HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
20 MARCH 2020

tenofovir disoproxil fumarate **(TDF)**
VIREAD (204 mg, 163 mg and 123 mg) film-coated tablets
VIREAD 33 mg/g granules

New indication

Key points

Favourable opinion for reimbursement in the indication extension for the treatment of chronic hepatitis B in paediatric patients aged 2 to <12 years, with compensated liver disease.

What therapeutic improvement?

Therapeutic improvement, in the same way as entecavir (BARACLUDE) and peginterferon alfa-2a (PEGASYS).

Role in the care pathway?

In children and adolescents, treatments for chronic hepatitis B must be prescribed as part of specific protocols and include specialised monitoring.

Where antiviral treatment is indicated, two first-line strategies can be discussed:

- peginterferon alfa-2a (PEGASYS) for a limited 48-week period,
- a nucleoside or nucleotide analogue for an extended period, i.e., tenofovir disoproxil fumarate (VIREAD) or entecavir (BARACLUDE), the only products to have a marketing authorisation in this indication.

Role of the medicinal product in the care pathway

VIREAD is a first-line treatment option, in the same way as entecavir (BARACLUDE) or peginterferon alfa-2a (PEGASYS) when antiviral treatment is indicated. However, despite an efficacy and safety profile in paediatric populations that appears to be similar to that in adults, its use in this growing population should take into account the risk of renal and bone toxicity. The SPC indicates that there are “uncertainties associated with the long term effects of bone and renal toxicity. Moreover, the reversibility of renal toxicity cannot be fully ascertained. Therefore, a multidisciplinary approach is recommended to adequately weigh on a case by case basis the benefit/risk balance of treatment, decide the appropriate monitoring during treatment (including decision for treatment withdrawal) and consider the need for supplementation”.

Special recommendations

The Committee reiterates that the expected benefit of treatment should be carefully evaluated in view of the safety data from clinical studies conducted in children and adolescents and that the decision to treat should be made on a case by case basis.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

◗ In the majority of children, hepatitis B is an asymptomatic chronic disease, with a low risk of severe complications (glomerulonephritis, D [delta] secondary infections, cirrhosis and hepatocellular carcinoma). The incidence of HBV is stable and low in children.

◗ These proprietary medicinal products are part of a curative treatment regimen.

◗ Their efficacy/adverse effects ratio is high, as long as the contraindications, special warnings and precautions for use are complied with.

◗ There are few alternatives with an MA in paediatric populations: entecavir (BARACLUDE) and peginterferon alfa-2a (PEGASYS).

◗ These proprietary medicinal products are first-line treatments.

◗ **Public health impact:**

Considering:

- the lack of seriousness of HBV infection in children in most cases due to its low rate of progression;
- the low prevalence of chronic hepatitis B in the paediatric population, in particular due to the method of virus transmission, the low frequency of perinatal contamination and the existence of a vaccine limiting the risks of infection;
- the reduction in morbidity and mortality related to hepatitis B corresponding to a public health need, particularly in children, for whom the treatment options remain limited;
- the fact that VIREAD is likely to provide a response to the medical need identified in children, based on data suggesting a virological efficacy profile comparable to that described in adults, but with uncertainties associated with the long-term effects of renal and bone toxicity in this growing population;
- the uncertainty in terms of the impact on morbidity and mortality of the antiviral treatment in children due to the low rate of progression of the disease and the lack of impact on development and quality of life in most cases;
- the lack of expected impact on the care and/or life pathway.

VIREAD is unlikely to have an additional impact on public health in this indication extension.

Consequently, the Committee considers that the clinical benefit of VIREAD is substantial in the indication extension for the treatment of chronic hepatitis B in paediatric patients aged 2 to <12 years, with compensated liver disease.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication extension and at the MA dosages, for the treatment of chronic hepatitis B in paediatric patients aged 2 to <12 years, with compensated liver disease.

01.2 Clinical Added Value

Considering:

- **demonstration of the efficacy versus placebo in terms of virological response, of the same magnitude as that observed in previous studies in adults and adolescents, with a good resistance profile,**
- **an effect size that appears to be similar to that described with the available alternatives but,**
- **uncertainties associated with the long term effects of bone and renal toxicity and,**
- **the limited number of therapeutic alternatives with an MA in children, i.e., entecavir (BARACLUDE) and peginterferon alfa-2a (PEGASYS),**

the Committee considers that VIREAD (tenofovir), in the same was as BARACLUDE and PEGASYS, provides a minor clinical added value (CAV IV) in the treatment of chronic hepatitis B in paediatric patients aged 2 to <12 years, with compensated liver disease.