Northwell Health Solutions

POLICY/GUIDELINE TITLE: Adult Treatment of Mild Cognitive Impairment and Mild Dementia due to Alzheimer's Disease with Anti-Amyloid Beta Monoclonal Antibodies – implications for the use of anticoagulants, antiplatelets and thrombolysis.	**SYSTEM POLICY AND PROCEDURE MANUAL**
DOCUMENT #: NEU.4258	**CATEGORY SECTION:**
System Approval Date: **Site Implementation Date:**	**Effective Date:** NEW **Last Reviewed/Approved: NEW**
Prepared by: Neurology Service Line; Medicine Service Line, Emergency Medicine Service Line	**Notation(s):** N/A

GENERAL STATEMENT of PURPOSE:

The purpose of this document is to provide a guideline in treating patients, treated with Anti-Amyloid Beta Monoclonal Antibodies for Mild Cognitive Impairment or Mild Dementia due to Alzheimer's Disease, who present at a Northwell Hospital Emergency Department or are hospitalized, with acute neurological or cardiovascular symptoms requiring anticoagulation, antiplatelets or thrombolysis.

POLICY

It is the policy of the Neurology Service Line to establish, educate and disseminate standardized, evidence-based guidelines for care. Attachment A: patients treated with Anti-Amyloid Beta Monoclonal Antibodies for Mild Cognitive Impairment **or** Mild Dementia due to Alzheimer's Disease.

SCOPE

This policy applies to all Northwell Health employees, as well as medical staff, volunteers, students, trainees, physician office staff, contractors, trustees and other persons performing work for or at Northwell Health; faculty and students of the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell or the Hofstra Northwell School of Nursing and Physician Assistant Studies conducting research on behalf of the Zucker School of Medicine on or at any Northwell Health facility.

DEFINITIONS

ARIA - Amyloid-related imaging abnormalities

ARIA-H – ARIA characterized by brain microhemorrhages and/or superficial siderosis.

ARIA-E - ARIA characterized by brain edema.

IV – intra-venous

IA – intra-arterial

PROCEDURE/GUIDELINES

Refer to Attachment A for guidelines.

CLINICAL REFERENCES/PROFESSIONAL SOCIETY GUIDELINES

- Aduhelm® [package insert]. Cambridge, MA: Biogen Inc.; 2/2023
- Leqembi® [package insert]. Nutley, NJ: Eisai Inc.; 7/2023
- N Reish, P Jamshidi, B Stamm, et al. Multiple Cerebral hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke. N Engl J Med 2023: 388:478-479
- J Cummings, P Aisen, L G Apostolova, A Atri, S Salloway, M Weiner. Aducanumab: Appropriate Use Recommendations. J Prev Alzheimers Dis. 2021;8(4):398-410
- J Cummings, L Apostolova, GD Rabinovici, et al. Lecanemab: Appropriate Use Recommendations. J Prev Alz Dis 2023;3(10):362-377
- CG Withington and R Turner. Amyloid-Related Imaging Abnormalities With Anti-amyloid Antibodies for the Treatment of Dementia Due to Alzheimer's Disease. Front Neurol. 2022; 13: 862369
- Salloway, S Chalkias, F Barkhof, et al. Amyloid-Related Imaging Abnormalities in 2 Phase 3 Studies Evaluating Aducanumab in Patients With Early Alzheimer Disease. JAMA Neurol. 2022 Jan 1;79(1):13-21.

REFERENCES to REGULATIONS and/or OTHER RELATED POLICIES

NEU #4257 IV Thrombolytic for Adult Ischemic Acute Stroke Patients
NEU #4251 Ischemic Stroke And Transient Ischemic Attack (TIA) in Adults
NEU #4252 Spontaneous Intracerebral Hemorrhage
NEU #4254 Endovascular Stroke Therapy

ATTACHMENTS

Attachment A - Guidelines for Patient Care treatment
Attachment B – Guidelines for Cerebral Hemorrhage Risk Flyer

FORMS

N/A

APPROVAL:	
Northwell Health Policy Committee	

System PICG/Clinical Operations Committee	

Standardized Versioning History:
Approvals: * =Northwell Health Policy Committee; ** = PICG/Clinical Operations Committee; ⧓ = Provisional; ❖ = Expedited

Attachment A

Guideline for Patient Care treatment

Patients undergoing treatment for Alzheimer's Disease with monoclonal antibodies [such as but not limited to: lecanemab (LEQEMBI®), aducanumab (ADUHELM®), and (KISUNLA™) donanemab] have demonstrated increased risk of cerebral hemorrhage.
The following guidelines are derived from experience in clinical trials, medications labels, appropriate use recommendations and published cases or case series.

I. Treatment with lecanemab, and medications in the same class, should not be offered to patients who require anticoagulation of any type, and anti-platelet treatment above aspirin 325mg or clopidogrel 75mg daily
    a. Discretion should be used in patients requiring short-term dual anti-platelet treatments, such as aspirin 81mg and clopidogrel 75mg daily or aspirin combined with other antiplatelet agents
    b. Patients at natural risk of bleeding (e.g. bleeding diathesis, known at-risk aneurysms, cerebral amyloid angiopathy etc.) should not be offered this anti-amyloid class of medications
    c. Caution must be taken in these patients when they need high dose antiplatelets or systemic anticoagulants for the treatment of thrombotic disorders including, but not limited to, pulmonary embolism, deep vein thrombosis, stent placement, etc.

II. Patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies) have an ABSOLUTE CONTRAINDICATION to receiving IV/IA thrombolysis (alteplase or tenecteplase) for acute stroke or other indications (See NEU #4257)
    a. Plan to discontinue Anti-Amyloid Beta Monoclonal Antibodies if significant risk of stroke or cardiac ischemia potentially requiring IV/IA thrombolysis
    b. It is reasonably safe to administer IV/IA thrombolytic agents 4+ weeks after the last Anti-Amyloid Beta Monoclonal Antibodies infusion.

III. In patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies), Mechanical Thrombectomy, with transient heparinization should be considered in appropriate cases.

IV. In patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies), DVT prophylaxis anticoagulation is allowed
    a. Consider discontinuing Anti-Amyloid Beta Monoclonal Antibodies for the duration of DVT prophylaxis anticoagulation
    b. It is reasonably safe to administer DVT prophylaxis anticoagulation 1-2 weeks after the last Anti-Amyloid Beta Monoclonal Antibodies infusion

V. In patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies) requiring anticoagulation:
    a. Use caution and entertain a risk/benefit discussion with patient/caregiver
    b. Plan to discontinue Anti-Amyloid Beta Monoclonal Antibodies if anticoagulation is required

c. It is reasonably safe to administer full anticoagulation 2+ weeks after the last Anti-Amyloid Beta Monoclonal Antibodies infusion.

VI. Recommendations for the use of anti-platelets in patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies):
   a. Single dose antiplatelets (e.g. aspirin up to 325mg daily, clopidogrel 75mg daily; ticagrelor or prasugrel in the usual therapeutic doses) are allowed
   b. Dual antiplatelets (e.g. ASA 81mg + clopidogrel 75 mg daily or ASA + other antiplatelet agents) are allowed
      i. Plan to discontinue Anti-Amyloid Beta Monoclonal Antibodies for the duration of the dual antiplatelets treatment
      ii. It is reasonably safe to administer dual or high-dose antiplatelets 2+ weeks after the last Anti-Amyloid Beta Monoclonal Antibodies infusion.

VII. In patients actively treated with lecanemab (or other anti-amyloid monoclonal antibodies), care should be taken in differentiating acute neurological symptoms due to ARIA from stroke, as ARIA can be a stroke mimic
   a. In case of suspected ARIA (E or H) urgent imaging should be obtained
   b. While a CT head may suffice to rule out significant lesions in the acute setting, a 3 Tesla brain MRI with 3D T2-FLAIR and susceptibility sequences (SWI preferred) is highly recommended
   c. While clear treatment recommendations for the treatment of ARIA-E/H do not exist, and most cases resolve spontaneously with discontinuation of lecanemab (or the others in the class), more severe cases have benefited from high-dose IV steroids with taper in the inpatient setting.

CEREBRAL HEMORRHAGE RISK

- **ALERT: this patient is being treated with anti-amyloid monoclonal antibodies,** e.g., lecanemab (legembi®), aducanumab (aduhelm®), donanemab
  - These treatments bear increased risk of cerebral hemorrhage.

⚠ If this patient presents with STROKE:

- **DO NOT treat with IV/IA thrombolytics**
  - Significant bleeding has been reported when IV thrombolysis (tPA) was administered in patients taking lecanemab and has resulted in fatal outcome
- **Thrombectomy** with transient heparinization is reasonably safe, and should be considered in appropriate cases
- **The use of anticoagulants may increase the risk of intracerebral haemorrhages in patients taking anti-amyloid monoclonal antibodies.**

⚠ **CAUTION** MUST BE TAKEN using antiplatelets and anticoagulants for the treatment of all thrombotic disorders including but not limited to: pulmonary embolism, deep vein thrombosis, stent placement, cerebral thrombectomy, etc.

- Anti-platelet treatment should not exceed ASA 325mg or clopidogrel 75mg daily
- Discretion should be used for short-term dual anti-platelet treatments, such as ASA 81mg + clopidogrel 75mg daily
- Caution must be taken for high-dose antiplatelets or systemic anticoagulants for the treatment of thrombotic disorders.

- The relative risk of treatment with anticoagulant/antiplatelet must be considered and discussed on a case-by-case basis.

- **Please, for any questions and concerns, consult Neurology and the Stroke Team**