NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Olipudase alfa for treating Niemann-Pick disease types A and B

Draft scope

Draft remit/evaluation objective

To evaluate the benefits and costs of olipudase alfa within its marketing authorisation for treating Niemann-Pick disease types A and B for national commissioning by NHS England.

Background

Niemann-Pick disease is a group of inherited autosomal recessive metabolic disorders. Niemann-Pick types A and B are caused by mutations in the SMPD1 gene. This gene mutation leads to a deficiency in an enzyme called acid sphingomyelinase, which breaks down a naturally occurring fatty substance called sphingomyelin. The deficiency in this enzyme leads to accumulation of sphingomyelin in cells throughout the body. In Niemann-Pick types A and B, build-up of sphingomyelin occurs in the liver, spleen and lungs. In Niemann-Pick type A sphingomyelin build-up also occurs in the brain leading to severe neurological problems. Niemann-Pick types A and B are also collectively known as Acid Sphingomyelinase Deficiency (ASMD)[1].

Signs and symptoms of Niemann-Pick type A develop within the first few months of life and include feeding difficulties; prolonged jaundice; enlargement of the liver and spleen and progressive loss of early motor skills, including ataxia. The prognosis for most children with Niemann-Pick type A is poor with a rapid decline in health leading to death by 2 to 5 years of age. Signs and symptoms of Niemann-Pick type B usually occur in childhood and include enlargement of organs, usually starting with the liver or spleen; poor growth; susceptibility to respiratory infections; bleeding problems and bone pain. Life expectancy for people with Niemann-Pick type B is highly variable depending on the severity of symptoms. Some people present with a type AB variant, with symptoms ranging from moderate to severe which may include neurological difficulties, cognitive impairment and ataxia[2].

It is estimated that around 1 in 10 million people are born with Niemann-Pick type A. It is more common in the Ashkenazi Jewish population, with an increased incidence of around 1 in 40,000[3]. Around 1 in 250,000 people are born with Niemann-Pick type B[4], suggesting around 240 people are born with Niemann-Pick type B per year in England and Wales[5].

There are currently no specific treatments or cure for Niemann-Pick type A or B. However, people with Niemann-Pick type A or B will benefit from supportive or palliative treatments. These may include treatment for neurological symptoms such as anticonvulsants, anticholinergic drugs and

tricyclic antidepressants. Other treatments may be given for insomnia, drooling, gastro-intestinal problems and other symptoms of the disease[2].

The technology

Olipudase alfa (brand name unknown, Sanofi Genzyme) is a recombinant human acid sphingomyelinase. It is an enzyme replacement therapy which aims to replace the deficient or defective enzyme acid sphingomyelinase. It is administered intravenously.

Olipudase alfa does not currently have a marketing authorisation in the UK for Niemann-Pick disease type A or B. It has been studied in clinical trials in children and adults.

Intervention(s)	Olipudase alfa
Population(s)	People with Niemann-Pick disease type A or type B (including type AB variant)
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • change in spleen volume • change in lung function • change in liver function • change in physical observations (including observations or measurements from examination of the skin, head, eyes, ears, nose and throat; lymph nodes; heart, vital signs, lungs and abdomen; extremities and joints and height) • change in neurological observations (including observations or measurements from examination of coordination; cranial nerves; extrapyramidal features; fundoscopy; gait; motor skills; peripheral nervous system; reflexes; sensory nervous system; strength and mental status) • change in biomarkers (including high sensitivity C reactive protein; ceramide; iron; cardiac troponin I; ferritin; interleukin-6; interlukin-8 and calcitonin) • mortality

	• adverse effects of treatment • health-related quality of life.
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• cost effectiveness using incremental cost per quality-adjusted life year • patient access schemes and other commercial agreements • the nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	• Guidance will only be issued in accordance with the marketing authorisation. • Guidance will take into account any Managed Access Arrangement for the intervention under evaluation
Related NICE	None.

recommendations and NICE Pathways	
Related National Policy	NHS England (2019) The NHS long term plan NHS England (2013) 2013/14 NHS standard contract for metabolic disorders (adult). Service Specification No. E06/S/a NHS England (2013) 2013/14 NHS standard contract for metabolic disorders (laboratory services). Service Specification No. E06/S/c NHS England (2018/2019) Manual for prescribed specialised services 2018/19. Chapter 62, Highly specialist metabolic disorder services (adults and children) Department of Health & Social Care (2021) The UK Rare Diseases Framework Department of Health & Social Care (2019) The UK strategy for rare diseases: 2019 update to the Implementation Plan for England Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 and 4.

Questions for consultation

How many people are currently being treated for Niemann-Pick disease types A and B in England?

Have all relevant comparators for olipudase alfa been included in the scope? Which treatments are considered to be established clinical practice in the NHS for Niemann-Pick disease types A and B?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

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 olipudase alfa 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 Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

References

1 National Organization for Rare Disorders (2019) Acid Sphingomyelinase Deficiency. Accessed September 2021

2 Patient UK (2016) Niemann-Pick Disease. Accessed September 2021

3 NPUK ASMD Niemann-Pick Disease Type A. Accessed September 2021

4 NPUK ASMD Niemann-Pick Disease Type B. Accessed September 2021

5 Office for National Statistics (June 2020) Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019. Accessed September 2021