NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Rebisufligene etisparvovec for treating mucopolysaccharidosis type IIIA ID6540

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of rebisufligene etisparvovec within its marketing authorisation for treating mucopolysaccharidosis type IIIA.

Background

Mucopolysaccharidosis type III (MPS type III, also known as Sanfilippo syndrome) is an inherited lysosomal storage disorder caused by a lack of the enzymes required to break down a long carbohydrate molecule called heparan sulfate. The enzyme deficiency leads to accumulation of heparan sulphate in the cells of several tissues and organs, causing progressive tissue damage, particularly to the brain and spinal cord. MPS III can be split into four subtypes (type A, B, C or D), each caused by deficiency of a different enzyme responsible for breaking down heparan sulfate. Type IIIA is caused by missing or altered heparan N-sulphatase. MPS type IIIA is the most common subtype of MPS type III globally and is the most severe subtype.[1]

Most cases of MPS type IIIA are diagnosed in early childhood, and early symptoms may include delays in speech and language development, behavioural issues, and impaired motor skills. The condition causes a wide range of symptoms that may also include hyperactivity, sleep disturbances, frequent respiratory infections, and gastrointestinal issues. Physical features associated with MPS type IIIA that may become more visible over time include coarse facial features, prominent eyebrows, and excess body hair.[2]

As the condition progresses over time, people begin to lose previously acquired cognitive or motor skills (including the ability to walk or speak). Neurological and physical decline can be further exacerbated by physical symptoms which can include musculoskeletal issues, an enlarged liver or spleen, cardiovascular complications, and vision or hearing loss. In the later stages, people may begin to have seizures and difficulty swallowing.[2] The average life expectancy for someone with MPS IIIA is around 15-20 years[3], but can vary depending on the severity and timing of symptoms.

Around 150 people are living with MPS type III in the UK, and between 2010 and 2020, 83 babies with MPS type III were born in the UK.[2] Incidence estimates suggest that MPS IIIA affects between 0.60 and 1.26 people per 100,000 UK live births.[4]

There is currently no cure for MPS type IIIA and current treatment is focused on managing symptoms and complications to improve quality of life. Management requires a multidisciplinary approach and may include behavioural therapies, educational support and medication to manage seizures and other physical complications. Speech therapy to support communication, and physiotherapy or specialist equipment to aid mobility, may also be part of care.[2] MPS type IIIA and other lysosomal storage disorders are usually managed in specialist centres in England.

The technology

Rebisufligene etisparvovec, also known as UX111 (brand name unknown,Ultragenyx Pharmaceutical) does not currently have a marketing authorisation in the UK for treating mucopolysaccharidosis type IIIA. It has been studied in single arm clinical trials in people who are at least 6 months of age with MPS type IIIA.

Intervention(s)	Rebisufligene etisparvovec
Population(s)	People with MPS type IIIA
Comparators	Established clinical management without rebisufligene etisparvovec
Outcomes	The outcome measures to be considered include: • cognitive and functional impairment • speech and communication • mobility • respiratory and cardiac function • change in spleen volume • change in liver volume • growth and development • vision and hearing • mortality • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related highly specialised technology appraisals:** Elosulfase alfa for treating mucopolysaccharidosis type 4A (2022) NICE highly specialised technology guidance 19.

Questions for consultation

Where do you consider rebisufligene etisparvovec will fit into the existing care pathway for MPS type IIIA in the NHS?

How is best supportive care for MPS type IIIA defined in the NHS?

Is there currently any screening in place in the NHS for MPS type IIIA?

Is there any available data on the prevalence of MPS type IIIA in England?

Would rebisufligene etisparvovec be used in a population with advanced disease?

Are the outcomes listed appropriate?

Are there any relevant subgroups that should be included in the scope?

Please select from the following, will rebisufligene etisparvovec be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would rebisufligene etisparvovec be a candidate for managed access?

Do you consider that the use of rebisufligene etisparvovec can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which rebisufligene etisparvovec will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE proposes to evaluate this technology through its Highly Specialised Technologies Evaluation Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on NICE's health technology evaluation processes is available at: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

References

1. Muschol N, Giugliani R, Jones SA et al. (2022) Sanfilippo syndrome: consensus guidelines for clinical care. Orphanet Journal of Rare Diseases 17(1):391.

2. MPS Society UK (2024) MPS III Sanfilippo – information for individuals, parents and families. Accessed January 2026.

3. Lavery C, Hendriksz CJ, Jones SA (2017). Mortality in patients with Sanfilippo syndrome. Orphanet journal of rare diseases 12(1):168.

4. Héron B, Mikaeloff Y, Froissart R et al (2011). Incidence and natural history of mucopolysaccharidosis type III in France and comparison with United Kingdom and Greece. American Journal of Medical Genetics Part A. 155(1):58-68