NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Intrathecal idursulfase for treating Mucopolysaccharidosis type II

Draft scope (pre-referral)

Draft remit/evaluation objective

To evaluate the benefits and costs of intrathechal idursulfase within its marketing authorisation for treating mucopolysaccharidosis type II for national commissioning by NHS England.

Background

Mucopolysaccharidosis type II (also known as MPS II and Hunter syndrome) is an inherited lysosomal storage disease caused by a lack of the enzyme iduronate sulfatase. This enzyme is required to break down molecules in the body called glycosaminoglycans (or mucopolysaccharides; such as dermatan sulfate and heparan sulfate). The enzyme deficiency leads to accumulation of glycosaminoglycans in the cells of several tissues and organs, resulting in progressive tissue damage.

Symptoms of mucopolysaccharidosis type II typically start to appear between the ages of 2 and 4, comprising a wide spectrum of severity[1]. The most common general clinical symptoms include enlarged tongue and tonsils, enlarged abdomen, coarse facial features, hearing loss, abnormal dentition, decreased joint range of motion, heart disease, lung disease, skeletal deformities, and short stature. For some people accumulation of glycosaminoglycans in the central nervous system leads to severe mental impairment and progressive neurological decline[2]. This is the most severe form of the disease with survival only until late childhood or adolescence. Those without central nervous system involvement may live long into adulthood depending on severity of their physical problems.

Except in very rare cases, only males are affected by mucopolysaccharidosis type II. The incidence in Europe is estimated to be 1 in 100,000 male births[3]. Between 1992 and 2002, 52 babies were born with mucopolysaccharidosis type II in the UK[3]. Expert opinion suggests that approximately 50-60% of patients have progressive neurological impairment[1].

Management of mucopolysaccharidosis type II requires a multi-disciplinary approach to treat the symptoms and its complications. An enzyme replacement therapy, intravenous idursulfase, is available to address the underlying lysosomal enzyme deficiency 'for the long-term treatment of patients with mucopolysaccharidosis II'[1]. However, intravenous idursulfase does not cross the blood brain barrier in clinically relevant amounts and therefore it does not treat central neurological impairment.

Additional supportive care for these patients may include anticonvulsants and behaviour modifying medications, treating hydrocephalus and preventing sleep apnoea. Mucopolysaccharidosis type II is usually managed in specialist centres in England.

The technology

Intrathecal idursulfase (HGT-2310, Shire) is a recombinant form of iduronate-2-sulfatase. It is intended to directly replace the lacking iduronate-2-sulfatase enzyme in people with mucopolysaccharidosis type II. The intrathecal formulation of idursulfase has been designed for direct administration into the cerebrospinal fluid to address neurocognitive decline.

Intrathecal idursulfase does not currently have marketing authorisation in the UK for treating mucopolysaccharidosis type II. It has been studied in clinical trials in combination with intravenous idursulfase, compared with intravenous idursulfase or in single arm trials, in children with mucopolysaccharidosis type II with cognitive impairment.

Intervention(s)	Intrathecal idursulfase in combination with intravenous idursulfase
Population(s)	Children with mucopolysaccharidosis type II with cognitive impairment
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • cognitive functioning • neuropsychological assessment, including adaptive functioning • walking ability • respiratory and cardiac function • hearing capacity • 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 any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2016) Manual for prescribed specialised services 2016/17 Chapters 62 and 71. NHS England (2013) 2013/14 NHS standard contract for lysosomal storage disorders service (children). E06/S(HSS)/c. NHS England (2013) Pre-implantation genetic diagnosis (PGD). Clinical commissioning policy. Reference: NHSCB/E01/P/a. NHS England (2013) 2013/14 NHS standard contract for paediatric medicine: palliative care. Reference: E03/S/h. **National Service Frameworks** Children, Young People and Maternity Services - archived Long Term Conditions (including neurological) - archived **Other policies**

	Department of Health (2016) NHS outcomes framework 2016 to 2017 Department of Health (2013) The UK strategy for rare diseases

Questions for consultation

Is inthrathecal idursulfase likely to be used in children with cognitive impairment, or to prevent cognitive impairment in children with MPS II?

Have all relevant comparators for intrathecal idursulfase been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for mucopolysaccharidosis II? Is hematopoietic stem cell transplantation used in practice?

Are the outcomes listed appropriate? Are there any other outcomes that should be included in the scope?

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 intrathecal idursulfase 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. NIHR 2016. *Intrathecal idursulfase (Elaprase) for Hunter syndrome (mucopolysaccharidosis type II)*.Horizon Scanning Research & Intelligence Centre, University of Birmingham. http://www.io.nihr.ac.uk/wp-content/uploads/migrated/Idursulfase-IT-March-2016.pdf

2. EMA 2007, *Elaprase: EPAR -Scientific Discussion* http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000700/WC500023005.pdf

3. MPS society UK. *MPS II Hunter* http://www.mpssociety.org.uk/diseases/mps-diseases/mps-ii/