OPINION ON MEDICINAL PRODUCTS

olipudase alfa

XENPOZYME 20 mg,

powder for solution for concentrate for solution for infusion

First assessment

Adopted by the Transparency Committee on 23 November 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement for the enzyme replacement therapy for the treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.

Therapeutic improvement?

Therapeutic improvement in the care pathway.

Role in therapeutic strategy?

There is currently no authorised or off-label treatment for ASMD. Reducing hepatosplenomegaly and hence correcting blood and lipid disorders, as well as improving respiratory function may improve the patient's state of health.

The current treatment of ASMD is multidisciplinary and symptomatic, and is based on:

- For cytopenia: blood transfusions (packed red blood cells) and antibiotic therapy (neutropenia),
- For lung involvement: corticosteroids or bronchodilators by the inhalation route. Anecdotal cases of pulmonary lavage, lung or bone marrow transplantation have been reported. Long-term oxygen therapies and/or continuous positive airway pressure (CPAP) therapy may also be required.
- For bone density: calcium and vitamin supplementation (vitamin D),
- For hypercholesterolaemia: high-dose statins (with close monitoring) and low-fat diet.

Splenectomy is not recommended as it is associated with a risk of pulmonary exacerbation and an increased risk of mortality.

Liver involvement must be monitored, including screening for oesophageal varix (non-selective beta-blocker prophylaxis) in patients with portal hypertension.

Lifestyle and dietary measures with a reduction in alcohol consumption, and a tailored diet must be implemented.

Role of the medicinal product

XENPOZYME (olipudase alfa) is a first-line treatment for the enzyme replacement therapy for the treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.

The Committee recommends that the decisions for treatment initiation and discontinuation of XENPOZYME (olipudase alfa) are made in ASMD reference and expert centers.

Committee's conclusions

Clinical Benefit

- Acid sphingomyelinase deficiency (ASMD) type B and A/B is a disease that is rare, progressive and serious as it is potentially life-threatening, incapacitating, with a significant impact on quality of life, affecting the paediatric and adult population.
- The proprietary medicinal product XENPOZYME (olipudase alfa) is a preventive medicinal product for the treatment of non- Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.
- The efficacy/adverse effect ratio is significant.
- There is currently no alternative for the treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.
- This product is a first-line treatment.

Public health benefit

Considering:

- the severity of the disease,
- its low prevalence,
- the unmet medical need,
- the response to the identified medical need, considering:
  - evidence of an additional impact on morbidity in adults, and suggested, at present, in children,
  - the lack of evidence of an impact on mortality in the adult and paediatric populations,
  - the expected impact on quality of life, despite the lack of probative data in adults and in children,
  - the expected impact on patients' care and life pathway, despite the lack of furnished data supporting this impact,

XENPOZYME (olipudase alfa) is likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of XENPOZYME (olipudase alfa) is significant in the marketing authorisation indication.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the marketing authorisation indication and at the marketing authorisation dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of the superiority of olipudase alfa versus placebo in adults after 52 weeks of treatment in terms of:
  - relative spleen volume variation of -39.9% (95%CI [-47.05; -32.80]; p<0.0001) and relative DLCO variation of +19.0% (95%CI [9.32; 28.70]; p=0.0004) (primary outcome measures),
  - relative liver volume variation of -26.6% (95%CI [-33.91; -19.28]; p<0.0001) and relative platelet count variation of +14.3% (95%CI [2.56; 26.10]; p=0.0185) (ranked secondary outcome measures),
- the efficacy which appears to be maintained at 104 weeks in adults, but based on limited data from the extension study,
- a suggested efficacy of olipudase alfa in children after 52 weeks of treatment on similar outcome measures to those assessed in adults in a non-comparative study,

but in view of:

- the lack of probative data on quality of life in adults and in children, while quality of life is particularly impaired in this disease,
- the lack of evidence of an impact on mortality in a condition in which life expectancy is reduced,
- the favourable safety profile in both populations, with however infusion-related reactions, of higher incidence in the paediatric population than the adult population, and serious adverse events linked with olipudase alfa treatment reported in children (anaphylactic shock, diffuse urticaria and ALAT > 10 UNL), with limited long-term safety follow-up in both populations,

the Committee deems that XENPOZYME (olipudase alfa) provides moderate clinical added value (CAV III) in the therapeutic strategy of enzyme replacement therapy for the treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.