HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
04 MARCH 2020

***trientine dihydrochloride*[1]**
CUFENCE 200 mg hard capsules

First assessment

Key points

Favourable opinion for reimbursement in the treatment of Wilson's disease in adults, adolescents and children ≥ 5 years intolerant to D-penicillamine therapy.

What therapeutic improvement?

No clinical added value in the management of Wilson's disease.

Role in the care pathway?

If left untreated, Wilson's disease is fatal. The prognosis depends on the severity of liver and neurological damage. The treatment of Wilson's disease includes a diet low in certain foods high in copper (chocolate, hazelnuts, shellfish, mushrooms, liver), zinc acetate or sulfate, which reduce the intestinal absorption of copper and, above all and primarily, D-penicillamine or trientine, which are copper chelating agents. The objective of treatment is to maintain serum free copper levels within acceptable limits. Zinc salts and/or D-penicillamine are recommended as first-line treatments, whereas trientine is recommended as a second-line treatment. Several adverse effects of D-penicillamine may lead to treatment discontinuation. These are mucocutaneous (early: rash, pruritus; late: gingivitis,

[1] Each hard capsule contains 300 mg trientine dihydrochloride equivalent to 200 mg trientine.

stomatitis, ulcerous lesions, drug eruption, pemphigus), renal (proteinuria), respiratory (interstitial lung disease and bronchiolitis obliterans), haematological (thrombocytopenia, agranulocytosis and bone marrow failure) and autoimmune disturbances (myasthenia, polymyositis and drug-induced lupus). In this case, patients are treated with trientine.

Role of the medicinal product in the care pathway

CUFENCE **(**trientine dihydrochloride**)** is a second-line treatment in patients intolerant to D-penicillamine.

Special recommendations

The Committee recommends that initial prescription of CUFENCE- trientine dihydrochloride (and CUPRIOR, another proprietary medicinal product containing trientine) along with any treatment changes be performed by a centre specialising in the management of Wilson's disease patients, to guarantee optimal clinical and biological monitoring and to include all these patients on the national Wilson's disease registry.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Wilson's disease (hepatolenticular degeneration) is a rare inherited disease with autosomal recessive transmission, characterised by the accumulation of copper, first in the liver, then in the brain and other tissues. Patients have primarily hepatic, neurological and psychiatric clinical symptoms.
◗ CUFENCE is a curative treatment.
◗ The efficacy/adverse effects ratio of trientine is high.
◗ There is a trientine-based therapeutic alternative (CUPRIOR), and zinc sulfate in some patients.
◗ Like CUPRIOR, CUFENCE is a second-line chelating agent indicated in adults, adolescents and children ≥ 5 years intolerant to D-penicillamine therapy (TROLOVOL).

Public health impact
Considering:
- the seriousness and the need for life-long chelating agent therapy,
- the rarity of Wilson's disease,
- the identified partially met medical need in the event of intolerance to D-penicillamine,
- the response to the identified need by the availability of a second medicinal product containing trientine in France, available in retail pharmacies, which can help significantly improve the care and life pathway of patients without adversely affecting morbidity and mortality, although this medicinal product must be stored in the refrigerator after the bottle is opened.

Like CUPRIOR, CUFENCE is likely to have an impact on public health.

Given all these elements, the Committee deems that the clinical benefit of CUFENCE is substantial in the MA indication.

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 in the marketing authorisation indication(s) and dosages.

Clinical Added Value

Given the demonstration of the efficacy of CUFENCE (INN) based solely on data of a low methodological quality, the Transparency Committee considers that CUFENCE provides no clinical added value (CAV V), in the same way as CUPRIOR (another medicinal product containing trientine), in the treatment of Wilson's disease in adults, adolescents and children ≥ 5 years intolerant to D-penicillamine therapy.