



OPEN ACCESS

Review

Lecanemab appropriate use recommendations for clinical practice in the UK

Catherine J Mummery ¹, Jill Rasmussen ², Dan Blackburn ³, Elizabeth Coulthard ⁴, R Rhys Davies ⁵, Rachel Dorsey ⁶, Nick C Fox ⁷, Akram A Hosseini ⁸, Chineze Ivenso ⁹, Matthew Jones ¹⁰, Sean P Kennelly ¹¹, Christopher Kipps ¹², Daniel Lashley ¹³, Graham Mackay ¹⁴, Rashi Negi ¹⁵, Ramin Nilforooshan ¹⁶, Peter Anthony Passmore ¹⁷, Richard Perry ⁶, Vanessa Raymont ^{18,19}, James Benedict Rowe ^{20,21}, Tom C Russ ^{22,23}, John-Paul Taylor ²⁴, Alistair Burns ^{19,25}

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/jnnp-2025-336597>).

For numbered affiliations see end of article.

Correspondence to

Dr Catherine J Mummery; cath.mummery@nhs.net

Received 25 April 2025

Accepted 17 September 2025

ABSTRACT

Lecanemab is an anti-amyloid monoclonal antibody, recently approved in the UK as a treatment for mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD) in adults who are apolipoprotein E ϵ 4 gene (*APOE4*) heterozygotes or non-carriers.

A group of UK neurologists, old age psychiatrists and geriatricians with expertise in AD convened to agree appropriate use recommendations for lecanemab in UK clinical practice. The primary focus of these recommendations is safety.

Eligibility criteria for lecanemab in the UK include (a) a clinical diagnosis of MCI or mild dementia due to AD, (b) the presence of amyloid- β pathology, confirmed using approved methods (ie, an amyloid positron emission tomography scan or cerebrospinal fluid assay) and (c) *APOE4* heterozygous or non-carrier status. Eligibility screening should be conducted in secondary care and those identified as being potentially eligible for lecanemab should be referred to a specialist centre for confirmation of the likely pathological diagnosis, *APOE4* counselling and testing and a multidisciplinary consensus decision regarding treatment eligibility. Lecanemab is administered as an intravenous infusion every 2 weeks, and those eligible for treatment should have brain magnetic resonance imaging (MRI) scans prior to the 1st, 5th, 7th and 14th infusions. Specific guidance is provided for safety monitoring and management of potential adverse reactions, including amyloid-related imaging abnormalities and infusion-related reactions. The introduction of lecanemab into UK clinical practice provides an important opportunity to improve services for all people living with dementia, not just those eligible for lecanemab treatment.

INTRODUCTION

Dementia is one of the biggest health and social care challenges of the 21st century.¹ Alzheimer's disease (AD) is the most common cause of dementia, for which treatment has historically been supportive only, including symptomatic drugs. Amyloid deposition in the brain starts many years before symptom onset.² Interventions to reduce brain amyloid,

aiming to slow progression of disease, are a step forward in the treatment of AD. Newer generation anti-amyloid immunotherapies slow cognitive decline in the medium term, in association with significant amyloid lowering in the brain.^{3–7}

Lecanemab is a humanised immunoglobulin gamma 1 anti-amyloid monoclonal antibody, which binds with high affinity to aggregated forms of amyloid-beta ($A\beta$), showing preferential activity for $A\beta$ protofibrils.^{8,9} Such protofibrils have been proposed to be more toxic to neurons than other $A\beta$ species, such as monomers and fibrils.^{10,11} Lecanemab was approved in the UK in August 2024 as a treatment for mild cognitive impairment (MCI) and mild dementia due to AD in adult patients who are apolipoprotein E ϵ 4 gene (*APOE4*) heterozygotes or non-carriers¹²; however, it is currently not reimbursed or state-funded in the UK/Ireland.¹³ Approval in the UK follows approvals in the USA, Japan, China, South Korea, Hong Kong, Israel, the United Arab Emirates, and subsequently in the European Union, and is based largely on the results of the Clarity AD trial.⁴ In this phase 3, international, 18-month, multicentre, double-blind, placebo-controlled, parallel-group trial, lecanemab 10 mg/kg was administered every 2 weeks as an intravenous infusion to people with MCI or mild dementia due to AD (N=1795).⁴ Active treatment resulted in moderate but statistically significant reductions in both disease progression (as measured using the Clinical Dementia Rating-Sum of Boxes (CDR-SB) for the primary endpoint) and amyloid burden (as measured using amyloid positron emission tomography (PET)), in comparison with placebo.⁴ Although lecanemab was generally well tolerated, it was associated with side effects, including infusion-related reactions (IRRs) and amyloid-related imaging abnormalities (ARIA), requiring careful monitoring and management.⁴ An open-label extension of Clarity AD is currently ongoing,^{14,15} as are other longer term lecanemab studies, such as the open-label extension of a phase 2 proof-of-concept trial, in which lecanemab reduced brain amyloid and rate of clinical decline across several clinical and biomarker endpoints over 18 months^{16,17};



► <https://doi.org/10.1136/jnnp-2025-337659>



© Author(s) (or their employer(s)) 2025. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ Group.

To cite: Mummery CJ, Rasmussen J, Blackburn D, et al. *J Neurol Neurosurg Psychiatry* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jnnp-2025-336597

also, the AHEAD 3–45 study, which comprises two sister trials (one phase 2, the other phase 3), that are assessing lecanemab for up to 4 years in people with preclinical AD with intermediate or elevated levels of brain amyloid deposition.¹⁸ Based on the inclusion criteria from the clinical trials of lecanemab and donanemab, it has been estimated that 30 200 people annually would be eligible for treatment with monoclonal antibodies for AD in the UK.¹⁹ However, this estimate included individuals who are homozygous for *APOE4*, who would not be eligible for lecanemab according to its current licence¹²; furthermore, not all those eligible would choose to proceed with treatment.

Following the approval of lecanemab by the US Food and Drug Administration (FDA),²⁰ the AD and Related Disorders Therapeutics Work Group published appropriate use recommendations for US clinical practice,²¹ and the American Academy of Neurology published practical guidance on logistical and organisational issues relating to emerging anti-amyloid treatments.²² Subsequently, a report was published by a team at the University of Washington Medicine Memory and Brain Wellness Center, outlining a framework for rolling out anti-amyloid monoclonal antibody treatments in US clinical practice.²³ Appropriate use recommendations have also been published for France²⁴ and Korea.²⁵ The approval by the UK Medical and Healthcare products Regulatory Agency (MHRA) differed from the FDA's approval in a number of ways, including the exclusion of *APOE4* homozygous patients. The objective of the current article is therefore to provide recommendations for lecanemab use in the UK, to facilitate its introduction into clinical practice by providing pragmatic guidance on how to prepare for, and address, the anticipated challenges of initiating a new type of therapy in the real-world UK setting.

The primary focus of these recommendations is the safe use of lecanemab. This will require significant changes in clinical practice, careful management of potential side effects and the gathering of long-term data. Since the available evidence is derived from patient populations carefully selected for inclusion in a clinical trial, it is sensible to adopt a cautious approach initially, both in terms of who should be deemed eligible for treatment in clinical practice, and how such patients should be monitored and managed. As new evidence and experience accrue, these recommendations will be reviewed and amended to provide updated guidelines. Recommendations may become more inclusive over time, increasing access, but for now they are similar to those adopted for the late-phase clinical trials. It is also important to note that the scope of this paper is to provide a framework of recommendations for best practice for the safe and effective delivery of lecanemab in the UK, and it is beyond its scope to address detailed structural and operational changes that will be required to meet the recommendations we make, which have been discussed elsewhere.^{26–28}

The introduction of lecanemab into UK clinical practice provides an important opportunity to improve services for all people living with dementia, not just those who are eligible for lecanemab treatment, including the provision of post-diagnostic support. It is hoped that the following recommendations will help improve the care and treatment for everyone affected by this devastating condition, including people with dementia, their families and carers.

METHODOLOGY

A group of UK neurologists, old age psychiatrists and geriatricians with expertise in AD met in January 2024 to review and discuss current clinical evidence for the use of lecanemab in patients

with MCI or mild dementia due to AD, with the aim of achieving consensus on guidance to form the basis of these appropriate use recommendations. Some experts had been involved in the lecanemab clinical development programme and so had first-hand experience of using the drug, which helped inform the recommendations. Further input has been obtained from primary care, pharmacy and radiology. During the initial meeting, discussion and debate resulted in key appropriate use recommendations we make, which were then iterated and fine-tuned during development of the manuscript to achieve a consensus.

FOR WHOM IS LECANEMAB SUITABLE?

The eligibility criteria for lecanemab treatment are based on the evidence available from the Clarity AD trial and the MHRA approval. These include (a) a clinical diagnosis of MCI or mild dementia due to AD, (b) the presence of A β pathology, confirmed using approved methods (ie, an amyloid PET scan or cerebrospinal fluid (CSF) assay) and (c) *APOE4* heterozygous or non-carrier status.¹² For eligibility, cognitive scores should lie between ≥ 22 and ≤ 30 on the Mini Mental State Examination (MMSE) or a score compatible with MCI or mild dementia due to AD using another cognitive screening instrument, such as the Montreal Cognitive Assessment (MoCA)²⁹ or Addenbrooke's Cognitive Examination (ACE, ACE-revised version or ACE-III).^{30–31} Patients with subjective cognitive symptoms only are not eligible for lecanemab treatment. Patients diagnosed with moderate or severe AD are also not currently eligible for lecanemab treatment, since the efficacy of treatment in these later disease stages has not been established.¹² Other key exclusionary criteria are outlined in table 1.^{12 32–34}

For patients with MMSE scores at the lower end of the defined range, it may be appropriate to include additional measures of functionality and/or frailty in order to confirm their suitability for treatment, given the rigours of the treatment schedule. The final decision should be determined by a multidisciplinary team (MDT) in a specialist treatment centre (see *Specialist treatment centre—Pathological confirmation, APOE testing and consensus eligibility decision* section). In addition to floor and ceiling effects, the MMSE has acknowledged limitations, particularly for individuals for whom English is not their first language, those with learning disability, those with atypical language or visual variants of AD and those who are hearing or visually impaired, or with premorbid dyslexia. However, other cognition measures are subjected to similar limitations as the MMSE. In addition, different memory services use different tests. For pragmatic purposes, we are recommending use of MoCA or ACE/ACE-III (the latter can provide an equivalent to MMSE³⁵; MoCA can be converted to an approximate MMSE equivalent).^{36–37} There may, therefore, be exceptional circumstances where there is a clear reason why an individual does not meet the MMSE criterion but otherwise appears eligible for treatment, which should be referred to the specialist centre MDT for the final decision regarding treatment. If variations or adjustments to the standard MMSE thresholds are considered, then the MDT must consider the possible effect on the risk–benefit of treatment and include this uncertainty in discussions with patients during the informed consent process. It should also be noted that current evidence for lecanemab is derived from a trial population of those defined as having AD; the subtype of AD has not been described. It is likely the majority would have amnesic AD, as this is the most common presentation; however, other presentations may have participated. As this has not been specifically assessed in the trials, recommendations therefore relate to the AD population

Table 1 Exclusionary criteria for lecanemab treatment

Exclusionary criterion	Other considerations
▶ Homozygous for <i>APOE4</i> ¹²	▶ Homozygous <i>APOE4</i> carriers have a higher risk of developing ARIA than heterozygous carriers and non-carriers ^{33 34}
▶ Diagnosis of moderate or severe AD ¹²	▶ Lecanemab efficacy in later disease stages has not been established ¹²
▶ Requirement for ongoing treatment with anticoagulants (since this increases the risk of cerebral haemorrhage) ^{12 32}	▶ Patients receiving dual <i>antiplatelet</i> therapy are eligible to receive lecanemab ▶ <i>However</i> , use of dual <i>antiplatelet</i> therapy should be considered as part of the MDT discussion on the totality of an individual's risks (comorbidities, <i>APOE4</i> status, frailty, etc.) when considering eligibility for treatment ▶ Prescribing clinician (eg, cardiologist, stroke specialist) should be consulted on the ongoing need for <i>antiplatelets</i> , where necessary
▶ Bleeding disorders that are not under adequate control*	▶ Lecanemab should be used with caution in those with a family history of haemorrhage
▶ History of clinically diagnosed TIAs in the past 12 months*	
▶ History of stroke in the past 12 months*	
▶ History of seizures in the past 12 months*	▶ There is currently no evidence for the effect(s) of lecanemab on seizure threshold ▶ However, a diagnosis of epilepsy, with no seizures for 12 months is not exclusionary
▶ History of ICH or severe cerebrovascular disease	
▶ Existing MRI scan that is indicative of severe cerebrovascular disease	
▶ Evidence of CAA on MRI: pre-treatment MRI findings of prior ICH, >4 microhaemorrhages, superficial siderosis or vasogenic oedema, which are suggestive of CAA ^{4 12}	
▶ Hypersensitivity to lecanemab or any of its excipients ¹²	

*Patients with these conditions were excluded from lecanemab clinical trials, and the safety and efficacy in these patients are unknown.¹²
AD, Alzheimer's disease; *APOE4*, apolipoprotein E ε4 gene; ARIA, amyloid-related imaging abnormalities; CAA, cerebral amyloid angiopathy; ICH, intracerebral haemorrhage; MDT, multidisciplinary team; TIA, transient ischaemic attack.

as a whole. There is no reason to think a difference in syndrome leads to a difference in benefit or risk; however, when discussing with an individual with an atypical variant, it is important to consider that they may underperform on standard cognitive tests. Therefore, in judging eligibility for treatment when cognitive performance is borderline, it should be assessed by the MDT on a case-by-case basis, and current evidence considered in discussions regarding informed consent between clinicians and patients/caregivers.

OVERVIEW OF RECOMMENDED PATIENT PATHWAY

Referral and assessment for lecanemab treatment should be undertaken in a timely manner, since long wait times may result in patients progressing out of the eligibility window for treatment (figure 1).

Primary care assessment

The majority of patients presenting with cognitive problems will be seen first in primary care. As such, general practitioners (GPs) represent the gateway through which patients with suspected dementia enter the healthcare system. They have an essential role in assessing whether patients with cognitive problems should be referred to secondary care for diagnostic tests and further assessment of their cognition, and consequently their eligibility for lecanemab.

In the future, it is possible that GPs may undertake diagnostic screening tests, such as blood biomarkers or digital cognitive tests, developed in close collaboration with secondary care as the pathway develops. At present, the role of primary care will be to exclude clinically those unlikely to have diseases leading to dementia as a cause of their symptoms and to perform an initial assessment, using their knowledge of the patient to facilitate appropriate referral to secondary care. As is currently the case, GPs should first exclude and/or treat other potential causes of cognitive impairment, such as physical illness (eg, history of alcohol use disorder, end-stage heart disease, life-limiting cancer), depression and the effects of existing medication(s).

This should include physical examination, depression screening (eg, Patient Health Questionnaire-9 (PHQ-9))³⁸ and appropriate blood tests to exclude reversible causes of cognitive decline (eg, vitamin B12 deficiency, thyroid dysfunction). Having ruled out other potential causes of cognitive impairment, a suitable screening tool should be employed to assess cognition. Ideally, we recommend using the MMSE or MoCA, but if time precludes the use of these, shorter cognition screening tools for dementia that are suitable for use in primary care include the Test Your Memory (TYM) test,^{39 40} the short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE),⁴¹ and the Clock-Drawing Test (CDT)⁴²; however, these shorter screening tools may not always identify MCI, especially in high functioning individuals.

Since patients with MCI may be eligible for lecanemab treatment, GP practices should consider contacting and re-referring any patients identified as having MCI in the previous 12 months by a Memory Assessment Service and discharged back to primary care (particularly if specified as having amnesic MCI). Re-referral of such patients to the Memory Assessment Service should explicitly request that they be screened for potential eligibility for lecanemab treatment, as outlined below for initial assessment for treatment eligibility (see *Secondary care assessment—local Memory Assessment Service* section).

Having ruled out other potential causes of cognitive impairment, patients with suspected neurodegenerative or vascular disease as a cause of MCI or mild dementia should be referred on to their local Memory Assessment Service. All information pertinent to potential eligibility for lecanemab treatment should be included in the referral to secondary care, including significant medical history (eg, transient ischaemic attacks (TIAs) or stroke), medication (eg, anticoagulants) and information relevant to the patient's ability to undergo lecanemab treatment safely (eg, contraindications to MRI). Patients requiring oral anticoagulation (warfarin, direct oral anticoagulants) would not normally be eligible

Neurodegeneration

Setting:

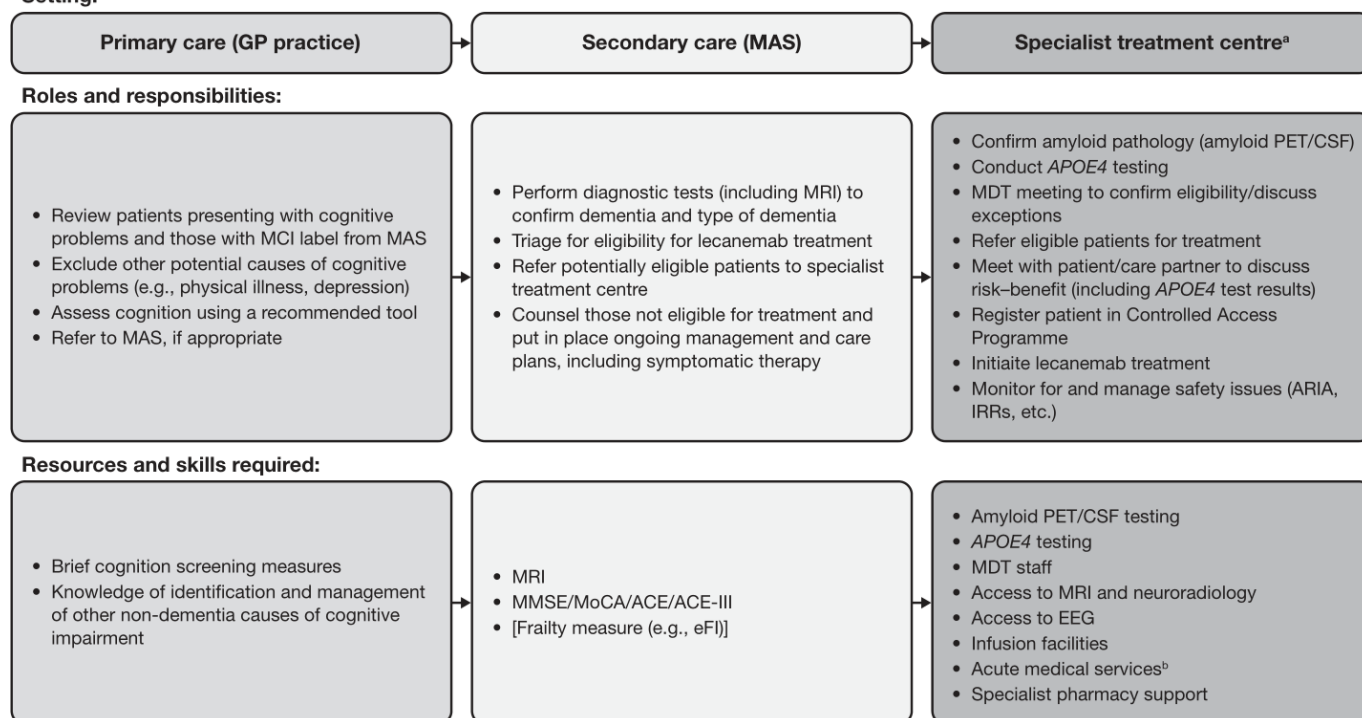


Figure 1 Overview of recommended patient pathway. ^aSpecialist treatment centre may be in secondary care or tertiary care. ^bIncluding crash trolley, antihistamines, steroids, epinephrine, etc. ACE, Addenbrooke's Cognitive Examination; *APOE4*, apolipoprotein E ε4 gene; ARIA, amyloid-related imaging abnormalities; CSF, cerebrospinal fluid; EEG, electroencephalogram; eFI, electronic Frailty Index; GP, general practitioner; IRR, infusion-related reaction; MAS, Memory Assessment Service; MCI, mild cognitive impairment; MDT, multidisciplinary team; MMSE, Mini-Mental State Assessment; MoCA, Montreal Cognitive Assessment; PET, positron emission tomography.

for lecanemab and referral for assessment should be avoided for these individuals.

Secondary care assessment—local Memory Assessment Service

Alongside the initial assessment, a person's eligibility for lecanemab treatment should be conducted in secondary care (most likely the local Memory Assessment Service, though in some areas neuroscience centres; patients may also be referred to the independent sector). This assessment should include confirmation of the clinical diagnosis of AD, including clinical and cognitive examination and MRI with relevant sequences (see the *MRI requirements and interpretation* section), together with careful assessment of exclusionary criteria (see the section *For whom is lecanemab suitable?* and [table 1](#)).

Lecanemab treatment involves fortnightly intravenous infusions and regular MRI monitoring to detect the potential occurrence of ARIA (see the section *ARIA monitoring and management* section); therefore, initial assessment should exclude any patients who are clearly unlikely to cope with the treatment schedule, such as those unable to undergo MRI scans (eg, MRI-incompatible pacemaker or unable to tolerate MRI due to claustrophobia). A detailed medical history should be obtained to identify any comorbidities and/or unstable medical conditions that may be affected by lecanemab therapy and/or impact the patient's ability to tolerate treatment. In general, patients should not discontinue a proven effective treatment for a comorbidity in order to take lecanemab, without specialist advice. It may also be appropriate to use a frailty measure, such as the electronic Frailty Index,^{43 44} to inform a clinical judgement as to whether or not a patient will be able to tolerate treatment.

Patients not eligible for lecanemab treatment will need to be managed and supported according to existing guidance, where available,⁴⁵ including appropriate post-diagnostic support,^{46 47} with symptomatic treatment and non-pharmacological interventions to reduce risks and burden for the person with dementia and carers. Additional management of patient expectations—and disappointments—will be of great importance, since it is estimated that only a minority of patients will initially be eligible for lecanemab treatment.¹⁹

Patients identified in local memory services as being potentially eligible for lecanemab should be referred to the specialist treatment unit within their service, or at a specialist centre, for confirmation of the likely pathological diagnosis, *APOE4* counselling and testing in the context of AD and a multidisciplinary consensus decision regarding treatment eligibility. Prior to referral to the treatment unit, patients and families should be informed about what is involved in lecanemab treatment (ie, fortnightly infusions and regular MRIs) and the potential risks of treatment (ie, ARIA and IRRs), as some people may not want to be considered for treatment. As with other agents that have been granted regulatory approval but are not yet funded by the NHS, patients and families should be informed that access to the treatment may require out-of-pocket payment, which could be significant. It should also be made clear that referral does not guarantee treatment with lecanemab, since further confirmatory assessments will be required.

Specialist treatment centre

The specialist treatment centre may be provided by a secondary care memory assessment service, or a regional hub if such a centre is not available locally.

- a. Pathological confirmation, *APOE4* testing and consensus eligibility decision

Relevant medical records will need to be reviewed, and any missing information requested from primary care or local memory services. It is likely that the patient will need to be seen to clarify any equivocal points and to ensure it is appropriate to undergo amyloid confirmation and *APOE4* testing. If no recent and suitable MRI is available (within the last 12 months, with no change in the patient's condition), an MRI will be required. Amyloid positivity will then need to be confirmed with either CSF examination or amyloid PET brain scan. We recommend using CSF amyloid biomarkers from an accredited lab and the use of licensed amyloid PET ligands. Plasma phosphorylated τ (p-tau)217 testing⁴⁸ is not currently recommended as a substitute for CSF/PET analysis in determining eligibility for lecanemab treatment, though blood biomarkers are likely to play a role in the future. Once amyloid positivity has been confirmed, *APOE4* counselling and testing will need to be performed. Patients found to be homozygous for *APOE4* will need to be supported and referred back to secondary care for appropriate management, since only *APOE4* heterozygotes or non-carriers are eligible for lecanemab treatment.¹² Counselling those found to be homozygous will be an important consideration and they will need to be informed that there is a 50% chance that their children will have at least one *APOE4* allele.

Polymorphism in *APOE* is a major risk factor for AD.^{49–50} The *APOE4* allele is associated with an increased risk of AD and the *APOE2* allele is associated with a decreased risk, relative to the more common *APOE3* allele.⁴⁹ Individuals who are heterozygous for *APOE4* have a 3–4-fold increased risk of late-onset AD, while those who are homozygous for *APOE4* have a 9–15-fold increased risk.⁴⁹ Approximately one in four of the general population carries at least one *APOE4* allele,⁵¹ and 10%–15% of patients with AD are homozygous carriers.³⁴ While *APOE4* homozygosity is associated with a high likelihood of developing AD pathology and biomarker changes, not all homozygous carriers will develop overt clinical dementia, indicating that the allele is not fully penetrant in terms of symptomatic disease.⁵²

Possessing one or two copies of *APOE4* is a key risk factor for developing ARIA.^{53–54} Homozygous carriers have a higher risk of developing ARIA than heterozygous carriers,^{33–34} as evidenced in both the initial lecanemab phase 2 proof-of-concept trial and the phase 3 Clarity AD trial (see the *Amyloid-related imaging abnormalities* (ARIA) section).^{4–17} Given the association between *APOE4* status and the risk of developing ARIA, *APOE4* testing is mandatory and only patients who are non-carriers or heterozygous for *APOE4* are eligible for lecanemab treatment in the UK.¹² Prior to *APOE4* testing, patients should be appropriately counselled (including the potential implications of test outcomes for family/offspring) and consented according to national or local guidelines, as applicable. Genetic counselling in this context may be conducted by the clinician: patients do not need to be referred to genetic counselling services.

Once it has been determined that a patient is either heterozygous for *APOE4* or a non-carrier, an MDT should discuss the eligibility of each patient and reach consensus on treatment. Having a consensus treatment decision has benefits both in terms of diagnosis and also in terms of managing patients who are not eligible for treatment.

- b. Discussion regarding the benefit–risk of lecanemab treatment

After the MDT has determined that a patient is potentially eligible for lecanemab treatment, the treating clinician should

arrange a meeting with the patient and their care partner/family to discuss the benefits and risks of treatment, including the results of *APOE* testing, as part of the informed consent procedure. The potential safety risks associated with lecanemab treatment should be clearly outlined, including the risks of ARIA (informed by their *APOE4* status), IRRs and other common or serious side effects (headache, rash, atrial fibrillation, hypersensitivity reactions).¹² Patient and carer educational material (eg, leaflets with graphical risk illustrations) should be provided to facilitate informed consent. If the MDT determines that a patient is not eligible for lecanemab treatment, a meeting should be arranged between the patient/care partner/family and their secondary care clinician, to inform them of the MDT decision and discuss their ongoing care pathway.

- c. Treatment

If the patient wishes to go ahead, the responsible clinician will then obtain informed consent and prescribe treatment. In order to receive treatment, all eligible patients must be entered into a central registration system implemented as part of a Controlled Access Programme.¹² Once registered, the patient will be given a unique identifier that is required prior to receiving the first infusion of lecanemab. The unique identifier and registration document should be uploaded onto the patient's electronic records. This will allow appropriate tracking and monitoring. Further information on the Controlled Access Programme can be obtained from lecanemab@uniphar.com.

The location of the treatment centre is likely to be initially at a specialist treatment centre/hub, with expertise in the use of similar drugs and pathways. The treatment centre must have all necessary resources in place to administer lecanemab safely and have immediate access to acute medical services in the event of safety concerns.

In addition to a recent brain MRI (within the last 12 months) before the first dose, MRIs should be performed prior to the 5th, 7th and 14th infusions.¹² We also recommend considering an additional MRI before the 26th infusion for individuals who are *APOE4* carriers or who have previously developed ARIA. Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment.¹² If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including an MRI.¹² See the *Safety monitoring and management* section for detail on ARIA.

It is very important that patients being treated with lecanemab should carry a Patient Alert Card at all times to alert medical staff to this fact. This card includes information on the prescribing service's 24-hour contact details and highlights important safety information, including the risks of thrombolysis and use of anti-coagulants in patients being treated with lecanemab. Copies of the Patient Alert Card can be obtained from Eisai Medical Information (EUMedinfo@eisai.net or telephone: 0208 600 1400). The use of lecanemab treatment and associated need for safety monitoring must also be clearly recorded and highlighted in hospital, GP and pharmacy records. Consideration should be given to setting up alerts in electronic patient records for when patients on lecanemab treatment present at accident and emergency (A&E) prior to admission and after they are admitted to hospital. Interaction with and education of staff working in emergency services (ambulances, A&E), the stroke treatment pathway and MRI departments (neuroradiologists, radiographers, etc) are critical. This is to ensure all are aware of the need for rapid access to MRI for patients treated with lecanemab, and the need to be vigilant about checking whether a patient is receiving lecanemab before considering diagnosis or starting therapy such as thrombolysis. Patients/care partners/families and

clinicians (including those working for emergency departments, primary care and NHS 111) should be educated on the symptoms/signs that may suggest an ARIA; and clinicians need to be educated on the threshold for needing an unscheduled MRI. There is no need to change the schedule for MRI monitoring on the basis of *APOE4* status, but the threshold for requesting an unscheduled MRI should be lower in patients known to have an increased risk of ARIA (see the *ARIA monitoring and management* section for further details).

LECANEMAB ADMINISTRATION

All contraindications to lecanemab should be checked prior to commencing treatment, since a patient's existing medication may have changed since eligibility for lecanemab treatment was confirmed. Vital signs should also be checked, and any uncontrolled hypertension or other abnormality would be a contraindication to lecanemab treatment at that time. Lecanemab is formulated as a 100mg/mL concentrate for intravenous infusion and treatment should be initiated and supervised by clinicians experienced in the diagnosis and treatment of AD.¹² The recommended dose is 10mg/kg administered as an intravenous infusion over approximately 1 hour, once every 2 weeks.¹² It must not be administered as an intravenous push or bolus injection.¹² Lecanemab is diluted prior to intravenous infusion.¹² Each vial contains lecanemab at a concentration of 100mg/mL and vials should be stored in a refrigerator (2–8°C).¹² Once the total volume of lecanemab solution required has been calculated (based on the patient's body weight), the required volume should be added to 250mL of 0.9% sodium chloride solution for injection and the infusion bag gently inverted (but not shaken) to mix completely.¹² Prior to infusion, the diluted lecanemab solution should be allowed to warm to room temperature.¹² The entire volume of the diluted solution should be administered over approximately 1 hour through an intravenous line containing a terminal 0.2micron in-line filter.¹² The infusion line should be flushed to ensure all lecanemab is administered.¹² Patients should be monitored for any signs or symptoms of an IRR, including fever and flu-like symptoms, nausea, vomiting, hypotension, hypertension and oxygen desaturation, and treated if needed.¹² Patients should be monitored for IRRs for 3 hours after the first infusion.²¹ Post-infusion monitoring can be reduced to 2 hours after the second and third infusions and to 30min for subsequent infusions, if no IRRs have occurred.²¹ Since delayed reactions can sometimes occur, a follow-up phone call should be made by the clinical team (usually the nurse coordinator) later in the day after each infusion to determine whether the patient has experienced any symptoms; any new symptoms should be detailed and the treating clinician informed. If an infusion is missed, the next dose should be administered as soon as possible after the due date.¹² If the infusion is given up to 5 days after its scheduled date, the dates of subsequent infusions and safety MRIs should remain unchanged, but if given more than 5 days late, then subsequent infusions and safety MRIs should be rescheduled accordingly. Since lecanemab dosing is based on weight, it is recommended that if a patient's weight changes by more than 10%, the prescribed dose should be revised. Patients' weight should be monitored at clinic regularly (eg, once every 3 months).

It is recommended that a treatment navigator (ie, a trained coordinator, preferably a nurse practitioner/clinical nurse specialist) orchestrates the patient's journey to ensure the safety and efficiency of the pathway and to ensure that the patient and family are kept informed at all times.

Other considerations regarding lecanemab treatment

Use of anticoagulants and antiplatelets

Lecanemab treatment should not be initiated in patients receiving ongoing anticoagulant therapy,¹² since anticoagulants increase the risk associated with ARIA. If anticoagulation needs to be started in a patient being treated with lecanemab, then lecanemab treatment should be paused until anticoagulation is no longer medically indicated,¹² and we recommend conducting an MRI prior to starting anticoagulation, at the treating clinician's discretion. Those receiving single antiplatelet therapy should be considered eligible for treatment, unless other exclusionary criteria are met. For patients receiving dual antiplatelet therapy, this should be discussed as part of the MDT discussion on the totality of the individual's risks (comorbidities, *APOE4* status, frailty, etc) when considering eligibility for treatment (table 1). It may be appropriate to consult the relevant clinician (cardiologist/stroke specialist/geriatrician) on the ongoing need for dual antiplatelet therapy. As previously stated, patients should not discontinue a proven effective treatment for a comorbidity in order to take lecanemab, without specialist advice.

Epilepsy/seizures

There is currently no evidence for the effect(s) of lecanemab on seizure threshold, so careful discussion of risk and benefit should be undertaken with patients with a history of epilepsy.

Our recommendation is that patients with no seizures in the previous 12 months may be considered eligible for lecanemab treatment, regardless of whether or not they are currently on antiseizure medications (ASMs), subject to clinical discussion; that is a well-controlled seizure disorder may not be exclusionary. Recommendations may change as further evidence becomes available.

Use of acetylcholinesterase inhibitors (AChEIs) or memantine

Neither the use of AChEIs or memantine, nor the timing of starting symptomatic therapy, should influence whether or not a patient is eligible for lecanemab treatment: normal care continues in parallel with lecanemab treatment.

People living alone

In Clarity AD, participants were required to have a minimum of 8 hours/week contact with a care partner.⁴ Since there are mildly affected individuals who are independent, working and capable of managing the lecanemab treatment schedule, those living alone should not be excluded from receiving lecanemab solely on this basis. However, it is important to discuss the impact of this for each patient, to assess potential risk of delayed detection of side effects such as ARIA, the practicalities of discussing risk–benefit, and keeping to the treatment schedule. Treatment of those living alone should therefore be at the clinician's discretion. If treated, it is important to ensure that those living alone have a sufficient support network and are able to provide information on any symptoms. The absence of a care partner should be systematically documented, as this could have implications for safety monitoring and adherence to treatment.

Genetic forms of AD

Patients with rare genetic forms of AD, such as autosomal dominant AD, should not be excluded from lecanemab treatment on that basis alone if they fulfil the eligibility criteria.

However, there is currently no evidence to support the use of lecanemab, and there is a higher rate of cerebral amyloid angiopathy (CAA), in individuals with AD and Down syndrome.¹² Lecanemab should not be used in individuals with evidence of CAA on MRI (as stated in the exclusionary criteria; table 1) and should be used with caution in those with a family history of brain haemorrhage.

People who have previously received treatment with lecanemab or another amyloid disease-slowing therapy

Patients who have previously received lecanemab or another amyloid disease-slowing therapy (eg, aducanumab) in a clinical trial setting, or whose lecanemab treatment is stopped due to unforeseen circumstances, should not be excluded from subsequently receiving lecanemab treatment if eligible according to the criteria outlined above. If previous anti-amyloid immunotherapy was associated with clinically significant ARIA, treatment with lecanemab should not be offered.

Patients whose amyloid has been effectively cleared by previous treatment should not be considered eligible for further treatment unless levels have reaccumulated. They would need to exceed the standard threshold of amyloid positivity prior to starting treatment. If known to be previously amyloid-depleted, we recommend a minimum of 6 months interval after cessation of anti-amyloid therapy before retesting for amyloid positivity.

There is currently no systematic evidence base to address the issues of switching anti-amyloid therapies. If a patient wishes to switch to lecanemab from another anti-amyloid therapy, we recommend a minimum washout period of 1 month before starting lecanemab treatment.

MRI REQUIREMENTS AND INTERPRETATION

MRI is key for initial diagnosis and eligibility, and for detection and differential diagnosis of ARIA: CT would not detect milder ARIA with oedema or sulcal effusions (ARIA-E) or ARIA with haemosiderin deposition (ARIA-H).⁵³ Scanning at 3.0T is preferred but the use of 1.5T is endorsed as a minimum standard due to the limited availability of 3.0T scanners. The acquisition sequences to identify ARIA include T2* gradient echo (GRE) or susceptibility weight imaging (SWI) to detect ARIA-H and T2-weighted fluid attenuated inversion recovery to detect ARIA-E.

MRI scans should be assessed by someone who has undergone specific training to identify ARIA. Ideally, an experienced neuroradiologist interprets the scans; at a minimum, the scan interpreter should have undergone at least some training for the detection of ARIA. It is recommended that a patient's earlier

scans (including their pretreatment scan) be made available as quickly as possible for comparative purposes, and that the same MRI scanner be used whenever possible, to ensure consistency and facilitate interpretation. Ideally, the lecanemab treatment protocol should stipulate that treating clinicians have access to MRI scan reports, including in the out-of-hours setting. It is also recommended that there is access to an 'ARIA specialist' to provide advice on ARIA interpretation, particularly for out-of-hours cases. This could be provided in neuroscience centres by having a pool of named expert neuroradiologists for ARIA interpretation and/or via a networking/buddying system with a small core of specialist sites initially (rather than having an ARIA specialist at every site).

SAFETY MONITORING AND MANAGEMENT

In the lecanemab clinical trials, the most commonly reported adverse reactions in patients who were *APOE4* heterozygotes or non-carriers and treated with lecanemab were IRRs (26%), ARIA-H (13%), fall (11%), headache (11%) and ARIA-E (9%).¹²

Amyloid-related imaging abnormalities (ARIA)

The accumulation and deposition of A β is involved in the pathophysiology of both AD and CAA.⁵⁵ In AD, A β deposition occurs mostly in the brain parenchyma, while in CAA, it occurs mostly in vascular walls.⁵⁵ Neuropathological studies have demonstrated that CAA occurs to some extent in >90% of patients with confirmed AD pathology.⁵⁶ Evidence suggests that ARIA may be caused by the disruption of blood vessels by CAA and that the risk is increased by the clearance of A β from these vessels, for example, by monoclonal anti-amyloid antibodies, although other mechanisms have also been hypothesised.⁵⁷ ARIA can manifest in two distinct forms that are identifiable using MRI: ARIA-E and ARIA-H, involving microhaemorrhage and superficial siderosis.^{58 59} (figure 2). ARIA-H typically accompany ARIA-E events.¹² Rarely, intracerebral haemorrhages >1 cm in diameter have occurred.¹²

Most ARIA are detected using routine surveillance MRIs and are asymptomatic, typically occurring early in the treatment course and decreasing in frequency with duration of drug exposure.^{53 54 57} ARIA-H are generally asymptomatic but the hemosiderin signal persists radiographically. ARIA-E are normally asymptomatic, but, when ARIA-E cause symptoms, they are non-specific and usually resolve completely.⁵⁴ ARIA-E symptoms include headache, confusion, nausea, vomiting, visual disturbance, neuropsychiatric symptoms, dizziness, fatigue and gait disturbances.¹² On rare occasions, individuals may experience severe neurological symptoms that may be life-threatening,

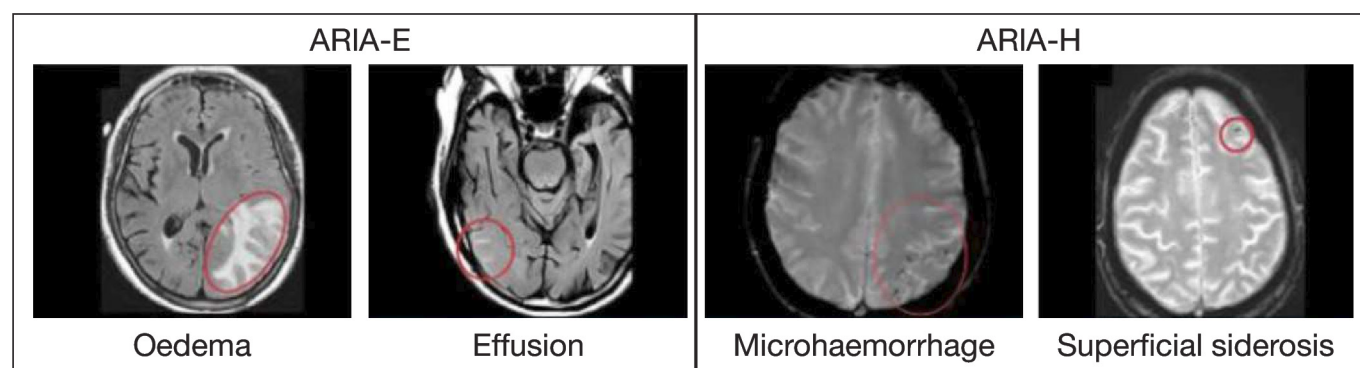


Figure 2 MRI imaging examples of ARIA-E and ARIA-H. Figure adapted from Hampel H, *et al*, with permission from Oxford University Press.⁵⁵ ARIA, amyloid-related imaging abnormalities; ARIA-E, ARIA with oedema or sulcal effusions; ARIA-H, ARIA with haemosiderin deposition.

Table 2 Incidence of ARIA during the phase 3 Clarity AD trial in *APOE4* non-carriers and heterozygotes^{4 12 14}

Category	<i>APOE4</i> non-carriers and heterozygotes		<i>APOE4</i> non-carriers		<i>APOE4</i> heterozygotes	
	Lecanemab N=757	Placebo N=764	Lecanemab N=278	Placebo N=286	Lecanemab N=479	Placebo N=478
ARIA-E, n (%)	67 (8.9)	10 (1.3)	15 (5.4)	1 (0.3)	52 (10.9)	9 (1.9)
Symptomatic ARIA-E, n (%)	12 (757)	0	4 (1.4)	0	8 (1.7)	0
ARIA-H, n (%)	98 (12.9)*	52 (6.8)*	32 (11.5)	11 (3.8)	66 (13.8)	41 (8.6)
Isolated ARIA-H, [†] n (%)	61 (8.1)	45 (5.9)	22 (7.9)	10 (3.5)	39 (8.1)	35 (7.3)
Intracerebral haemorrhage, n (%)	4 (0.5)	2 (0.3)	1 (0.4)	1 (0.3)	3 (0.6)	1 (0.2)

Treatment with lecanemab may be paused or discontinued, according to the algorithm shown in [table 3](#) (see also *ARIA monitoring and management* below).¹²
 *Among *APOE4* non-carriers and heterozygotes, six patients (0.8%) treated with lecanemab and one patient (0.1%) treated with placebo experienced symptomatic ARIA-H; symptomatic ARIA-H data for the individual *APOE4* non-carrier and *APOE4* heterozygote subgroups are not available.
[†]ARIA-H without ARIA-E.
APOE4, apolipoprotein E ε4 gene; ARIA, amyloid-related imaging abnormalities; ARIA-E, ARIA with oedema or effusions; ARIA-H, ARIA with hemosiderin deposits.

including encephalopathy, focal neurological issues, seizures and status epilepticus.^{12 54 60 61} For patients experiencing severe symptoms, hospitalisation and specific supportive treatment (eg, intensive care, corticosteroids, ASMs) may be required.^{54 60 61} Close working relationships between specialist centres, acute teams, stroke physicians, neurology and radiology are critical in this situation.

In Clarity AD, ARIA-E were observed in 8.9% (67/757) of patients who were *APOE4* non-carriers or heterozygotes treated with lecanemab, compared with 1.3% (10/764) of patients treated with placebo ([table 2](#)).^{4 12 14} Symptomatic ARIA-E occurred in 1.6% (12/757) of patients treated with lecanemab, and no patients treated with placebo.¹² ARIA-H were experienced by 12.9% (98/757) of patients who were *APOE4* non-carriers or heterozygotes treated with lecanemab, compared with 6.8% (52/764) of patients treated with placebo.¹² Symptomatic ARIA-H occurred in 0.8% (6/757) of patients treated with lecanemab and 0.1% (1/764) of patients treated with placebo.¹² There was no increase in isolated ARIA-H (ie, ARIA-H occurring in the absence of ARIA-E) in patients treated with lecanemab, compared with placebo.¹⁴ Intracerebral haemorrhage occurred in 0.5% (4/757) of patients who were *APOE4* non-carriers or heterozygotes treated with lecanemab, compared with 0.3% (2/764) of patients treated with placebo.¹² As previously mentioned, lecanemab treatment is not licensed in the UK for use in patients who are homozygous for *APOE4*.¹²

ARIA monitoring and management

In a suspected ARIA case, the full clinical picture must be considered before a diagnosis is confirmed.⁵⁸ Vigilance is required to differentiate ARIA from other conditions, including ischaemic stroke, subarachnoid haemorrhage and posterior reversible encephalopathy syndrome.⁵⁸ As previously stated, MRIs should be performed and reviewed prior to the 5th, 7th and 14th infusions,¹² and we also recommend considering an additional MRI before the 26th infusion for individuals who are *APOE4* carriers or who have previously developed ARIA.

Knowing if a patient is on a monoclonal antibody that removes amyloid (such as lecanemab) helps with determining an ARIA diagnosis.⁵⁸ ARIA should be considered the presumed diagnosis when signal abnormalities on MRI are identified in patients recently exposed to anti-amyloid monoclonal antibodies in whom no evidence of any other cause or underlying lesion can be found. Since ARIA can present with focal neurological findings that mimic ischaemic stroke, MRI should be used to evaluate stroke-like symptoms in patients on lecanemab to distinguish ARIA from ischaemic stroke. In addition to the

acquisition sequences outlined for ARIA, diffusion-weighted imaging (DWI) should be carried out to exclude an ischaemic stroke in such patients. It is vital that anyone treating a patient on lecanemab presenting acutely with focal neurological symptoms/signs is made aware that they are on lecanemab, so that the correct imaging can be done and diagnosis made. The standard stroke pathway involves computerised tomography angiography (CTA) scanning, which would not reliably pick up ARIA and is therefore not sufficient for a patient who has received lecanemab: MRI is required. In addition, treatment with thrombolytic therapy would risk significant haemorrhage—close liaison with stroke and other acute colleagues is necessary to ensure that patients receiving lecanemab are not treated with thrombolytic therapy, except in life-threatening circumstances with no alternative management options (eg, pulmonary embolism with haemodynamic compromise) when the benefit of thrombolytic therapy may outweigh the associated risk.¹² The decision on whether or not to instigate a standard stroke pathway once lecanemab treatment has been stopped should be made on an individual patient basis, as there is currently no evidence to guide this.

Regarding the timing of unscheduled MRIs, if a patient presents with focal neurological symptoms/signs (ie, symptoms/signs that mimic ischaemic stroke) and has already undergone CTA scanning and stroke has been ruled out, they should have an MRI within 24 hours, but if a patient presents with non-specific symptoms that may suggest an ARIA (such as headache, confusion, nausea, dizziness, visual changes, gait difficulty), they should be scanned within a few days. In both situations, lecanemab treatment should be paused until the results of the unscheduled scan are known.

ARIA-E, ARIA-H microhaemorrhage and ARIA-H superficial siderosis can be categorised by MRI severity ([table 3A](#)).¹² Dosing recommendations for individuals who experience ARIA-E or ARIA-H are based on MRI radiographic severity and whether clinical symptoms are asymptomatic or symptomatic, as summarised in [table 3B](#).¹²

Dosing may continue in patients with asymptomatic, mild radiographic ARIA-E or ARIA-H based on clinical judgement and the Summary of Product Characteristics (SPC) recommends enhanced clinical monitoring and follow-up MRIs starting 2 months after occurrence and every 1 or 2 months thereafter until the ARIA-E has resolved or the ARIA-H has stabilised;¹² however, where possible, we recommend starting follow-up MRIs 1 month after occurrence.

In patients with symptomatic or moderate and severe radiographic ARIA-E, the SPC states that lecanemab dosing should be suspended and a follow-up MRI should be performed to assess

Table 3 (A) Grading of ARIA MRI severity and (B) dosing recommendations for patients with ARIA¹²

(A) Grading of ARIA MRI severity				
ARIA type		MRI severity		
		Mild	Moderate	Severe
ARIA-E		FLAIR hyperintensity confined to sulcus and/or cortex/subcortex white matter in one location <5 cm	FLAIR hyperintensity 5–10 cm in single greatest dimension, or more than 1 site of involvement, each measuring <10 cm	FLAIR hyperintensity >10 cm with associated gyral swelling and sulcal effacement. One or more separate/independent sites of involvement may be noted
ARIA-H microhaemorrhage		≤4 new incident microhaemorrhages	5–9 new incident microhaemorrhages	≥10 new incident microhaemorrhages
ARIA-H superficial siderosis		1 focal area of superficial siderosis	2 focal areas of superficial siderosis	>2 areas of superficial siderosis
(B) Dosing recommendations for patients with ARIA				
Clinical symptom severity		MRI severity		
		Mild	Moderate	Severe
ARIA-E	Asymptomatic	May continue dosing based on clinical judgement*	Suspend dosing [†]	Suspend dosing [†]
	Symptomatic	Suspend dosing [†]		
ARIA-H	Asymptomatic	May continue dosing based on clinical judgement*	Suspend dosing [‡]	Permanently discontinue treatment
	Symptomatic	Suspend dosing [‡]		
*With enhanced clinical monitoring and follow-up MRIs starting 2 months after occurrence and every 1 or 2 months thereafter until ARIA-E resolution or ARIA-H stabilisation.				
[†] Suspend dosing for any symptomatic or radiographically moderate or severe ARIA-E and perform a follow-up MRI to assess for resolution 2–4 months after initial identification; once the MRI demonstrates radiographic resolution and symptoms, if present, resolve, resumption of dosing should be guided by clinical judgement.				
[‡] Suspend dosing for any symptomatic or radiographically moderate ARIA-H and perform a follow-up MRI to assess for stabilisation 2–4 months after initial identification; once the MRI demonstrates radiographic stabilisation and symptoms, if present, resolve, resumption of dosing should be guided by clinical judgement.				
ARIA, amyloid-related imaging abnormalities; ARIA-E, ARIA with oedema or sulcal effusions; ARIA-H, ARIA with haemosiderin deposition; FLAIR, fluid attenuated inversion recovery.				

for resolution 2–4 months after initial identification;¹² however, we recommend that follow-up MRIs be performed every month until the event has resolved, where possible. Once the MRI demonstrates radiographic resolution and symptoms, if present, resolve, resumption of lecanemab treatment should be guided by clinical judgement.¹² It should be noted that recurrence after resumption of lecanemab treatment is more common in *APOE4* heterozygotes than in *APOE4* non-carriers.¹²

In patients with symptomatic or moderate radiographic ARIA-H, the SPC states that lecanemab dosing should be suspended and a follow-up MRI should be performed to assess for stabilisation 2–4 months after initial identification;¹² however, as for symptomatic or moderate and severe radiographic ARIA-E, we recommend that follow-up MRIs should be performed every month until the ARIA-H has stabilised, where possible. Once the MRI demonstrates radiographic stabilisation and symptoms, if present, resolve, resumption of dosing should be guided by clinical judgement,¹² taking account of the exclusionary criteria outlined in table 1. Following an ARIA-H event, recurrence after resumption of lecanemab treatment is very common in both *APOE4* non-carriers and heterozygotes: in Clarity AD, the recurrence rate in *APOE4* non-carriers and heterozygotes who continued lecanemab treatment after experiencing ARIA-H (with or without concurrent ARIA-E) was 35.9% (28/78).¹²

Lecanemab treatment should be permanently discontinued in patients who experience a severe radiographic ARIA-H event or intracerebral haemorrhage.¹²

In the event of symptomatic ARIA E requiring hospital admission, early initiation of high-dose glucocorticoid treatment should be considered (eg, methylprednisolone 1 g/day intravenous for 5 days, followed by an oral steroid tapered over several weeks).²¹ Severe forms of ARIA, such as CAA-related inflammation and Aβ-related angiitis, may require treatment with non-steroid immunosuppressants.⁶² Monitoring for seizures should

be part of the management protocol.²¹ If a seizure occurs while on lecanemab treatment, the patient must always be scanned for an ARIA, regardless of whether or not they have a history of epilepsy. Until there is further evidence, the decision as to whether to continue lecanemab treatment in a patient who experiences an ARIA-related seizure should rely on current guidance on ARIA severity (see *Stopping lecanemab treatment* below), alongside clinical judgement and shared decision-making with the patient/carer regarding the severity of symptoms including seizures.

Further information on the identification and management of ARIA is found here: <https://www.medicines.org.uk/emc/rmm/100590/Document>.

Management of IRRs

In Clarity AD, IRRs were the most commonly reported adverse event, experienced by 26.4% of individuals treated with lecanemab (compared with 7.4% of those treated with placebo).⁴ The majority were mild to moderate (grade 1 or 2; 96%) and occurred with the first dose (75%).⁴ The incidence of IRRs was similar regardless of *APOE4* status.¹² However, it should be noted that IRRs do not necessarily occur just at the start of treatment. In the clinical trial setting, most IRRs, including severe reactions, occurred during the infusion or within approximately 2.5 hours after infusion completion.¹²

Symptoms of IRRs include fever and flu-like symptoms (chills, generalised aches, feeling shaky and joint pain), nausea, vomiting, hypotension, hypertension and oxygen desaturation.¹² In the event of IRRs, it is recommended that the infusion rate be decreased and discontinued if necessary, depending on grade (online supplemental table S1^{4 63 64}).¹² IRRs should be treated with antihistamines, paracetamol, non-steroidal anti-inflammatory drugs or corticosteroids, as necessary, and as per

local hospital protocol. It is also recommended that prophylactic treatment (antihistamines, paracetamol, non-steroidal anti-inflammatory drugs or corticosteroids) be considered for patients with recurrent IRRs.¹²

General management and interdisciplinary liaison

It is critical to have in place a plan and protocol for the management of any safety issues, including ARIA and IRRs. This must include clear and effective communication between relevant disciplines (such as neuroradiology, stroke and acute medicine) and overall trust management. Since there needs to be access to an acute medical team in the event of symptomatic ARIA and IRRs, it is recommended that lecanemab be administered in an appropriate clinical setting for the first 6 months, when there is the greatest risk of ARIA occurrence. It will initially take time for staff to build confidence in administering lecanemab and monitoring and managing safety issues, and it is therefore recommended that a networking/buddying initiative be in place to help provide the necessary expertise and support when a new site is starting up. Home infusion may be considered after 6 months if there have been no safety issues (ARIA, IRRs, etc), with appropriate supervision by the treatment centre and according to local resources regarding fast access to MRI scanning and acute treatment services. Antihistamines, paracetamol, non-steroidal anti-inflammatory drugs and corticosteroids should be available, if needed, whenever lecanemab is administered.

STOPPING LECANEMAB TREATMENT

Lecanemab treatment should be discontinued in patients experiencing radiographically severe ARIA-H or intracerebral haemorrhage > 1 cm in diameter, or if any medical condition develops that requires anticoagulant treatment.¹² It is also recommended that discontinuation of lecanemab treatment be considered in patients experiencing grade 3 or higher IRRs.^{4 21} Hypersensitivity reactions (including angioedema, bronchospasm and anaphylaxis) have occurred in patients treated with lecanemab.¹² Infusion of lecanemab should therefore be stopped promptly upon the first observation of any signs/symptoms consistent with a hypersensitivity-type reaction and appropriate therapy should be initiated as per local protocol.¹²

The duration of lecanemab treatment in Clarity AD was 18 months.⁴ Emerging evidence from the open-label extension of Clarity AD suggests that lecanemab may continue to slow disease progression, as measured by CDR-SB, over 3 years compared with a matched control group; further evidence is needed to confirm this.^{4 15} No new safety signals have yet been observed with lecanemab treatment over 3 years.^{14 15} Treatment duration should take into account clinical needs, service capacity and patient and clinician choice. Treatment with lecanemab should be stopped once the patient progresses to moderate AD, since the efficacy of continued treatment in patients with moderate AD has not been established.¹² Progression to moderate AD should be determined by the treating clinician on a case-by-case basis using clinical judgement informed by the results of a suitable cognitive performance test indicative of moderate status (eg, MMSE <20). Cognitive performance should be assessed every 6 months or if there is a clinical indication.

CURRENT CHALLENGES

It must be acknowledged that the current reimbursement status of lecanemab in the UK has implications for healthcare equity. Moreover, the need for long-term infusion schedules, frequent MRI monitoring for ARIA and specialised staffing requirements

will provide challenges to the existing NHS infrastructure, limiting access initially even if reimbursement is approved. As previously mentioned, our recommendations aim to provide pragmatic guidance on how to administer lecanemab effectively and safely in UK clinical practice, and while it is beyond the scope of this article to address how such recommendations translate into the current structure of the UK healthcare system, we acknowledge long-term planning is required to successfully implement anti-amyloid immunotherapies and other disease-modifying therapies into clinical practice; issues which have been addressed elsewhere.^{26–28} The current decision by NICE means that, at least in the short term, only a small minority of those eligible for lecanemab treatment will be likely to receive it. The slow start may facilitate development of UK treatment pathways and prioritisation of critical bottlenecks to resolve; in addition, we will be accumulating real-world evidence from other countries where lecanemab is approved, feeding into our understanding of the best pathway for treatment.^{63–68} The management of AD is changing as our understanding of pathophysiology improves. As has been the case with other conditions (such as multiple sclerosis and stroke), dramatic changes in a model of care may initially be viewed as being unsustainable but can ultimately lead to substantial improvements in patient outcomes. Therefore, although the system of care for AD needs altering for the effective and safe delivery of lecanemab treatment, this is the time for such change, and a relatively slow initial uptake may enable the development of appropriate skills and pathways over time.

OPPORTUNITIES

Collaborative, multidisciplinary working

Many different groups of healthcare professionals will need to be involved to roll out lecanemab successfully, including GPs, neurologists, old age psychiatrists, geriatricians, radiologists, radiographers, geneticists, stroke physicians, cardiologists, nurses, pharmacists, emergency services and A&E staff, NHS 111 staff and laboratory staff. It is important that there is wide representation in decisions relating to setting up the lecanemab treatment pathway, since multidisciplinary collaboration will be crucial to its safety and success. Education, supervision and training of sites will be required, and access to educational material is vital for all those involved in the lecanemab treatment pathway, including patients and care partners as well as clinical staff and care support workers. Educational resources will need to be adapted appropriately for each stakeholder group, including information and safety materials for patients, families and care homes; these resources could include digital applications as well as printed leaflets. A collaborative 'treatment network' approach, where GPs, memory clinics and other specialist services collaborate closely, would help address these educational needs.

Development of a patient registry

It is recommended that all patients treated with lecanemab be included in a registry, which should be electronic and include an agreed template for monitoring of ARIA, IRRs and the emergence of significant medical events (eg, myocardial infarction, TIA, stroke). This will need to be embedded within clinical practice and provide sufficient information to build a body of evidence on long-term use of lecanemab. A common minimum dataset is being developed across sites likely to start therapies early. These data will facilitate timely revision of treatment recommendations and speed up equity of access.

Looking to the future

There are currently many unanswered questions regarding lecanemab treatment, which will need to be addressed in post-marketing studies. It is important to reiterate that the recommendations presented in this article are focused on the need to ensure safety. The recommendations are expected to evolve as further evidence emerges and experience with lecanemab increases, and this will likely improve equity of access to treatment, which is an acknowledged limitation of the current recommendations.

It is also important to reiterate that the introduction of lecanemab provides opportunities to improve services for all patients with dementia, regardless of whether or not they are eligible for lecanemab treatment. All patients would benefit from improvements in multidisciplinary collaboration, and patients ineligible for lecanemab treatment can be assessed for other appropriate forms of intervention and support. Indeed, every case presents an opportunity to improve patient care; for example, a patient excluded from lecanemab treatment due to severe vascular changes could be assessed for ways to improve their vascular risk profile. For patients receiving lecanemab, the requirement for fortnightly infusion of the drug provides an opportunity to provide support for the impact of AD and its treatment and to help patients and care partners plan for the future. Services should explore ways to offer an equivalent level of support to patients not receiving lecanemab. There are also opportunities for developing new methods to improve access to treatment, such as the use of ultrafast MRI to cut time and cost of MRIs and so increase accessibility. At the time of writing, lecanemab has just been approved in the UK for monthly IV maintenance dosing. Consequently, after receiving 18 months of 10 mg/kg once every two weeks, patients may be transitioned to the maintenance dosing regimen of 10 mg/kg once every four weeks (or continue with the previous regimen).⁶⁹ Furthermore, a subcutaneous formulation may become available in the UK in the future, and it is likely that blood-based biomarkers for the detection of amyloid pathology may soon become available and affect the pathways for referral, diagnosis and screening for eligibility—developments that will further improve access to treatment and necessitate timely updates to these appropriate use recommendations.

Author affiliations

¹National Hospital for Neurology and Neurosurgery, University College London, London, UK

²Primary Care Specialist Dementia, Mental Health and Learning Disability, Surrey, UK

³Neuroscience, School of Medicine and Population Health, The University of Sheffield, Sheffield, UK

⁴Bristol Medical School, University of Bristol, Bristol, UK

⁵The Walton Centre NHS Foundation Trust, Liverpool, UK

⁶Imperial College London, London, UK

⁷National Hospital for Neurology and Neurosurgery and Queen Square Institute of Neurology, University College London, London, UK

⁸Nottingham University Hospitals NHS Trust, Nottingham, UK

⁹Aneurin Bevan University Health Board, Newport, UK

¹⁰Manchester Centre for Clinical Neurosciences, Salford Royal Hospital, Salford, UK

¹¹Department of Medical Gerontology, School of Medicine, Trinity College Dublin, Dublin, Ireland

¹²University Hospital Southampton NHS Foundation Trust, Southampton, UK

¹³University Hospitals Plymouth NHS Trust, Plymouth, UK

¹⁴Aberdeen Royal Infirmary, Aberdeen, UK

¹⁵Midlands Partnership NHS Foundation Trust, Lichfield, UK

¹⁶Surrey and Borders Partnership NHS Foundation Trust, Surrey, UK

¹⁷Queen's University Belfast, Belfast, UK

¹⁸Oxford University, Oxford, UK

¹⁹Oxford Health NHS Foundation Trust, Oxford, UK

²⁰Cambridge Centre for Frontotemporal Dementia, University of Cambridge, Cambridge, UK

²¹Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

²²Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

²³Neuroprogressive & Dementia Network, NHS Research Scotland, Dundee, UK

²⁴Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK

²⁵Manchester University, Manchester, UK

Acknowledgements Editorial assistance was provided by John Scopes of mXm Medical Communications, funded by Eisai UK. Multiple members of the NIHR Dementia Translational Research Collaboration collaborated to co-author this publication

Contributors CM: concept, drafting, editing and critical revisions of manuscript; and guarantor of the paper. JR, DB, EC, RRD, RD, NCF, AAH, CI, MJ, SPK, CK, DL, GM, RNe, RNi, PAP, RP, VR, JBR, TCR, JPT, AB: concept, editing and critical revisions of manuscript.

Funding The panel meeting for the development of this article was organised and funded by Eisai UK. Editorial support for the preparation of this article was funded by Eisai UK (grant number N/A).

Competing interests CM has provided consultancy to Alector, Biogen, Eisai, Ionis, Lilly, MSD, Neurimmune, Novartis, Prevail, Roche/Genentech, Wave. She is an advisor to the Drug Delivery Foundation. She has received honoraria for advisory boards, teaching and education from Biogen, Eisai and Lilly, and received academic funding award from Biogen. She is supported by the NIHR UCLH Biomedical Research Centre. JR is serving as a member of Data Monitoring Committees for several companies, including Lilly. She has received honoraria for advisory boards, teaching and education from Eisai. DB has no competing interests. EC has received consultancy fees from Biogen, Eisai and Lilly over the last 3 years. RD has no competing interests. RD has received honoraria for education work, advisory boards and support for conference attendance from Biogen, Novartis, Sanofi, Merck, Roche and Janssen. NCF has provided consultancy to AbbVie, Biogen, Eisai, Lilly, Roche/Genentech and Siemens. AAH has provided consultancy to Eisai and Lilly; and has received honorarium an honourarium from Biogen for teaching and education. She has received funding from the UKRI (MR/T005580/1) and the NIH (R56AG074467), and serves as Chair of the Association of British Neurologists Cognitive Specialist Interest Group. The views expressed are those of the authors and do not necessarily reflect those of the UKRI, the NIH or the ABN. CI is Academic Secretary Faculty of Old Age Psychiatry, Royal College of Psychiatrists, and Speciality Lead for Dementia and Neurodegeneration Health and Care Research Wales. She has received ad hoc payments for advisory roles with Biogen, Eisai, Lilly, Roche and Novo Nordisk. MJ has received honoraria/honoraria for giving educational talks for Eisai and Biogen. SPK has received honoraria/honoraria for consultancy/advisory board contributions from Roche, Biogen, Merck, Nutricia and Eisai. He has also received honoraria from Roche, Nutricia and Eisai for speaker and educational material development. CK has provided consultancy to Eisai and Lilly. DL has received honoraria/honoraria from Eisai. GM has no competing interests. He has research sessions supported by his NRS clinical research fellowship. RN has no competing interests. RN has received honoraria/honoraria from Eisai, Lilly, Roche and Janssen. PAP has provided consultancy to Eisai, Biogen and Lilly. RP has provided educational sessions and advisory expertise for Roche, MSD, Lilly, Eisai, and Biogen. VR has no competing interests. JBR has provided consultancy to AstronauTx, Astex, Alector, Asceneuron, Booster Therapeutics, CuraSen, Cumulus Neuroscience, Eisai, Ferrer, Invicro, Prevail and SV Health; and received academic funding awards from Janssen, Lilly, GSK, and AstraZeneca. He is supported by the NIHR Cambridge Biomedical Research Centre (NIHR203312; the views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care). TCR has no competing interests. He is supported by the University of Edinburgh, the Chief Scientist Office of the Scottish Government, NHS Lothian, Alzheimer Scotland, NIH, the Blood Biomarker Challenge, and the Rosetrees Trust/Race Against Dementia. JPT has provided consultancy to Eisai and is supported by the NIHR Newcastle Biomedical Research Centre (the views expressed are those of the author and not necessarily those of the NIHR or the Department of Health and Social Care). AB acts as a consultant for Eisai, Lilly and TauRx; trustee for Dementia UK; and advisor to Alzheimer's Research UK. He also carries out clinical assessments and medico-legal work on a private basis.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and

is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Catherine J Mummery <https://orcid.org/0000-0002-6739-0803>
Jill Rasmussen <https://orcid.org/0000-0003-4365-0428>
Dan Blackburn <https://orcid.org/0000-0001-8886-1283>
Elizabeth Coulthard <https://orcid.org/0000-0002-0017-9595>
R Rhys Davies <https://orcid.org/0000-0002-8157-078X>
Nick C Fox <https://orcid.org/0000-0002-6660-657X>
Akram A Hosseini <https://orcid.org/0000-0003-0133-9842>
Chineze Ivenso <https://orcid.org/0009-0003-3690-2698>
Sean P Kennelly <https://orcid.org/0000-0002-3721-0197>
Christopher Kipps <https://orcid.org/0000-0002-5205-9712>
Daniel Lashley <https://orcid.org/0009-0002-6758-0540>
Graham Mackay <https://orcid.org/0000-0002-4316-2320>
Rashi Negi <https://orcid.org/0009-0006-4918-3647>
Ramin Nilforooshan <https://orcid.org/0000-0001-9801-183X>
Peter Anthony Passmore <https://orcid.org/0000-0002-5738-6800>
Richard Perry <https://orcid.org/0000-0002-4536-9018>
Vanessa Raymont <https://orcid.org/0000-0001-8238-4279>
James Benedict Rowe <https://orcid.org/0000-0001-7216-8679>
Tom C Russ <https://orcid.org/0000-0001-9797-2188>
John-Paul Taylor <https://orcid.org/0000-0001-7958-6558>
Alistair Burns <https://orcid.org/0000-0002-9837-0645>

REFERENCES

- Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet* 2020;396:413–46.
- Hampel H, Hardy J, Blennow K, et al. The Amyloid- β Pathway in Alzheimer's Disease. *Mol Psychiatry* 2021;26:5481–503.
- Zhang Y, Chen H, Li R, et al. Amyloid β -based therapy for Alzheimer's disease: challenges, successes and future. *Sig Transduct Target Ther* 2023;8:248.
- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. *N Engl J Med* 2023;388:9–21.
- Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in Early Alzheimer's Disease. *N Engl J Med* 2021;384:1691–704.
- Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. *JAMA* 2023;330:512–27.
- Budd Haeberlein S, Aisen PS, Barkhof F, et al. Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. *J Prev Alzheimers Dis* 2022;9:197–210.
- Magnusson K, Sehlin D, Syvänen S, et al. Specific uptake of an amyloid- β protofibril-binding antibody-tracer in A β PP transgenic mouse brain. *J Alzheimers Dis* 2013;37:29–40.
- Tucker S, Möller C, Tegerstedt K, et al. The murine version of BAN2401 (mAb158) selectively reduces amyloid- β protofibrils in brain and cerebrospinal fluid of tg-ArcSwe mice. *J Alzheimers Dis* 2015;43:575–88.
- Ono K, Tsuji M. Protofibrils of Amyloid- β are Important Targets of a Disease-Modifying Approach for Alzheimer's Disease. *Int J Mol Sci* 2020;21:952.
- Tolar M, Hey J, Power A, et al. Neurotoxic Soluble Amyloid Oligomers Drive Alzheimer's Pathogenesis and Represent a Clinically Validated Target for Slowing Disease Progression. *Int J Mol Sci* 2021;22:6355.
- Eisai Ltd. Leqembi (lecanemab) summary of product characteristics. 2024. Available: <https://www.medicines.org.uk/emc/product/15908>
- National Institute for Health and Care Excellence. Final draft guidance finds benefits of 2 Alzheimer's treatments remain too small to justify the additional cost to the NHS. 2025. Available: <https://www.nice.org.uk/news/articles/the-benefits-of-alzheimers-treatments-donanemab-and-lecanemab-remain-too-small-to-justify-the-additional-costs-says-nice-in-final-draft-guidance> [Accessed 20 Aug 2025].
- Honig LS, Sabbagh MN, van Dyck CH, et al. Updated safety results from phase 3 lecanemab study in early Alzheimer's disease. *Alzheimers Res Ther* 2024;16:105.
- van Dyck CH, Sperling RA, Dhadda S, et al. Is there Evidence for a Continued Benefit for Long-Term Lecanemab Treatment? A Benefit/Risk Update from Long-Term Efficacy, Safety and Biomarker Data. *Alzheimers Dement* 2024;20.
- Satlin A, Wang J, Logovinsky V, et al. Design of a Bayesian adaptive phase 2 proof-of-concept trial for BAN2401, a putative disease-modifying monoclonal antibody for the treatment of Alzheimer's disease. *Alzheimers Dement (N Y)* 2016;2:1–12.
- Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-A β protofibril antibody. *Alzheimers Res Ther* 2021;13:80.
- Rafii MS, Sperling RA, Donohue MC, et al. The AHEAD 3-45 Study: Design of a prevention trial for Alzheimer's disease. *Alzheimers Dement* 2023;19:1227–33.
- Laurell AAS, Venkataraman AV, Schmidt T, et al. Estimating demand for potential disease-modifying therapies for Alzheimer's disease in the UK. *Br J Psychiatry* 2024;224:198–204.
- US Food and Drug Administration. (Lecanemab-irmb) prescribing information. 2023. Available: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761269s000lbl.pdf
- Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: Appropriate Use Recommendations. *J Prev Alzheimers Dis* 2023;10:362–77.
- Ramanan VK, Armstrong MJ, Choudhury P, et al. Anti-amyloid Monoclonal Antibody Therapy for Alzheimer Disease: Emerging Issues in Neurology. *Neurology (Ecricon)* 2023;101:842–52.
- Rosenbloom MH, O'Donohue T, Zhou-Clark D, et al. A Framework for the Administration of Anti-amyloid Monoclonal Antibody Treatments in Early-Stage Alzheimer's Disease. *CNS Drugs* 2024;38:493–505.
- Villain N, Planche V, Lilamand M, et al. Lecanemab for early Alzheimer's disease: Appropriate use recommendations from the French federation of memory clinics. *J Prev Alzheimers Dis* 2025;12:100094.
- Park KH, Kim GH, Kim C-H, et al. Lecanemab: Appropriate Use Recommendations by Korean Dementia Association. *Dement Neurocogn Disord* 2024;23:165–87.
- Belder CRS, Schott JM, Fox NC. Preparing for disease-modifying therapies in Alzheimer's disease. *Lancet Neurol* 2023;22:782–3.
- Dobson R, Patterson K, Malik R, et al. Eligibility for anti-amyloid treatment: preparing for disease-modifying therapies for Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2024;95:796–803.
- Cooper C, Marshall CR, Schott JM, et al. Preparing for disease-modifying dementia therapies in the UK. *Nat Rev Neurol* 2024;20:641–2.
- Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
- Mioshi E, Dawson K, Mitchell J, et al. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int J Geriatr Psychiatry* 2006;21:1078–85.
- Hsieh S, Schubert S, Hoon C, et al. Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. *Dement Geriatr Cogn Disord* 2013;36:242–50.
- Magid-Bernstein J, Girard R, Polster S, et al. Cerebral Hemorrhage: Pathophysiology, Treatment, and Future Directions. *Circ Res* 2022;130:1204–29.
- Cogswell PM, Barakos JA, Barkhof F, et al. Amyloid-Related Imaging Abnormalities with Emerging Alzheimer Disease Therapeutics: Detection and Reporting Recommendations for Clinical Practice. *AJNR Am J Neuroradiol* 2022;43:E19–35.
- Abushakra S, Porsteinsson AP, Sabbagh M, et al. APOE ϵ 4/ ϵ 4 homozygotes with early Alzheimer's disease show accelerated hippocampal atrophy and cortical thinning that correlates with cognitive decline. *Alzheimers Dement (N Y)* 2020;6:e12117.
- Matias-Guiu JA, Pytel V, Cortés-Martínez A, et al. Conversion between Addenbrooke's Cognitive Examination III and Mini-Mental State Examination. *Int Psychogeriatr* 2018;30:1227–33.
- Roheger M, Xu H, Hoang MT, et al. Conversion Between the Mini-Mental State Examination and the Montreal Cognitive Assessment for Patients With Different Forms of Dementia. *J Am Med Dir Assoc* 2022;23:1986–9.
- Fasnacht JS, Wuest AS, Berres M, et al. Conversion between the Montreal Cognitive Assessment and the Mini-Mental Status Examination. *J Am Geriatr Soc* 2023;71:869–79.
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
- Brown J, Pengas G, Dawson K, et al. Self administered cognitive screening test (TYM) for detection of Alzheimer's disease: cross sectional study. *BMJ* 2009;338:b2030.
- Brown JM, Wiggins J, Dawson K, et al. Test Your Memory (TYM) and Test Your Memory for Mild Cognitive Impairment (TYM-MCI): A Review and Update Including Results of Using the TYM Test in a General Neurology Clinic and Using a Telephone Version of the TYM Test. *Diagnostics (Basel)* 2019;9:116.
- Jorm AF. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychol Med* 1994;24:145–53.
- Mendez MF, Ala T, Underwood KL. Development of scoring criteria for the clock drawing task in Alzheimer's disease. *J Am Geriatr Soc* 1992;40:1095–9.
- Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing* 2016;45:353–60.
- NHS England. Identifying frailty. 2024. Available: <https://www.england.nhs.uk/ourwork/clinical-policy/older-people/frailty/frailty-risk-identification/> [Accessed 13 May 2024].
- National institute for health and care excellence. Clinical knowledge summary (CKS): Dementia. 2024. Available: <https://cks.nice.org.uk/topics/dementia/> [Accessed 18 Apr 2024].
- Bamford C, Wheatley A, Brunskill G, et al. Key components of post-diagnostic support for people with dementia and their carers: A qualitative study. *PLoS One* 2021;16:e0260506.

- 47 Levin KA, Lithgow S, Miller M, *et al.* Post-diagnostic support for dementia: What can be learned from service providers' experiences, model variation and information recording. *Health Educ* 2018;118:320–38.
- 48 Ashton NJ, Brum WS, Di Molfetta G, *et al.* Diagnostic Accuracy of a Plasma Phosphorylated Tau 217 Immunoassay for Alzheimer Disease Pathology. *JAMA Neurol* 2024;81:255–63.
- 49 Yamazaki Y, Zhao N, Caulfield TR, *et al.* Apolipoprotein E and Alzheimer disease: pathobiology and targeting strategies. *Nat Rev Neurol* 2019;15:501–18.
- 50 Lambert JC, Ibrahim-Verbaas CA, Harold D, *et al.* Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nat Genet* 2013;45:1452–8.
- 51 Gharbi-Meliani A, Dugravot A, Sabia S, *et al.* The association of APOE ϵ 4 with cognitive function over the adult life course and incidence of dementia: 20 years follow-up of the Whitehall II study. *Alz Res Therapy* 2021;13:5.
- 52 Van Cauwenberghe C, Van Broeckhoven C, Sleegers K. The genetic landscape of Alzheimer disease: clinical implications and perspectives. *Genet Med* 2016;18:421–30.
- 53 Barakos J, Purcell D, Suhy J, *et al.* Detection and Management of Amyloid-Related Imaging Abnormalities in Patients with Alzheimer's Disease Treated with Anti-Amyloid Beta Therapy. *J Prev Alzheimers Dis* 2022;9:211–20.
- 54 Filippi M, Cecchetti G, Spinelli EG, *et al.* Amyloid-Related Imaging Abnormalities and β -Amyloid-Targeting Antibodies. *JAMA Neurol* 2022;79:291.
- 55 Hampel H, Elhage A, Cho M, *et al.* Amyloid-related imaging abnormalities (ARIA): radiological, biological and clinical characteristics. *Brain (Bacau)* 2023;146:4414–24.
- 56 Janson CG. AD and CAA: Independent risk factors for dementia. *Sci Transl Med* 2015;7.
- 57 Sperling RA, Jack CR, Black SE, *et al.* Amyloid-related imaging abnormalities in amyloid-modifying therapeutic trials: Recommendations from the Alzheimer's Association Research Roundtable Workgroup. *Alzheimers Dement* 2011;7:367–85.
- 58 Barakos J, Sperling R, Salloway S, *et al.* MR Imaging Features of Amyloid-Related Imaging Abnormalities. *AJNR Am J Neuroradiol* 2013;34:1958–65.
- 59 Sperling R, Salloway S, Brooks DJ, *et al.* Amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with bapineuzumab: a retrospective analysis. *Lancet Neurol* 2012;11:241–9.
- 60 Salloway S, Chalkias S, Barkhof F, *et al.* Amyloid-Related Imaging Abnormalities in 2 Phase 3 Studies Evaluating Aducanumab in Patients With Early Alzheimer Disease. *JAMA Neurol* 2022;79:13.
- 61 VandeVrede L, Gibbs DM, Koestler M, *et al.* Symptomatic amyloid-related imaging abnormalities in an APOE ϵ 4/ ϵ 4 patient treated with aducanumab. *Alzheimers Dement (Amst)* 2020;12:e12101.
- 62 Regenhardt RW, Thon JM, Das AS, *et al.* Association Between Immunosuppressive Treatment and Outcomes of Cerebral Amyloid Angiopathy-Related Inflammation. *JAMA Neurol* 2020;77:1261–9.
- 63 Doessegger L, Banholzer ML. Clinical development methodology for infusion-related reactions with monoclonal antibodies. *Clin Transl Immunology* 2015;4:e39.
- 64 US Food and Drug Administration. Guidance for industry: toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials 2007. 2007. Available: <https://www.fda.gov/media/73679/download> [Accessed 29 May 2025].
- 65 Shields LBE, Hust H, Cooley SD, *et al.* Initial Experience with Lecanemab and Lessons Learned in 71 Patients in a Regional Medical Center. *J Prev Alzheimers Dis* 2024;11:1549–62.
- 66 Sabbagh MN, Zhao C, Mahendran M, *et al.* Characterizing the Journey of Early Alzheimer's Disease in Patients Initiating Lecanemab Treatment in the United States: A Real-World Evidence Study. *Neurol Ther* 2025;14:1115–27.
- 67 Bregman N, Nathan T, Shir D, *et al.* Lecanemab in clinical practice: real-world outcomes in early Alzheimer's disease. *Alzheimers Res Ther* 2025;17:119.
- 68 Paczynski M, Hofmann A, Posey Z, *et al.* Lecanemab Treatment in a Specialty Memory Clinic. *JAMA Neurol* 2025;82:655–65.
- 69 Eisai. LEQEMBI® (lecanemab) IV Maintenance Dosing for the Treatment of Early Alzheimer's Disease Approved in the United Kingdom; press release.. 2025. Available: <https://www.eisai.com/news/2025/news202579.html> [Accessed 1 December 2025].