These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Amyloid Beta Directed Therapies: Lecanemab-irmb (Leqembi) and Donanemab-azbt (Kisunla) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy and/or URAC Specialty Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG029
Effective: 3/24/2023
Reviewed: 6/1/2025
Revised: 6/1/2025
Approved by: Kathleen Patrick, President, 3/24/23, 6/1/25

I. BACKGROUND

Lecanemab-irmb (Leqembi) and donanemab-azbt (Kisunla) are amyloid beta-directed therapies used in the treatment of Alzheimer's disease. They target a human, immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. These medications should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. Alzheimer's disease is a neurodegenerative disorder characterized by a number of neuropathological changes, including accumulation of amyloid-β (Aβ) plaques. Lecanemab-irmb and donanemab-azbt selectively target and reduce soluble and insoluble Aβ in the brain in a dose-dependent manner. The following defines specific guidelines that will ensure the safe and effective use and administration of parenteral beta amyloid directed therapies.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. Confirm the presence of amyloid beta pathology prior to treatment initiation and evidence of mild cognitive impairment (MCI) or mild dementia. Safety and efficacy when initiating treatment in earlier or later disease stages have not been established.

C. The decision to administer a first doses in the home or ambulatory infusion suite will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age
4. Other relevant social and/or medical history

D. Physician orders must include:

1. Drug and dose
2. Route of administration
3. Frequency of administration
4. Emergency medications
5. Orders for pre-medications
6. Line care protocol
7. Routine lab monitoring, if applicable

E. Baseline labs or tests prior to starting therapy:

1. Recent MRI scan within the last year of initiating treatment.
2. Apolipoprotein E ε4 (ApoE ε4) genetic testing is recommended to determine the risk of amyloid related imaging abnormalities (ARIA).

F. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*).

III. PHARMACOLOGIC OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information.

A. Indications: Treatment of Alzheimer's disease (mild cognitive impairment or mild dementia stage)

B. Dosing:

1. Lecanemab: 10 mg/kg of actual body weight every 2 weeks with no titration schedule. After 18 months, the 10mg/kg every 2 weeks may be continued, or the patient may transition to a frequency of every 4 weeks.

2. Donanemab: 700 mg every four weeks for three doses, then 1400 mg every four weeks

IV Infusion (every 4 weeks)	Donanemab Dosage
Infusions 1, 2, and 3	700 mg
Infusion 4 and beyond	1,400 mg

1. Dosing is based off actual body weight. Amyloid beta-directed therapies have not been studied in extremes of body weights.

C. Dose Adjustments:

1. Doing Recommendations for renal or hepatic impairment: Currently, there are no dosage adjustments for renal or hepatic impairment.

2. Dosing Recommendations for Patients with ARIA-E (for both lecanemab and donanemab):

Clinical Symptom Severity[1]	ARIA-E Severity on MRI		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing	Suspend dosing[2]	Suspend dosing[2]
Mild	May continue dosing based on clinical judgment	Suspend dosing[2]	
Moderate or Severe	Suspend dosing[2]		

[1] Mild: discomfort noticed, but no disruption of normal daily activity.
Moderate: discomfort sufficient to reduce or affect normal daily activity.
Severe: incapacitating, with inability to work or to perform normal daily activity.
[2] Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; consider a follow-up MRI to assess for resolution 2 to 4 months after initial identification. Resumption of dosing should be guided by clinical judgment.

1. Dosing Recommendations for Patients with ARIA-H (for both lecanemab and donanemab)

Clinical Symptom Severity	ARIA-H Severity on MRI		
	Mild	**Moderate**	**Severe**
Asymptomatic	May continue dosing	Suspend dosing[1]	Suspend dosing[2]
Symptomatic	Suspend dosing[1]	Suspend dosing[1]	

[1] Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment; consider a follow-up MRI to assess for stabilization 2 to 4 months after initial identification.
[2] Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; use clinical judgment in considering whether to continue treatment or permanently discontinue LEQEMBI.

D. Duration: Duration of therapy is dependent on patient response and adverse reactions.

E. Contraindications: Both lecanemab and donanemab are contraindicated in patients with known hypersensitivity to either drug or to any of the excipients.

F. Warning/Precautions:

1. **Amyloid related imaging abnormalities** - edema (ARIA-E), which can be observed on MRI as brain edema or sulcal effusions, and **amyloid related imaging abnormalities hemosiderin deposition** (ARIA-H), which includes micro hemorrhages.

   a. Enhanced clinical vigilance for ARIA is recommended during the first several doses of treatment and during titration.

      1) Lecanemab: obtain baseline brain MRI and MRIs prior to the 5th, 7th, and 14th infusions.
      2) Donanemab: obtain baseline brain MRI and MRIs prior to the 2nd, 3rd, 4th, and 7th infusions

ARIA Type	Radiographic 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 to 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	Less than or equal to 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more new incident microhemorrhages
ARIA-H superficial siderosis	1 new[a] focal area of superficial siderosis	2 new focal areas of superficial siderosis	Greater than 2 new focal areas of superficial siderosis

[a] Includes new or worsening superficial siderosis.

b. Seizure, including status epilepticus, which can be serious and life-threatening, has been associated with ARIA.
c. If a patient experiences symptoms that could be suggestive of ARIA, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrate radiographic stabilization (i.e., no increase in size or number of ARIA-H).
d. The risk of developing ARIA is increased in patients with apolipoprotein E ε4 (ApoE ε4) homozygotes. About 15% of patents with Alzheimer's disease are ApoE ε4 homozygotes. Testing for ApoE ε4 is recommended to be completed prior to starting therapy to inform the risk of developing ARIA.

2. Hypersensitivity and Infusion Reactions

a. Hypersensitivity reactions including angioedema and urticaria were reported during clinical trials. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate emergency kit therapies per protocol.
b. Infusion reactions: The majority (75%) of infusion related reactions occurred within the first lecanemab infusion. The majority of infusion related reactions with donanemab occurred within the first four infusions. Infusion related reactions with both therapies were mild to moderate in nature. Signs and symptoms of infusion related reactions include fever and flu-like symptoms, chills, general aches, nausea, vomiting, hypotension, hypertension, erythema, headache, and chest pain.

3. Pregnancy and Lactation

a. There are no adequate data on amyloid beta-directed therapies used in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.
b. There are no data on the presence of amyloid beta-directed therapies in human milk, the effects on the breastfed infant, or the effects of the drug on milk production.

G. Pharmacokinetics

1. Volume of distribution:

a. Lecanemab: 3.24 L
b. Donanemab: 3.36 L

2. Metabolism: Lecanemab and donanemab are both degraded by proteolytic enzymes
3. Half-life:

    a. Lecanemab: 5-7 days
    b. Donanemab: 12.1 days

H. Adverse Reactions

1. Hypersensitivity: hypersensitivity related reaction (3% with donanemab), infusion-related reaction (9-26%)
2. Nervous system: Headache (11-14%), Brain edema [ARIA-E, including sulcal effusion (10-24%)], altered mental status, confusion, delirium, disorientation.
3. Cardiovascular: Atrial fibrillation (3% lecanemab)
4. Dermatologic: Urticaria (6% lecanemab)
5. Gastrointestinal: Diarrhea (8% lecanemab), nausea and vomiting (6% lecanemab)
6. Hematologic & oncologic: Hemosiderosis [ARIA-H, including microhemorrhage and superficial siderosis (6-31%)], lymphocytopenia (38% lecanemab), neutropenia (22% lecanemab).
7. Respiratory: Cough (9% lecanemab)

I. Drug Interactions: drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMIMISTRATIVE GUIDELINES

A. Administration: IV infusions should be given immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. A low protein binding **0.2 micron in line filter** is required for administration of lecanemab.

C. Do not co-administer with other products in the same IV line

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. IV access supplies as applicable

    a. Peripheral IV access supplies for patients requiring peripheral IV access
        1. IV start Kit
        2. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
        3. Extension set 8" with needless connector

    b. Port access supplies for patients with a port
        1. Port needle (ex. 22 Gauge x ¾ to 1" safe step)
        2. Needless connector
        3. Central line dressing change kit

c. IV pole
d. IV administration set (flow regulator or gravity tubing) with in line or add-on 0.2-micron filter
e. Syringes (10-50mL) with needles (20 G x 1")
f. Sharps container

B. Prescription items:

1. Lecanemab-irmb drug or donanemab-azbt vial(s)
2. 0.9% Sodium Chloride stock bag [100mL (donanemab), 250 mL (lecanemab and higher donanemab dose)] dilution bag
3. 0.9% Sodium Chloride Injection 50 mL post-infusion flush bag (lecanemab)
4. Standard flushes per protocol
5. Anaphylaxis kit per protocol

C. How Supplied:

1. Lecanemab: Preservative-free, sterile, clear to opalescent, and colorless to pale yellow solution in 100 mg/mL concentration available as 2 or 5 mL single-dose vials.

2. Donanemab: Preservative-free, sterile clear to opalescent, colorless to slightly yellow to slightly brown solution. Donanemab supplied in one vial per carton as follows: 350 mg/20 mL (17.5 mg/mL) single-dose vial.

D. Storage and Handling:

1. Store in original carton until use to protect from light
2. Store in a refrigerator at 2°C to 8°C (36°F to 46°F)
3. Do not freeze or shake

E. Compatibility:

1. Dilution with 0.9% Sodium Chloride for both lecanemab and donanemab.
2. No compatibility tests for other intravenous agents currently exist.

F. Procedures:

1. Explain the reasoning for visit and use of lecanemab or donanemab.
2. Don gloves.
3. Establish venous access prior to preparation of drug.
4. Counsel patient on warnings, precautions, and potential side effects including but not limited to: ARIA-E, ARIA-H, infusion reactions, neurologic adverse effects including delirium, falls, and altered mental status, and atrial fibrillation.
5. Prepare Product

a. Lecanemab:

1) Calculate the dose (mg), the total volume (mL) of solution required, and the number of drug vials needed based on the patient's actual body weight and the dose ordered.

2) Visually inspect drug vial for particulate matter and discoloration prior to administration to ensure solution is clear to opalescent and colorless to pale yellow. Do not use if opaque particles, discoloration, or other foreign particles are present.
3) Remove the flip-off cap from the vial. Insert the sterile syringe needle into the vial through the center of the rubber stopper.
4) Withdraw the required volume from the vial(s) and add to an infusion bag containing 250 mL of 0.9% Sodium Chloride Injection, USP. Discard any remaining contents of the drug vial.
5) Gently invert the infusion bag containing the diluted solution to mix completely. Do not shake.

b. Donanemab:

1) Withdraw an appropriate amount of saline from stock bag. For the 700 mg dose, utilize a 100 mL 0.9% sodium chloride stock bag. Remove 20-40mL of 0.9% sodium chloride from 100 mL bag and discard. For the 1400 mg dose, utilize a 250 mL 0.9% sodium chloride diluent bag. Remove 60-80mL of 0.9% sodium chloride from 250 mL bag and discard.
2) Visually inspect drug vial for particulate matter and discoloration prior to administration to ensure solution is clear to opalescent, colorless to slightly yellow to slightly brown.
3) Withdraw required volume of donanemab and add to the 0.9% sodium chloride bag to the recommended total volume for a final concentration of 4 mg/mL to 10 mg/mL.

Donanemab dose (mg)	Donanemab volume (mL)	Volume of 0.9% Sodium Chloride Injection Diluent (mL)	Final Volume of Diluted Solution to be Infused (mL)	Final Concentration of Diluted Solution (mg/mL)
700 mg	40 mL	30 to 135 mL	70 to 175 mL	700mg /175 mL (4mg/mL) to 700mg/70 mL (10mg/mL)
1,400 mg	80 mL	60 to 270 mL	140 mL to 350 mL	1400mg/350 mL (4mg/mL) to 1400 mg/140mL (10mg/mL)

4) Gently invert the infusion bag containing the diluted solution to mix completely. Do not shake.

6. Infusion Rates:

a. Lecanemab: Infuse diluted solution over one hour.
b. Donanemab: Infuse diluted solution over 30 minutes

7. Post infusion flush: After administration of lecanemab or donanemab, flush the entire administration tubing with 0.9% Sodium Chloride Injection to ensure all of the medication is administered. Spike the 50mL 0.9% Sodium Chloride Injection bag and administer the flush at the same rate as the infusion of lecanemab or donanemab.

8. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete

IV. CLINICAL MONITORING

A. Prior to therapy

1. Confirmation of the presence of amyloid beta pathology
2. Baseline MRI
3. Apolipoprotein E ε4 (ApoE ε4) genetic testing

B. During therapy

1. Signs and symptoms of disease progression
2. Signs and symptoms of hypersensitivity reactions
3. Signs and symptoms suggestive of amyloid-related imaging abnormalities (ARIA) (e.g., headache, altered mental status, dizziness, visual disturbance, seizure, nausea)
4. Brain MRI Imaging

    a. Lecanemab: Obtain an MRI prior to the 5th, 7th, and 14th infusions
    b. Donanemab: Obtain an MRI prior to the 2nd, 3rd, 4th, and 7th infusions

Please refer to the package insert for the most up to date guidance on this medication.

REFRENCES

Leqembi (lecanemab) [prescribing information]. Nutley, NJ: Eisai Inc; January 2023.

Kisunla (donanemab-azbt) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; July 2024.

United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

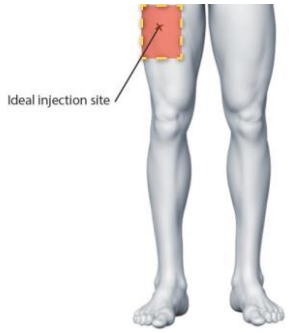
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampule.**
3. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**
5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampule.

9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

Call 911 or have someone drive you to the emergency department.