HAUTE AUTORITÉ DE SANTÉ

ASSESS HEALTH TECHNOLOGIES

OPINION ON MEDICINAL PRODUCTS

avalglucosidase alfa

NEXVIADYME 100 mg,

powder 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

- **Pompe disease**
- **Sectors: Community and Hospital**

Key points

Approval of reimbursement for long-term enzyme replacement therapy in patient with Pompe disease (α-glucosidase acid deficiency).

Therapeutic improvement?

No therapeutic improvement in the care pathway.

Role in therapeutic strategy?

Multidisciplinary therapeutic treatment of the disease is coordinated by a hospital practitioner in concert with a reference or expert centre for metabolic or neuromuscular diseases and in concert with the primary care physician. The specific treatment of Pompe disease is based on enzyme replacement therapy. The objectives of treatment are as follows: improve or stabilise cardiac hypertrophy and function in cases of initial impairment (infantile-onset form); stabilise or slow down degradation of muscle weakness, or prevent or delay loss of deambulation; stabilise or slow down respiratory function degradation, and prevent or delay use of assisted ventilation.

The specific treatment of Pompe disease is based on enzyme replacement therapy. Treatment initiation is subject to multidisciplinary validation by experts from an accredited reference centre.

Role of the medicinal product

NEXVIADYME (avalglucosidase alfa) is the second replacement enzyme to be granted a marketing authorisation for Pompe disease, after MYOZYME (alglucosidase alfa).

In late-onset forms of the disease, considering the findings of the clinical non-inferiority study versus alglucosidase alfa conducted on treatment-naive patients, NEXVIADYME (avalglucosidase alfa) is a first-line treatment, in the same way as MYOZYME (alglucosidase alfa) for the treatment of patients with late-onset forms.

In the absence of robust comparison in infantile-onset forms, it is not possible to rank NEXVIADYME (avalglucosidase alfa) in relation to MYOZYME (alglucosidase alfa), and it represents a new first-line treatment option.

Considering the data from the review of temporary authorisations of use and the mini COMET study, NEXVIADYME (avalglucosidase alfa) treatment may be proposed to patients failing to respond to MYOZYME (alglucosidase alfa) treatment.

Committee's conclusions

Clinical Benefit

Late-onset forms of Pompe disease

- Pompe disease or glycogen storage disease type 2 is a progressive and chronic hereditary disease which progressively reduces functional capacities and lowers life expectancy in patients. The disease cause motor disability with an impact on all aspects of life: work, family, social. Treatment involves specific constraints (repeated hospitalisation, potential side-effects). The clinical symptoms in patients with the late-onset form of the disease (the most common form) are highly variable and unpredictable.
- The proprietary medicinal product NEXVIADYME (avalglucosidase alfa) is a replacement medicinal product.
- The efficacy/adverse effect ratio of NEXVIADYME (avalglucosidase alfa), which appears to be on the same scale as that of MYOZYME (alglucosidase alfa), is significant in the short term, but has yet to be defined in the longer term in view of the level of evidence of the efficacy data on disease progression and overall survival in patients.
- A therapeutic alternative is available: the proprietary medicinal product MYOZYME (alglucosidase alfa).
- NEXVIADYME (avalglucosidase alfa) is a first-line treatment

Public health benefit

Considering:

- the severity of the disease and its rare nature,
- the partially met medical need,
- the lack of additional response to the identified medical need in view of the findings of the non-inferiority study versus alglucosidase alfa and the lack of demonstrated additional impact on long-term disease progression and on overall survival in patients,
- the lack of demonstrated additional impact on delivery of care,
- the lack of demonstrated additional impact on the care or life pathway,

NEXVIADYME (avalglucosidase alfa) is not likely to have an additional impact on public health in late-onset forms of Pompe disease.

Considering all of these elements, the Committee deems that the actual clinical benefit of NEXVIADYME (avalglucosidase alfa) is low in the treatment of late-onset forms of Pompe disease.

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 above-mentioned indication and at the marketing authorisation dosages.

Recommended reimbursement rate: 15%

Infantile-onset forms of Pompe disease

- Pompe disease or glycogen storage disease type 2 is a hereditary metabolic disease primarily affecting the muscles. Infantile-onset forms are less frequent, but more severe, forms of the disease. Their rapid progression is life-threatening for children in the short term, with death occurring before 2 years of age.
- The proprietary medicinal product NEXVIADYME (avalglucosidase alfa) is a replacement medicinal product.
- The efficacy/adverse effect ratio of NEXVIADYME (avalglucosidase alfa) is significant in the short term, but not defined in the medium and long term due to the lack of data demonstrating its impact on disease-induced heart and muscle impairment.
- A therapeutic alternative is available: the proprietary medicinal product MYOZYME (alglucosidase alfa).
- NEXVIADYME (avalglucosidase alfa) is a first-line treatment

Public health benefit

Considering:

- the severity of the disease and its rare nature,
- the partially met medical need,
- the partial and short-term response of NEXVIADYME (avalglucosidase alfa) to the identified medical need (lack of data on neurological impairment-related disability and quality of life),
- the lack of demonstrated additional impact on delivery of care,
- the lack of demonstrated additional impact on the care or life pathway,

NEXVIADYME (avalglucosidase alfa) is not likely to have an additional impact on public health in infantile-onset forms of Pompe disease.

Considering all of these elements, the Committee deems that the actual clinical benefit of NEXVIADYME (avalglucosidase alfa) is significant in the treatment of infantile-onset forms of Pompe disease.

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 above-mentioned indication and at the marketing authorisation dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Late-onset forms of Pompe disease

Considering:

- the findings of a study demonstrating the non-inferiority, but not superiority, of NEXVIADYME (avalglucosidase alfa) versus MYOZYME (alglucosidase alfa) in terms of transient benefit on the functional clinically relevant outcome measure, namely FVC assessed after 49 weeks of treatment in hitherto enzyme therapy treatment-naive patients,
- the uncertainties around the long-term efficacy of NEXVIADYME (avalglucosidase alfa),
- the safety profile of NEXVIADYME (avalglucosidase alfa) which appears to be favourable,

the Committee deems that NEXVIADYME (avalglucosidase alfa) provides no clinical added value (CAV V) in the therapeutic strategy of late-onset forms of Pompe disease.

Infantile-onset forms of Pompe disease

Considering:

- the predominantly non-comparative exploratory data from a multi-cohort phase II study, on patients with an infantile-onset form of the disease (which is a more severe form of the disease than the late-onset form) who demonstrated cardiac or muscle parameter stabilisation, lack of degradation, while these patients were previously treated with alglucosidase alfa and exhibited a decline or poor response under this first treatment,
- the lack of data as to the longer-term progression of heart, muscle and neurological impairments ultimately leading to disability, and on overall survival in patients;
- the severity of this form of Pompe disease and the partially met medical need,
- the safety profile of NEXVIADYME (avalglucosidase alfa) which appears to be favourable in the paediatric population,

the Committee deems that NEXVIADYME (avalglucosidase alfa) provides no clinical added value (CAV V) in the therapeutic strategy of infantile-onset forms of Pompe disease.