# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

# SINGLE TECHNOLOGY APPRAISAL

# APPEAL HEARING

## Advice on lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043]:

## Decision of the panel

### *Introduction*

1. An appeal panel was convened on 13 January 2026 to consider an appeal against NICE's final draft guidance to the NHS on lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease [ID4043].

2. The appeal panel consisted of:

- Jon Cohen — Chair
- Frank Smith — Non-executive Director, NICE
- Kawitha Helme — Industry Representative
- Stephen Hoole — Health Service Representative
- Rosemary Harris — Lay Representative

3. None of the members of the appeal panel had any competing interest to declare.

4. The panel considered an appeal submitted by Eisai Ltd ("the Company" / "Eisai").

5. Eisai was represented by:

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| • Chris Parker | Market Access Director UK and Ireland |
| • Nick Burgin | Chief Operating Officer for Eisai in EMEA and Global President for Value and Access |
| • Michael Rushworth | Senior medical advisor |
| • Clive Ballard | Professor of Age Related Disease and Old Age Psychiatry |
| • Adela Williams | Legal Representative |

6. In addition, the following individuals involved in the appraisal were present and available to answer questions from the appeal panel:

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| • Jacoline Bouvy | Programme Director, Medicines Evaluation, NICE |
| • Ross Dent | Associate Director, NICE |

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| • Lizzie Walker | Principal Technical Adviser, NICE |
| • Andy Fox | Member, Technology Appraisal Committee D |
| • Will Sullivan | Member, Technology Appraisal Committee D |

7. The appeal panel's legal adviser, Alistair Robertson (DAC Beachcroft LLP) was also present.

8. Under NICE's appeal procedures, members of the public are admitted to observe appeal hearings and several members of the public and NICE staff observed the proceedings which were held via Zoom.

9. There are two grounds under which an appeal can be lodged:

Ground One: In making the assessment that preceded the recommendation, NICE has:

(a) Failed to act fairly; and/or

(b) Exceeded its powers.

Ground Two: The recommendation is unreasonable in light of the evidence submitted to NICE.

10. Mark Chakravarty, the lead non-executive director for appeals, in preliminary correspondence had confirmed that Eisai had potentially valid grounds of appeal under Grounds 1 and 2.

11. The appraisal that is the subject of the current appeal provided advice to the NHS on lecanemab for treating mild cognitive impairment or mild dementia caused by Alzheimer's disease.

12. The numbering of appeal points in this document reflects those that were used during the hearing. The text of this document does not represent a verbatim account of the proceedings nor a documentation of the order of events that took place but rather, provides a brief summary of Eisai and committee submissions for the points that were discussed relevant to the decisions of the panel.

13. Before the appeal panel inquired into the detailed complaints the following made a preliminary statement:

    a. Nick Burgin on behalf of Eisai; and

    b. Andy Fox on behalf of NICE.

14. Some appeal points were discussed together in the hearing (which is reflected in the summary of the discussion below). They were then considered separately by the panel and the conclusions in this decision letter are presented as such.

**Appeal point 1(a)1: The disclosure of information regarding infusion costs very shortly before the third Appraisal Committee meeting (ACM3) without opportunity for consideration or comment by consultees was procedurally unfair.**

15. Adela Williams introduced this appeal point for Eisai. She explained that the preferred infusion cost estimates were central to the outcome of the appraisal of lecanemab, and described the figures ultimately preferred by the committee (i.e. NHS England's "Infusion

Cost Estimates Document") to have been controversial and with an unclear basis.

16. Eisai had sought clarification (as early as in response to consultation on the first draft guidance) as to the basis of NHS England's Infusion Cost Estimates Document, but this was not provided after either the first or second draft guidance. It was, however, provided four working days before the third committee meeting. Adela Williams explained that the additional information was not considered by the External Assessment Group ("EAG"), and the time available did not afford Eisai adequate opportunity to consider the information provided, and to carry out the complex and detailed analysis required to understand the figures.

17. Eisai did provide a preliminary response to NHS England's Infusion Cost Estimates Document, but this was not reviewed by the EAG nor was it included in the committee papers ahead of the third committee meeting.

18. Adela Williams expressed Eisai's view that fairness required an adequate period in which to consider NHS England's Infusion Cost Estimates Document, particularly given it was central to the outcome of the appraisal. Further, she noted that no reason had been offered by NHS England as to why the data were not provided earlier. Eisai requested them during both first and second draft guidance consultation periods.

19. Ross Dent, for NICE, explained that NICE had requested further information as to the basis of NHS England's infusion cost estimates at several points during the appraisal, including during draft guidance consultation. He confirmed that NICE had not withheld any information from Eisai in relation to the infusion cost estimates, and

that the information was shared with Eisai as soon as it was provided to NICE.

20. Ross Dent described for the panel's benefit what NHS England's Infusion Cost Estimates Document contained. He explained that the information contained in the document was not a new cost estimate, and was instead an explanatory note about how NHS England had reached the estimate previously provided, alongside a workbook of HRG codes considered.[1] He noted that although NICE would have preferred receiving the document earlier, it cannot compel NHS England to provide information.

21. Ross Dent distinguished between having adequate opportunity for (1) consideration of the new information; and (2) consultation on its contents. He noted that the NICE technology appraisal and highly specialised technologies guidance: the manual ("the Manual") does not provide an opportunity for Eisai (or any other stakeholder) to respond to each and every piece of evidence, particularly where it is presented outside the draft guidance consultation periods. Similarly, there is no opportunity for one stakeholder to respond directly to another stakeholder's consultation response.

22. Ross Dent explained the committee's view as to whether or not it considered the 4-day window to have been adequate:

    a. First, he explained, the committee papers were shared earlier than usual ahead of the third committee meeting, approximately 15 working days before the meeting. Usually, the papers would be shared approximately 5 working days before a committee meeting, and therefore he did not consider the truncated period

[1] A Healthcare Resource Group ("HRG") code is a standardised, five character code used to categorise patient activity derived from NHS patient records.

of 4 days for consideration of NHS England's Infusion Cost Estimates Document to have been a significant outlier.

b. Secondly, as Eisai had responded with preliminary views (in circumstances where NICE would not usually have expected a written response to another stakeholder's evidence), this suggested that Eisai had had an opportunity to consider the infusion cost estimates document.

c. Finally, Eisai did not request that the third committee meeting be delayed, nor did it suggest prior to the third committee meeting that further time was needed to consider the information.

23. Jacoline Bouvy, for NICE, added that NHS England's Infusion Cost Estimates Document was made available and discussed at the third committee meeting.

24. The panel noted that it understood that Eisai's written response to NHS England's Infusion Cost Estimates Document was not included in the papers for the third committee meeting, and asked whether Eisai had an opportunity to contribute to the discussion relating to the document during the third committee meeting.

25. Ross Dent explained that during committee meetings, questions are directed through the chair of the committee. A representative from NHS England was present during the third committee meeting and was questioned rigorously by the committee as to the content of NHS England's Infusion Cost Estimates Document. He noted that some of the questions put to the NHS England representative had been informed by Eisai's questions, and that this is reflected in the final draft guidance ("FDG").

26. The panel asked whether it was standard procedure for a company to be able to participate in discussions during committee meetings.

Ross Dent answered that it is possible to raise a hand and ask a question, but that questions would be directed through the chair of the committee rather than directly to the NHS England representative.

27. Chris Parker, for Eisai, answered a question from the panel as to whether or not Eisai did in fact contribute to the discussion at the third committee meeting on this point. He explained that although Eisai had raised some of the specific concerns which it had also raised in its preliminary written response to NHS England's Infusion Cost Estimates, this was necessarily limited given the time available to consider the information and identify concerns ahead of the third committee meeting.

28. The panel asked whether the committee was hindered in its decision-making by the lack of EAG critique of NHS England's Infusion Cost Estimates, given the impact of those data on the most plausible incremental cost effectiveness ratio ("ICER").

29. Ross Dent explained that the information was provided to the EAG at the same time as it was made available to Eisai, but that the EAG had not submitted any response to it. With reference to previous discussions with the EAG, he noted that as NHS England has a dedicated team for pricing treatments, the EAG did not consider that it would have much to add to NHS England's Infusion Cost Estimates.

30. Jacoline Bouvy highlighted that the FDG details the history of the committee's approach to infusion cost estimates. The committee had recognised the importance of these estimates on the cost effectiveness of lecanemab from the first committee meeting onwards. NHS England's Infusion Cost Estimates Document provided shortly before the third committee meeting was, she

described, additional contextual information to supplement the estimates already provided. Given that NHS England had subsequently provided the information which the committee had requested to supplement its estimate, the committee was assured as to the plausibility of the estimate, and considered it to be sufficiently transparent information on which to reach its decision.

31. Jacoline Bouvy explained that, given the nature of the information provided (i.e. to supplement the estimates previously provided), the committee did not consider there to be any need for further input on those estimates in circumstances where it had already set out its views on those estimates in the first and second committee meetings.

32. The panel highlighted that it understands the practical and financial implications of delaying committee meetings, but that speed should be balanced against fairness. The panel asked how the committee sought to balance those two objectives.

33. Jacoline Bouvy responded that the committee first considers whether information provided at a late stage is new or whether it is already known to the committee and stakeholders. Then, the committee considers the extent to which that information is decision modifying. If information was brand new and potentially decision-modifying, the committee would offer an opportunity for stakeholders to comment.

34. In appraising lecanemab, she explained, that was not the case. It was clear from the first committee meeting that there was a big difference between the infusion cost estimates provided by each stakeholder. The committee was alive to that disparity, and recognised that it would need to understand the basis on which those estimates had been reached in order to ensure that it relied on

the most plausible estimate. She noted that the estimates put forward by NHS England and Eisai remained the same between the second and third committee meetings. After the second committee meeting, the committee had asked NHS England for further information about the basis on which it had reached its estimates, which was received four days before the third committee meeting. At that stage in the appraisal process, there had already been two draft guidance consultations and plenty of opportunity for stakeholders to express their view on the draft recommendation. In those circumstances, the threshold for holding a third draft guidance consultation, to the detriment of speed of outcome and associated cost, would have been higher. She reminded the panel that there are circumstances in which the committee is perfectly content to hold third draft guidance consultation, but that this was not considered necessary in this appraisal.

35. In response to a question from the panel, Eisai confirmed that the response to a freedom of information request made by Eisai to NHS England in relation to the infusion cost estimates had not been shared with the committee, as the response was received after the third committee meeting.

36. Adela Williams, for Eisai, noted that irrespective of the fact that the Manual does not explicitly offer stakeholders an opportunity to respond to information provided by other stakeholders, stakeholders should be allowed to do so where fairness requires.

37. Adela Williams drew the panel's attention to paragraph 3.20 of the FDG. She highlighted the fact that, by the end of the second committee meeting, the committee could not decide on the appropriate source of infusion costs. By the end of the third committee meeting, the committee had changed its position and accepted NHS England's proposed infusion cost estimates. It is

Eisai's view that the change in position was as a result of the new information provided four days before the third committee meeting. Adela Williams described this as an illustration of the significance of the document, and that it influenced the committee's decision. In the time available to it, Eisai had sought to review the information provided, to test whether it was a reliable basis for decision making. Various errors and concerns were identified by Eisai during that period and had there been more time, Eisai would have been able to provide a more comprehensive / detailed response to the document.

38. Jacoline Bouvy drew the panel's attention to paragraph 3.17 of the second draft guidance, where the committee concluded that it was "*unable to determine a preferred cost for use in modelling. But the committee concluded that the most appropriate cost was likely closer to the NHS England estimate based on the infusion cost for coronavirus monoclonal antibodies than the Company's estimates. It also noted that, irrespective of the infusion cost used, all cost-effectiveness estimates were significantly above the range considered cost-effective".*

39. Ross Dent and Jacoline Bouvy both confirmed that neither of the infusion cost estimates provided by NHS England nor Eisai would have resulted in an acceptable ICER. Adela Williams responded with her view that the impact on the ICER is immaterial to the panel's assessment of whether or not the late provision of information amounted to procedural unfairness.

40. Concluding this appeal point, Jacoline Bouvy noted that the substance of the information (and whether or not it is likely to change the committee's decision) is highly material to the committee's decision to consult further or to issue final draft guidance.

41. The appeal panel concluded as follows. The panel noted that 5 days was the usual timeframe stipulated by NICE for companies to respond to new data and therefore 4 days was shorter than usual, albeit this would not of itself be unfair.

42. The panel also noted that Eisai had not requested for the third committee meeting to be delayed and that Eisai had only been able to submit a partial response within the allotted time but that subsequent analysis by Eisai had detected errors in NHS England's Infusion Cost Estimate Documents used to inform the cost estimate.

43. The panel reasoned that for a decision of this significance, given the high impact the infusion cost had on the final ICER, Eisai should have been given more time and opportunity to scrutinise the data and respond fully, rather than the limited time offered with the consequential partial response provided.

44. Whilst the panel acknowledged that rescheduling the meeting would have been logistically difficult, they were of the opinion that the administrative difficulty did not outweigh fairness to allow Eisai time to respond fully to this crucial data.

45. The panel also did not accept the argument from NICE that the infusion cost data provided by NHS England was merely explanatory rather than influential. The panel noted that at the second committee meeting the committee was undecided as to whether to accept the NHS England calculated costs or those provided by Eisai. It was only after they received NHS England's Infusion Cost Estimates Document, shortly before the third committee meeting, that they reached a decision. Therefore, the infusion cost data were highly influential, and informed the committee’s view decisively.

46. The appeal panel therefore upheld this appeal point on the grounds that while they recognise the pressure to proceed efficiently, it was unfair not to give Eisai adequate time to respond to such vital and influential data.

**Appeal point 1(a)2: The committee has not provided adequate reasons for rejecting Eisai's infusion costs.**

47. Adela Williams introduced this appeal point for Eisai. She explained that the infusion cost estimates submitted by Eisai were estimated to be comparable to the costs of chemotherapy. This was agreed by clinical experts, on the basis that lecanemab infusion is not complex, nor does it require intensive monitoring. She noted that the FDG does not refer to the fact that these costs were supported by expert views. Instead, she described the FDG as containing speculative views advanced by NHS England, that lecanemab is complex to prepare, can cause adverse reactions and that the patients receiving lecanemab might have more complex needs than those receiving simple parenteral chemotherapy. All of which, Eisai claims, are not supported by evidence.

48. Jacoline Bouvy, for NICE, explained that the committee carefully considered the issue of infusion costs across all three committee meetings and both pieces of draft guidance – all of which is summarised across four pages of the FDG. The reference case requires evidence on resource use and costs to relate to NHS and PSS (“personal social services”) resources and should be assessed using the prices relevant to the NHS and PSS. As a result, the committee considered that it should base its decision on realistic cost estimates, and in this instance those cost estimates which it considered appropriate were informed by NHS England's estimates given its role in the system.

49. Jacoline Bouvy explained that at the second committee meeting the committee reached the view that the methodology provided by Eisai was vague, and the scope of the estimates was necessarily limited because only three people were consulted to estimate the resource use and the three answers varied considerably. The rationale for why the committee could not rely on the estimate provided by Eisai is explained in the FDG. Jacoline Bouvy rejected any implication that the committee simply accepted NHS England's estimates purely because they were provided by NHS England. She explained that, given the significance of the estimates to the cost effectiveness analysis, the committee recognised the need for bringing a level of scrutiny to its deliberations (which is why it asked NHS England for further information/transparency to support its decision making).

50. Adela Williams disagreed with Jacoline Bouvy, noting that the mere existence of four pages discussing the matter did not indicate that the evidence had been carefully considered. Given that there is little experience in administering lecanemab by infusion, it was essential that the proxy HRG codes put forward by NHS England were scrutinised and tested to ensure that they were appropriate. Adela Williams drew the panel's attention to the three reasons advanced at paragraph 3.20 of the FDG for rejecting Eisai's infusion cost estimates:

> "*It* [NHS England] *advised against using a chemotherapy infusion cost because lecanemab:*
>
> - *Is more complex to prepare*
> - *Has the potential for more adverse reactions*
> - *People having it might have more complex needs than people having chemotherapy infusions."*

51. Taking each in turn:

    a. Adela Williams said that clinical evidence did not support the view that lecanemab was more complex to prepare,

    b. Adela Williams said that clinical evidence did not support the suggestion of a higher likelihood of reaction.

    c. Clive Ballard gave his clinical insight in relation to the needs of those receiving lecanemab. He noted that although people with mild cognitive impairment / mild dementia caused by Alzheimer's disease deteriorate after time (and consequently have more co-morbidities then) – at the stage of illness at which lecanemab is indicated, patients are functioning at an almost independent level. The co-morbidity in this cohort is comparable to the age matched group in the population. Patients in this group are not generally frail, with many travelling to infusion centres unaccompanied, and therefore in his experience there was no reason to assume additional complexity / complex co-morbidities in the patient population.

52. Summarising, Adela Williams referred to Clive Ballard's view as reflective of the expert evidence offered to the committee – which was not captured by the FDG. She suggested that NHS England's Infusion Cost Estimates were accepted simply because it had been provided by NHS England, and that the reasons for rejecting Eisai's infusion costs provided in the FDG were not supported by expert evidence.

53. The panel noted that NICE is obliged, in evaluating the cost effectiveness of a technology, to consider what the NHS would pay for the technology – i.e. the "real world" costs. Eisai's figure, on the other hand, was premised on a micro-costing study.

54. In response to a question from the panel, Adela Williams thought that it was unfair for the committee to have relied on NHS England's infusion costs estimates, despite NHS England's considerable experience in producing such estimates. In her view this was unfair on the basis that such evidence should not be relied on solely by virtue of the status of the provider. Fairness requires that other stakeholders can test the veracity of the data which is heightened where only proxy HRG costs are available. Eisai would have liked to test whether the identified proxies were fair and reasonable. In Eisai's view, Adela Williams explained, the proxies selected by NHS England were flagrantly inappropriate.

55. Chris Parker provided some background to Eisai's micro costing – and highlighted that this detail was provided in response to the second draft guidance. Clive Ballard added that the costs incurred in the clinical trials for lecanemab had been costed by local NHS systems directly – and included staffing, overheads etc.

56. The panel noted that the FDG sets out a broad range of various estimates considered by the committee before ultimately settling on an infusion cost of £432. The panel asked whether the breadth of estimates caused the committee any concern as to the precision with which they were estimated. Jacoline Bouvy explained that the committee had no reason to doubt the information provided by any stakeholder, including NHS England. She also added that the changing estimates was one reason prompting a second draft guidance to be issued – as a change occurring at that stage in the appraisal process requires the committee to consider whether it has been adequately scrutinised.

57. Will Sullivan, for NICE, explained that it was wrong to suggest that that NHS England's estimates were taken at face value – the FDG illustrates the fact that the committee challenged and tested the

estimates provided – which, in part, caused the breadth of estimates. He noted that the committee was conscious that lecanemab is a novel treatment in a service that does not yet exist in the NHS.

58. Andy Fox, for NICE, recalled intensive questioning and challenge over the issue of infusion cost estimates during committee meetings to test the solidity of the evidence on which the stakeholders relied. He did not consider it unreasonable to accept NHS England's estimate if it, as a clinical commissioner, puts forward an appropriate tariff which was subject to robust scrutiny.

59. The panel observed that the micro-costing exercise carried out by Eisai was based on clinical expert input, whereas NHS England's Infusion Cost Estimates were drawn from comparator therapies. The panel asked whether the committee took that difference into account in its decision making.

60. Jacoline Bouvy said that there is a difference between clinical observation of an infusion and the appropriate national tariff for providing that treatment (which incorporates overheads, administration costs, staffing etc). Clive Ballard disagreed with this distinction, explaining that the clinicians involved in clinical trials of lecanemab did not simply observe the infusions, but had been involved with local commissioners in costing the treatment.

61. Jacoline Bouvy described the considerable work that NHS England and NICE had undertaken to ensure the system was prepared for such treatment, including work on system design and implementation, and so the estimates had not been reached lightly.

62. Chris Parker, for Eisai, noted that the costs on which Eisai had relied (i.e. simple parenteral chemotherapy infusion) already incorporated

adverse event costs, which counters the committee's concerns as expressed at paragraph 3.20 of the FDG.

63. Will Sullivan explained that additional information provided in NHS England's Infusion Cost Estimates Document provided further detail on how the estimates were derived and the sources of that information. This meant that, although there were no data for this specific service / disease area, it provided the committee with a range of plausible figures – all of which being far from Eisai's estimates derived from micro costing.

64. The appeal panel concluded as follows. The panel acknowledged that unlike Eisai's infusion cost estimate, the NHS England infusion costs were not itemised and therefore could not be fully validated by the EAG, committee or Eisai.

65. Whilst they acknowledged Eisai's argument that the NHS England data were possibly inaccurate and did not reflect "real-world", the panel were reminded that NHS England was the main payor and that the therapy was not currently available on the NHS and therefore any infusion cost calculation is an estimate and liable to some degree of inaccuracy. Furthermore, the Manual provides that the perspective adopted in the reference case on costs should be that of the NHS.

66. The panel reminded itself that this ground 1 appeal point was concerned with the adequacy of reasons provided by the committee, and not the reasonableness of the committee's conclusion. The panel was persuaded that the reasons provided by the committee in the FDG for declining to follow Eisai's estimate of infusion costs, and adopting the NHS estimate, are sufficient for the reader to understand the drivers of the committee's conclusion. The

committee adequately explained how it had reached its decision, on the basis of the evidence available to it.

67. The panel agreed that the committee discussed this point adequately, and whilst they may wish to revise the FDG to highlight their uncertainty in reaching their decision to accept the NHS England infusion cost at face value, and why they chose this estimate in preference to Eisai's estimate, the committee had not been unfair in how they reached their decision.

68. The appeal panel therefore dismissed the appeal on this point.

**Appeal point 1(a)3: The committee has omitted to explain why it has rejected the data from Clarity AD in concluding no effect of lecanemab in delaying progression to moderate or severe AD and has adopted an inconsistent approach to that followed in the appraisal of donanemab.**

69. Chris Parker introduced this appeal point for Eisai. Eisai's position was that the committee had failed to explain adequately why it did not take into account the effect of lecanemab in delaying progression to moderate or severe Alzheimer's disease.

70. Paragraph 3.12 of the FDG illustrates the committee's consideration of transitions between health states. Chris Parker explained that it was procedurally unfair for the committee to have accepted that the treatment effect is statistically significant, but then fail to accept Eisai's modelling of disease progression. He noted that the committee frequently accepts qualitative evidence in the absence of statistical evidence, and that preferring the EAG's approach of disabling this effect in the model was illogical and not adequately explained in the FDG.

71. Will Sullivan, for NICE, explained the two factors considered by the committee in reaching its preferred assumptions on modelling

transitions between health states. First, the treatment effect itself, and secondly the bias in the model. He explained that Eisai's model cycled through mild cognitive impairment, mild dementia, moderate and severe dementia with monthly cycles between those health states. Eisai's model, he explained, contained a bias that underestimated the relative state occupancy in severe Alzheimer's disease of lecanemab versus standard of care compared with the observed state occupancy in the Clarity AD trial. Chris Parker was describing only the overall treatment effect of lecanemab, whereas the committee had focussed on occupancy within the trial and whether that was appropriately modelled by Eisai to demonstrate the treatment effect.

72. Will Sullivan explained that the EAG had highlighted this concern, and that by the third committee meeting the matter remained outstanding. The committee took into account both factors – the treatment effect itself and the bias in the model – in reaching its preferred assumption on modelling transitions between health states. He noted also that the exact number of patients transitioning between health states is confidential. Ultimately, the committee was of the view that the EAG's modelling (i.e. to disable the relative treatment effect for the transition from mild to severe Alzheimer’s disease from its base case) was most appropriate.

73. The panel noted that it is apparent from the appeal papers that there was disagreement between Eisai and the EAG on this matter. The panel asked whether Eisai had put forward evidence that the treatment effect of lecanemab was clinically significant. Chris Parker confirmed that Eisai had submitted throughout the appraisal process evidence to support the clinical meaningfulness of the overall effect of lecanemab in delaying disease progression. He explained that Eisai did not have data specifically on the transition between mild to

severe disease, on the basis that transitioning between mild to severe within one cycle would be very rare in practice. On the broader progression, Eisai submitted data on transitions between each health state sequentially.

74. Chris Parker expressed the view that, together with the evidence that Eisai had submitted before the third committee meeting, the evidence it provided on the treatment effect of lecanemab in delaying disease progression at the third committee meeting should have been sufficiently powerful to change the direction of travel in the committee's view. While it is fair to say that the numbers are small and there is uncertainty, there were ways in which that uncertainty could have been managed / mitigated short of disabling the effect entirely.

75. Jacoline Bouvy, for NICE, explained that the additional information presented by Eisai on this topic at the third committee meeting, although helpful, was based on low patient numbers. In the absence of compelling evidence to the contrary, the committee was comfortable with the EAG's approach of disabling transition probability in the mode.

76. Chris Parker noted that the low patient numbers were a result of the fact that this population have early Alzheimer's disease and therefore it is rare to cycle through multiple states within the space of a month as modelled. Will Sullivan said that it was Eisai's choice to model monthly transition probabilities – it could have modelled different movements in a more flexible manner, for example.

77. The panel then turned to consider whether the approach was inconsistent with the approach taken in the appraisal of donanemab for mild cognitive impairment / mild dementia caused by Alzheimer's disease [ID6222] ("donanemab appraisal").

78. Chris Parker said that the circumstances were the same in the donanemab appraisal – with similarly small data sets. In appraising donanemab, he said, there was no discussion as to how the model matched observed state occupancy in Clarity AD. The FDG did not explain why different decisions were reached in relation to the two technologies, which undermined the Eisai's confidence in the committee's decision making.

79. Will Sullivan explained that the committee had spent considerable effort to align the appraisals of donanemab / lecanemab where it was appropriate to do so – but noted that there were different evidence bases for the two technologies and different EAGs, and so there were instances where it was appropriate to diverge. He explained that the manner in which transition probabilities were modelled in the donanemab appraisal did not give rise to the same concern in relation to the alignment between state occupancy and the trial data.

80. Chris Parker noted that, to the best of Eisai's knowledge, there was no evidence to support the idea that the transition probabilities modelled for donanemab aligned any better to the observed trial data than lecanemab.

81. Jacoline Bouvy reiterated Will Sullivan's comments, and highlighted that in appraising lecanemab, the EAG had raised the disparity between modelled transition probabilities and observed trial data as a key issue. The same issue was not considered key in appraising donanemab. Jacoline Bouvy recognised that there were differences between both appraisals, but they did not, in her view, amount to unfair inconsistency.

82. Concluding this appeal point for Eisai, Chris Parker noted that none of the reasons now advanced by the committee in relation to the

impact of bias on the modelling had been adequately explained in the FDG. Jacoline Bouvy disagreed, and drew the panel's attention to the explanation provided at paragraph 3.15 of the FDG.

83. The appeal panel concluded as follows. The panel were persuaded that the committee had legitimate concerns that Eisai's modelling was biased toward fewer patients in the severe state and that this did not adequately reflect the Clarity AD data.

84. The panel acknowledged that the committee had requested that this was addressed but had not received a response from Eisai. The panel also recognised that the evidence of benefit provided by Eisai was modest.

85. The panel acknowledged that whilst *prima facie* it would seem intuitive that two similar drugs should have similar effects on Alzheimer's disease progression the panel accepted that it was fair that the committee considered each drug individually.

86. The panel also noted that the committee were advised by different EAGs who relied on the different data and trial designs available to them, particularly around timing and reason of drug discontinuation, to inform their modelling and in advising the committee. This could legitimately result in different conclusions to be drawn by the committee.

87. The panel were persuaded that the committee had considered the issue of inconsistency, and accepted that when the committee reached different conclusions in the two appraisals they did not act unfairly by attributing this difference to differences in modelling assumptions of waning between lecanemab and donanemab.

88. The panel therefore concluded that the committee were justified to take the decision they did and they did not act unfairly in doing so.

89. The appeal panel therefore dismissed the appeal on this point but suggested that the FDG be revised to clarify this distinction between the two appraisals.

**Appeal point 2.1: The committee's assessment of utility values for carers does not reflect the balance of the available evidence.**

90. Adela Williams introduced this appeal point for Eisai. Carers bear a substantial toll of the burden of Alzheimer's disease, and therefore the assessment of carer utility is of central importance to the appraisal of any treatment for it. NICE's manual expresses a preference for EQ-5D to measure utility values. There is no inflexible requirement to use EQ-5D in every appraisal, and in some cases, EQ-5D may not be appropriate. She explained that Eisai had repeatedly highlighted the fact that the impact on carer quality of life may be underestimated by EQ-5D. This was supported by evidence from the Clarity AD trial. Despite this, NICE concluded that the GERAS[2] study data should be used as it was carried out in the UK and used EQ-5D to measure carer utility values. The GERAS study itself acknowledged that EQ-5D was not sensitive enough, and to mitigate this, the committee accepted the EAG's proposal that caregiver utility values should be multiplied by 1.8. It was Eisai's view that multiplying an inappropriate figure by 1.8 does not account for the inadequacy of the tool deployed.

91. Adela Williams explained Eisai's view that the vignette study submitted by Eisai (using data from the donanemab trials) better captured carer utility values and the committee had failed to provide

[2] Reed C, Barrett A, Lebrec J et al. How useful is the EQ-5D in assessing the impact of caring for people with Alzheimer's disease? *Health & Quality of Life Outcomes (2017) 15:16*

reasons for rejecting those data. Rejecting these data was also contrary to clinical expert input.

92. Will Sullivan, for NICE, acknowledged the substantial burden that Alzheimer's disease poses to carer health-related quality of life. That is why the committee was prepared to take the unusual step of quantitatively accounting for this impact in modelling. He explained that the committee requires sufficient evidence to demonstrate that EQ-5D is not an appropriate tool in the specific circumstances of the appraisal. The Manual explains the need for a generic measure of utility values, and while there is provision to deviate from EQ-5D where appropriate, there must be sufficient evidence to justify such departure in those exceptional cases. He acknowledged that Eisai had collected EQ-5D data from patients and carers, and had identified a body of published evidence on EQ-5D utilities in carers in their submission dossier.

93. Will Sullivan explained that the GERAS study was a large, UK based sample – which aligned well with the provisions of the Manual to assess impact on utility decrement across health states that were not captured by the clinical trials (i.e. moderate / severe dementia).

94. The panel noted that, during the appraisal process, specialist and patient organisations had expressed the view that the true impact of Alzheimer's disease on carer utility was not well represented by EQ-5D. The panel asked whether this impacted the committee's assessment of the face validity of the carer utility values – and asked whether the committee took the evidence of patients and specialist organisations into account in its decision making on this issue.

95. Will Sullivan noted that it is not uncommon for stakeholders to feel that a generic measure of utility values does not represent the impact well, by virtue of its being a generic measure. If the

committee is made aware that certain aspects are not properly captured by EQ-5D, then this is taken into account.

96. Jacoline Bouvy, for NICE, reiterated Will Sullivan's comments, that it was not uncommon to hear that EQ-5D, being a generic instrument, did not capture specific aspects of the condition. However, that does not equate to compelling evidence that EQ-5D cannot measure the domains at all. Several EQ-5D domains are relevant to mild cognitive impairment / mild dementia caused by Alzheimer's disease (specifically anxiety/depression, self-care and participation in daily activities). The committee expected that all those domains would be impacted for someone caring for a person in a severe disease state.

97. Jacoline Bouvy explained that the Manual makes provision for other tools to be used in circumstances where EQ-5D is not appropriate, and evidence supports that conclusion – specifically in relation to content validity and whether key dimensions of health are missing. The committee recognised the limitations of the GERAS study – but did not consider that those limitations equated to sufficient evidence to justify departing from EQ-5D in favour of a vignette study.

98. The panel then enquired whether the committee considered the Zarit Burden Interview to be appropriate for decision making. Will Sullivan and Jacoline Bouvy explained that a tool such as EQ-5D is used to record health measures. That is then translated to a utility value for the purpose of cost effectiveness analysis. The Zarit Burden Interview does not translate to a utility value which is why it could not be relied on for cost utility analysis.

99. Clive Ballard, for Eisai, provided his clinical view of the impact on carers – and highlighted that a number of EQ-5D domains are entirely irrelevant to this patient population and their carers. He explained that in addition to the inadequacy of EQ-5D demonstrated

in the GERAS study, the Mini-mental State Examination ("MMSE") thresholds used to define disease states were also flawed (particularly whether the MMSE scores for severe dementia were plausible).

100. The panel pointed out that the reasons for preferring the carer utility values in the GERAS study are explained in the FDG, and asked Eisai to explain why it did not consider the explanation to be sufficient.

101. Chris Parker, for Eisai, noted that the main concern was in respect of the construct validity. He highlighted what he described as a clear issue – that 38% of carers caring for those in this patient population in the community reported "perfect health" consistently across all disease states, which does not appear plausible.

102. Adela Williams noted that Eisai was not suggesting that the Zarit Burden Interview should have been used to produce utility values, instead it was evidence of the deficiencies of EQ-5D in accurately measuring the impact. She also added that the definition of health-related quality of life ("HRQoL") focussed on overall physical mental and social wellbeing – not merely the absence of disease. The World Health Organisation adopt a similar definition.

103. Ross Dent, for NICE, explained that the committee took into account a study (Pennington, 2020)[3] which analysed NICE's use of carer HRQoL in cost utility analysis. He explained that the utility values derived from GERAS are not out of line with the range of utility values in the Pennington study.

[3] Pennington BM. Inclusion of carer health-related quality of life in National Institute for Health & Care Excellence appraisals. *Value Health (2020) 23:1349*

104. Will Sullivan explained that the onus is on the company to generate the evidence that would enable consideration of a tool other than EQ-5D. The committee can question the propriety of the measurement method used during the course of the appraisal, and this can (and often does) form part of discussion at committee meetings.

105. Chris Parker explained that Eisai's preference was for the vignette study submitted in response to the second draft guidance to have been used – this was, in Eisai's view, the most clinically plausible estimate of caregiver utility.

106. Adela Williams expressed Eisai's view that the decision to use carer utility values derived from GERAS was unreasonable in the context of the overall evidence available to the committee, as it showed that EQ-5D did not capture the relevant aspects of carer utility. She referred to the evidence heard by the committee from clinicians and patients, and the conclusions of the authors of the GERAS itself.

107. Jacoline Bouvy noted that the vignette was not without its own limitations, and that this is explained in the FDG.

108. Lizzie Walker, for NICE, explained that the 1.8 multiplier applied to caregiver utility value was derived from the utility values of primary carers in GERAS. By extrapolating the utility value of a primary carer and multiplying by 1.8, this would increase the overall utility value on all a person's carers. Usually, NICE would assess the secondary carer as having a lesser burden than is on the primary carer, and so adopting the 1.8 multiplier extrapolated primary carer burden to a secondary carer.

109. The panel asked whether the committee felt that the 1.8 multiplier was appropriate mitigation – and whether, if EQ-5D was the wrong

measurement tool, it was logical to multiply a potentially inappropriately derived value by 1.8.

110. Lizzie Walker explained that EQ-5D was still considered appropriate by the committee, but recognised that it may underestimate, which the committee sought to address by multiplying the primary carer utility value by 1.8.

111. Adela Williams concluded with the Eisai's view that multiplying an inadequate figure does not result in an adequate figure.

112. The appeal panel concluded as follows. The panel judged that the overwhelming evidence from the academic literature, expert advice and carers themselves demonstrated that the EQ-5D tool was inadequate to assess carer utility values, and that it was illogical for the committee to continue to use the EQ-5D, despite it being the preferred model in the Manual, when it was aware that the carer utility values calculated were grossly under-estimated and remote from other (vignette) models provided by both the EAG and company.

113. The panel were convinced that the committee knew the important impact Alzheimer’s disease had on carers and that this had been the reason to use a quantitative rather than qualitative approach to this issue, notwithstanding the inherent issues of using EQ-5D.

114. Whilst the panel acknowledged the committee’s attempt to compensate for the inadequacy of EQ-5D by applying a 1.8 multiplier they were not persuaded that this had provided adequate redress.

115. The panel reasoned that the committee had the discretion to use other methods when EQ-5D is inadequate and to not do so in this case was unreasonable.

116. The appeal panel therefore upheld the appeal on this point.

**Appeal point 2.3: The assessment of the additional aspects of lecanemab treatment is unbalanced and unreasonable.**

117. Adela Williams introduced this appeal point for Eisai. She drew the panel's attention to paragraph 3.31 of the FDG, which includes "uncaptured harms". She explained that there is evidence to support each instance of uncaptured benefit listed in the FDG. The list of uncaptured harms, on the other hand, is in Eisai's view novel and potentially discriminatory. "False hope" is a feature of any therapy, and those who are ineligible will simply not commence treatment (which will be addressed through counselling). Infrastructure costing falls outside NICE's remit. Difficulties with diagnosing Alzheimer's disease is also not an issue specific to lecanemab, but is as a result of the current state of dementia care in England. She expressed the view that all of the purported uncaptured harms listed are unsupported by evidence and are irrelevant.

118. Adela Williams expressed Eisai's view that, as a result, the conclusion reached in relation to uncaptured aspects is unsustainable.

119. Adela Williams noted that the obvious way in which uncaptured benefits can be taken into account is by varying the acceptable ICER threshold in accordance with section 6.3.5 of the Manual, which was not done in the appraisal of lecanemab. In short, she said, the uncaptured aspects in the FDG were patently unreasonable and potentially discriminatory.

120. Lizzie Walker, for NICE, explained that the uncaptured aspects section of the FDG addressed the comments received from all stakeholders, including patient and professional groups. She

explained that the committee received a number of comments which were supportive of the negative draft guidance, highlighting the risks and harms of lecanemab, which was very unusual. The committee considered it important to highlight the uncaptured harms reported by stakeholders as well as the benefits to ensure that stakeholder and public opinion was captured in a balanced manner in the FDG. Section 6.3.2 of the Manual provides that the FDG should address risks/harms – and therefore the committee considered it reasonable to address risk/harm in addition to benefit.

121. Responding specifically to Adela Williams' comment that it was inappropriate to have considered infrastructure cost risk, Lizzie Walker drew the panel's attention to section 6.2.34 of the Manual where "*committees must consider the nature, scale and consequences of the decision uncertainty and the risks to patients and the NHS*" (emphasis added).

122. Lizzie Walker explained that scenario analysis did address some of the uncaptured benefits/harms to the extent they could be quantified – but many cannot be quantified – and so are considered qualitatively.

123. Andy Fox, for NICE, reiterated that the uncaptured harms in question were brought to the committee's attention by stakeholders, rather than being the committee's own view. He explained that it was right for the committee to consider the significant impact a recommendation can have on the NHS, not all of which would necessarily be positive.

124. The panel asked whether the committee agreed with Adela Williams' submission that the uncaptured benefits outweighed the uncaptured harms. Andy Fox explained that the committee did not consider the

evidence base for uncaptured benefits to have been any stronger than that for uncaptured harms.

125. Clive Ballard, for Eisai, explained that while it is true that there will be benefits/harms with screening – this is inherent with the evolution of an innovation in the field of dementia care. Listing that as a potential risk could impede practice and innovation and is contrary to international consensus.

126. The panel noted that section 6.3.5 of the Manual provides that consideration of uncaptured benefits/harms becomes particularly important when the ICER is close to an acceptable threshold. If the most plausible ICER is far away from what would be acceptable, then the uncaptured benefits/harms necessarily become less relevant.

127. Adela Williams disagreed, noting that it is important for stakeholders to understand the factors that the committee will weigh in its decision making, and that those factors should be applied consistently, regardless of the ICER.

128. Jacoline Bouvy, for NICE, explained that the FDG captures the committee's consideration of uncaptured benefits and harms, but ultimately concludes that neither the benefits of harms put the committee in a position to be able to adjust its decision-making threshold in one direction or the other. Not adjusting the ICER threshold does not equate to failing to take these factors into consideration entirely.

129. Adela Williams added that Eisai is not suggesting that uncaptured harms ought to have been disregarded entirely, but that it was unreasonable for the committee to have considered them if these aspects were not analysed or assessed to test their validity.

130. The appeal panel concluded as follows. The panel noted that the "uncaptured harms" whilst not often considered were included to reflect stakeholder feedback and therefore it was not unreasonable of the committee to include them to reassure stakeholders that their concerns had been considered.

131. The panel was also reminded that it explicitly states in the Manual that the impact of any treatment on NHS resources should be considered.

132. The panel acknowledged that uncaptured benefits and harms are by their very nature qualitative data and attributing anything more than an estimate of their impact is implicit. Furthermore, the panel noted that irrespective of the weighting of uncaptured benefit to harm, this would not have made a material difference to the recommendation made by the committee.

133. The panel were persuaded that the committee considered these uncaptured outcomes carefully and that it was not unreasonable for them to conclude that their impact may increase or decrease the ICER threshold, particularly when they could not be measured, and therefore it was reasonable to not change the ICER boundary.

134. The appeal panel therefore dismissed the appeal on this point.

**Appeal point 2.4: The approach to treatment waning accepted by the Committee is arbitrary and unreasonable.**

135. Chris Parker introduced this appeal point for Eisai. He described the strong correlation between amyloid burden and treatment waning. When amyloid levels dropped below the negativity threshold there would be continued treatment effect. He explained that the re-accumulation rate was based on the Phase 2 study and was also consistent with the rates in anti-amyloid therapies.

136. The committee preferred the EAG's approach to treatment waning which was based on time since treatment discontinuation rather than rate of amyloid re-accumulation. It assumed that when stopping treatment after 18 months, waning started 1 year after stopping and took 4 years to reach full loss of treatment effect. Chris Parker described this preference for the EAG's base case as inconsistent with the approach taken in appraising donanemab, where the committee had assumed total duration of effect (full and waned) of 9 years in the model. Chris Parker noted that there was no explanation for this divergence in the FDG.

137. Andy Fox, for NICE, explained that there was no clear evidence as to the correlation between amyloid clearance and symptom burden. There was also uncertainty in the data sources used to inform the amyloid re-accumulation in the model. He noted that the uncertainty resulted in an in-depth discussion about treatment waning assumptions in the committee meetings.

138. Will Sullivan, for NICE, noted that care should be taken in assuming that donanemab and lecanemab have similar treatment waning effects, as donanemab had an 18 month stopping rule and so there were inevitable differences. He disagreed with the characterisation of the EAG's modelling as being arbitrary, and noted that both Eisai and EAG's position on amyloid re-accumulation changed during committee meetings.

139. The panel asked Eisai whether the concerns identified in the FDG (that Eisai's modelled amyloid re-accumulation rate was from a study with a small sample size and very limited follow-up) explained its approach, and therefore was not arbitrary.

140. Chris Parker accepted that there is uncertainty which was heightened given that continuous treatment was still ongoing by the

time Eisai was submitting evidence to the committee. He explained that the Phase 2 data were the best available evidence, and that it was reassuring that the amyloid re-accumulation rate was consistent with other data from anti amyloid accumulation.

141. The panel noted that ground 2 appeal points require an assessment of the reasonableness of the committee's approach. The FDG sets out the position of the EAG, the company and committee and reaches a decision on that basis. In light of that, the panel asked whether Eisai considered the committee's conclusions to have been unreasonable, or whether they simply disagreed with the conclusion.

142. Chris Parker explained that Eisai's evidence was supported by a variety of clinical expert opinion throughout the appraisal, which in Eisai's view counted again the EAG's evidence.

143. Will Sullivan explained that the committee recognised the relationship between amyloid clearance, disease progression and the effect of lecanemab. The uncertainty lies in the extent of that relationship – and that the effect may not be as strong as the hypothesis may have suggested.

144. The panel noted that in the donanemab appraisal, the committee accepted that there was an association between amyloid clearance and disease progression, notwithstanding that the evidence was not particularly strong. On the other hand, in the lecanemab appraisal – the committee had concluded that the uncertainty was such that the committee could not attribute any weight to that association. The panel asked how the committee reconciled that difference.

145. Will Sullivan disagreed with the panel's suggestion that the committee had not attributed any weight to the link between amyloid clearance and disease progression. He explained that the sole

difference between lecanemab and donanemab in this regard is that donanemab has an 18 month stopping rule. This means that patients who stop at 18 months in that trial could be responding very well, leading to the potential for different assumptions for those patients who stop simply because the trial ends, rather than for other reasons.

146. Ross Dent, for NICE, explained the difference between the assessment of treatment waning in the lecanemab and donanemab appraisals. Whereas in appraising donanemab, there was follow up evidence, this was not the case in lecanemab.

147. Jacoline Bouvy, for NICE, concluded this appeal point by explaining that the differing stopping rules meant that different assumptions about treatment effect waning were necessary. The differences in the evidence presented to support those assumptions in appraising lecanemab and donanemab differed, including the differences in how both the treatments were given in the trials – which explains the different approaches preferred (and is as also explained in the FDG).

148. The appeal panel concluded as follows. The panel acknowledged that there remained uncertainty amongst experts on the validity of using amyloid clearance and re-accumulation as a clinical surrogate and that the EAG rejected the validity of Eisai's disease progression analysis due to concerns over the small sample size and limited follow-up.

149. The panel noted that lecanemab and donanemab have different trial designs, reasons for stopping treatment, and, as a result, different treatment durations, all of which could legitimately influence the waning effect, resulting in different EAG modelling and advice, and, in turn, different committee conclusions drawn.

150. The appeal panel were convinced that the committee had carefully considered the data and its limitations in reaching their conclusions on treatment waning and therefore dismissed the appeal on this point.

**Appeal point 2.5: The committee's decision to rely on an unverified cost estimate for APOE4 gene testing costs rather than a transparent estimate from an alternative source is unreasonable.**

151. Adela Williams introduced this appeal point for Eisai. The marketing authorisation indication for lecanemab stipulates that people are eligible for treatment if they are heterozygous (or have a homozygous deletion) for apolipoprotein Eε 4 (ApoE ε4) ("APOE4"). The cost of APOE4 testing was subsequently incorporated into the economic analysis. NHS England considered that the appropriate figure for APOE4 testing according to the proxy HRG code was £250. Eisai had provided a figure of £41.10, which was obtained from the Scottish Health Service. Adela Williams explained that this was rejected by the committee on the basis that NHS England's modelled proxy HRG related to England, and was therefore purportedly more reflective of real-world practice. The very substantial difference between Eisai and NHS England costs for APOE4 testing caused concern for Eisai about the reliability of NHS England's estimates.

152. Adela Williams reiterated her earlier comments that it was not appropriate for the committee to have accepted NHS England's cost estimates purely by virtue of the fact of NHS England's role in the system, in circumstances where NHS England had not provided any basis for its calculation.

153. Lizzie Walker, for NICE, explained that because there are no available estimates for APOE4 testing in England, this requires more

input than usual from NHS England as to what is likely to reflect real world practice. NHS England is a credible source for NHS costing, explained Lizzie Walker. She added that in the first and second committee meetings, Eisai also used a figure of £250 for APOE4 costing – it was only in the third meeting that Eisai adopted the figure of £41.10.

154. The committee noted in the FDG that the APOE4 testing costs had a very small impact on the ICER, and therefore Lizzie Walker explained that the level of interrogation given to the preferred assumption, when challenged in the third committee meeting, was appropriate in light of the decision risk.

155. The panel asked whether NHS England's estimate of £250 included the cost of genetic counselling. Lizzie Walker noted that it was included in the model but separately to the £250. Chris Parker, for Eisai, explained that Eisai's estimate was also exclusive of the genetic counselling cost.

156. Chris Parker explained that the total cost for APOE4 testing would include the laboratory cost of the test itself, the genetic counselling and the outpatient appointment for the test. The two respective estimates relevant to this appeal point (£41.10 and £250) both related to the costs of the laboratory costs – rather than all three elements combined.

157. Ross Dent, for NICE, noted that the disparity between the two estimates did not arise until the third committee meeting. The NHS England representative was questioned about this at the committee meeting, and they explained that £250 would be the real-world cost. Ross Dent explained that it would be incongruous for NICE to make a recommendation relying on Scottish Health Service estimates

when NHS England had explicitly advised NICE on the costs that it would pay for APOE4 testing.

158. The panel asked the committee whether it understood the cause for the disparity between both estimates. Jacoline Bouvy, for NICE, explained that there is an assumption made by Eisai that the Scottish Health Service estimate is accurate, which was not necessarily established during the appraisal process. She explained that appraisal processes are constrained by limited time and resource availability – and given the very modest impact that APOE4 testing costs had on the ICER, this was not a matter that the committee scrutinised with the same rigour as, for example, infusion costs.

159. In response to Jacoline Bouvy's comment about whether or not the Scottish Health Service estimate was accurate, Chris Parker noted that there was no transparency as to how NHS England had reached its estimated cost either.

160. Clive Ballard, for Eisai, explained that, in research settings, the APOE4 testing that he had commissioned from various university laboratories over 20 years usually cost around £50 per test.

161. Lizzie Walker noted that the only alternative cost presented to NHS England's was the Scottish Health Service estimate.

162. Will Sullivan, for NICE, stressed that, compared to infusion cost estimates, the impact of testing costs on the ICER is very small, and that this was discussed at the third appraisal meeting. Adela Williams argued that it is the principle, rather than the impact on the ICER, that is in dispute here – and that accepting NHS England's figures at face value without appropriate scrutiny sets a troubling precedent.

163. The appeal panel concluded as follows. The panel observed a clear discrepancy between Eisai's cost estimate and the NHS figure provided and later used by the EAG and committee. However, the panel placed significant weight on the principle of proportionality in reaching their decision; the APOE4 testing had a very small impact on the ICER and the panel agreed that the committee was not obliged to interrogate every discrepancy in depth, particularly as there were time constraints on the committee as the issue arose only in the third committee meeting, and the impact of APOE4 cost on the ICER would not have materially affected the committee's recommendation.

164. The panel were reminded that NHS England was the main payor and therefore, whilst the cost estimate provided from NHS England was not itemised, it was reasonable to accept this estimate.

165. The panel were persuaded that as the APOE4 testing costs were not consequential on the committee's decision, it was therefore justified and reasonable for the committee to pragmatically accept the NHS cost estimate at face value.

166. The appeal panel therefore dismissed the appeal on this point.

***Conclusion and effect of the appeal panel's decision***

167. The appeal panel therefore upheld the appeal on appeal points 1(a)1 and 2.1, and dismissed all other appeal points.

168. The appraisal of this technology is remitted to the appraisal committee in order to allow them to reconsider the assessment of utility values for carers, and to ensure that stakeholders are afforded adequate time to respond to NHS England's Infusion Cost Estimates Document.

169. The panel also suggested that, in relation to point 1(a)3, the committee should consider making it clearer in the FDG the reasons why they did not consider that there was any inconsistency in their approach to data on delaying progression comparing lecanemab and donanemab.

170. There is no possibility of further appeal against this decision of the appeal panel. However, this decision and NICE's decision to issue the final guidance may be challenged by applying to the High Court for permission to apply for a judicial review. Any such application must be made within three months of NICE publishing the final guidance.