYAL (only 2 doses per day) of a nature to improve medium and long-term compliance in patients requiring 4 to 6 doses daily with current alkalising treatments, but
    - with a demonstration of non-inferiority of SIBNAYAL compared to standard alkalising therapy that has not been adequately established, and the absence of demonstration of an additional impact on morbidity and mortality,

SIBNAYAL (potassium citrate/potassium bicarbonate) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SIBNAYAL (potassium citrate/potassium bicarbonate) is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list and/or the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages.

◗ **Recommended reimbursement rate: 35%**

Clinical Added Value

Considering:
- an expected improvement in care conditions given the delivery form of this pharmaceutical product, which should simplify the dosing regimens currently practised (expert opinion);
- the normalisation of plasma bicarbonate levels in patients receiving SIBNAYAL (potassium citrate/potassium bicarbonate) observed at up to 48 months, but with a demonstration of non-inferiority, in terms of plasma bicarbonate levels, of SIBNAYAL (potassium citrate/potassium bicarbonate) that has not been formally established compared to standard alkalising therapy in patients with distal renal tubular acidosis, and a small number of patients assessed;
- the absence of demonstration of an efficacy on nephrocalcinosis, nephrolithiasis, bone parameter, stature and growth given the limited assessment period under SIBNAYAL (data in 27 patients after 48 months of follow-up);
- the medical need already partially met by current alkalising therapies, mainly used in pharmacy-compounded form,

the Transparency Committee considers that SIBNAYAL (potassium citrate/potassium bicarbonate) provides a minor clinical added value (CAV IV) compared to the alkalising therapy currently used in pharmacy-compounded preparation form in the treatment of distal renal tubular acidosis in the MA indication.