NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Sebelipase alfa for treating Wolman disease ID3995

Final scope

Final remit/evaluation objective

To evaluate the benefits and costs of sebelipase alfa for treating Wolman disease for national commissioning by NHS England.

Background

Lysosomal acid lipase (LAL) deficiency is an inherited autosomal recessive lysosomal storage disorder.[1] It is caused by a deficiency of the LAL enzyme resulting in abnormal accumulation of lipids in cells primarily in the gastrointestinal, hepatic and cardiovascular systems. LAL deficiency is caused by a marked decrease or loss in LAL enzyme activity and affects people of all ages from infancy through adulthood.

Wolman disease is a type of LAL deficiency that presents in babies and children under 2 years as rapidly progressing multisystem disease.[1] Wolman disease is characterised by intestinal failure and severe malabsorption, growth failure, hepatosplenomegaly and progressive liver fibrosis and cirrhosis.[2,3] The condition normally results in death in the first 6 months of life, usually due to multiple organ failure. For the smaller group of children diagnosed slightly later (under 2 years), there is still usually evidence of growth failure in the first 6 months of life.[3]

Cholesteryl ester storage disease is a type of LAL deficiency presenting later in life, mostly in childhood (over 2 years) and adolescence.[4] It tends to have less severe presenting symptoms but can lead to hepatic and cardiovascular problems including hepatomegaly, cirrhosis, liver failure, dyslipidaemia and accelerated atherosclerosis.[4]

The prevalence of LAL deficiency in England is unknown based on currently available information. It is estimated that on average 1 or 2 babies with Wolman disease are born every 1 or 2 years. The estimated incidence rate for Wolman disease is approximately 1 in 350,000 births, and for cholesteryl ester storage disease, it is 2.5 in 100,000 births.[5,6] LAL deficiency affects males and females equally.

Enzyme replacement therapy with sebelipase alfa is the only licensed treatment option for LAL deficiency, including the subgroup with Wolman disease.[1] Currently, sebelipase alfa is not routinely commissioned by NHS England,[7] however most babies and children with Wolman disease are treated with sebelipase alfa through clinical trials or a company compassionate use program. Treatment for Wolman disease without sebelipase alfa is usually palliative and supportive, because of the severe,

multiorgan and rapidly progressive nature of the condition. A minimal or fat free diet may be used to reduce accumulation of LAL substrates (cholesteryl esters and triglycerides) in the body (also called dietary substrate reduction).[8] Intravenous nutritional support is also provided.[1] Medication may be needed to supplement adrenal hormones as adrenal gland dysfunction is common. Hematopoietic stem cell transplant may be used in some people.[8]

The NICE evaluation of sebelipase alfa for treating LAL deficiency (ID737) has been paused while this evaluation for treating Wolman disease is undertaken.

The technology

Sebelipase alfa (Kanuma, Alexion AstraZeneca Rare Disease) is a recombinant human lysosomal acid lipase. It is an enzyme replacement therapy that aims to replace the deficient enzyme LAL. Sebelipase alfa is indicated for long-term enzyme replacement therapy in patients of all ages with LAL deficiency. It is given by intravenous infusion.

Intervention(s)	Sebelipase alfa
Population(s)	People with Wolman disease
Comparators	Established clinical practice without sebelipase alfa
Outcomes	The outcome measures to be considered include: • mortality • body weight and nutritional parameters (including growth) • haematological parameters (including serum ferritin, need for blood transfusions) • lipid parameters (including total, low-density lipoprotein and high-density lipoprotein cholesterol, and triglycerides) • liver function (including transaminase level) • liver disease progression (including hepatomegaly) • adrenal gland function (for example, need for adrenal hormone supplementation) • neurological development parameters • cardiovascular events • anti-drug antibodies • adverse effects of treatment (including

	infusion-associated reactions) • health-related quality of life (for patients and carers).
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	If the evidence allows the following subgroups will be considered: • people who have received hematopoietic stem cell transplant • and people who have not received hematopoietic stem cell transplant. The availability, including of a well-matched donor, and cost of hematopoietic stem cell transplant should be taken into account. 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 National Policy	***NHS England*** NHS England (2019) The NHS long term plan NHS England (2018) Manual for prescribed specialised services 2018/19 see Chapter 62 Highly specialist metabolic disorder services (adults and children) NHS England (2017) NHS Medicines for Children's Policy NHS England (2013) 2013/14 NHS standard contract metabolic disorders (children) ***Other policies*** 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 (2018) The UK Strategy for Rare Diseases. Second Progress Report from the UK Rare Diseases Policy Board Department of Health and Social Care (2018) Rare Diseases Glossary. Glossary of commonly used terms and rare diseases initiatives

	Department of Health and Social Care (2018) The UK Strategy for Rare Diseases. Rare Diseases implementation plan for England Welsh Government (2017) Rare diseases implementation plan UK Rare Disease Forum (2016) Delivering for patients with rare diseases: Implementing a strategy A report from the UK Rare Disease Forum Department of Health (2016) NHS outcomes framework 2016 to 2017 Department of Health, Social Services and Public Safety (2015) Providing high quality care for people affected by rare diseases – the Northern Ireland implementation plan for rare diseases Department of Health (2013) The UK strategy for rare diseases

References

1. National Organization for Rare Disorders. (2021) Wolman disease. Accessed September 2021.
2. Orphanet. (2021) Wolman disease. Accessed September 2021.
3. Jones SA, Valayannopoulos V, Schneider E et al. (2016) Rapid progression and mortality of lysosomal acid lipase deficiency presenting in infants. Genet Med 18(5):452–458.
4. National Organization for Rare Disorders. (2021) Cholesteryl ester storage disease. Accessed September 2021.
5. Aguisanda F, Thorne N, Zheng W. (2017) Targeting Wolman Disease and Cholesteryl Ester Storage Disease: Disease Pathogenesis and Therapeutic Development. Curr Chem Genom Transl Med 11:1–18.
6. Online Mendelian Inheritance in Man (OMIM). (2021) Lysosomal acid lipase deficiency. Accessed September 2021.
7. NHS England. (2021) NHS England drugs list v16.1, 2021-2022. Accessed November 2021.
8. Potter JE, Petts G, Ghosh A et al. (2021) Enzyme replacement therapy and hematopoietic stem cell transplant: a new paradigm of treatment in Wolman disease. Orphanet J Rare Dis 16:235.