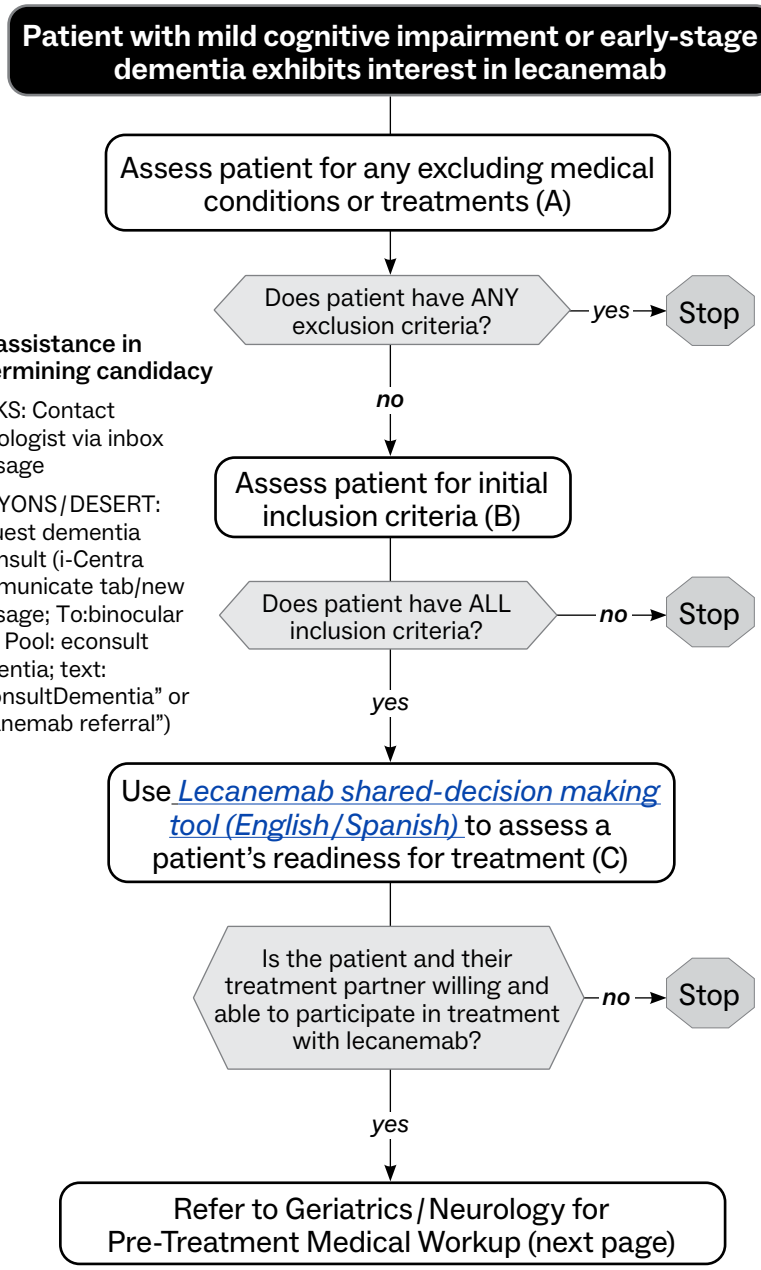
Leqembi (lecanemab-irmb)

Criteria, treatment, and management of ARIA

This guideline was developed by Intermountain's Neurosciences Clinical Program in collaboration with Pharmacy, Imaging, Primary Care, Geriatrics, Neurology, and Telehealth. It includes clinical workflows and considerations to help healthcare professionals identify patients who are eligible for treatment with lecanemab and manage potential side effects such as amyloid-related imaging abnormalities (ARIA) during treatment.

Preliminary Screening (Primary Care)



For assistance in determining candidacy

PEAKS: Contact neurologist via inbox message

CANYONS/DESERT: Request dementia e-consult (i-Centra communicate tab/new message; To:binocular icon; Pool: econsult dementia; text: ".econsultDementia" or "lecanemab referral")

(A) Lecanemab Exclusion Criteria

If the patient has ANY of the previously diagnosed conditions or is currently receiving any of the following treatments, they should NOT receive lecanemab.

Previously Diagnosed Medical Conditions

- ☐ Medical, neurological, and/or behavioral health conditions that may contribute to or cause cognitive impairment
- ☐ TIA, stroke, or seizure in the past 12 mos.
- ☐ Uncontrolled epilepsy
- ☐ Inherited disorders of cognition (e.g. Down's syndrome, Huntington's disease, Autosomal dominant alzheimer's disease)
- ☐ Uncontrolled sleep apnea
- ☐ Uncontrolled immunological disease
- ☐ Untreated HIV
- ☐ Bleeding disorders
- ☐ Major depressive disorder outside of maintenance phase
- ☐ Active suicidality or hospitalization with suicidal behavior within the last 5 years
- ☐ Active substance abuse disorder

Medical Treatments

- ☐ Anticoagulation
- ☐ Chemotherapy
- ☐ Immunotherapy including: IVIG, monoclonal antibodies or immunosuppression (steroids are not considered exclusionary)
- ☐ Plasmapheresis
- ☐ Implanted device that contraindicates urgent MRI scan (e.g. pacemaker, vagus or spinal cord stimulator)

B) Lecanemab Inclusion Criteria

Patient must have ALL of the following to be treated with lecanemab.

- ☐ Clinical presentation consistent with MCI or early-stage dementia
- ☐ Slowly progressive cognitive decline which is not attributable to another medical condition
- ☐ MoCA between 16 and 25 (patient can complete cognitive testing)
- ☐ Age between 50 and 90
- ☐ BMI between 17 and 35
- ☐ Patient is able to undergo urgent MRI scan (no pacemaker, vagus or spinal cord stimulator, etc.)

C) Shared decision discussion points

- ☐ Treatment partner required
- ☐ Participation in additional testing including lumbar puncture, genetic testing, and MRI scans
- ☐ Attend infusion treatments every two weeks
- ☐ Attend monitoring MRI scans of the brain
- ☐ Understand the risks of lecanemab therapy including:
  - Amyloid-related imaging abnormalities (ARIA) risk
  - Impact on future medication (thrombolytics)
  - Cost uncertainties (drug, infusion, imaging)

These guidelines apply to common clinical circumstances, and may not be appropriate for certain patients and situations. The treating clinician must use judgment in applying guidelines to the care of individual patients.

Pre-Treatment Medical Workup (Geriatrics / Neurology + Navigator)

Intermountain providers (all regions): Contact nurse navigators at (844) 444 – 0019 before beginning pre-treatment medical workup.

Geriatric / Neurology Provider		Exclusion Parameters
Order base-line MRI	Epic: *MRI Brain Amyloid Baseline* iCentra: *Brain Amyloid/Alzheimer's Imaging Baseline* Brain Amyloid/Alzheimer's Imaging Baseline Assessment PowerPlan	• >4 microhemorrhages (≤10 mm at greatest diameter) • ≥1 macrohemorrhage (>10 mm at greatest diameter) • Superficial siderosis • >2 lacunar infarcts or large vessel stroke • Small vessel disease with Fazekas score of 3 • Aneurysm or vascular malformation • Acute/subacute findings which may account for cognitive presentation (vasogenic edema, acute/subacute stroke, acute/subacute cerebral contusion, infectious lesion, space-occupying lesions)
Order Genetic Screening for Apolipoprotein E (APOE) allele	Epic:[580820] Apolipoprotein E (APOE) Genotyping, Alzheimer's Disease risk (ARUP) iCentra: APOE (Apolipoprotein E (APOE) Genotyping, Alzheimer Disease risk (ARUP))	Consider exclusion if patient is homozygous for APOE ε4. APOE ε4 homozygotes have a significantly higher risk of symptomatic and serious ARIA. Discuss with patient.
Order Amyloid Plaque Visualization (CSF lumbar puncture)	Epic: *Lumbar Puncture Panel* iCentra: *XR Lumbar Puncture Amyloid Protocol* Epic:[523286] Alheimer's Disease Markers, CSF iCentra: ADMCSF [Alzheimer's Disease Markers, CSF (ARUP)]	No amyloid plaque present

In iCENTRA, all orders for the pre-treatment medical workup (Baseline-MRI, APOE, and Amyloid-CSF) can be placed simultaneously by using the PowerPlan: *RAD - Brain/Amyloid Alzheimer's Imaging Baseline Assessment*

Nurse Navigator		
Schedule medical work-up at one of the following Intermountain facilities: • Intermountain medical center; Murray, UT • Lutheran Medical Center; Wheat Ridge, CO (LP and infusion only) • McKay-Dee Hospital; Ogden, UT • Saint Joseph Hospital; Denver, CO		• St. George Regional Hospital; St. George, UT • St. Mary's Medical Center; Grand Junction, CO • St. Vincent Regional Hospital; Billings, MT • Utah Valley Hospital; Provo, UT
Schedule Base-line MRI	**Peaks** Lutheran:(303) 403-7871 Saint Joseph: (303) 812-3344 St. Mary's: (303) 298-6900 St. Vincent: (406) 237-4373 **Canyons/Desert** R1 scheduling (801) 906-2700	• Schedule base-line MRI on a 3T machine that can be utilized on all future follow-up MRIs. • Baseline MRI should occur before LP for amyloid plaque visualization, though it can occur the same day. • Advise patient to stop multi-vitamins or any supplements containing biotin (B7) 12 hours before MRI and LP. • MRIs occurring after the LP must occur >24 hrs after LP.
Amyloid Plaque Visualization using CSF lumbar puncture	• Schedule LP – Verify you have correct collection tube: ARUP supply #58810. Call lab if needed. – Refer to *Alzheimer's Disease Markers, CSF | ARUP Laboratories Test Directory for specimen collection instructions.* • Schedule a separate lab draw for APOE; CSF requires its own blood panel for CSF oligoclonal banding;	

Post Medical Workup

- Counsel with patient based on results.
- Shared decision making on whether to proceed. See *Lecanemab shared-decision making tool (English/Spanish)*

Preparing for Treatment

Providers	
Order lecanemab Leqembi (lecanemab-irmb) prescribing information	• Epic:Lecanemab (Leqembi) for Mild Cognitive Impairment or Mild Alzheimer's Disease-related Dementia • iCentra: INF Adult Leqembi (add medical action plan to flag ED with critical note warning)
	Orders for amyloid work-up or therapy should include ≥1 of the following ICD 10 codes • G30.0 Alzheimer's disease with early onset • G30.1 Alzheimer's disease with late onset • G30.8 Other Alzheimer's disease • G30.9 Alzheimer's disease unspecified • G31.84 Mild Cognitive Impairment, so stated
Obtain patient's formal consent	*Intermountain Informed Consent (English)/(Spanish)*
Nurse Navigators	
Enroll patient in CMS registry	CMS *Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease CED Study Registry*. Items needed for enrollment : • National Provider Identifier (NPI) • Medicare Beneficiary ID (MBI) • Provider contact info, (physical/email) • Clinical Dx: MCI due to AD or early dementia due to AD • Date of Clinical Dx • Amyloid testing dates and results • Cognitive tests and date: MoCA, other • Functional test: *FAQ test* or other • Clinical Dementia Rating (CDR) (optional) • Anticoagulation/antiplatelet status • Date of ARIA-E or ARIA-H occurrence
Schedule lecanemab infusion every two weeks at authorized center. Note: Pharmacy will need to order drug. Allow a few days for delivery. Preauthorization is required for treatment.	• Intermountain Medical Center Infusion Center (801-507-3980) • Lutheran Cancer Center (303) 403–3611 • McKay-Dee Infusion Center (801) 387–5265 • Saint Joseph Cancer Center (303) 318–3434 • St. George Infusion Center (435) 251–4600 • St. Mary's Infusion Center (970) 298–7500 • St. Vincent Neuro Infusion Center (406) 237–5581 • Utah Valley Infusion Center (801) 357–7341
Provide patient wallet card	• Give patients *Lecanemab (Leqembi®) Med Card (English)/(Spanish)* to present to emergency department in case of stroke symptoms.

Monitoring during Lecanemab Treatment

Providers	Notes
Order monitoring MRIs 1,2,and 3	• Epic: MRI Brain Amyloid • iCentra: MRI Brain Amyloid on Therapy
If patient or caregiver report signs and symptoms of ARIA	• If mild signs or symptoms, perform follow-up MRI. • If stroke-like signs or symptoms, perform Emergency MRI. • Do not administer thrombolytics. See Management of ARIA (next page)
Ongoing treatment and follow-up	• Depending on clinical response, lecanemab may be continued > 18 mos.
Nurse Navigator	**Notes**
Schedule monitoring MRIs 1,2,and 3	• MRIs should be conducted: – Between infusion 4 and 5 – Between infusions 6 and 7 – Between infusion 13 and 14 Additional imaging procedures may be needed. The amyloid-specific orderable codes must be used to drive imaging protocols and locations. • Ensure follow-up MRIs are performed on same machine, reschedule MRI's as needed. • If an MRI is not performed prior to the 5th, 7th, or 14th infusion, it is essential to delay these infusions until the MRI is obtained. • Regular MRI monitoring should continue for as long as the patient remains on lecanemab. After the initial 14 weeks, the frequency of MRI scans should be determined based on clinical judgement.
Fill out dose and imaging spreadsheet	• Every two weeks through infusion 14, to ensure scheduled tests/infusion have occurred.
Have patient and their caregivers monitor for clinical signs of ARIA	• Review signs of bleeding or swelling in the brain found in *Lecanemab shared-decision making tool (English/Spanish)* with patients and their caregivers.
Update CMS lecanemab registry every 6 months	*Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease CED Study Registry*

Management of amyloid-related imaging abnormalities (ARIA)

Classify ARIA Type and Severity			
ARIA Type	**Radiographic Severity**		
	Mild	**Moderate**	**Severe**
ARIA-E (edema & effusion)	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 (microhemorrhage)	≤4 new incident microhemorrhages	5–9 new incident microhemorrhages	≥10 new incident microhemorrhages
ARIA-H (superficial siderosis)	1 focal area of superficial siderosis	2 focal areas of superficial siderosis	>2 focal areas of superficial siderosis

FLAIR- Fluid-attenuated inversion recovery. Leqembi (lecanemab-irmb) prescribing information Table 3. ARIA MRI Classification Criteria (https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=77aa4a86-b786-457a-b894-01de37199024) Accessed 12/27/23

Dosing Recommendations for Patients with ARIA-E			
Clinical Symptoms Severity	**Radiographic Severity of ARIA-E on MRI**		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing	Suspend dosing	Suspend dosing
Mild Discomfort noticed, but no disruption of daily activity	May continue dosing based on clinical judgement		
Moderate or Severe Moderate: discomfort sufficient to reduce or affect normal daily activity Severe: incapacitating, with inability to work or perform normal daily activity	Suspend dosing		

Leqembi (lecanemab-irmb) prescribing information Table 1. Dosing Recommendations for Patients with ARIA-E (https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=77aa4a86-b786-457a-b894-01de37199024) Accessed 12/27/23

Dosing Recommendations for Patients with ARIA-H			
Clinical Symptoms Severity	**Radiographic Severity of ARIA-H on MRI**		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing	Suspend dosing	Suspend dosing
Symptomatic	Suspend dosing		

Leqembi (lecanemab-irmb) prescribing information Table 2. Dosing Recommendations for Patients with ARIA-H (https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=77aa4a86-b786-457a-b894-01de37199024) Accessed 12/27/23

After Suspended Dosing of Lecanemab	
Continue monitoring symptoms	Do not restart lecanemab until symptoms resolve
Perform monthly MRIs until ARIA resolves	Do not restart lecanemab until radiographic stabilization
Use clinical judgement and shared decision making to determine whether to continue treatment or permanently discontinue lecanemab	