Information Note: Acute Management of Potential Adverse Treatment Effects of Lecanemab

For suggested local cascade to:

Primary Care Teams, NHS 111, Ambulance Services, Accident and Emergency Departments, Hospital Pharmacy Teams, Local Medical Committees, Local Pharmaceutical Committees, Stroke Units, Local Memory Clinics, Psychiatry Teams, Neurosurgery Departments, Neurology Departments, Imaging Teams, Independent Sector Clinics

Purpose

Although not currently available in the NHS, Eisai (the manufacturer and market authorisation holder for lecanemab (Leqembi®)) has begun to make the drug available for patients to access through independent sector clinics. This note provides a short briefing for clinical teams who may subsequently be asked to support referrals for private treatment or otherwise assess, advise and possibly treat a small number of patients who could present with potential adverse treatment effects, including symptomatic Amyloid-Related Imaging Abnormalities (ARIA).

This information note has been drafted in relation to lecanemab. However please note that a second monoclonal antibody (donanemab (Kisulna®), manufactured by Eli Lilly) has received a GB licence and may also be made available in the independent sector in the next few weeks. Further medicines-specific information will be made available by the company in due course, but information in this note on the clinical management of ARIA will be relevant to both medicines.

Summary

- Alzheimer's Disease, the most common cause of dementia[1], is in part caused by an abnormal build-up of proteins within the brain.
- Lecanemab is a medication that targets these abnormal proteins and is now licensed for use in Great Britain. However, in line with the current draft NICE recommendation, lecanemab will not be available in the NHS in England, but may be available through independent sector providers.
- Routine consultations, additional investigations and interventions directly associated with lecanemab must be provided by the private provider delivering lecanemab and funded by the patient or their insurer.
- Though often asymptomatic, for a small number of patients receiving lecanemab serious symptoms may present clinically. These symptoms may present as new-onset confusion, headache, dizziness and nausea, or occasionally as more severe neurological emergencies including seizures, focal neurological deficits and reduced level of consciousness.
- ARIA reflects swelling in one or more areas of the brain (ARIA-E for o**e**dema), or small spots of bleeding in or on the surface of the brain (ARIA-H for **h**aemorrhage).
- Eisai has provided a guide for healthcare professionals, and patients taking the drug should have been given a patient information leaflet and encouraged to carry a patient alert card.
- Following history and examination with suspected symptomatic ARIA, in a hospital setting, an MRI brain scan and corticosteroid therapy should be considered.

[1] Dementia is the term used to describe a decline in cognition and level of social functioning due to an underlying progressive brain disease. Alzheimer's disease (AD) is the most common cause of dementia. Part of the AD process involves an abnormal build-up of the proteins amyloid-beta and tau in the brain, developing into structures called plaques and tangles. These interfere with the normal functioning of, and cause damage to, brain cells, ultimately leading to the clinical symptoms of the condition.

- Anti-coagulation and thrombolysis should be avoided in patients on lecanemab except for immediately life-threatening indications with no alternative management and where the benefits outweigh the risks.
- Suspected adverse drug reactions should be reported to the MHRA through the Yellow Card scheme and to Eisai.

Lecanemab

Alzheimer's disease (AD) is the most common cause of dementia. Lecanemab is the first Disease Modifying Treatment for AD to have been licensed for use in Great Britain. This monoclonal antibody-based treatment targets amyloid plaques in the brain. Lecanemab modestly slows the pace of decline in those experiencing the earliest symptomatic stages of the disease (mild cognitive impairment, or mild dementia, associated with AD). The drug is administered intravenously every 2 weeks, with regular MRIs required as part of treatment safety monitoring. If tolerated, treatment can continue until a patient has progressed from mild to moderate AD.

NICE draft guidance consultation

NICE's draft recommendation (to be finalised following a period of formal consultation) is that lecanemab should *not* be routinely offered in the NHS, based on an assessment of the drug's clinical and cost-effectiveness. However, the manufacturer has advised that lecanemab will be made available to independent sector clinics.

Responsibilities of the independent sector provider

All planned elements of care specific to privately or self-funded lecanemab treatment should be provided and funded outside of the NHS. This includes, but is not limited to, clinical consultations, additional tests or investigations over and above routine Alzheimer's care, drug costs, infusion clinic attendance and planned treatment monitoring / scanning. Whilst patients (and independent sector clinics) are encouraged to advise NHS clinicians about the initiation of lecanemab treatment, NHS services should not be asked, nor agree to provide, these routine elements of the lecanemab treatment pathway (in the absence of a positive NICE recommendation on routine use in the NHS). The NHS would, however, be expected to provide and fund any unplanned / emergency elements of care, including the acute management of potential adverse treatment effects. This includes the management of symptomatic Amyloid-Related Imaging Abnormalities (ARIA).

What is ARIA?

ARIA reflects swelling in one or more areas of the brain (ARIA-E for o**e**dema), or small spots of bleeding in or on the surface of the brain (ARIA-H for **h**aemorrhage). Treatment with lecanemab increases the risk of ARIA. Whilst most ARIA is discovered incidentally on routine brain scans, does not cause any symptoms and may be managed by the patient's private provider, in a small number of patients serious symptoms can occur. Clinically, symptomatic ARIA can present as a new onset of confusion, headache, dizziness and nausea (Vukmir, 2024). The most severe manifestations can include seizures, focal neurological deficits and reduced level of consciousness; these symptoms can mimic other pathologies such as stroke. It is these acute presentations that are most likely to need to be managed (and funded) by the NHS.

Approach to symptomatic ARIA

Clinicians involved in the management of patients receiving lecanemab are encouraged to access the guide for healthcare practitioners published by the medicine manufacturer, Eisai. Patients initiated on lecanemab should have also received a patient information leaflet and have been encouraged to carry a patient alert card.

If ARIA is suspected following history taking and examination, immediate advice from a radiologist on appropriate MRI imaging techniques should be sought. CT scans can be inconclusive, particularly in detecting subtle ARIA-E or microhaemorrhages due to ARIA-H.

However, if MRI is unavailable, CT brain can be performed in an emergency scenario as it should identify life-threatening oedema or haemorrhage. Close neurological monitoring should be established. Administration of corticosteroid therapy should be considered (Salloway et al., 2022). Dosing with lecanemab (see summary of product characteristics) should be suspended until ARIA has been ruled in or out and the severity determined.

If a patient is on lecanemab, anti-coagulation should be avoided due to the increased risk of causing or exacerbating intracerebral haemorrhage (Vukmir, 2024), particularly in the context of suspected or confirmed ARIA. Use of thrombolytic agents, for example for the treatment of acute ischaemic stroke, should be avoided in patients on lecanemab, particularly with suspected or confirmed ARIA – except for immediately life-threatening indications with no alternative management and where the benefits outweigh the risks.

Suspected adverse drug reactions should be reported to the MHRA through the Yellow Card scheme. Adverse events should also be reported to Eisai Ltd on 0208 600 1400 or EUmedinfo@eisai.net

V1.0 1st November 2024

References

Salloway, S. *et al.* (2022) 'Amyloid-Related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease,' *JAMA Neurology*, 79(1), p. 13. https://doi.org/10.1001/jamaneurol.2021.4161.

Vukmir, R.B. (2024) 'Amyloid-related imaging abnormalities (ARIA): diagnosis, management, and care in the setting of amyloid-modifying therapy,' *Annals of Clinical and Translational Neurology*, 11(7), p. 1669–1680. https://doi.org/10.1002/acn3.52042.