NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Elosulfase alfa for treating mucopolysaccharidosis type IVA (review of highly specialised technologies guidance 2)

Draft scope

Remit/evaluation objective

To evaluate the benefits and costs of elosulfase alfa within its marketing authorisation for treating mucopolysaccharidosis type IVA for national commissioning by NHS England.

Background

Mucopolysaccharidosis type IVA (also known as MPS IVA and Morquio A syndrome) is an inherited lysosomal storage disorder caused by a lack of the enzyme N-acetylgalactosamine-6-sulfatase. This enzyme is required to break down long carbohydrate molecules known as glycosaminoglycans (such as keratan sulphate). The enzyme deficiency leads to accumulation of glycosaminoglycans in the cells of several tissues and organs, causing progressive tissue damage. Mucopolysaccharidosis type IVA may be considered distinct from type IVB, which is also associated with accumulation of keratan sulphate but is caused by a deficiency in a different enzyme (beta-galactosidase).

Mucopolysaccharidosis type IVA causes a wide spectrum of symptoms including joint and skeletal abnormalities, hearing loss, corneal clouding and heart valve disease. The joint and skeletal abnormalities associated with this condition lead to short stature, difficulties with breathing and movement, spinal instability and spinal cord compression. The first signs and symptoms typically appear in early childhood, with over 70% of people presenting with unusual skeletal features within the first 2–3 years of life. People who are severely affected may survive only until late childhood or adolescence, whereas those with less severe forms of the condition may live long into adulthood. People with mucopolysaccharidosis type IVA often need surgery on the neck, hip, knee or leg before age 10.

Incidence estimates suggest that mucopolysaccharidosis type IVA affects approximately 1 person per 220,000 live births, equating to about 3 new diagnoses per year in England. In 2015, there were 88 people living with mucopolysaccharidosis type IVA in England.

Management of mucopolysaccharidosis type IVA requires a multi-disciplinary approach to treat the symptoms and address the complications. This may include surgery for skeletal problems, respiratory support, drugs to treat heart valve lesions, dental and eye care, pain relief and hearing aids and ventilating tubes to manage deafness and middle ear effusions. Mucopolysaccharidosis

type IVA can also be treated with enzyme replacement therapy (elosulfase alfa), which is currently available in the NHS in England through a managed access agreement.

Mucopolysaccharidosis type IVA and related conditions (collectively termed lysosomal storage disorders) are usually managed in specialist centres in England.

This evaluation is a review of NICE highly specialised technologies guidance on elosulfase alfa for treating mucopolysaccharidosis type IVA (HST2), in line with the completion of the managed access agreement.

The technology

Elosulfase alfa (Vimizim, BioMarin) is a recombinant form of human N-acetylgalactosamine-6-sulfatase. It is intended to directly replace the lacking N-acetylgalactosamine-6-sulfatase enzyme in people with mucopolysaccharidosis type IVA. It is administered by intravenous infusion.

Elosulfase alfa has a marketing authorisation in the UK for treating mucopolysaccharidosis type IVA in people of all ages. The summary of product characteristics states that treatment with elosulfase alfa should be supervised by a physician experienced in managing patients with mucopolysaccharidosis type IVA or other inherited metabolic diseases.

Intervention(s)	Elosulfase alfa
Population(s)	People with mucopolysaccharidosis type IVA
Comparators	Established clinical management without elosulfase alfa
Outcomes	The outcome measures to be considered include: • endurance • mobility • respiratory and cardiac function • growth and development • vision and hearing • sleep apnoea • fatigue • pain • mortality • 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 evidence considered in the evaluation of elosulfase alfa (HST2) and any further evidence that has become available since, including evidence collected in the elosulfase alfa managed

	access agreement.
Related NICE recommendations and NICE Pathways	Elosulfase alfa for treating mucopolysaccharidosis type Iva (2015). NICE Highly Specialised Technologies guidance 2. Related NICE Pathways: Metabolic conditions (2019) http://pathways.nice.org.uk/
Related national policy	NHS England interim commissioning policy in development UK strategy for rare diseases, November 2013. https://www.gov.uk/government/publications/rare-diseases-strategy 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 manual for prescribed specialised services 2018/19, service 71: lysosomal storage disorder service (adults and children), October 2017. https://www.england.nhs.uk/publication/manual-for-prescribed-specialised-services/ NHS England Highly Specialised Services 2018, December 2018 https://www.england.nhs.uk/commissioning/publication/highly-specialised-services-2018/

Questions for consultation

Have there been any changes to the management of mucopolysaccharidosis type IVA or the commissioning of services that would affect the proposed scope for this evaluation?

- Have all relevant comparators for elosulfase alfa been included in the scope? How is established clinical management without elosulfase alfa defined?
- Are the outcomes listed appropriate?
- Are there any subgroups of people in whom elosulfase alfa 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 elosulfase alfa is 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)?