NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

Lumasiran for treating primary hyperoxaluria type 1

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of lumasiran within its marketing authorisation for treating primary hyperoxaluria type 1.

Background

Primary hyperoxaluria type 1 is a genetic disorder caused by mutations of the AGXT gene, which causes excess oxalate production leading to oxalate crystals building up in the kidneys and urinary tract. Signs and symptoms of primary hyperoxaluria type 1 vary in severity and may begin any time from infancy to early adulthood. Children with primary hyperoxaluria type 1 who have symptoms during infancy generally have the most severe disease course, characterised by rapid progression to renal failure. Symptoms may include recurrent kidney stones; blood in the urine; and urinary tract infections. Left untreated, primary hyperoxaluria type 1 can result in end-stage renal disease accompanied by systemic oxalate deposition in the eyes, skin and bone marrow, which is life-threatening.[1] It is estimated that about a third of people with primary hyperoxaluria type 1 have end-stage renal disease at diagnosis and only a quarter of people will retain kidney function 30 years after diagnosis.[2]

Around 120 people in the UK have hyperoxaluria as of October 2021, according to the National Registry of Rare Kidney Diseases (RaDaR).[3] Approximately three quarters of people with primary hyperoxaluria are diagnosed as type 1.[4] The median age at diagnosis is around 7 to 10 years in people with primary hyperoxaluria.[5] The incidence of primary hyperoxaluria type 1 in Europe has been estimated as 1 in 100,000 live births per year.[6]

The aim of treatment for people with primary hyperoxaluria type 1 is to reduce oxalate levels, therefore preventing complications associated with hyperoxaluria, such as the formation of kidney stones or worsening kidney function. This can be done by taking vitamin B6, which may reduce oxalate levels in some people.[7] Several dietary measures can also be taken to try and prevent kidney stones forming, for example drinking lots of fluids and avoiding foods with high levels of oxalate. In clinical practice, for infants with rapidly progressing disease, haemodialysis and hyperhydration are used to try to stop progression. Depending on the response to other treatments and the disease severity, options include; a combined liver kidney transplant or a sequential liver kidney transplant or an isolated liver transplant.[8]

The technology

Lumasiran (Oxlumo, Alnylam) is an RNA interference agent which uses gene silencing to target glycolate oxidase. This reduces oxalate production and therefore has the potential to prevent the build-up of oxalate in people with primary hyperoxaluria type 1 and prevent subsequent complications, such as worsening kidney disease. It is administered as a subcutaneous injection.

Lumasiran has a marketing authorisation in the UK for the treatment of primary hyperoxaluria type 1 (PH1) in all age groups. It is being studied in a clinical trial compared with placebo in adults and children aged 6 years and older with primary hyperoxaluria type 1. It is also being studied in a single-arm trial in children aged up to 5 years and a single-arm trial in infants and adults with advanced hyperoxaluria type 1 and severely reduced kidney function.

Intervention(s)	Lumasiran
Population(s)	People with primary hyperoxaluria type 1
Comparators	• established clinical management without lumasiran (including vitamin B6 and an oxalate-controlled diet) • liver transplant with or without a combined or sequential kidney transplant • haemodialysis • hyperhydration
Outcomes	The outcome measures to be considered include: • oxalate levels in urine • oxalate levels in plasma • change in Estimated Glomerular Filtration Rate (eGFR) • need for liver transplant with or without kidney transplant • mortality • adverse effects of treatment • health-related quality of life.
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	• overall magnitude of health benefits to patients

Effectiveness	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: infants with rapid and progressive disease; children with a family history confirmed by cord blood testing; and children and adults presenting with kidney stones. • Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2019) The NHS long term plan NHS manual for prescribed specialist services (2018/2019). See 15. Adult specialist renal services, 69. Liver transplantation service (adults and children) 127. Specialist renal services for children

	Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1-4. NHS standard contract for metabolic disorders (adult, 2013/2014) NHS standard contract for metabolic disorders (children, 2013/2014) NHS standard contract for metabolic disorders (laboratory services, 2013/2014)

References

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