NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using etranacogene dezaparvovec in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders 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 clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- 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 age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: July 2023

Note that this document is not NICE's final guidance on etranacogene dezaparvovec. 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 stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using etranacogene dezaparvovec in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 26 July 2023
- Second evaluation committee meeting: 13 September 2023
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Etranacogene dezaparvovec is not recommended, within its marketing authorisation, for treating moderately severe or severe haemophilia B (congenital factor IX deficiency) in adults without a history of factor IX inhibitors (antibodies against factor IX).

1.2 This recommendation is not intended to affect treatment with etranacogene dezaparvovec that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

People with moderately severe or severe haemophilia B usually have long-term treatment with factor IX (FIX) concentrates to prevent bleeding episodes (prophylaxis) and on-demand FIX concentrates to stop bleeding during a bleeding episode. A small number of people with the condition opt to only have on-demand treatment.

Evidence from a clinical trial suggests that etranacogene dezaparvovec reduces the number of bleeding episodes a person has each year. But there is not enough evidence on how well it works in the long term.

An indirect comparison of etranacogene dezaparvovec with FIX prophylaxis treatments suggests that it improves bleeding outcomes. But there are problems with this evidence, such as differences between studies in the methods used, and the definition and measurement of bleeding outcomes. So, the indirect comparison results are highly uncertain.

The cost-effectiveness estimates for etranacogene dezaparvovec are uncertain because of uncertainties in the long-term clinical evidence and some of the assumptions used to estimate cost effectiveness. They are also above what NICE

considers an acceptable use of NHS resources. So etranacogene dezaparvovec is not recommended.

2 Information about etranacogene dezaparvovec

Marketing authorisation indication

2.1 Etranacogene dezaparvovec (Hemgenix, CSL Behring) has a conditional marketing authorisation 'for the treatment of severe and moderately severe Haemophilia B (congenital Factor IX deficiency) in adult patients without a history of Factor IX inhibitors'.

Dosage in the marketing authorisation

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

Price

2.3 The list price per treatment for a single dose of etranacogene dezaparvovec is £2,600,000.

2.4 The company has a commercial arrangement, which would have applied if etranacogene dezaparvovec had been recommended.

3 Committee discussion

The evaluation committee considered evidence submitted by CSL Behring, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of the condition

3.1 Haemophilia B is an X-linked, congenital bleeding condition characterised by a deficiency of coagulation factor IX (FIX). It mainly affects men, but can affect women in rare cases. The severity of haemophilia B generally correlates with the level of FIX in the blood and is defined as either severe

(FIX level below 1%), moderate (FIX level 1% to 5%), or mild (FIX level 5% to less than 40%). Moderately severe haemophilia does not have a standard definition but is generally considered to be a FIX level below or equal to 2%. The main symptom of haemophilia is prolonged bleeding but other complications include bleeding into joints and muscles without having had an injury. Patient experts explained that bleeds are not only physically painful but can also have a substantial psychological impact on people with the condition and their family. They often have anxiety or worry about their condition, causing great mental distress. The patient experts explained that FIX prophylaxis treatment for moderately severe or severe haemophilia B (see section 3.2) often requires self-infusion or infusion by caregivers as often as every 2 to 3 days, which is a substantial treatment burden. They added that this makes planning difficult, especially when travelling, and impairs ability to be spontaneous. Because of the heavy treatment burden, 1 patient expert described a one-off treatment with etranacogene dezaparvovec, with potential to stop the need for regular FIX prophylaxis, as life-changing. The committee concluded that moderately severe or severe haemophilia B substantially affects health-related quality of life.

Treatment pathway and proposed positioning

3.2 The clinical management of haemophilia B usually involves long-term FIX prophylaxis treatment and/or on-demand treatment with FIX concentrates. FIX prophylaxis treatment involves regular administration of standard half-life FIX concentrates (every 2 to 3 days) or extended half-life FIX concentrates (every 1 to 2 weeks) to prevent bleeding. On-demand treatment is administration of FIX concentrates at the time of a bleeding event. The company noted that, despite being eligible for regular FIX prophylaxis treatment, a small number of people with the condition, opt to only have on-demand treatment because of personal choice or clinical challenges. The company proposed that etranacogene dezaparvovec would mainly replace FIX prophylaxis treatment but could also replace on-

demand only treatment. The comparators included in the company submission were 4 FIX prophylaxis treatments available on the NHS:

- nonacog alfa (BeneFIX, standard half-life)
- eftrenonacog alfa (Alprolix, extended half-life)
- albutrepenonacog alfa (Idelvion, extended half-life) and
- nonacog beta pegol (Refixia, extended half-life).

The committee concluded that FIX prophylaxis treatment was the most appropriate comparator.

Clinical evidence

The HOPE-B trial

3.3 The primary clinical-effectiveness evidence was from the HOPE-B trial. HOPE-B is an ongoing phase 3, open-label, single-dose, single-arm multinational trial evaluating etranacogene dezaparvovec in adult males with moderately severe or severe haemophilia B who had routine FIX prophylaxis treatment (n=54). HOPE-B included a lead-in period (minimum 6 months) in which people had FIX prophylaxis treatment. After the lead-in period, people had a dose of etranacogene dezaparvovec. Because there was no control arm, outcomes assessed during the lead-in period were compared with outcomes in the post-treatment follow-up period. The company submission presented data up to 24 months after treatment with etranacogene dezaparvovec.

Annualised bleeding rate and change in FIX levels

3.4 The HOPE-B primary outcome is annualised bleeding rate (ABR). Several bleeding outcomes were reported, including various types of bleeds: all bleeds, joint bleeds, spontaneous bleeds and bleeds that needed FIX treatment. At 7 to 24 months after etranacogene dezaparvovec, results showed that:

- the adjusted ABR for all bleeding episodes decreased from 4.19 to 1.51, a reduction of 64% (p=0.0002)
- the adjusted annualised spontaneous bleeding rate decreased from 1.52 to 0.38, a reduction of 75% (p=0.0005)
- the adjusted annualised joint bleeding rate decreased from 2.35 to 0.46, a reduction of 80% (p<0.0001)
- the adjusted ABR for bleeds that needed FIX treatment decreased from 3.65 to 0.99, a reduction of 73% (p=0.0001).

The committee noted that at 7 to 24 months post-treatment, 27 out of 54 people had bleeds (average of 2.7 bleeds per person). It noted that the average number of bleeds after treatment was not substantially different from the lead-in period (average of 3.4 bleeds per person). A clinical expert explained that this may be because people may need a period of relearning in the first couple of years after having etranacogene dezaparvovec, to differentiate between joint pains and bleeds. However, a scan would be needed to confirm whether the pain was because of a bleed. Therefore, it was possible that people in the trial recorded bleeds in their patient diary when they were actually experiencing joint pain. A key secondary outcome was the change in FIX level between baseline and the post-treatment period. At 24 months post-treatment, the mean (least square) increase in endogenous FIX level from baseline was 34.13 IU/dl (p<0.001). The committee concluded that bleeding rates were lower after etranacogene dezaparvovec than during the lead-in period.

Calculation of change in FIX levels

3.5 The EAG highlighted that the company did not report participants' FIX levels during the lead-in period but instead estimated baseline FIX levels based on their historical haemophilia B severity. This approach meant it was not possible to compare FIX levels during routine prophylaxis treatment in the lead-in period with FIX levels after treatment with etranacogene dezaparvovec. The company said it used this approach because FIX levels would vary depending on the type, brand, dose and

frequency of FIX prophylaxis treatment that people were having. It also noted that FIX levels fluctuate after FIX prophylaxis treatment so it would be challenging to identify a representative measurement. It added that a benefit of etranacogene dezaparvovec would be more stable FIX levels because of endogenous production (that is, the body producing its own FIX). The company believed that using a historical estimate of baseline FIX levels instead of actual measurements better represents endogenous FIX production in the lead-in period and leads to a fairer comparison between treatments. The EAG considered that it was not possible to determine how etranacogene dezaparvovec affects FIX levels without comparing FIX levels during FIX prophylaxis with levels after etranacogene dezaparvovec. It added that understanding the change in FIX levels after treatment with etranacogene dezaparvovec would corroborate the other clinical outcomes, and show how etranacogene dezaparvovec reduces bleeds (for example, by increasing FIX levels). A clinical expert said that FIX levels tend to fluctuate after FIX prophylaxis treatment, and that the risk of bleeds is particularly high when FIX levels are low. They added that etranacogene dezaparvovec treatment stabilises FIX levels and so reduces the risk of bleeding from low FIX levels. The committee considered that a representative measure of peoples' actual FIX levels during the lead-in period would be useful. But, it understood the company's rationale and accepted the company's approach for reporting change in FIX levels. The committee concluded that etranacogene dezaparvovec produces a clinically meaningful increase in endogenous FIX levels.

Magnitude of clinical benefits

3.6 The EAG noted the clinical benefits reported in HOPE-B may have been overestimated. It suggested that reduced physical activity during the COVID-19 pandemic may have meant there were fewer bleeding episodes needing on-demand FIX replacement. The EAG also noted that after the lead-in period, the trial protocol prohibited prophylactic FIX replacement for FIX levels of 5% or more but investigating clinicians could

give FIX replacement at their discretion. The EAG considered that clinicians may be less likely to give ad hoc FIX replacement within the trial than in routine practice, to adhere as closely as possible to the preferred study procedures. It considered it plausible that use of FIX replacement would be higher in clinical practice than in HOPE-B. The company highlighted that FIX replacement use remained substantially reduced up to 24 months post-treatment. It suggested that if the COVID-19 pandemic had lowered activity levels, increased activity after the pandemic would have led to more bleeds and increased use of FIX replacement, which was not the case. It also highlighted that the reduction in annualised spontaneous bleeding rates (not related to trauma or activity) from the lead-in period to 7 to 18 months post-treatment, was maintained at 24 months post-treatment. The patient experts shared their experience that activity levels actually increased during the COVID-19 pandemic. Clinical experts added that there was no noticeable difference in reported bleeding events during the pandemic. The clinical experts also noted that decisions about giving FIX replacement would be based on normal clinical practice and not influenced by a trial setting. The committee considered it plausible that physical activity (or its intensity) may have increased during the COVID-19 pandemic and recalled that bleeding events did not noticeably change during the pandemic. The committee concluded that the COVID-19 pandemic and trial protocol did not have a substantial impact, if any, on the magnitude of clinical benefits reported in HOPE-B.

Indirect treatment comparisons

3.7 Because HOPE-B was a single-arm trial the company did indirect treatment comparisons to compare the clinical effectiveness of etranacogene dezaparvovec with FIX prophylaxis. The company used the inverse probability of treatment weight method for the comparison with Idelvion because participant-level data was available for both treatments. A matching-adjusted indirect comparison method was used for the comparisons with Alprolix, Refixia and BeneFIX because only summary data was available. The indirect treatment comparisons suggested

statistically significant improvements in bleeding outcomes for etranacogene dezaparvovec compared with each of the comparators. The results are considered confidential by the company so cannot be reported here. The EAG believed that the indirect treatment comparisons used the best available methods, but the different methods used in the studies seriously undermined the results of comparisons. The EAG noted that the comparator studies differed from HOPE-B in several important ways, principally relating to analysis populations, outcome definitions and background care. The committee understood the EAG's concerns but acknowledged these limitations related to the quality of the studies used in the indirect treatment comparisons rather than the methods used to do the indirect treatment comparisons. The committee concluded that the magnitude of improvement in bleeding outcomes for etranacogene dezaparvovec compared with FIX prophylaxis treatments was uncertain and would take this into account in its decision making.

Economic model

Company's modelling approach

3.8 The company presented a cohort-based Markov model. The modelled cohort moved through 4 health states which were based on bleeding events. These were 'no bleed', 'non-joint bleed', 'joint bleed' and 'death', with everyone starting in the 'no bleed' state. Bleeding rates from HOPE-B and the company's indirect treatment comparisons (see section 3.7) were used to calculate transition probabilities between the health states. The committee concluded that the company's model structre was appropriate for decision making.

Comparators in the economic model

3.9 In HOPE-B, people who had etranacogene dezaparvovec were also given ad hoc FIX replacement (on-demand) for bleeding episodes. The company's economic model excluded on-demand supplementary FIX replacement because this would be expected to be equal between arms.

The EAG agreed with this approach. The company modelled treatment with etranacogene dezaparvovec followed by FIX prophylaxis treatment after etranacogene dezaparvovec failure (see section 3.10). The company's model comparison was:

- etranacogene dezaparvovec followed by FIX prophylaxis treatment after etranacogene dezaparvovec failure, compared with
- FIX prophylaxis treatment.

The company presented both a fully incremental analysis (which included 8 treatment combinations) and a pairwise analysis (which included 4 comparisons). The clinical experts explained that in current clinical practice, the choice of FIX prophylaxis treatment is based on a variety of factors including the dosing schedule, FIX activity levels, bleeding patterns, mechanism of action and availability of each treatment. A clinical expert said that the most frequently prescribed treatments in clinical practice are extended half-life treatments. This is primarily because less-frequent dosing is needed (see section 3.2). The committee concluded that it would consider both the fully incremental and pairwise results but requested the company provide a further scenario analysis using a 'basket of comparators' weighted by market share in the NHS. The committee concluded this further scenario would be helpful in evaluating cost-effectiveness.

Definition of treatment failure

3.10 The company's economic model included a predicted failure rate of etranacogene dezaparvovec based on extrapolations of observed data from Shah et al. (2022) (see section 3.11). The company base case defined treatment failure (that is, the FIX level at which FIX prophylaxis treatment would be restarted) as a FIX level below 2%, based on advice from 8 NHS clinicians. Once etranacogene dezaparvovec failed, it was assumed that people resumed treatment with 1 of the 4 FIX prophylaxis treatments. The EAG consulted with an NHS clinician who advised that a

FIX level of 2% to 5% would be considered as a 'trough' (a minimum level when people are routinely having FIX prophylaxis treatment). They also advised that this level may be too low for people to engage safely in some routine activities such as certain sports. The EAG also noted that people in HOPE-B only stopped FIX prophylaxis treatment when FIX levels were more than 5%. The EAG's base case therefore considered that FIX prophylaxis treatment was more likely to be reintroduced when FIX levels dropped below 5% rather than 2%. The clinical experts explained that restarting FIX prophylaxis treatment is based on many factors, including: bleeding symptoms, FIX level and personal preference. One clinical expert said an appropriate definition of treatment failure would be a FIX level between 2% and 3% and another said below 3%. The committee considered that the definition of treatment failure, and when people need to restart FIX prophylaxis treatment, would vary based on a number of factors, including bleeding symptoms and activity levels. The committee concluded that it is appropriate to model restarting FIX prophylaxis treatment at a FIX level between 2% and 3%. It requested the company also provide a scenario in which FIX prophylaxis treatment is restarted at a FIX level of 3%.

Durability of treatment effect

Shah et al. analysis

3.11 Because only 24 months of follow up data was available from HOPE-B, the company used analyses by Shah et al. (2022) to estimate the long-term durability of entranacogene dezaparvovec treatment. The analysis combined observed data from HOPE-B (52 out of 54 people in the trial) and AMT-061-01 (n=3), a phase 2b trial of etranacogene dezaparvovec (total n=55). Two out of 54 people from HOPE-B were excluded from the analysis: 1 person who only had a partial dose because of an adverse reaction and 1 person with a poor response to treatment and a notably high adeno-associated virus 5 (AAV5) neutralising antibody titre. In the Shah et al. (2022) analysis, Bayesian and frequentist linear mixed models

were used to predict FIX levels for up to 25.5 years at an individual and population level. Both models predicted that no more than 6 out of 55 people (10.9%) would have FIX levels below 2%, up to 25.5 years post-infusion. The company also used a supplementary analysis from Shah et al. (2022) which extended to 60 years in its economic model. The EAG noted that the economic model results were highly sensitive to the mean durability estimates. The committee discussed the 2 people excluded from the Shah et al. (2022) analysis. It noted that the summary of product characteristics for etranacogene dezaparvovec states that high titres of pre-existing neutralising anti-AAV5 antibody may reduce treatment efficacy, but does not state that this is a contraindication to administration. The company confirmed that the decision to give or withhold etranacogene dezaparvovec when there is a high neutralising antibody titre would be based on individual clinical judgement. This introduced some uncertainty as to whether it was appropriate to exclude the person who had a poor response to treatment. The committee also questioned whether it was appropriate to exclude the person who only had a partial dose. The company said that this person only had 10% of the dose and it would not be appropriate to evaluate the effectiveness of etranacogene dezaparvovec based on a dose below the licensed dose. However, the committee considered that because the person was intended to have the full dose, they should have been included in the Shah et al. (2022) analysis. The committee was concerned that the excluded data could bias the estimates. It requested that the company provide 2 scenario analyses which include:

- the person who had a partial dose because this would be more reflective of clinical practice
- all participants including the person who had a partial dose and the person with poor response to treatment and a notably high neutralising anti-AAV5 antibody titre.

Long term treatment durability

3.12 The EAG highlighted the low number of people available to inform the Shah et al. (2022) analysis and the short follow-up of the source data. Only 6 out of 55 people (10.9%) in the analysis had 24 months of follow-up data, and 30 months follow-up data was available for only 3 out of 55 people (5.45%), which was then extrapolated to 60 years. The company considered that it was plausible that etranacogene dezaparvovec has a long-term therapeutic effect based on other studies showing that effects of recombinant AAV vector-based gene therapies can be maintained over long periods of time. The most recently published follow-up of a trial for another haemophilia B gene therapy showed stable FIX expression over a period of 8 years (Nathwani et al. [2018]). The company noted that in HOPE-B, at 18 months post-treatment, none of the people who expressed endogenous FIX (52 out of 54 people) restarted FIX prophylaxis treatment, and FIX levels remained above 5% in about 95% of people. However, the EAG considered that the extrapolations were highly uncertain because of the low number of people in the analysis and the lack of long-term data. The committee also discussed 6-year data on AMT-060, an earlier form of etranacogene dezaparvovec (using the same vector and cassette design, but with a wild-type FIX transgene). The company believed that this data showed there is no treatment waning effectiveness for AMT-060, which supports the long-term durability of etranacogene dezaparvovec because the products are similar. The EAG noted that the crude mean FIX activity levels over years 1 to 3 and years 3.5 to 6, may suggest, on the balance of probabilities, a decline in FIX levels. However, the EAG said that neither its nor the company's claim can be demonstrated at conventional levels of statistical significance because of the small sample size (n=9). The EAG understood there to be several reasons why gene therapies for haemophilia using an AAV vector may have reduced durability. Evidence from HOPE-B suggested that treatment effect may be reduced in specific subgroups of people who have etranacogene dezaparvovec. These subgroups included people who

had corticosteroids to treat transaminase increases, people who developed AAV5 neutralising antibodies and people with moderate or severe liver steatosis at baseline. The EAG considered it plausible that reduced treatment effect over time may be more likely in these groups. The EAG also noted it received expert advice that suggested that the rate of cell turnover in the areas of the body targeted by etranacogene dezaparvovec, and subsequent illnesses and other treatments that affect these areas of the body or the broader mechanisms of treatment, may lead to reduced efficacy over time. Cells in the liver are responsible for producing FIX, and study participants with liver conditions were either excluded from the study or showed reduced treatment efficacy. The EAG also understood that the liver has a higher rate of cell turnover than other areas of the body. The committee concluded that the long-term durability of etranacogene dezaparvovec was a considerable uncertainty, which had a notable impact on the cost-effectiveness estimates. It considered that the AMT-060 sample size was too small to support robust conclusions on the long-term durability of etranacogene dezaparvovec. It further concluded that the uncertainty relating to longer-term durability of etranacogene dezaparvovec would only be reduced by longer-term data collection.

Acceptable ICER

3.13 NICE's manual for health technology evaluations notes that judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the incremental cost-effectiveness ratio (ICER). The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented.

The committee noted concerns around the high level of uncertainty, specifically:

- the results of the indirect treatment comparison (see section 3.7)

- the Shah et al. (2022) durability extrapolation including the:
  - small sample size
  - lack of long-term data
  - exclusion of the person who had a partial dose and
  - exclusion of the person with poor response to treatment and a notably high AAV5 neutralising antibody titre (see section 3.11).

Because of the high level of uncertainty in the clinical and economic evidence, the committee agreed that an acceptable ICER would be towards the lower end of the range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per quality adjusted life year [QALY] gained).

Cost-effectiveness estimates

3.14 The committee noted that neither the company nor the EAG's base cases or scenario analyses included all its preferred assumptions. The committee agreed that it would prefer to see the following scenarios:

- treatment failure defined as FIX level of 3% (see section 3.10).
- a 'basket of comparators' weighted by use in the NHS (see section 3.9).
- updated Shah et al. (2022) analysis to include the person who had a partial treatment dose (see section 3.11) and a further scenario which also includes both the person who had a partial dose and the person with poor response to treatment and a notably high AAV5 neutralising antibody titre (see section 3.11).

The committee recalled that the only difference between the company's and EAG's base-case models was the definition of treatment failure which was 2% and 5%, respectively. The committee considered the company's and EAG's probabilistic base-case cost-effectiveness results. Because etranacogene dezaparvovec and the comparators have confidential commercial arrangements, the exact ICERs are confidential and cannot

be reported here. The committee considered both the fully incremental and pairwise results:

In both the company and EAG base-case models:

- in the fully incremental analyses, etranacogene dezaparvovec was not the most cost-effective treatment strategy. Both ICERs were above £100,000 per QALY gained.
- in pairwise analyses, etranacogene dezaparvovec dominated 3 out of 4 of the comparators (that is, it resulted in lower costs and higher QALYs).

The committee concluded that neither the company nor the EAG's base cases or scenario analyses included its preferred assumptions.

Other considerations

Managed access

3.15 The committee was aware that NICE's health technology evaluations manual states that a recommendation with managed access can be an option for patient access to medicines when immature evidence or evidence gaps results in significant uncertainty for committee decision making. It recognised that etranacogene dezaparvovec is a promising treatment and that the ongoing HOPE-B trial could provide further data to address some of the uncertainty about the treatment's long-term durability. However, the committee may only consider a recommendation with managed access after seeing a managed access proposal and a feasibility assessment by NICE. The committee concluded that it was unable to consider a recommendation with managed access because it had not been provided with a managed access proposal.

Equality

3.16 The committee noted that haemophilia B is rare in women and HOPE-B did not include women. It was aware of clinical advice received by the EAG that the few women who experience severe and moderately severe

haemophilia B would be affected similarly as men. The committee considered that any recommendation made would not need to differentiate between men and women.

Uncaptured benefits

3.17 The committee also noted benefits of etranacogene dezaparvovec that were not included in the economic model. It noted that etranacogene dezaparvovec is expected to reduce long-term joint damage because it reduces bleeding events which are associated with joint damage. It also noted that etranacogene dezaparvovec might lower mortality, which would lead to higher QALY benefit. However, the effect of etranacogene dezaparvovec on mortality has not been shown. The committee concluded that these uncaptured benefits did not have a material effect on the decision-making at the first committee meeting. This is because they were unlikely to outweigh the committee's concerns about the cost-effectiveness estimates and the degree of uncertainty around the ICER.

Conclusion

3.18 The committee concluded that it could not recommend etranacogene dezaparvovec for treating moderately severe or severe haemophilia B. The cost-effectiveness estimates are highly uncertain, do not contain all of the committee's preferred assumptions and are above the range that NICE usually considers an acceptable use of NHS resources. Further analyses are needed to yield more robust cost-effectiveness estimates (see sections 3.13 and 3.14).

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered 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

Megan John

Chair, technology appraisal committee D

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.

Dilan Savani

Technical lead

Victoria Kelly

Technical adviser

Kate Moore and Celia Mayers

Project managers

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