NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Evaluation consultation document

Givosiran for treating acute hepatic porphyria

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using givosiran in the context of national commissioning by NHS England. The highly specialised technologies evaluation committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts, patient experts and NHS England.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the draft recommendations made by the committee. NICE invites comments from the consultees and commentators for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of the criteria considered by the committee, and the clinical and economic considerations reasonable interpretations of the evidence?
- Are the provisional recommendations sound and a suitable basis for guidance on the use of givosiran in the context of national commissioning by NHS England?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: June 2021

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final evaluation document.
- Subject to any appeal by consultees, the final evaluation document may be used as the basis for NICE's guidance on using givosiran in the context of national commissioning by NHS England.

For further details, see the interim process and methods of the highly specialised technologies programme.

The key dates for this evaluation are:

Closing date for comments: 2 July 2021

Second evaluation committee meeting: TBC

Details of membership of the evaluation committee are given in section 6.

1 Recommendations

1.1 The committee was minded not to recommend givosiran as an option for treating acute hepatic porphyria in people 12 years and older.

1.2 The committee recommends that NICE requests further information from the company, which should be made available for the second evaluation committee meeting. This should include:

- a revised clinical and cost-effectiveness analysis comparing givosiran with prophylactic haem arginate and including the committee's preferred assumptions
- an exploratory analysis of how the starting age for treatment affects cost effectiveness and
- an exploratory analysis of how the number of people stopping treatment at menopause in both arms of the clinical trial affects cost effectiveness.

Why the committee made these recommendations

Acute hepatic porphyria is a rare, progressive and potentially life-threatening condition that can significantly affect the quality of life of people with the condition, and their families and carers. People can have acute attacks with extreme pain, nausea and fatigue, which sometimes lead to seizures and paralysis. They can also have chronic pain and fatigue. Standard treatment in the NHS is prophylactic haem arginate, which is offered to most people with recurrent severe attacks despite it being used outside its marketing authorisation. Therefore, givosiran should be compared with haem arginate.

Clinical trial evidence shows that givosiran reduces the frequency of attacks compared with best supportive care without haem arginate. No evidence or analysis was provided comparing givosiran with prophylactic haem arginate. It is uncertain how effective givosiran is in the long term and how it will be used in clinical practice.

Also, it is not known if the starting age for treatment and the number of people stopping treatment at menopause affect cost effectiveness. So givosiran's cost effectiveness is unknown and further information is needed before a recommendation can be made.

2 The condition

2.1 Acute hepatic porphyria (AHP) is a rare inherited metabolic disorder caused by a deficiency of the enzymes needed to make haem. It is characterised by high levels of porphyrin precursors, including delta-aminolevulinic acid and porphobilinogen, in the liver and other tissues. High levels of these substances damage nerve cells and can provoke acute attacks of physical pain. Acute attacks are very rare before puberty and usually start between 15 and 35 years. They are more common in women, who may be at increased risk of having an acute attack during or after pregnancy. Acute attacks are often triggered by factors such as drugs, alcohol, hormones, and infection. AHP is life-threatening because it can lead to seizures and paralysis during acute attacks. Also, people may stop breathing. It can be debilitating in the long term because of chronic pain, fatigue, nausea and vomiting. AHP is progressive, with attack frequency and severity increasing over time. The condition varies from person to person. There are 4 types of AHP: acute intermittent porphyria, hereditary coproporphyria, variegate porphyria and aminolevulinate dehydratase porphyria. Acute intermittent porphyria is the most common form of AHP in the UK and has the highest symptom burden.

2.2 The prevalence of AHP is estimated to be 1 in 100,000 people in Europe, which equates to about 560 people in England. Most people fully recover after 1 attack or a few attacks, but attacks can be recurrent in about 10% of people. People with recurrent severe attacks often have chronic symptoms and may not fully recover from an attack. According to the National Acute Porphyria Service, there are 35 people in the UK having treatment for recurrent severe attacks.

2.3 Treatment options for AHP aim to stop or manage symptoms. They include pain management, stopping medication that could have triggered symptoms, gonadotrophin releasing hormone (GnRH) analogues for hormone-induced attacks in women, and oral or intravenous glucose for acute attacks. Haem arginate is indicated for treating acute attacks of AHP. It is also used outside its marketing authorisation to prevent attacks. Liver transplant may be an option for some people with recurrent severe attacks when other treatment options have not worked.

3 The technology

3.1 Givosiran (Givlaari, Alnylam) is a small-interfering ribonucleic acid that suppresses delta-aminolevulinic acid synthase 1 production by the liver. This reduces the level of toxic precursors of porphyrin. Givosiran has a marketing authorisation in the UK for 'treating acute hepatic porphyria in adults and adolescents aged 12 years or older'. It is administered by subcutaneous injection. The recommended dose is 2.5 mg per kg body weight once a month.

3.2 Very common adverse reactions (that is, occurring in 1 in 10 people or more) include injection site reactions, nausea and fatigue. Elevated transaminases and anaphylactic reactions have led to people stopping treatment. For full details of adverse reactions and contraindications, see the summary of product characteristics.

3.3 The price for givosiran is £41,884.43 per 189-mg vial (excluding VAT; company's evidence submission). The company has a commercial arrangement (simple discount patient access scheme), which would have applied if the technology had been recommended.

4 Consideration of the evidence

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

Burden of disease

4.1 The patient and clinical experts explained how recurrent severe hepatic porphyria (AHP) affects all aspects of the lives of people with the condition, and their families and carers. It has a significant effect on a person's independence, their ability to work and to have a social life. People with recurrent attacks (that is, 4 or more attacks in 12 months) live in fear of having a severe attack that results in hospital admission. This can be worrying for them and their families and carers. Recovery from a severe attack can take a couple of months, but some people do not recover fully. The patient experts explained that even between attacks, people with recurrent severe attacks are often unable to take part in usual family and social activities because of debilitating long-term pain and fatigue. This can have a substantial emotional effect on them and their families. AHP can be life-threatening if not appropriately treated, although the clinical experts highlighted that mortality has significantly reduced since the use of haem arginate. The committee concluded that AHP is rare, serious and potentially life-threatening, affecting the lives of people with the condition, their families and carers.

Unmet need

4.2 The clinical experts explained that there is no treatment with a marketing authorisation for preventing recurrent attacks of AHP. About 95% of people have haem arginate outside its marketing authorisation to prevent recurrent attacks. But its effect reduces over time and many people still have severe attacks, needing hospital admission. According to the clinical

and patient experts, haem arginate does not reduce chronic pain and fatigue. Also, it can be associated with iron overload, which can cause chronic liver inflammation. Haem arginate is given intravenously once a month but this often needs to be increased to 2 to 4 times a month. It is given through a central venous catheter, which can be difficult to maintain. The clinical experts explained that women of childbearing age could take GnRH analogues to manage hormone-induced attacks but very few chose to do so. GnRH analogues suppress ovulation and are associated with oestrogen deficiency so they are only used for up to 2 years. After this people usually have haem arginate. The clinical experts explained that previously people had a liver transplant when haem arginate was no longer an option. Although transplant can be a cure it is rarely done because of the person's health and lack of a donor organ. The clinical experts confirmed that referral for liver transplant is now often delayed in the hope that more effective and safer treatment options will become available. The committee recognised that there is a significant unmet need for effective and safe treatment options for people with recurrent acute attacks of AHP.

Diagnosis

4.3 The clinical experts explained that AHP is diagnosed by testing urine for porphobilinogen, aminolevulinic acid, and porphyrin. Given the rarity of the condition and its many unspecific symptoms, diagnosis of AHP is often delayed, or it is misdiagnosed. Genetic tests are now available. The clinical experts confirmed that these are not routinely used but help to confirm the initial diagnosis and identify the type of AHP. However, the tests do not indicate whether the condition will be severe and recurrent.

Impact of the new technology

Experience with givosiran in NHS clinical practice

4.4 The clinical experts confirmed that 6 people in England have had givosiran for preventing recurrent severe attacks as part of an

international clinical trial. The patient and clinical experts explained that there were minor side effects including nausea, but this only lasted for a short time. They also highlighted that givosiran reduced the frequency of attacks quickly. Attacks that did occur were less severe and people did not need hospitalisation. People still had symptoms such as chronic pain and fatigue, which lessened with time. The committee concluded that people with AHP and their clinicians would welcome givosiran as a treatment option for preventing recurrent severe attacks.

Comparators

4.5 The company submission only included evidence comparing givosiran with best supportive care. This was different to the NICE scope, which specified haem arginate, GnRH analogues and liver transplant as comparators. The committee recalled that haem arginate was established NHS clinical practice for preventing recurrent acute attacks (see section 4.2). It noted that haem arginate was used outside its marketing authorisation and referred to the highly specialised technologies interim methods and process guide section 59. This states that comparators can be considered even though they do not have a marketing authorisation if they are part of established NHS clinical practice for the indication. The ERG explained that there is a lack of data on prophylactic haem arginate for preventing recurrent acute attacks. The clinical experts confirmed that it is challenging to collect such data in clinical practice because haem arginate is used for both prevention and acute treatment of severe attacks. The committee recalled that GnRH analogues and liver transplant are rarely used in NHS clinical practice for preventing recurrent severe attacks (see section 4.2). The committee agreed that all treatment options currently used in NHS clinical practice should have been considered. It concluded that prophylactic haem arginate is the most appropriate comparator for this appraisal.

Clinical evidence

4.6 The clinical evidence for givosiran included:

- ENVISION (N=94), a double-blind randomised placebo-controlled trial assessing the efficacy and safety of givosiran (n=48) compared with placebo (n=46). This trial was in people who had at least 2 attacks in 6 months that needed hospitalisation, an urgent healthcare visit or intravenous haem arginate. Givosiran was administered by subcutaneous injection (2.5 mg per kg body weight) once a month. After the 6-month trial period, people could join a 30-month open-label extension study (ENVISION OLE), assessing the efficacy and safety of givosiran. People could have 2 different doses of givosiran (1.25 mg per kg body weight [n=37], and 2.5 mg per kg body weight [n=56]). People in both arms also had best supportive care, which included managing chronic symptoms and acute attacks.

- A phase 1 or 2 (n=40) randomised dose-finding study that assessed the safety of givosiran. Part C (n=17) of this study recruited people with AHP and recurrent acute attacks (that is, at least 2 attacks in 6 months that needed hospitalisation, an urgent healthcare visit or intravenous haem arginate). This part of the trial was a double-blind evaluation of 4 different doses of givosiran (n=13) compared with placebo (n=4). Follow up was 168 days.

The committee agreed that evidence from ENVISION and ENVISION OLE was relevant to this appraisal.

Generalisability of ENVISION and ENVISION OLE to NHS clinical practice

4.7 ENVISION was an international trial that included 4 people from the UK (4.3% of people enrolled). Most people had a diagnosis of acute intermittent porphyria (n=89) and only 4 people had other types of AHP. Everyone had 2 or more attacks in 6 months that needed hospitalisation, an urgent healthcare visit or intravenous haem arginate. The clinical experts confirmed that people with AHP having treatment in the NHS and for whom givosiran would be an option, have similar characteristics to people in ENVISION. The committee acknowledged that a small trial such

as ENVISION may not represent the full population who would have givosiran. The clinical experts explained that best supportive care in other countries is similar to that in NHS clinical practice although it would usually include prophylactic haem arginate. This was not allowed in ENVISION. The committee concluded that people in ENVISION, other than not having prophylactic haem arginate, would have similar characteristics to those seen in NHS clinical practice.

4.8 Everyone who completed ENVISION entered ENVISION OLE. Most people (n=56) had the dose of givosiran specified in the summary of product characteristics (2.5 mg per kg body weight) but 37 people had a lower dose (1.25 mg per kg body weight). People could swap between doses. The clinical experts confirmed that everyone having givosiran in the UK as part of an ongoing clinical trial has 2.5 mg per kg body weight. The committee agreed that there was some uncertainty about the generalisability of ENVISION OLE to NHS clinical practice but concluded that it was acceptable for decision making.

Study outcomes

4.9 The primary outcome of ENVISION was annualised rate of porphyria attacks (that is, attacks needing hospitalisation, an urgent healthcare visit, or intravenous haem arginate at home). At 6 months people in the givosiran arm had fewer attacks (3.2; 95% confidence interval [CI] 2.25 to 4.59) than people in the best supportive care arm (12.5; 95% CI 9.35 to 16.76). This was a relative reduction of 74% (95% CI 59% to 84%). There were fewer attacks with givosiran compared with best supportive care across the 3 categories of attacks. The difference was smallest for attacks needing hospitalisation and was not statistically significant (relative reduction 49% 95% CI -4% to 75%). The committee concluded that givosiran was effective in reducing severe attacks compared with best supportive care.

4.10 In ENVISION health-related quality-of-life data were collected using the EuroQol 5-dimensions 5-level questionnaire (EQ-5D-5L). Results were mapped to EQ-5D-3L to obtain utility values. There was no statistically significant difference between the treatment arms at 6 months (least squares mean change from baseline in visual analogue scale: givosiran 6.8, placebo 2.8; treatment difference 4.0, 95% CI -3.3 to 11.4). The committee noted that fewer attacks did not lead to improved health-related quality of life and considered this to be unexpected. It was aware that health-related quality of life is affected by many factors including chronic symptoms and psychological factors. It recalled that chronic symptoms may not reduce as quickly as the frequency of attacks and that 6 months might be too short to capture givosiran's full benefits. The committee concluded that givosiran was likely to affect health-related quality of life but it was unclear how large such an effect would be.

Cost to the NHS and value for money

Company's model

4.11 The company's economic model compared givosiran with best supportive care. The Markov model contained 4 health states and 1 absorbing state (death). The health states were defined by the number of severe attacks (attacks needing hospitalisation, an urgent healthcare visit or intravenous haem arginate) in 12 months:

- asymptomatic (0 attacks)
- symptomatic (4 or less attacks)
- recurrent (4 to 24 attacks)
- severe (more than 24 attacks).

People entered the model in the symptomatic, recurrent or severe health state. At the end of each 6-month cycle they could move to another health state, remain in the same health state or move to the absorbing state.

4.12 The hypothetical group of people in the model was assumed:

- to be 42 years at model entry
- to be 86% women and
- to have the same characteristics as people in ENVISION.

4.13 The company's economic analysis adopted an NHS perspective and had a 60-year 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.

Long-term effectiveness of givosiran

4.14 Data collected from ENVISION and ENVISION OLE during the first 18 months informed the health state of people entering the model. It also informed how they moved (or transitioned) from 1 health state to another in the givosiran arm of the model. The company's base case used these transitions up to 5 years in model. After 5 years people remained in the health state they were in at this time and moving to another health state was no longer allowed. The clinical experts confirmed that givosiran decreases the frequency of acute attacks in a few weeks. They expected that this effect would last for as long as a person has givosiran. The committee recalled that givosiran can also reduce chronic symptoms but this happened over several months (see section 4.4). The committee concluded that after 18 months people should remain in the health state they were in at that time. Only moving to the death state, in line with mortality in the general population, should be possible.

Long-term effectiveness of best supportive care

4.15 Data collected from ENVISION during the first 6 months informed the health state of people entering the model. It also informed how they moved from 1 health state to another in the best supportive care arm of the model. The company's base case used these transitions for the first 6 months in the model; after this moving to another health state was not allowed. The committee understood that most people in the ENVISION best supportive care arm had previously had haem arginate. This was

either to treat acute attacks or as prophylactic treatment. The committee acknowledged that the 6-month results for best supportive care might include a treatment withdrawal effect. The clinical experts explained that if untreated, acute attacks get more frequent and severe, and the condition generally deteriorates over time. The committee agreed that the effect of prophylactic haem arginate is unknown. Also, stopping people moving to another health state after 6 months for the best supportive care arm might be conservative because it assumes that the disease stabilises early on. It concluded that stopping people moving to another health state after 6 months was acceptable, but this added to the uncertainty in the model.

Stopping treatment

4.16 In ENVISION only 1 person stopped givosiran and this was because of adverse events. The clinical experts explained that in NHS clinical practice people might also have treatment breaks. For example, if the disease was asymptomatic (no attacks in 12 months) or there were few attacks (less than 4 in 12 months). They confirmed that there is little experience with treatment breaks; it is unclear when treatment would be stopped and how long breaks would last. Routine monitoring of symptoms and biochemistry would continue every 6 months during treatment breaks. The committee understood that clinicians would prefer to offer treatment for the minimum time and that people prefer a life without treatment. The committee concluded that because of the uncertainty about stopping and starting criteria for givosiran and their effect on outcomes it was not appropriate to include them in the model.

Time on treatment

4.17 The committee was aware that most people with recurrent severe attacks are women of childbearing age. The clinical experts explained that attacks often stop at menopause so treatment is no longer needed for most women. In the model, more people in the givosiran arm had no attacks at menopause and stopped treatment than in the best supportive care arm. The committee noted that it should have been presented with an

exploratory analysis estimating the effect of varying the numbers of women stopping treatment in both arms. Because there are fewer men with AHP there is less clinical experience, and it is unclear whether attacks in men also stop or diminish with age. The committee noted that few people might need lifelong treatment but it was unclear how many this might be.

4.18 Because of the short follow-up time in ENVISION (up to 18 months) there is only limited clinical data on how long people stay on treatment. So fitting an appropriate parametric model was challenging. Based on clinical plausibility, the company fitted a log-logistic model to the Kaplan–Meier curve based on observed data from ENVISION and ENVISION OLE. Because cost-effectiveness results change substantially with time-on-treatment estimates, the ERG explored alternative methods. This included a piecewise approach using the Kaplan–Meier curve based on observed data followed by the log-normal model. The committee concluded that time-on-treatment estimates were very uncertain but accepted the company's approach using a log-logistic model.

Quality-of-life data used in the model

4.19 To look at the effect on quality of life, the model used a 2-step approach to include the chronic symptoms of the disease and the acute attacks. EQ-5D-5L data collected in ENVISION (see section 4.10) was not used in the model. Instead, the company used utility values for each chronic symptom from the literature. It used data from the EXPLORE study, a natural history study of people with AHP, for utilities associated with acute attacks. The clinical experts explained that it is challenging to use trial data to determine the quality of life for people who have acute attacks. They suggested that ENVISION utilities could be used for the chronic symptoms. The committee cautioned that these did not appear plausible because they suggested higher quality of life in more severe health states. It agreed that the company's approach of summing the effect of single chronic symptoms was flawed. It preferred the ERG's approach of using

utilities from relapsing–remitting multiple sclerosis as the best available proxy for the chronic symptoms. The committee concluded that using utilities from relapsing–remitting multiple sclerosis to model the chronic symptoms and from EXPLORE to model the acute attacks was reasonable.

Number of people with chronic symptoms

4.20 The ERG challenged the sources of treatment costs for chronic symptoms and how costs were included in the model. The committee agreed that a micro-costing approach should only be used when each symptom needed separate resources. Also, costs should come from the most recent publications, the Personal and Social Services Research Unit or health resource groups. The clinical and patient experts explained that people with chronic pain often use opioids and that opioid dependency was an issue for some people. The committee agreed to include costs of opioid dependency in the model. It concluded that including the costs of treating chronic symptoms added uncertainty and this should be further explored using alternative cost sources.

Age at model entry

4.21 Clinical experts advised that people are diagnosed with AHP in their 20s or 30s. Often people in their 30s start treatment with haem arginate to prevent recurrent acute attacks. The median age of people entering the model in the company's base case was 42 years. Because most people in the givosiran arm stopped treatment at menopause age at model entry, this had a substantial effect on the cost-effectiveness results. The clinical experts confirmed that the median age of people who have prophylactic treatment for recurrent severe attacks and would be eligible for givosiran in the NHS is early 40s. However if givosiran was recommended, anyone newly diagnosed with recurrent severe attacks would become eligible at diagnosis so people starting treatment would be younger. The committee concluded that the starting age for treatment is an important model driver.

An analysis of the effect of varying starting age should be provided using information from people with AHP currently having treatment in the NHS.

Applying QALY weighing

4.22 The interim process and methods of the highly specialised technologies programme specifies that a most plausible incremental cost-effectiveness ratio (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. This is revealed through the number of additional unadjusted QALYs gained and by applying a 'QALY weight'. It understood that a weight between 1 and 3 can be applied when the QALY gain is between 10 and 30 unadjusted QALYs. The committee discussed the QALY gains associated with givosiran compared with best supportive care. It agreed that these are likely to be above 10 and that applying a QALY weight might be appropriate compared with best supportive care. A comparison of givosiran with prophylactic haem arginate was not provided. Therefore, the committee could not conclude whether it was appropriate to apply a QALY weight for that comparison.

Cost-effectiveness results

4.23 The committee's preferred base-case assumptions were:

- allowing people to move between health states in the first 18 months after which they remain in the same health state in the givosiran arm (see section 4.14)
- allowing people to move between health states in the first 6 months after which they remain in the same health state in the best supportive care arm (see section 4.15)

- using the log-logistic model to extrapolate time on treatment (see section 4.18)
- using utilities from relapsing–remitting multiple sclerosis (see section 4.19)
- continuing treatment until menopause for most women and throughout the time horizon of the model for men and some women (see section 4.17)
- including the costs of opioid dependency (see section 4.20).

4.24 The committee recalled that the most appropriate comparator was prophylactic haem arginate (see section 4.5). It noted that this was not included in the company or ERG's cost-effectiveness analysis. It concluded that it could not establish whether givosiran could be considered an effective use of NHS resources without further information.

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

4.25 The committee discussed the effects of givosiran beyond its direct health benefits and the evidence of the patient experts. The patient and clinical experts explained that all aspects of people's lives, and those of their families and carers, are affected by the condition. Most people with AHP cannot live independent lives and rely on family and carers at least some of the time. If people have to give up work they will be worse off financially. The committee agreed that the carer disutilities used in the model were higher than expected for a disease that usually starts in adults. The patient experts explained that givosiran had completely changed their experience of living with AHP. Recurrent attacks needing hospitalisation and chronic pain decreased substantially, so they seldom needed painkillers. The committee concluded that givosiran may affect people beyond its direct health benefits, but it noted that the full effect of these benefits had not been quantified. The committee considered these benefits in its decision making.

Other factors

4.26 The committee noted that AHP is more common in women than men. However, it concluded that its recommendation applies equally, regardless of gender, so this difference is not in itself an equality issue.

4.27 The committee discussed the innovative nature of givosiran, noting that the company and clinical experts considered the drug's mechanism of action to be a step change in managing AHP. The patient experts explained that having givosiran available would change the course of their condition. The committee took this into account in its decision making.

Conclusion

4.28 The committee concluded that AHP is a rare, serious and potentially life-threatening condition that can affect the lives of patients, their families and carers. It recognised that there is an unmet need for effective and safe treatment options for preventing recurrent severe attacks. It agreed that givosiran provided substantial clinical benefit compared with best supportive care. Givosiran could potentially improve quality of life for patients, their families and carers. Treatment with haem arginate is established clinical practice in the NHS because it provides some clinical benefit. However, evidence comparing givosiran with haem arginate was not provided. So the committee was minded not to recommend givosiran as an option for treating AHP.

4.29 The committee recommended that NICE requests further information from the company, which should be made available for the second evaluation committee meeting. This should include:

- a revised clinical and cost-effectiveness analysis comparing givosiran with prophylactic haem arginate and including the committee's preferred assumptions
- an exploratory analysis of how the starting age for treatment affects cost effectiveness and

- an exploratory analysis of how the number of people stopping treatment at menopause in both arms of the clinical trial affects cost effectiveness.

5 Proposed date for review of guidance

5.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Peter Jackson
Chair, highly specialised technologies evaluation committee
June 2021

6 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 to be appraised. If it is considered that there is a conflict of interest, the member is excluded from participating further in that appraisal.

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.

NICE project team

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

Verena Wolfram
Technical lead

Sally Doss
Technical adviser

Gavin Kenny
Project manager

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