NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Sebelipase alfa for treating Wolman disease ID3995

Draft scope

Draft remit/evaluation objective

To evaluate the benefits and costs of sebelipase alfa within its marketing authorisation 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.

LAL deficiency is sub-classified as Wolman disease in babies and cholesteryl ester storage disease in children and adults.[1,2] Babies presenting with Wolman disease experience a rapidly progressive condition characterised by malabsorption, growth failure, and liver fibrosis and cirrhosis normally resulting in death in the first 6 months of life, usually due to multiple organ failure.[3,4] Cholesteryl ester storage disease presenting later in life, mostly in childhood and adolescence, tends to be a less severe disease.

The prevalence of LAL deficiency in England is unknown based on currently available information. It is estimated that approximately 3 to 4 babies with the most rapidly progressive disease are born each year. The estimated incidence rate for Wolman disease is less than 1 in 100,000 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] Treatment for Wolman disease is directed towards medical management and is aimed at controlling symptoms and managing complications. A minimal or fat free diet is 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.

A NICE evaluation of sebelipase alfa for treating LAL deficiency (ID737) has been superseded by this evaluation for treating Wolman disease.

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 • 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 • need for liver transplant • adrenal gland function (for example, need for adrenal hormone supplementation) • cardiovascular events • adverse effects of treatment • 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	• 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

Questions for consultation

How is Wolman disease defined clinically? How is it differentiated from LAL deficiency and cholesterol ester storage disease?

What is the incidence and prevalence of Wolman disease in England? Wolman disease is defined as LAL deficiency in babies. Are people who have

been diagnosed with Wolman disease as a baby, still be considered to have Wolman disease in childhood, adolescence and adulthood? What is the age range of people with Wolman disease?

Would people with Wolman disease be treated with sebelipase alfa? Would sebelipase alfa be used in the context of a highly specialised service? When would treatment be initiated?

Does treatment continue indefinitely? Are there any stopping criteria for sebelipase alfa in people with Wolman disease? Would people who have had a hematopoietic stem cell transplant be likely to continue treatment with sebelipase alfa?

Have all relevant comparators for sebelipase alfa been included in the scope? Which treatments are considered to be established clinical practice in the NHS for Wolman disease? Is hematopoietic stem cell transplantation a comparator for sebelipase alfa that should be included?Are the outcomes listed appropriate? Are there any that should be added (or removed) to make this more relevant to Wolman disease specifically (not LAL deficiency in general)? Is the need for liver transplant a relevant outcome to consider for people with Wolman disease?

Are there any subgroups of people in whom sebelipase alfa is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately? Would these subgroups include: people with very rapidly progressing LAL deficiency; people who may be candidates for hematopoietic stem cell transplant; people who have had a liver transplant? Would people with Wolman disease be treated with sebelipase alfa with the aim of subsequently having a hematopoietic stem cell transplant?

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 sebelipase 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. (2021) Wolman disease. Accessed September 2021.
2. National Organization for Rare Disorders. (2021) Cholesteryl ester storage disease. Accessed September 2021.
3. Orphanet. (2021) Wolman disease. Accessed September 2021.
4. 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.
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.