PROCYSBI (cysteamine), metabolism product

Minor improvement in the treatment of proven nephropathic cystinosis by comparison with CYSTAGON.

Main points

- PROCYSBI 25 mg and 75 mg have Marketing Authorisation in the treatment of proven nephropathic cystinosis.
- The presentation takes the form of prolonged-release gastro-resistant hard capsules, which need to be taken only once every 12 hours.
- It is an alternative to CYSTAGON (same active ingredient, but immediate release), which is the only other medicinal product with Marketing Authorisation in nephropathic cystinosis.
- PROCYSBI was found to be non-inferior to CYSTAGON in terms of maintenance of intraleukocytic cystine levels in patients managed with CYSTAGON.

Therapeutic use

- Once diagnosed, nonspecific symptomatic treatment should be instituted to offset the effects of Fanconi syndrome and the loss of fluid and electrolytes. The extrarenal complications caused by the accumulation of cystine in all organs likewise need to be managed in order to improve the patient's survival and quality of life.
- Cysteamine is currently the only available specific treatment for depletion of the lysosomal cystine content. The aim of treatment is to maintain the intraleukocytic cystine concentration below 1 nmol hemicystine per mg protein. This treatment should be initiated immediately after diagnosis of the condition and needs to be continued indefinitely for the rest of the patient's life.
- Patients with renal failure undergo dialysis while waiting for a kidney transplant. If they receive a kidney transplant, cysteamine treatment must be continued in order to limit the accumulation of cystine in other organs.
- CYSTAGON, the immediate-release formulation of cysteamine, is the only medicinal product that is currently available. In practice its dosage regimen, which involves four doses and in particular a night-time dose, and the adverse effects associated with cysteamine (notably halitosis) make good compliance with treatment difficult.
- Cysteamine is also available in the form of eye drops (Temporary Usage Authorisation) for the prevention of corneal deposits, against which the oral form of the substance is ineffective.

Role of the medicinal product in the therapeutic strategy

By decreasing the frequency of administration compared with CYSTAGON, PROCYSBI could help improve treatment compliance – and thus delay progression of the disease – and patients’ quality of life.

Clinical data

- The efficacy of PROCYSBI has been compared with that of CYSTAGON in a study that included 43 patients aged over 6 years (average 12 years) with nephropathic cystinosis in whom the intraleukocytic cystine concentration was controlled and below 2.0 nmol hemicystine per mg protein under CYSTAGON. Eligible patients were randomised to receive one of the following two treatment regimens: PROCYSBI for 3 weeks, then CYSTAGON for 3 weeks, or CYSTAGON then PROCYSBI for the same periods.
- During the treatment periods, PROCYSBI was found to be non-inferior to CYSTAGON in terms of maintenance of the intraleukocytic cystine concentration: 0.44 ± 0.06 nmol in the CYSTAGON group versus 0.52 ± 0.06 nmol in the
PROCYSBI group, i.e. a difference between treatments of $0.08 \pm 0.03$, 95% CI [0.01; 0.15], $p < 0.0001$ (per-protocol population).

- In a follow-up study over a period of 36 months, 40 patients who completed this study as well as 14 children under 6 years and 6 renal transplant patients received PROCYSBI. Interim results indicate that the intraleukocytic cystine concentration is maintained below 1 nmol hemicystine per mg protein after 31 months.
- The observed safety profile of prolonged-release cysteamine bitartrate in clinical trials is consistent with the profile known for the immediate-release cysteamine formulation. There are currently only limited clinical data evaluating PROCYSBI in children under 6 years and in transplant patients.

**Special prescribing conditions**

- Medicine for hospital prescription

**Benefit of the medicinal product**

- The actual benefit* is substantial.
- PROCYSBI provides clinical added value** (CAV IV, minor) by comparison with CYSTAGON in the management of patients with nephropathic cystinosis.
- Recommends inclusion on the list of reimbursable products for hospital use.

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1 * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

2 ** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

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