HAUTE AUTORITÉ DE SANTÉ

RARE DISEASE
Focus
July 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ELAPRASE (idursulfase), enzyme replacement

Minor improvement in Hunter syndrome

Main points

- ELAPRASE has Marketing Authorisation in the long-term treatment of patients with Hunter syndrome (mucopolysaccharidosis type II).
- It is the only enzyme replacement therapy available for managing these patients.
- Its short-term efficacy has been demonstrated on the 6-minute walk test (6MWT) versus placebo (52 weeks). There are no data showing neurological improvement on treatment.
- There are insufficient data to establish its medium and long-term efficacy. Given the long-term results in real life, one may question the relevance of the criteria used to assess the long-term efficacy of idursulfase treatment.

Therapeutic use

Mucopolysaccharidosis type II (MPS II) or Hunter syndrome is a lysosomal storage disease, of the mucopolysaccharidoses group.
The early forms of the disease (diagnosis around age 2 to 4) are the most severe; patients present brain damage leading to cognitive impairments and early death (age 10). The late forms of the disease are more moderate; survival is extended and intellectual abilities are preserved. Complications are mainly musculoskeletal and cardiorespiratory.

Enzyme replacement therapy is a first-line treatment. Symptomatic treatments, requiring a multidisciplinary team approach, may also be used. Allogeneic bone marrow transplantation can be proposed, although the clinical benefit is limited insofar as it does not impede intellectual deterioration.

Role of the medicinal product in the therapeutic strategy

ELAPRASE is the first enzyme replacement therapy available for the treatment of these patients. Clinical trials have shown short-term improvement in walking and respiratory involvement and significant results on reducing liver and spleen size and on improvement of cardiac involvement.

Clinical data

A placebo-controlled, randomised, double-blind study was done in 96 patients with MPS II, aged 5 to 31, treated for 52 weeks.

During the 2-year follow-up phase, predicted forced vital capacity was significantly improved relative to the initial status only once during the analysis (at 16 months) and not significantly improved for all the other analysis periods, that is at 4, 8, 12, 18, 20, 24, 30 and 36 months. The effect of ELAPRASE on lung function has not been established.
The results were variable regarding the 6-minute walk test (6MWT) over time; a significant improvement was observed at 16, 20, 24 and 36 months but its clinical relevance is disputable (gain of 20 to 40 m) and no statistically significant difference was observed at 18 and 30 months.
In the long-term follow-up study, the lack of a control group, the number of lost to view and the clinical relevance of the results observed raise questions and do not justify long-term maintenance of the efficacy of this treatment.

Another study evaluated the safety of ELAPRASE in children below the age of 5 years. Evaluation of efficacy was a secondary endpoint and a reduction in urine glycosaminoglycans and liver and spleen volume up to 60% were observed.

In one multi-centre, open-label observational cohort that included 647 patients, reductions were observed, relative to baseline, in median urine GAG levels and in median 6-minute walk test results.

According to the SPC, the most common adverse effects (>10%) are: headache, hypertension, flushing, wheezing, dyspnoea, abdominal pain, nausea, dyspepsia, diarrhoea, vomiting, hives, rash, itching, fever, chest pain, swelling at the infusion site and reaction to the infusion

Special prescribing conditions

- Medicines for hospital prescription reserved for certain specialists (physician experienced in the management of patients with MPS II or other inherited metabolic diseases).

Benefit of the medicinal product

- The actual benefit of ELAPRASE is substantial.
- Given the lack of quality data to justify treatment efficacy beyond the first year, the Transparency Committee believes that ELAPRASE provides minor clinical added value (CAV IV) in the management of Hunter syndrome.
- Recommends inclusion on the list of reimbursable products for hospital use.

HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 01 July 2015 (CT-13992) and is available at **www.has-sante.fr**

[i] * 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.

** 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".