CHENODEOXYCHOLIC ACID LEADIANT
(chenodeoxycholic acid), bile-acid based medicinal product

Low clinical benefit in cerebrotendinous xanthomatosis but no clinical benefit demonstrated within the therapeutic strategy

Main points

- CHENODEOXYCHOLIC ACID LEADIANT has MA in the treatment of congenital primary bile acid synthesis deficiency due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX))
- Three retrospective analyses of the medical records of patients treated with chenodeoxycholic acid show a reduction in blood cholestanol concentration (biological criterion), with conflicting results on the clinical symptoms.
- The use of chenodeoxycholic acid is established in this disease.
- The safety profile appears to be favourable.

Therapeutic strategy

- Early diagnosis and treatment of CTX are essential for avoiding the gradual deposition of cholestanol and cholesterol, responsible for neurological damage. Treatment for CTX, currently only symptomatic, includes anti-epileptics, cholesterol-lowering agents or anti-diarrheal agents and chenodeoxycholic acid (CDCA). Despite the absence of conclusive clinical data, it could be useful to treat patients early on, in order to delay the onset of symptoms and disease progression.

- **Role of the medicinal product in the therapeutic strategy**

  CHENODEOXYCHOLIC ACID LEADIANT is first-line replacement treatment in the management of congenital primary bile acid synthesis deficiency due to a lack of sterol 27-hydroxylase in adults and infants from one month of age. HMG-CoA reductase inhibitors may be used in combination.

Clinical data

- The data available on the efficacy and safety of CDCA are based on the retrospective analysis of the medical records of 3 cohorts of patients with CTX and a literature review. These studies and analyses all demonstrate a reduction in serum cholestanol concentration following treatment with CDCA. Two studies, one carried out in a centre in the Netherlands (35 patients included) and the other in a centre in Italy (28 patients included), show a slight improvement in the neurological disability scores: EDSS score (multiple sclerosis reference scale) and Rankin score, between inclusion and each visit under CDCA treatment.
- The efficacy data comprise numerous biases, in particular due to the high number of missing data, the highly heterogeneous intervals separating the measures at the same visit, cholestanol and urinary bile alcohol tests which are not specified, and which changed over the study period, lack of precision as to concomitant treatments. Also, CDCA treatment was introduced late on due to a late diagnosis, this could explain the low clinical efficacy.
- The safety data from these retrospective studies or from literature do not show any specific signals with CDCA.
Special prescription requirements

- Medicinal product subject to hospital prescription.
- Prescription by endocrinology, diabetes and metabolic diseases, gastro-enterology and hepatology, neurology or paediatric specialists.

Benefit of the medicinal product

- The actual clinical benefit* of CHENODEOXYCHOLIC ACID LEADIANT is low.
- CHENODEOXYCHOLIC ACID LEADIANT does not provide any clinical added value ** (CAV V) in the therapeutic strategy.
- Assessment favourable to be approved for hospital treatment.

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV rating from I, major, to IV, minor. A CAV rating of V (equivalent to "no CAV") denotes a "lack of clinical improvement"