HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
04 MARCH 2020

sevelamer (carbonate)
RENVELA 2.4 g powder for oral suspension in sachets

New indication

Key points

Favourable opinion for reimbursement only as second-line treatment for the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m2) with chronic kidney disease. RENVELA should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease.

What therapeutic improvement?

No clinical added value in its indication.

Role in the care pathway?

The treatment of hyperphosphataemia in chronic kidney disease (CKD) requires a combination of several measures: dietary control of phosphorus intake, dialysis and, usually, treatment with a phosphorus chelating agent. In practice, a calcium salt is generally prescribed as first-line treatment (off-label), as in adults, and used in the context of pharmacy compounded preparations.

Role of the medicinal product in the care pathway

RENVELA (sevelamer carbonate) is a second-line phosphorus chelating agent to be used preferentially in the event of adverse effects such as hypercalcaemia following the use of a calcium-based chelating agent as first-line treatment.

Special recommendations

The 2.4 g sachet packaging form is not appropriate for the prescribing conditions in this indication and in accordance with the dosage and treatment duration. The SPC specifies that “if a dose of 0.4 g is to be administered, please use the dedicated 0.8 g powder presentation with dosing spoon”. However, given that the contents of the sachet must be used within 30 minutes following dilution and cannot be stored, this leads to substantial product losses.

In practice, in children, sevelamer is usually started at a dose of 800 mg two to three times daily, it being possible to increase this dose up to 1,600 mg per day. Therefore this presentation is not suitable for young children. In young children, the RENVELA 0.8 g sachets presentation, also available, is more appropriate.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Hyperphosphoraemia, due to its bone and cardiovascular complications in particular, can be a serious situation in paediatric patients with chronic kidney disease given that it may be more difficult to control than in adults.
In addition to cardiovascular complications, calcium-phosphate metabolism disorders, anaemia and increased susceptibility to infections, in particular, chronic kidney disease also exposes children to a risk of growth retardation. It impairs their quality of life and has a social impact.
◗ This medicinal product is part of a preventive treatment regimen.
◗ The efficacy/adverse effects ratio of sevelamer carbonate in children with chronic kidney disease over 6 years of age and with a body surface area (BSA) of > 0.75 m² is high.
◗ No other phosphate chelating agents are currently authorised in this paediatric population in this indication. However, since they reduce the intestinal absorption of dietary phosphorus, phosphorus chelating agents are used to control the hyperphosphataemia associated with chronic kidney disease in children. The proprietary medicinal products available in France, despite only having an MA in adults, are used (off-label or as part of a pharmacy compounded preparation) in the paediatric population.
◗ The Committee considers that RENVELA (sevelamer carbonate) is a second-line phosphorus chelating agent to be used preferentially in the event of adverse effects such as hypercalcaemia following the use of a calcium-based chelating agent as first-line treatment.
It should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease.

Public health impact:
Considering:
- the seriousness of hyperphosphataemia complications in children with chronic kidney failure and its prevalence,
- the partially met medical need,
- the only partial response to the identified need, particularly in the event of hypercalcaemia under calcium-based phosphorus chelating agent treatment (available data establishing only a short-term effect on blood phosphorus levels and leading to their normalisation in less than a third (27%) of patients in the available placebo-controlled study),
- the absence of any demonstrated impact on quality of life and the organisation of care,

RENVELA (sevelamer carbonate) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of RENVELA 2.4 g powder for oral suspension in sachets is substantial only as second-line treatment in the indication "for the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m2) with chronic kidney disease".

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use only as second-line treatment in the indication "for the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m2) with chronic kidney disease" and at the marketing authorisation dosages.

Clinical Added Value

Considering:

- **the demonstrated superiority of sevelamer carbonate (RENVELA) on the reduction of blood phosphorus levels after 2 weeks compared to placebo in a randomised, double-blind trial in children - mainly adolescents - with hyperphosphataemia associated with chronic kidney disease,**
- **the limited clinical relevance of the result for this primary outcome measure, assessed in the very short term (2 weeks) in this chronic disease,**
- **the limited interest of the exploratory results of the additional, non comparative follow-up study with only 27% of the children demonstrating normalisation of phosphorus levels at 6 months,**
- **the lack of any demonstrated impact on the quality of life of the children,**
- **the absence of demonstration of an impact on morbidity and mortality, the study duration not enabling this to be assessed,**
- **and the absence of comparative data versus another phosphorus chelating agent containing a calcium salt (carbonate, acetate),**

the Transparency Committee considers that RENVELA provides no clinical added value (CAV V) as second-line treatment for the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m2) with chronic kidney disease.