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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.

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GUIDELINES FOR IN-HOME INTRAVENOUS AMYLOID BETA-DIRECTED THERAPIES

Section: Nursing
Compliance: ACHC Infusion Pharmacy and/or URAC Specialty Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: NUR260
Effective: 3/24/23
Reviewed:
Revised:
Approved by: Kathleen Patrick, President, 3/24/23

I. BACKGROUND

Leqembi (Lecanemab-irmb) and Aduhelm (Aducanumab-avwa) are amyloid beta-directed therapies used in the treatment of Alzheimer disease (AD). They both 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. AD is a neurodegenerative disorder characterized by a number of neuropathological changes, including accumulation of amyloid-β (Aβ) plaques. Lecanemab-irmb and Aducanumab-avwa 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 Lecanemab-irmb and Aducanumab-avwa.

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.

C. All patients should receive the initial dose in a controlled setting due to the high incidence of infusion and anaphylaxis reactions. Appropriateness of subsequent doses for home administration will be reviewed. Date of prior infusion should be provided.

D. First dosing in the home should be avoided due to associated risk and potential side effects. The decision to administer subsequent doses in the home by a home infusion nurse 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 ≥18 years

4. 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.
5. Other relevant social and/or medical history

E. 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

F. Baseline labs or tests prior to starting therapy.
1. Recent MRI scan within the last year of initiating treatment

G. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGIC OVERVIEW

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

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

B. Dosing
1. Lecanemab-irmb
a. 10 mg/kg of actual body weight every 2 weeks with no titration schedule
2. Aducanumab-avwa
a. Initial titration is described in the table below. After titration schedule, infusions 7 and thereafter are 10mg/kg of actual body weight every 4 weeks and at least 21 days apart.

IV Infusion (every 4 weeks)	Aducanumab Dosage
Infusion 1 and 2	1 mg/kg
Infusion 3 and 4	3 mg/kg
Infusion 5 and 6	6 mg/kg
Infusion 7 and beyond	10 mg/kg

3. 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
a. Currently, there are no dosage adjustments for renal or hepatic impairment.
2. Dosing Recommendations for Patients with ARIA-E

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.

1. Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment.

a. Aducanumab-avwa

b. Lecanemab-irmb

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.

3. Dosing Recommendations for Patients with ARIA-H
   a. Aducanumab-avwa

Clinical Symptom Severity	ARIA-H Severity on MRI		
	Mild	Moderate	Severe
Asymptomatic	May continue dosing at current dose and schedule	Suspend dosing[1]	Suspend dosing[2]
Symptomatic	Suspend dosing[1]	Suspend dosing[1]	

1. Suspend until MRI demonstrates radiographic resolution and symptoms, if present, resolve; resumption of dosing should be guided by clinical judgment.
2. Suspend until MRI demonstrates radiographic stabilization and symptoms, if present, resolve; use clinical judgment in considering whether to continue treatment or permanently discontinue ADUHELM.

   b. Lecanemab-irmb

D. Contraindications
   1. None

E. Warning/Precautions
1. Amyloid Related Imaging Abnormalities
a. 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.

ARIA Type	Radiographic Severity		
	Mild	Moderate	Severe
ARIA-E	FLAIR hyperintensity confined to sulcus and or cortex/subcortical white matter in one location < 5 cm	FLAIR hyperintensity 5 to 10 cm, or more than 1 site of involvement, each measuring < 10 cm	FLAIR hyperintensity measuring > 10 cm, often with significant subcortical white matter and/or sulcal involvement. One or more separate sites of involvement may be noted.
ARIA-H microhemorrhage	≤ 4 new incident microhemorrhages	5 to 9 new incident microhemorrhages	10 or more 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

b. Enhanced clinical vigilance for ARIA is recommended during the first several doses of treatment and during titration
i. Aducanumab-avwa - obtain baseline brain MRI and MRIs prior to the 5th infusion (first dose of 6 mg/kg), 7th infusion (first dose of 10mg/kg), 9th infusion (third dose of 10 mg/kg), and 12th infusion (sixth dose of 10 mg/kg)
1) Events of intracerebral hemorrhage greater than 1 cm in diameter have been reported infrequently in patients taking Aducanumab-avwa and use of antithrombotic or thrombolytic medications while taking tis medication may increase the risk of bleeding in the brain.
ii. Lecanemab-irmb - obtain baseline brain MRI and MRIs prior to the 5th, 7th, and 14th infusions
c. Seizure, including status epilepticus, which can be serious and life-threatening, has been associated with ARIA.
d. 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 demonstrates radiographic stabilization (i.e., no increase in size or number of ARIA-H)
2. Infusion-Related 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.
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.

F. Pharmacokinetics
    1. Half-life
        a. Aducanumab-avwa ~ 25 days
        b. Lecanemab-irmb ~ 5-7 days
    2. Vd
        a. Aducanumab-avwa ~ 9.63 L
        b. Lecanemab-irmb ~ 3.22 L

G. Adverse Reactions
    1. Hypersensitivity: Infusion-related reaction, Angioedema
    2. Nervous system: Headache, Brain edema (ARIA-E, including sulcal effusion), Seizure (associated with ARIA), Altered mental status, confusion, delirium, disorientation, falling
    3. Cardiovascular: Atrial fibrillation
    4. Dermatologic: Urticaria
    5. Gastrointestinal: Diarrhea
    6. Hematologic & oncologic: Hemosiderosis (ARIA-H, including microhemorrhage and superficial siderosis), lymphocytopenia
    7. Immunologic: Antibody development
    8. Respiratory: Cough

H. Drug Interactions
    1. Efgartigimod Alfa: May diminish the therapeutic effect of Fc Receptor-Binding Agents

IV. ADMIMISTRATIVE GUIDELINES

A. Administration
    1. Dilution required prior to administration. Administer by IV infusion over 60 minutes through an IV line with a **sterile, low-protein binding, 0.2 micron in-line filter**. Discard unused portion.
    2. IV infusions should be given immediately after dilution. Use within 1 hour of preparation per current USP Immediate-Use Guidelines.

B. Duration
    1. Duration of therapy should be dependent on patient response and adverse reaction. No specific duration is noted in package insert.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
    1. Alcohol Swabs
    2. Gloves
    3. Tape
    4. Port Access Needle (Ex: 22 Gauge x ¾" Safe-step)
    5. IV Pole
    6. IV injection cap
    7. Dressing change kit
    8. Extension set 8"
    9. IV administration set with 0.2-micron filter

10. IV start kit for peripheral line
11. IV peripheral catheter (Ex: 24 Gauge x ¾" or 22 Gauge x 1")
12. Syringes with needles
13. Sharps container

B. Prescription items:
    1. Aducanumab-avwa or Lecanemab-irmb drug vial(s)
    2. 0.9% Sodium Chloride Injection (100mL for Aducanumab-avwa or 250 mL for Lecanemab-irmb) dilution bag
    3. 0.9% Sodium Chloride Injection (50 mL) post-infusion flush bag

C. How Supplied
    1. Aducanumab-avwa
        a. Preservative-free, sterile, clear to opalescent, and colorless to yellow solution in 100 mg/mL concentration available as 1.7 or 3 mL single-dose vials
    2. Lecanemab-irmb
        a. 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

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
    4. Aducanumab-avwa
        a. If no refrigeration is available Aducanumab-avwa may be stored unopened in its original carton to protect from light at room temperature up to 25°C (77°F) for up to 3 days

E. Compatibility
    1. Dilution with 0.9% Sodium Chloride
    2. No compatibility tests for other intravenous agents currently exist

F. Procedures: Preparation of the product, Infusion rates, post infusion monitoring time
    1. Explain the reasoning for visit and use of Aducanumab-avwa or Lecanemab-irmb.
    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. 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.
        b. 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.
        c. Remove the flip-off cap from the vial. Insert the sterile syringe needle into the vial through the center of the rubber stopper.
            i. Aducanumab-avwa
                1) Withdraw the required volume from the vial(s) and add to an infusion bag of 100 mL of 0.9% Sodium Chloride Injection, USP. Discard any remaining contents of the drug vial.

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

ii. Lecanemab-irmb

1) 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.
2) Gently invert the infusion bag containing the diluted solution to mix completely. Do not shake.

d. Infusion Rates

i. Infuse diluted solutions over approximately one hour.

6. Post infusion monitoring
    a. The package insert does not specify post-infusion monitoring time. Refer to policy NUR002.

G. CLINICAL MONITORING

Assessment/Clinical Monitoring: Therapy or disease-specific assessment and monitoring prior to subsequent refills; standardized question sets or telehealth tools may be incorporated.

A. Prior to therapy
    1. Confirmation of the presence of amyloid beta pathology
    2. Baseline MRI

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. Aducanumab-avwa
            i. Obtain brain MRIs prior to the 5th infusion (first dose of 6 mg/kg), 7th infusion (first dose of 10mg/kg), 9th infusion (third dose of 10 mg/kg), and 12th infusion (sixth dose of 10 mg/kg)
        b. Lecanemab-irmb
            i. Obtain an MRI prior to the 5th, 7th, and 14th infusions.

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

REFRENCES

Aduhelm (Aducanumab) [prescribing information]. Cambridge, MA. Biogen, Inc. 2021
Leqembi (lecanemab) [prescribing information]. Nutley, NJ: Eisai Inc; January 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

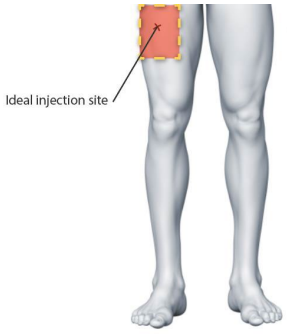
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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.