NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health technology Appraisal

Lumasiran for treating primary hyperoxaluria type 1

Draft scope (pre-referral)

Draft remit/appraisal 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. 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, 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 January 2020, according to the National Renal Rare Disease Registry (RaDaR).[3] Approximately three quarters of people with primary hyperoxaluria are diagnosed as type 1.[4,5] Almost half of all cases of primary hyperoxaluria are diagnosed before the age of 15.[4] 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.[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. Depending on the response to other treatments and the disease severity, options include; a combined liver kidney transplant, a sequential liver kidney transplant; an isolated kidney transplant, or an isolated liver transplant.[8]

The technology

Lumasiran (brand name unknown, 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

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complications, such as worsening kidney disease. It is administered as a subcutaneous injection.

Lumasiran does not currently have a marketing authorisation in the UK for the treatment of primary hyperoxaluria type 1. 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.

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) • kidney transplant • combined kidney-liver transplant
Outcomes	The outcome measures to be considered include: • oxalate levels in urine • change in Estimated Glomerular Filtration Rate (eGFR) • need for kidney or kidney/liver transplant • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
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 only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE	None

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recommendations and NICE Pathways	
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)

Questions for consultation

Have all relevant comparators for lumasiran been included in the scope? Is transplant considered a comparator to this technology?

Which treatments are considered to be established clinical practice in the NHS for primary hyperoxaluria type 1?

Would lumasiran be given in addition to established clinical management or replace current established clinical management?

Are the outcomes listed appropriate?

Are there any other subgroups of people in whom lumasiran 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 lumasiran 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 lumasiran

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- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider lumasiran 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)?

Do you consider that the use of lumasiran can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

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3. National Renal Rare Disease Registry (RaDaR). 2020. Available from: https://rarerenal.org/wp-content/uploads/2020/01/RaDaR-recruitment-January-2020.pdf Accessed January 2020

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5. Lieske JC, Monico CG, Holmes WS, et al. International Registry for Primary Hyperoxaluria. *American Journal of Nephrology*. 2005, 25, 290–296

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7. Hoyer-Kuhn, H, Kohbrok S, Volland R, et al. Vitamin B6 in Primary Hyperoxaluria I: First Prospective Trial after 40 Years of Practice. *Clinical Journal of American Society of Nephrology*. 2014, 9 (3), 468–477.

8. Marion B, Coulter-Mackie CT, White DL, et al. Primary Hyperoxaluria Type 1. GeneReviews. July 17, 2014; http://www.ncbi.nlm.nih.gov/books/NBK1283/.

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