NICE National Institute for Health and Care Excellence

NICE guidance

Lumasiran for treating primary hyperoxaluria type 1

Highly specialised technologies guidance
Published: 19 April 2023

www.nice.org.uk/guidance/hst25

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Lumasiran is recommended, within its marketing authorisation, as an option for treating primary hyperoxaluria type 1 (PH1) in people of all ages. It is recommended only if the company provides lumasiran according to the commercial arrangement.

Why the committee made this recommendation

PH1 is a rare, inherited condition that can significantly affect the quality of life of people with the condition, and their families and carers. In PH1, the liver produces excess oxalate which combines with calcium in the tissues to form toxic crystals. These crystals can cause recurrent kidney stones, kidney damage and in severe cases kidney failure and multiorgan damage. Standard care includes supportive measures, dialysis and a liver–kidney transplant depending on a person's kidney function.

Clinical trial evidence suggests that, after 6 months of treatment, lumasiran plus standard care reduces a person's oxalate levels compared with standard care alone. The impact of PH1 and advanced kidney disease on people's quality of life in the economic model is uncertain. This makes the cost-effectiveness estimates uncertain. Despite this, lumasiran is likely to provide important clinical benefits for people with PH1 and is considered an appropriate use of NHS resources within the context of a highly specialised service. So, lumasiran is recommended for use in the NHS.

2 Information about lumasiran

Marketing authorisation indication

2.1 Lumasiran (Oxlumo, Alnylam Pharmaceuticals) is indicated 'for the treatment of primary hyperoxaluria type 1 (PH1) in all age groups'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for lumasiran.

Price

2.3 The list price of lumasiran is £61,068.98 per 94.5 mg vial (excluding VAT; Monthly Index of Medical Specialities [MIMS] online, accessed February 2023). The company has a commercial arrangement. This makes lumasiran available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The evaluation committee considered evidence submitted by Alnylam Pharmaceuticals, the views of people with the condition, those who represent them and clinical experts, NHS England and a review by the evidence review group (ERG). See the committee papers for full details of the evidence. In forming the recommendations, the committee took into account the full range of factors that might affect its decision, including in particular the nature of the condition, the clinical effectiveness, value for money and the impact beyond direct health benefits.

Nature of the condition

Primary hyperoxaluria type 1 and burden of disease

3.1 Primary hyperoxaluria type 1 (PH1) is a rare, inherited condition which affects a person's oxalate metabolism. Oxalate is normally filtered by the kidneys and removed in the urine. In PH1, a genetic mutation causes the liver to produce excess oxalate which builds up in the kidneys and urinary tract. The excess oxalate binds with calcium in the tissues to form toxic calcium oxalate crystals. These crystals can join together to form kidney stones and over time impair kidney function. If left untreated, this can result in end-stage kidney disease. Oxalate crystals may also be deposited across the body such as in the eyes, bones and joints (known as systemic oxalosis). Systemic oxalosis can cause severe disabling complications and affect the growth and development of children.

3.2 The committee noted stakeholder submissions from the patient and professional organisations and a clinical expert. It understood that PH1 has the potential to reduce a person's life expectancy, particularly in those children who experience the most severe symptoms and rapid disease progression. The submissions described the significant physical and psychosocial impact of living with PH1 for people with the condition, their families and carers. The patient expert explained that symptoms also include loss of appetite, fatigue, depression and anxiety, which can be debilitating for some people with PH1. They described how PH1 significantly impacts a person's quality of life, their ability to do daily activities

and maintain employment because of the disease itself or because of caring responsibilities. The patient expert explained that parents and carers live in constant fear that their child's condition will deteriorate rapidly and that this has a substantial emotional effect on them. They described how PH1 in children often prevents them from being able to attend school because of ill health and this can affect their education and make them feel isolated. The patient experts explained how achieving an increased fluid intake (hyperhydration) and having to use the toilet more frequently because of this can be difficult to manage. They described how this can be particularly challenging for children during school time because teachers and other pupils often lack an understanding of the condition. The clinical experts explained that for people needing dialysis, the dialysis schedule is higher than usual intensity. The patient experts explained how people with PH1 and their carers struggle to have a social life and maintain relationships with family members and friends. They also described how the condition affects family planning, with some people with PH1 opting not to have children because of the burden of the disease and the impact on the wider family network. The committee noted comments which reiterated the severity of the condition, particularly for children with recurrent kidney stones and systemic oxalosis. The committee concluded that PH1 is rare, serious and potentially life-threatening, affecting the lives of people with the condition, their families and carers.

Unmet need

3.3 Standard care for PH1 depends on a person's kidney function. In people with no kidney impairment, treatment includes supportive measures such as an oxalate-controlled diet, hyperhydration, crystallisation inhibitors and pyridoxine (vitamin B6) supplementation. In people with more advanced stages of kidney impairment, dialysis may be started to slow the build-up of oxalate around the body or replace lost kidney function. In people with end-stage kidney disease, a liver–kidney transplant may be needed to eliminate the source of excess oxalate production and restore lost kidney function. Treatment of kidney stones may be needed at all stages of disease.

3.4 A stakeholder submission highlighted that pyridoxine is effective for less than 25% of all people with PH1. There are currently no disease-modifying drugs available for people whose disease does not respond to pyridoxine. The

committee understood that people with PH1 need more frequent dialysis sessions (6 to 7 times per week) compared with conventional haemodialysis schedules (3 times per week) for other non-PH1 conditions. The clinical expert explained that despite the intensive dialysis schedules in PH1, they are usually not enough to consistently lower plasma oxalate levels, which begin to rise within hours of a dialysis session. The patient expert felt that their child's experience of dialysis before having a liver transplant resulted in a poor quality of life for their child and them for several years. They explained the burden of travelling to the hospital for haemodialysis sessions 5 to 6 times per week, alongside providing home peritoneal dialysis for 7 nights per week. The committee noted from the stakeholder submissions how current treatments are perceived as restrictive and difficult to adhere to, needing regular hospital admissions and outpatient follow up. It understood that many people struggle with the need to drink large volumes of fluids alongside medication and that having a transplant is associated with additional morbidity and risk of death. The committee noted comments which highlighted that the wait for a transplant is an additional worry for people with PH1. It was aware that current treatments did not include a pharmacological option specifically licensed for the treatment of PH1. The committee recognised that there is a significant unmet need for effective and safe treatments for people with PH1.

Impact of the new technology

Experience of lumasiran in NHS clinical practice

3.5 The committee understood that a small number of people (the actual number is confidential and cannot be reported here) in England have had lumasiran through the Medicines and Healthcare products Regulatory Agency's early access to medicines scheme (EAMS) and as part of several international clinical trials (see section 3.9 to 3.11). The company submission highlighted that data collection was not mandated for people having lumasiran through the EAMS in the UK. However, the clinical expert submission highlighted that increased survival has been seen in children with infantile oxalosis treated with lumasiran through the EAMS. The clinical expert also commented that data from the EAMS reflected the clinical trial data for lumasiran. They explained that lumasiran normalised or near-normalised

urinary oxalate excretion, which therefore stabilised kidney function and reduced the number of kidney stone events. The committee noted comments that treatment with lumasiran had improved the quality of life for people with PH1 and their families. It concluded that people with PH1 and their clinicians would welcome lumasiran as a treatment option for treating PH1.

Comparators

3.6 The company submission included evidence comparing lumasiran plus standard care with standard care alone. Standard care included pyridoxine, an oxalate-controlled diet, liver transplant with a combined or sequential kidney transplant, haemodialysis and hyperhydration. The ERG commented that the company had excluded isolated liver transplant as part of standard care, but that it was included in the final scope for this appraisal. The company considered that an isolated liver transplant is not part of standard clinical practice and may be associated with poorer outcomes compared with a liver–kidney transplant. The ERG considered that the company had not provided any evidence to support this assumption and the impact of exclusion was uncertain. The clinical expert explained that registry data from Europe (OxalEurope) indicates that people who have had an isolated liver transplant experience a higher risk of mortality and complications compared with those who have a liver–kidney transplant. The clinical expert highlighted that clinical practice is moving away from isolated liver transplant and more towards a liver–kidney transplant in people with signs of kidney impairment. The committee recalled comments from the patient expert who described how their child had had an isolated liver transplant. The committee considered that a small number of people may have an isolated liver transplant before the onset of advanced kidney damage. However, it accepted that most people would have a liver–kidney transplant in NHS clinical practice. Therefore, the committee concluded that the company's approach to exclude isolated liver transplant as a part of standard care was reasonable.

Expected use of the technology

3.7 The population included in the company's model was based on the key ILLUMINATE trials (see section 3.9) and reflected the full marketing authorisation

for lumasiran (people of all ages with PH1). The company considered that in clinical practice lumasiran would be used in people with PH1 who have not already had an isolated liver transplant or a liver–kidney transplant. Within this group, the company considered that all children with elevated oxalate levels despite standard care should be offered treatment with lumasiran. In adults, those offered lumasiran would include people in later stages of chronic kidney disease, with exceptions for those in earlier stages of kidney disease with disease progression or severe comorbidities. The company highlighted that it was currently unknown if lumasiran would be started in people with early-stage kidney disease without rapid signs of disease progression.

3.8 The committee discussed the company's expected use of lumasiran in clinical practice. Clinical experts explained that lumasiran would be offered to children with evidence of calcium oxalate deposition (such as in the kidneys) but whose kidney function had not declined. It would also be offered to all children with reduced kidney function or evidence of a severe infantile phenotype. This early use of lumasiran may prevent morbidity in early childhood caused by infantile oxalosis. Clinical experts explained that lumasiran would likely be offered to adults if there is evidence of rapid deterioration in kidney function and to people who have frequent and severe kidney stone formation. The clinical expert explained that an emergency use of lumasiran may be considered for adults with end-stage kidney disease but who have not been diagnosed with PH1 at the time of kidney transplant. If kidney function declined after transplant, the diagnosis of PH1 would likely be considered, and if confirmed, treatment with lumasiran could be started. The committee discussed if lumasiran may be used after a liver–kidney transplant if a person's oxalate levels remained high. The clinical experts explained that because a liver transplant would restore the activity of the liver-specific enzyme responsible for excess oxalate production, it would not be appropriate to use lumasiran after a successful isolated liver or liver–kidney transplant. The clinical experts explained that although a liver transplant prevents any new production of oxalate, people with systemic oxalosis would still have a high residual oxalate burden in the body that needs to be cleared. They considered that because of how lumasiran works, it would not help to normalise a person's oxalate burden after a liver–kidney transplant. At the second committee meeting, the clinical experts explained that in some people, the early use of lumasiran had the potential to avoid the need for dialysis and a liver transplant. The committee concluded that because having a liver transplant resolves the

underlying condition, lumasiran would not be indicated for people who have had a liver transplant. It further concluded that the company's expected use of lumasiran in people with PH1 largely aligned with how clinicians would expect to use lumasiran in clinical practice.

Clinical evidence

3.9 The clinical evidence for lumasiran included:

- ILLUMINATE-A, a randomised, double-blind, placebo-controlled trial (6-month duration, completed) with an extension period when both arms have lumasiran (3-month blinded extension, 51-month open-label period, ongoing until January 2024)
- ILLUMINATE-B, a phase 3, single-arm, open-label trial (6-month duration, completed) with an extension period (54 months, ongoing until August 2024)
- ILLUMINATE-C, a phase 3, single-arm, open-label trial (6-month duration, completed) with an extension period (54 months, ongoing until July 2025)
- ALN-GO1-001B, a phase 1/2 randomised, placebo-controlled dosing study (completed)
- ALN-GO1-002, a phase 2, open-label extension safety study of people previously enrolled in ALN-GO1-001B (ongoing until June 2023).

  The committee noted that the ERG did not recognise the ALN-GO1-001B study as a full randomised controlled trial because only 1 person was allocated to the placebo group in each of the 3 lumasiran cohorts. So, the committee focused on the results from the randomised phase of the ILLUMINATE-A study because this provided comparative evidence of the treatment effect for lumasiran compared with standard care.

Study outcomes

3.10 The ILLUMINATE-A study assessed the efficacy of lumasiran (n=26) administered

by subcutaneous injection (3 mg per kg once monthly for the first 3 doses, followed by a maintenance dose every 3 months) compared with matched placebo (n=13). People in both arms were able to continue treatment with their standard care, which was stable before enrolling in the trial. The trial was in people aged 6 years and over with PH1 and no kidney impairment. The study included 16 study sites, including 3 UK sites with a small number of people (the actual number is confidential and cannot be reported here). The primary outcome of ILLUMINATE-A was the percentage change in 24-hour urinary oxalate excretion from baseline to month 6 for lumasiran compared with placebo. People in the lumasiran arm had a significantly greater reduction in urinary oxalate excretion than people in the placebo arm (effect size -53.5%, 95% confidence interval -62.3% to -44.8%). The absolute change in 24-hour urinary oxalate, as well as percentage and absolute changes in plasma oxalate, were all reduced more in people in the lumasiran arm compared with people in the placebo arm. The levels of estimated glomerular filtration rate (eGFR), which is a measure of kidney function, remained relatively stable for both treatment groups. The rate of kidney stone events (per person per year) 12 months before the trial compared with during the 6-month double-blind period reduced in people in the lumasiran arm and increased in people in the placebo arm. However, the treatment groups were not comparable at baseline. The committee concluded that lumasiran plus standard care was effective in reducing oxalate levels compared with standard care alone.

3.11 In ILLUMINATE-A health-related quality-of-life data was collected using the EuroQol 5-dimensions questionnaire (EQ-5D). The mean change from baseline to month 6 in the EQ-5D visual analogue scale was reported for people in the lumasiran and placebo arms (the actual numbers are confidential and cannot be reported here). The ERG noted that the comparability of treatment groups at baseline could not be assessed from the data provided by the company. Assuming comparability, the ERG advised that the difference in changes in EQ-5D was not clinically significant. The committee considered that it was unclear why reductions in oxalate levels seen with lumasiran treatment did not lead to a clinically meaningful improvement in health-related quality of life. It was aware that health-related quality of life is affected by many factors including chronic symptoms and psychosocial factors. It considered that the 6-month randomised phase in the ILLUMINATE-A study might be too short to capture lumasiran's full benefits. The committee concluded that treatment with lumasiran was likely to

affect health-related quality of life but it was unclear how large such an effect would be.

Quality and generalisability of clinical evidence

3.12 The committee considered the ERG's critique that the company's submission included a low volume of robust evidence. The ERG considered that there were examples of treatment groups not being comparable at baseline (such as rates of kidney stone events), which makes conclusions for these outcomes difficult. The ERG highlighted that it had limited confidence that some of the observed effects in the non-randomised evidence truly reflect the treatment effects of lumasiran. The committee heard how larger randomised controlled trials comparing lumasiran with relevant comparators would decrease clinical uncertainty but that these are not possible because of the rare nature of PH1. The committee understood that people with PH1 have their condition managed at 1 of the 4 centres which form the Hyperoxaluria Rare Disease Collaborative Network or other specialist centres with advice and support from the network. It noted that if lumasiran was recommended it would be provided within these centres. It noted that the ILLUMINATE-A trial included people from 3 of the Hyperoxaluria Rare Disease Collaborative Network centres and that this increased the generalisability of the trial results to those who would have lumasiran in NHS clinical practice. The committee acknowledged the limitations in the evidence base but concluded that it was appropriate for decision making given the rarity of the condition.

Proportion of people who would have lumasiran in clinical practice

3.13 The company estimated the proportion of people for whom lumasiran would be suitable using data from the National Registry of Rare Kidney Diseases (RaDaR), which reports on the overall hyperoxaluria population in the UK. The ERG noted that because recruitment to RaDaR is voluntary, the number of recruits to the database will likely be a subset of the total number with the disease. The ERG considered that the total population for whom lumasiran would be suitable may be larger than stated in the company's submission. The clinical experts estimated

the proportion of people who would likely have lumasiran if it was recommended. They explained that in adults there would be an initial spike in using lumasiran, which would level out rapidly. In children under the age of 2, the clinical experts considered that all people (around 3 or 4 per year) would have treatment with lumasiran. In older children use would be in those with nephrocalcinosis (calcium oxalate deposits in the kidneys) or evidence of declining kidney function. The clinical experts considered that around 40% of people in this age group would be offered lumasiran. However, the patient expert explained that their preference would be to wait until their child experienced symptoms of disease progression before starting treatment so that they could live a normal life for as long as possible. The committee concluded that it was unclear on the exact population size that lumasiran would be suitable for but recognised that the number would be small.

Company's model

3.14 The company's economic model compared lumasiran plus standard care (from now, referred to as lumasiran) with standard care in a simulated cohort of people with PH1. The Markov model used chronic kidney disease (CKD) stages as health states because the company considered that no disease-specific classification exists for categorising disease severity in PH1. Each of the CKD stages (1 to 2, 3a, 3b, 4, and 5 or end-stage kidney disease) were defined by a person's eGFR. In the model, it is assumed that having a lower eGFR indicates a worse kidney function and higher CKD stage. In addition to these health states, the model included post-transplant and death states.

3.15 The modelled cohort included people of all ages, and reflected the expected use of lumasiran in clinical practice (see sections 3.7 to 3.8). For example, in response to consultation, the company adjusted the health state distribution of the cohort at model start to assume that 50% of all adults in the CKD 1 to 3a health states had rapid progression. This was based on clinical expert opinion expressed at the first committee meeting that suggested lumasiran would only be started in adults in CKD 1 to 3a health states who experienced rapid progression.

3.16 In each 6-month cycle, people could progress to the next CKD stage or stay in the same CKD stage if they had not had a transplant. Transition to a less severe

CKD stage was not permitted in either cohort in the model, on the basis that lost kidney function cannot be recovered. For CKD 4 and end-stage kidney disease health states, a threshold of 50 micromol per litre of plasma oxalate was used to distinguish between uncontrolled and controlled oxalate levels. Only people in the lumasiran cohort could move to states with controlled oxalate levels. In the later CKD health states, people in both arms of the model were able to have a liver–kidney transplant. Health states after transplant depended on a person's plasma oxalate levels before transplant. Treatment with lumasiran was continued across all CKD stages.

3.17 The company's economic analysis adopted an NHS perspective and had a lifetime time horizon. A discount rate of 3.5% per year was used for both costs and health outcomes. The committee was satisfied that the model structure reflected the general course of the condition.

Modelling of disease progression

3.18 The company's model assumed that plasma oxalate levels are suitable to be used as a surrogate outcome to predict change in kidney function. The company referenced an observational study (Shah 2020), which showed that the rate of decline in eGFR was associated with plasma oxalate. It used plasma oxalate data from ILLUMINATE-A and the relationship between plasma oxalate and eGFR (reported in Shah 2020) to model disease progression for people in CKD 1 to CKD 3b health states on standard care. The ERG was uncertain about the extent to which urinary or plasma oxalate levels can predict kidney function, mortality and health-related quality of life in people with PH1. It considered that this may result in uncertainty when attempting to interpret the treatment effect for lumasiran. The committee noted comments from the clinical expert submission, which highlighted that in clinical practice urinary oxalate excretion is a more widely accepted marker of the risk of future decline in kidney function in people with PH1 who can pass urine. This aligned with Shah (2020), which reported that urinary oxalate was a better predictor of change in kidney function in the early stages of kidney disease. The clinical experts explained that measures of plasma oxalate levels are helpful in monitoring kidney function in people whose kidneys are unable to produce urine. The clinical experts stated that in children urinary oxalate levels are used as a marker of prognosis in those who can pass urine and

that plasma oxalate levels are a useful marker of prognosis in those with end-stage kidney disease. In adults, it is predominantly urinary oxalate levels that are used for clinical decision making. The clinical expert explained that plasma oxalate levels in adults can play a role in clinical decision making around the time of a kidney transplant or when a person is having dialysis. The committee noted consultation comments that a higher value for defining uncontrolled oxalate may represent a more suitable threshold for the damaging effect of oxalate. Also, variability in plasma oxalate measurements across laboratories can make it difficult to identify a precise threshold value. The ERG explained that assuming a different cut-off for uncontrolled oxalate in the model had a minor effect on the cost-effectiveness estimates. The committee concluded that applying measures of plasma oxalate levels is appropriate and relevant in predicting kidney function in people with PH1.

3.19 The company's model assumes that disease progression (in terms of decreasing eGFR) for people on standard care in CKD 1 to 3b health states depends on changes in plasma oxalate levels over time. The ERG considered that disease progression would also likely happen in people who sustain a steady, but very high, plasma oxalate level over time. The observational evidence from Shah (2020) did not distinguish between the 2 (company's and ERG's assumptions). The committee noted that in response to clarification, the company had provided an exploratory analysis that stratified the risk of progression through CKD stages based on data from the ILLUMINATE studies. In the analyses, people in the CKD 1 to 3b cohorts were split into 2 separate strata. These were people with what it termed normal or near normal oxalate levels and people with above normal oxalate levels. The ERG was uncertain if the company's scenario addressed the issue about time spent at a steady but very high plasma oxalate level over time. It considered that clinical opinion may be useful to validate the modelled length of time spent in each CKD stage for people having standard care (starting in CKD stages 1 to 3b). The clinical experts explained that if a person's disease responds to pyridoxine and they have a stable urinary oxalate level with no evidence of nephrocalcinosis, they are likely to remain in a stable disease state for about 10 years. However, people with nephrocalcinosis are likely to experience a relatively rapid decline in kidney function. Also, people who have recurrent kidney stones and acute kidney injury would experience a greater decline in kidney function. The committee discussed how the company's model assumes that the lumasiran cohort will not experience any disease progression.

However, in the ILLUMINATE studies oxalate levels in people having lumasiran were at a level at which progression was seen in the study by Shah (2020). In contrast, the company made the assumption that if a person's plasma oxalate levels were not increasing, as would be expected in people having lumasiran, then their kidney function should be stable. The company explained that oxalate-lowering treatments such as lumasiran reduce a person's oxalate levels to a higher than normal but stable level. The committee discussed whether the company's model may reasonably estimate the effect of lumasiran on kidney function. It noted, based on the results of company's exploratory analysis, that any uncertainty in relation to this was likely to have a small impact on the incremental cost-effectiveness ratio (ICER).

3.20 In response to consultation on the first evaluation consultation document, the company updated its base case to use data from a study by Singh (2022) to calculate the transition probability from CKD 3b to CKD 4 health states and from CKD 4 to end-stage kidney disease health states for people on standard care. Singh (2022) reported the rate of eGFR decline as a function of CKD stage in people with PH1. The original model had used survival curves from a study of people with PH1 (Harambat 2010) to model disease progression from CKD 4 to end-stage kidney disease health states. The ERG noted that the survival curves in Harambat (2010) were not specific to people with PH1 who were already in CKD 4 but included people who were in various stages of CKD. So, it considered than an incorrect approach was used in the original model which had now been corrected. The committee noted that this change significantly reduced the ICER because it meant that people on standard care would be more likely to transition to the end-stage kidney disease health state than before. It concluded that the company's modelling of disease progression was sufficient for decision making.

Probability of transplant

3.21 The company initially estimated the rate of liver–kidney transplant for the CKD 4 and end-stage kidney disease health states depending on whether a person's oxalate level was controlled or uncontrolled. These rates were transformed into 6-month cycle probabilities. For the first and second committee meetings, the company assumed that 100% of people in the CKD 4 and end-stage kidney disease health states with controlled oxalate levels would be placed on a

transplant waiting list. For these people the probability of transplant was estimated based on the rates of liver–kidney transplants for people on the transplant waiting list seen in clinical practice in the NHS. For people whose oxalate levels were uncontrolled, the probability of transplant was based on the observed rates of transplant in people with PH1 in a French cohort. This was updated by the company for the second committee meeting with an estimate based on review of data of people in the OxalEurope registry who had a liver or kidney transplant across 8 countries in Europe (Metry 2022). The study by Metry (2022) did not stratify people according to their oxalate level. The ERG suggested a different way to calculate the probability of transplant using Metry (2022), which resulted in an estimate that people would be twice as likely to have a transplant in a 6-month model cycle than the company's estimate. This difference arose because the ERG considered that it was important to include people from the study who had had a sequential or a combined liver–kidney transplant, whereas the company had only included people from the study who had had a combined liver–kidney transplant. The ERG also used the average age of the study cohort who had been in the registry from birth to estimate its transplant probability rather than the maximum follow up from the study.

3.22 At the first meeting the ERG suggested that the difference in assumed probability of having a transplant between people with controlled and uncontrolled plasma oxalate lacked face validity. In the company's model the probability of having a transplant was much higher in the controlled oxalate group than the uncontrolled oxalate group. The ERG considered that the probability of transplant for people with uncontrolled oxalate levels was underestimated in the model. The clinical experts explained that many children are prevented from having a kidney transplant, but not a liver transplant. This is mainly because of the weight criteria needed for kidney transplant, the risk of kidney failure after transplant (because of nephrocalcinosis) and mortality. However, older children would be less likely to be prevented from having a liver–kidney transplant if they have had reasonable kidney function in early childhood. The clinical expert explained that in adults, high levels of urinary oxalate would be indicative for people to have a transplant as soon as possible. The company and ERG, in response to the first consultation, used data from Metry (2022) to derive transplant rates in people with uncontrolled oxalate. This resulted in a similar difference in the probability of transplant in the group of people whose oxalate was controlled and uncontrolled, as had been presented by the company in the first meeting. The committee

sought further clarification from the clinical experts about whether this reflected clinical practice. The clinical experts explained that, contrary to the assumption in the company's model, people with high plasma oxalate levels are more likely to have a transplant because they might experience faster disease progression. The clinical experts also stated that young people would have a liver transplant as soon as possible after diagnosis to eliminate the source of excess oxalate production. The clinical experts stated that high oxalate levels may affect the success of a kidney transplant and that it would be better for this to be controlled before a kidney transplant. The committee considered that, by using the assumed different transplant rates for people whose oxalate levels were controlled and uncontrolled, the company's model did not reflect clinical practice. In response to the second consultation the company updated its model using data from Metry (2022) and the ERG's approach (see section 3.21), to calculate the same probability of transplant for people with controlled and uncontrolled oxalate levels. The committee concluded that the company's updated model was reflective of transplant rates in clinical practice for people with PH1 and was appropriate for decision making.

Utility values used in the company's base case

3.23 The company derived utility values for people in CKD 1 to CKD 3b health states using pooled EQ-5D data from ILLUMINATE-A. Utility values for people in CKD 4 and end-stage kidney disease health states could not be obtained from ILLUMINATE-A because the trial included people with relatively preserved kidney function. Although EQ-5D data was collected in ILLUMINATE-C, which included people with advanced kidney disease, it was not considered appropriate by the company (see section 3.25). Therefore, the company did a health-state vignette study to estimate utilities for the CKD 4 and end-stage kidney disease health states for people with uncontrolled oxalate on high-intensity dialysis. This involved surveying a sample of the general population and asking them to complete a quality-of-life measure based on the vignette. The vignette study produced different sets of utility values depending on whether the EQ-5D-5L questionnaire, visual analogue scale or time-trade-off method was used. For the remaining health states, the company used data from the ILLUMINATE-A study and the literature to estimate utility values. The company base case used the EQ-5D-5L-based valuation of the vignettes (mapped to EQ-5D-3L) to estimate

utilities for the CKD 4 and end-stage kidney disease health states (for people with uncontrolled oxalate and on high-intensity dialysis) and the post-transplant health states in the model.

Different methods of deriving utility values from the vignette study give different results

3.24 To assess the validity of the different methods to derive utility values from the vignette study, the ERG compared the utility values for vignettes describing people with PH1 and relatively preserved kidney function with the utility values derived from ILLUMINATE-A. The ERG considered that the utilities derived from the EQ-5D-5L-based valuation of the vignettes for the CKD 1 to 3b health states lacked face validity when compared with the utility values measured in the ILLUMINATE-A study. It considered that the utilities derived from the time-trade-off valuations of the vignettes aligned better with the utility values measured in the ILLUMINATE-A study. At the first committee meeting, the ERG preferred the time-trade-off valuations of the vignettes to estimate utilities for the CKD 4 and end-stage kidney disease (for people with uncontrolled oxalate and on high-intensity dialysis) and post-transplant health states. The committee agreed that the EQ-5D-5L utility values for CKD 1 to 3b health states from the vignette study were inconsistent with the values seen in the ILLUMINATE-A study. The company highlighted that current NICE guidance prefers the EQ-5D over the time-trade-off method for vignette valuation. In response to the second consultation, the company also stated that many of the time-trade-off scores derived from the vignette study were implausibly high for a person with advanced stages of CKD and PH1. It presented a scenario that excluded individual time-trade-off scores above the expected utility value for people without PH1 in CKD 4 and end-stage kidney disease. The committee noted that the ERG was unable to validate the results of the company's scenario, based on the information provided by the company. It did not consider that the company's adjustment of the time-trade-off utility estimates, by excluding some of the sample's responses, was appropriate. The committee agreed with the company that using EQ-5D is the preferred approach for valuing vignette studies according to the NICE methods guide. It noted that while both approaches allow individual respondees' estimates of quality of life to be a minus value (meaning that quality of life is 'worse than death'), the time-trade-off approach resulted in a small number of extreme

negative values that were far apart from the remaining utility scores. Because of this, it considered that that the utilities derived using the time-trade off-approach may also be less valid. The committee considered that it needed to see EQ-5D data measured in the ILLUMINATE-C study to determine the most appropriate estimates of utility values for the late CKD health states for decision making.

3.25 The company stated that there was not enough robust EQ-5D data from ILLUMINATE-C from which utility values could be derived, because of the small sample size of the study. However, for the second committee meeting it provided EQ-5D scores at initial valuation for a small number of people from ILLUMINATE-C (mainly children with advanced kidney disease on dialysis). The company considered that the utility values from this subgroup showed closer agreement with the utilities derived by the EQ-5D-5L valuations of the vignettes for children in later stages of disease. The committee noted at the second committee meeting that the company had not presented all the available data from ILLUMINATE-C and that there was variation between the individuals' scores from the company's subgroup. It discussed the ERG's scenario analysis, which applied the average utility value seen from this subgroup to children in the CKD 4 health state and all people in end-stage kidney disease health states with uncontrolled oxalate levels. This average utility value was between the EQ-5D-5L and time-trade-off derived utilities from the vignette study. Using this average directly observed utility value had a large effect on the ICER compared with using the company's preferred vignette approach. The committee would have liked the company to provide the average EQ-5D score across all people included in ILLUMINATE-C to validate the utilities derived from the vignette study. In the absence of this data, the committee preferred to use the EQ-5D utility average from the subgroup in ILLUMINATE-C to estimate utilities for the late CKD health states (as per the ERG's scenario analysis). The committee noted that the choice of utility values had a large impact on the cost-effectiveness estimates.

3.26 In response to the second consultation, the company stated that it considered that individual EQ-5D index scores from adults in ILLUMINATE-C were unsuitable for decision making. This was because some adults reported EQ-5D scores higher than those reported by people without PH1 (in CKD 4 or end-stage kidney disease) and the general population norm values. The company stated that such high scores lacked credibility given that people in this trial had advanced PH1 and would be having frequent dialysis. It suggested that a possible explanation for

this could be that some people may have adapted to their condition and so did not see their disease symptoms as impacting their quality of life when completing the EQ-5D questionnaire. The company described such an effect as a disability paradox. It suggested that this might have affected EQ-5D scores for adults more than for children, because they would have had more time to adapt to their disease. The committee noted how some of the EQ-5D scores from the subgroup of children from ILLUMINATE-C indicated health states worse than death. The clinical expert explained that health states worse than death are plausible in infantile oxalosis because of the presence of co-morbidities affecting various parts of the body (such as the eyes, heart, bone marrow and skin), which results in a high burden of care. The company presented the ERG's scenario from the second committee meeting (using the EQ-5D utility average from a subgroup in ILLUMINATE-C) but considered that the small sample size of the subgroup introduced uncertainty around the estimate. It considered that the vignette valuations were more robust because they were elicited from a larger sample of the general population and would not be biased by the effect described by the company (disability paradox). The committee recognised that there was uncertainty in using the EQ-5D utility average from the subgroup of children from ILLUMINATE-C but considered that this was the best source of utility data to estimate utilities for people with PH1 and advanced kidney disease. This was because the utility values were measured directly from children (or their caregivers) in the trial. The committee acknowledged that there may be potential for some people with the condition to adapt to it and report better quality of life than may be expected. It recalled that the EQ-5D scores reported directly by people with PH1 in ILLUMINATE-A were also higher than the EQ-5D-5L utilities derived from the vignette study for the CKD 1 to 3b health states. The committee considered that this difference in utility value estimates derived directly from people with PH1 and from the vignette study for people with advanced kidney disease and for people with less severe disease with relatively preserved renal function was unlikely to be fully explained by people with PH1 adapting to the condition. It discussed that if such an effect was true then it would be likely be present for other chronic conditions which may have a severe impact on a person's quality of life. The committee noted that it had not adjusted for such an effect in previous evaluations of highly specialised technologies, in line with current NICE guidance. It considered that the company's approach to use EQ-5D data from ILLUMINATE-A to estimate utilities for the earlier CKD health states (CKD 1 to 3b) was appropriate. The committee further concluded that the EQ-5D

utility average from the subgroup in ILLUMINATE-C should be used to estimate utilities for the late CKD health states (as per the company and ERG scenarios). But, this utility value estimate was highly uncertain because it was derived from a small subgroup that did not include adults.

Dialysis assumptions

3.27 In the model, it is assumed that all people in the standard care arm (both CKD 4 and end-stage kidney disease states) have high-intensity dialysis for 7 days per week. In the lumasiran arm, no people with CKD 4 have any type of dialysis and all people with end-stage kidney disease have normal-intensity dialysis.

3.28 The ERG considered there to be a disconnect between the dialysis schedules suggested by the company's clinical experts and the schedules used in the model. The clinical experts explained that the ideal dialysis regimen for people with uncontrolled oxalate levels is high-intensity haemodialysis 7 days per week. However, they explained that this is not manageable in NHS clinical practice because of the limited capacity of haemodialysis units and the disruption that intensive dialysis causes to family life. The clinical experts explained that in most cases, the frequency of dialysis is reduced to around 3 to 4 times per week with a maximum of 6 days per week. The clinical experts explained that a home haemodialysis programme is primarily used for the age group they described as infants, and allows parents to do dialysis at home more frequently, reducing the burden of travelling to and from the hospital. The committee noted that home haemodialysis would need a significant commitment from parents and carers and that it may not be suitable for all families. The clinical experts explained that they would consider dialysis for children and adults with stage 4 CKD to prevent disease progression ahead of transplant, but that it is more frequently used for people with end-stage kidney disease. The committee discussed that if lumasiran was equivalent to a transplant, it would expect that people would still be having dialysis alongside treatment to remove the established oxalate from the body. The patient expert explained that their child was now having home haemodialysis 5 times per week after having a liver transplant to lower oxalate levels in the body. The committee accepted that people having lumasiran with end-stage kidney disease would be likely to have less intensive dialysis. It discussed the ERG's scenario that reduced the percentage of people on standard care having

dialysis in the CKD 4 health state, in line with the company's clinical expert opinion. The committee considered that this would likely underestimate the use of dialysis in this population based on comments made by the clinical experts at the committee meeting. It concluded that it would have preferred for the company to have provided scenario analyses that varied the intensity of dialysis schedules for people having standard care in the CKD 4 health state and lumasiran in end-stage kidney disease.

3.29 At the second committee meeting, the company updated its base-case assumptions for people having dialysis in the CKD 4 health state. It reduced the proportion of adults on standard care having high-intensity dialysis (from 100% to 25%) and increased the proportion of children on lumasiran having normal-intensity dialysis (from 0% to 50%). The company also presented scenarios exploring alternative proportions of adults with CKD 4 on standard care having dialysis (50% or 0%). The clinical experts reiterated that most people would have dialysis in hospital for a maximum of 6 days per week, and that this would still be considered as high-intensity dialysis compared with dialysis schedules for people without PH1. The committee concluded that the company's scenario, which assumed that 50% of adults and 100% of children in CKD 4 would be on high-intensity dialysis, aligned better with clinical expert opinion compared with the company's revised base-case assumptions. At the third committee meeting, the company updated its base-case assumptions for people having dialysis in the CKD 4 health state in line with the committee's preferred scenario from the second committee meeting. It applied the dialysis rates from this scenario to people on standard care having high-intensity dialysis as well as people on lumasiran having normal-intensity dialysis. This was because the committee had previously considered that people on lumasiran would still need dialysis to remove established oxalate deposits from the body. The company also reduced the frequency of high-intensity dialysis in the model from 7 days to 6 days per week, based on clinical opinion heard in the second committee meeting. The committee was satisfied that the company's updated modelling assumptions reflected the expected use of dialysis in people with PH1 on standard care or lumasiran.

Survival after transplant

3.30 The company used data from a study in people with PH1 to model overall survival after a liver–kidney transplant. The study estimated survival curves based on a person's pre-operative condition (very good, good, fair and poor). The company assumed that:

- survival for people in very good and good condition in the study would be reflective of survival for people in the post-transplant state with controlled oxalate levels
- survival for people in fair and poor condition would be reflective of survival for people in the post-transplant state with uncontrolled oxalate levels.

The ERG noted that survival in the study was based on all people having standard care. Therefore, it preferred to assume that estimates of overall survival from the study were representative of survival for all people in the standard care group. The committee agreed with the ERG's approach and noted that the change in post-transplant survival for the standard care group had a small impact on the ICER. In response to consultation, the company updated its base case to align with the committee's preferred assumption on survival after transplant for people on standard care.

Lumasiran continuation rule

3.31 At the second committee meeting, the company suggested that a person with onset of PH1 during childhood with mature kidneys could potentially clear a higher rate of oxalate than they were able to as a child with immature kidneys. The company considered that in the absence of severe renal impairment, it could be appropriate to pause lumasiran treatment in such people with criteria for restarting treatment if they experience signs of progression. The committee noted that the company had not included a continuation rule in its base case because there is no data available to inform the proportion of people that would remain stable after lumasiran treatment interruption. This was reiterated by the clinical experts at the committee meeting. The committee discussed the company's scenario analyses, which modelled different proportions of people to restart treatment with lumasiran over time (10%, 30%, 50%, 70%, 90%). It noted

that the results of the scenario analyses suggested a large impact on the ICER. The clinical experts explained that there may be some groups of people for whom pausing treatment with lumasiran may be appropriate if they have stable kidney function over time (such as women who wish to start a family and those whose disease responds to vitamin B6). They explained that it would be unlikely that treatment with lumasiran would be stopped because of the risk of long-term damage to the kidneys, which would have been prevented by remaining on treatment. The clinical experts considered that a more sensible approach would instead focus on titrating the dose of lumasiran or altering the frequency of dosing in people with stable kidney function. The committee concluded that because there was no evidence to show the impact of a stopping rule with lumasiran treatment it could not take these scenarios into account in its decision making.

Discount rate

3.32 Both the company and ERG presented scenario analyses using different discounting for costs (3.5%) and health outcomes (1.5%), which significantly reduced the ICERs. The company explained that different discounting would be more appropriate given the natural history of PH1 and the timescale over which health benefits of lumasiran are accrued. The committee was aware that in line with NICE's guide to the methods of technology appraisal (2013), in cases when a treatment restores people who would otherwise die or have a very severely impaired life to full or near full health, analyses that use a non-reference-case discount rate for costs and outcomes may be considered. However, the non-reference-case discount rate is 1.5% for both costs and health outcomes. The committee recalled comments from the clinical and patient experts which highlighted that while treatment with lumasiran would prevent excess oxalate production, most people would still have a high oxalate burden in the body that would need treatment to clear. It concluded that while lumasiran would offer benefits to people with PH1, it was not a curative treatment and so the application of a lower discount rate was not appropriate.

Drug wastage

3.33 The committee understood that lumasiran would be supplied in a 94.5 mg vial and that the dosing schedule would depend on a person's body weight. The ERG considered that costs from drug wastage are high for lumasiran, which could be reduced if smaller vials were available. The committee understood that the company did not envisage supplying lumasiran in smaller vial quantities to reduce wastage. It discussed that the summary of product characteristics for lumasiran stated that it would be provided in a single-use vial and therefore vial sharing could not happen. The committee recalled that it can only recommend the use of lumasiran within its marketing authorisation.

Cost to the NHS and value for money

Applying QALY weighting

3.34 The interim process and methods of the highly specialised technologies programme specifies that a most plausible ICER of below £100,000 per quality-adjusted life year (QALY) gained for a highly specialised technology is normally considered an effective use of NHS resources. For a most plausible ICER above £100,000 per QALY gained, judgements about the acceptability of the highly specialised technology as an effective use of NHS resources must take account of the size of the incremental therapeutic improvement. When the undiscounted QALY gain is between 10 and 30, the committee understood that a weight of between 1 and 3 may be applied if there is compelling evidence that the treatment offers significant QALY gains. The committee discussed the QALY gains associated with lumasiran. It noted that for the scenario considered most plausible by the committee, the undiscounted QALY gain was greater than 30. It recalled that this scenario included its preference to use the average EQ-5D utility from the subgroup of children from ILLUMINATE-C to estimate the utilities for the late CKD health states (see section 3.26). The committee noted that this utility estimate was highly uncertain given the small sample size of the subgroup and variation of utility values across the subgroup. It considered that there was further uncertainty about whether the same QALY gains would be achieved for adults, given that the company had not reported any EQ-5D data from

ILLUMINATE-C for this population. The committee took this uncertainty into consideration. It concluded that although it was satisfied that lumasiran would offer significant QALY gains, there was too much uncertainty around the exact QALY gains for the whole population to consider this "compelling" and to apply a weighting of 3.0. So, it decided that a QALY weight of 2.0 should be applied in its consideration of whether lumasiran gave good value for money.

Cost-effectiveness results

3.35 At the third meeting, the committee was satisfied that the cost-effectiveness estimates from the model were appropriate for decision making following the company's model revisions in response to the second evaluation consultation document. This included using the same transplant rate for people with controlled and uncontrolled oxalate (see section 3.22) and updated dialysis assumptions for people on standard care and lumasiran (see section 3.29). The company presented results for its updated base-case analysis with a further revised confidential patient access scheme for lumasiran. This was updated again by the company after the third meeting. The company's base-case deterministic and probabilistic ICERs for lumasiran compared with standard care were below £200,000 per QALY gained (the exact ICERs are confidential and cannot be reported here). The committee's preferred deterministic and probabilistic ICERs for lumasiran compared with standard care were around £200,000 per QALY gained (the exact ICERs are confidential and cannot be reported here). Taking into account the decision to apply a QALY weighting of 2.0 (see section 3.34), the committee considered that its preferred ICERs were likely to be within the range NICE normally considers an effective use of NHS resources for a highly specialised technology.

Impact of the technology beyond direct health benefits and on the delivery of the specialised service

3.36 The committee discussed the effects of lumasiran beyond its direct health benefits and recalled the submissions from various stakeholders. It understood that lumasiran would be more convenient to administer as a subcutaneous injection in hospitals or in the community setting and the dosing schedule is less

onerous compared with current treatments. It noted that because lumasiran is administered by injection, this may be difficult for some people, particularly in young children or those with needle phobia. However, lumasiran would still be considered if the potential benefits of treatment outweighed these challenges. The patient expert explained that all aspects of people's lives, and those of their families and carers, are affected by the condition. The committee understood that PH1 can affect a child's education because of ill health or because of their treatment regimen, which may limit their opportunity to eventually gain full time employment. The patient expert described how caring responsibilities for parents can be particularly demanding. The patient expert described that a parent or carer may frequently have to take time off work, for example to take their child to hospital for regular dialysis sessions. This may mean that they are worse off financially and their quality of life is negatively affected. The committee noted comments that lumasiran would result in reduced disease burden and allow people with PH1 and their caregivers to retain their independence and return to work. It considered that the company's modelling assumptions to estimate caregiver disutility were appropriate. The patient expert explained that people with PH1 would be willing to try a new treatment, such as lumasiran, if it would improve their own quality of life and that of their families. The committee concluded that lumasiran may affect people beyond its direct health benefits, but it noted that the full effect of these benefits had not been quantified. It considered these benefits in its decision making.

Other factors

Equality issues

3.37 The committee discussed the potential equality issues raised during scoping and later stages of the appraisal. It noted comments from stakeholders that because of the way PH1 is inherited, it disproportionately affects populations in which consanguineous marriages are common. Therefore, PH1 is more common in people from Middle Eastern, North African, and South Asian family backgrounds. The committee noted other stakeholder comments which highlighted that PH1 disproportionately affects young people, their families and carers. The committee considered that issues related to differences in prevalence or incidence of a

disease cannot be addressed in a highly specialised technology evaluation. It noted stakeholder comments that people who have clinical features of PH1 but are not referred for assessment to a specialist centre because of geographical distance or inadequate referral pathways may experience inequalities in care. People who have been diagnosed with metabolic kidney stone disease may also struggle to access and attend specialist centres because of where they live. The committee considered that issues about healthcare implementation could not be addressed in the evaluation. A stakeholder commented that the PH1 gene can be found in all people and is not limited to a single ethnic group. So, if lumasiran was recommended then it should be offered to anyone in need of this treatment. The committee was mindful of its obligations in relation to the Equality Act 2010 and that it can only recommend the use of lumasiran within its marketing authorisation. The committee concluded that there were no equality issues relevant to the recommendations.

Innovation

3.38 The committee discussed the innovative nature of lumasiran, noting that the company and clinical experts considered the drug's mechanism of action to be a step change in managing PH1. The company highlighted that lumasiran is the first pharmacological option that can normalise or near normalise oxalate production in people with PH1. The committee noted stakeholder comments that treatment with lumasiran could prevent disease progression, reduce the number of kidney stone procedures and the need for dialysis and a transplant. The committee took this into account in its decision making.

Conclusion

3.39 The committee took into account the nature of PH1, the clinical effectiveness, value for money and the impact beyond direct health benefits. It acknowledged that PH1 is rare, serious and potentially life-threatening, affecting the lives of people with the condition, their families and carers. It recognised that there is a significant unmet need for effective and safe treatments for people with PH1. The clinical evidence suggested that lumasiran plus standard care was effective in reducing oxalate levels compared with standard care alone. The committee

understood that treatment with lumasiran would likely improve the health-related quality of life for people with PH1. The committee's preferred utility estimate for people with PH1 and advanced kidney disease was highly uncertain, and this made the cost-effectiveness results from the model uncertain. Taking this uncertainty into consideration, it agreed that limiting a QALY weight to 2.0 was appropriate for decision making. The committee also considered other benefits of lumasiran that were not fully captured in the company's modelling and stakeholder comments about the innovative nature of lumasiran. It noted that the expected use of lumasiran would be in a smaller number of people than the population modelled by the company that reflected the marketing authorisation. When using the committee's preferred assumptions and applying the confidential discount for lumasiran and agreed QALY weighting, the ICERs were likely to be within the range that NICE normally considers an appropriate use of NHS resources for highly specialised technologies. So, lumasiran is recommended as an option for treating PH1.

4 Implementation

4.1 Section 8(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication. Because lumasiran has been available through the early access to medicines scheme, NHS England and integrated care boards have agreed to provide funding to implement this guidance 30 days after publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE highly specialised technologies guidance. When a NICE highly specialised technologies guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final evaluation document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has PH1 and the doctor responsible for their care thinks that lumasiran is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The highly specialised technologies evaluation committee is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered that there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Peter Jackson
Chair, highly specialised technologies evaluation committee

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Anita Sangha
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Project managers

ISBN: 978-1-4731-5142-0