NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technology Evaluation

Sebelipase alfa for treating lysosomal acid lipase deficiency

Draft scope (pre-referral)

Draft remit/evaluation objective

To evaluate the benefits and costs of sebelipase alfa within its marketing authorisation for treating lysosomal acid lipase deficiency for national commissioning by NHS England.

Background

Lysosomal acid lipase (LAL) deficiency is an inherited autosomal recessive lysosomal storage disorder. It is caused by a deficiency of the LAL enzyme resulting in abnormal accumulation of lipids in cells, organs and tissues, primarily in the gastrointestinal, hepatic and cardiovascular systems. LAL deficiency in infants is known as early onset LAL deficiency or Wolman disease. This is the most severe form of the disease normally resulting in death in the first 6 months of life, mainly due to growth failure. LAL deficiency in children and adults is known as late onset LAL deficiency or cholesteryl ester storage disease. It is typically diagnosed in childhood or adolescence and involves hepatic and cardiovascular problems including hepatomegaly, cirrhosis, liver failure, dyslipidemia and accelerated atherosclerosis, normally resulting in death before the age of 30.

The prevalence of LAL deficiency in England is unknown. It is estimated that there are approximately 3 to 4 people with early onset LAL deficiency, and approximately 20 to 40 people with late onset LAL deficiency in England. There were 36 admissions for LAL deficiency during 2010-11. LAL deficiency affects men and women equally.

There is currently no treatment for LAL deficiency. Although enzyme replacement therapies are used for treating people with lysosomal storage disorders characterised by specific lysosomal enzyme deficiencies, none are currently available for treating people with LAL deficiency. Medical management is aimed at controlling symptoms and managing complications. Bone marrow transplantation, with intravenous nutritional support, has been used on an experimental basis for treating people with early onset LAL deficiency. A low-fat diet and cholesterol-lowering drugs such as statins are used to lower high levels of cholesterol and other fats in the blood in people with late onset LAL deficiency. These treatments have limited efficacy and have not been shown to improve the underlying disease.

The technology

Sebelipase alfa (brand name unknown, Synageva BioPharma) is a recombinant human lysosomal acid lipase, an enzyme replacement therapy. It is given by intravenous infusion.

Sebelipase alfa does not currently have a marketing authorisation in the UK. It has been studied in clinical trials, without a comparator, in children with early onset LAL deficiency and, in comparison with placebo, in children and adults with late onset LAL deficiency.

Intervention(s)	Sebelipase alfa
Population(s)	• People with early onset lysosomal acid lipase deficiency (Wolman disease) • People with late onset lysosomal acid lipase deficiency (cholesteryl ester storage disease)
Comparators	Established clinical practice without sebelipase alfa
Outcomes	The outcome measures to be considered include: • mortality • transaminase level • cholesterol level (LDL and HDL) • triglycerides level • liver function • liver volume • spleen volume • growth parameters • 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
Impact of the new technology	• clinical effectiveness of the technology • 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)
Cost to the NHS and Personal Social Services (PSS), and Value for Money	• budget impact in the NHS and PSS, including patient access agreements (if applicable) • robustness of costing and budget impact information • technical efficiency (the incremental benefit of the new technology compared to current treatment) • productive efficiency (the nature and extent of the other resources needed to enable the new technology to be used) • allocative efficiency (the impact of the new technology on the budget available for specialised commissioning)
Impact of the technology beyond direct health benefits, and on the delivery of the specialised services	• 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 • staffing and infrastructure requirements, including training and planning for expertise.
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 in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	None
Related National policy	NHS England Manual for prescribed specialised services, service 71: lysosomal storage disorder service (adults and children), November 2012. http://www.england.nhs.uk/wp-

	content/uploads/2012/12/pss-manual.pdf NHS England Standard Contract for Lysosomal Storage Disorders Service (Children), 2013. http://www.england.nhs.uk/wp-content/uploads/2013/06/e06-lyso-stor-dis-child.pdf NHS England Standard Contract for Metabolic Disorders (Adult), 2013. http://www.england.nhs.uk/wp-content/uploads/2013/06/e06-metab-disorders-adult.pdf

Questions for consultation

Which treatments are considered to be established practice for treating people with lysosomal acid lipase deficiency?

Should liver transplantation be included as a comparator?

Should people with early onset LAL deficiency and late onset LAL deficiency be considered separately?

How are early onset and late onset LAL deficiency diagnosed in the NHS respectively?

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?

Are the outcome measures listed in the scope appropriate? Is there any other relevant outcome measure that should be included?

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: http://www.nice.org.uk/media/DE4/9A/HSTCombinedInterimProcessMethods.pdf.