RESOURCE

CME OUTFITTERS

Quick-Reference ATT Landscape

Purpose

Amyloid-targeting therapies (ATTs) are reshaping the care of early Alzheimer's disease (AD). This quick guide equips pharmacists with essential, at-a-glance information on how these therapies work, who they're for, how to monitor them safely, and what operational steps are needed for successful implementation.

This resource is intended as a quick, at-a-glance reference to support learning during the activity and practical application afterward.

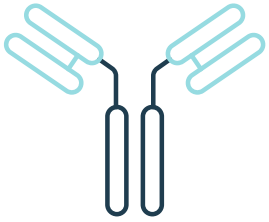
Decoding the ATT Landscape

Mechanisms, Evidence, and the Evolving Role of Pharmacy

What Are Amyloid-Targeting Therapies?

Quick Scan

- **WHO:** Patients living with mild cognitive impairment (MCI) or mild AD, amyloid-positive
- **WHAT:** Disease-modifying anti-amyloid monoclonal antibodies (mAbs)
- **KEY RISK:** amyloid-related imaging abnormalities (ARIA)
- **KEY BOTTLENECK:** magnetic resonance imaging (MRI) + workflow coordination



Disease-modifying monoclonal antibodies

Indicated for MCI due to AD or mild AD dementia

Require biomarker confirmation

Central safety risk: ARIA

Mechanism of Action

Agent	Amyloid Target	Stage of Pathology	Practical Implication for Pharmacy
Lecanemab	Primarily soluble Aβ protofibrils	Earlier aggregation	Fixed dosing; MRI cadence critical
Donanemab	Pyroglutamate-modified plaque Aβ	Established plaque	Treat-to-clear; positive emission tomography (PET) coordination

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Approval Status ATTs (U.S. and EU)

Agent	Regulatory Status (U.S.)	Regulatory Status (EU)	Shared Implementation Requirements
Lecanemab	FDA approved 2023	EC approved (April 2025; based on CHMP positive opinion November 2024); national access varies by country	Baseline MRI; ARIA monitoring per label (MRI schedule); multidisciplinary coordination
Donanemab	FDA approved 2024	EC approved (September 2025; based on CHMP positive opinion 24 July 2025); national access varies by country	Baseline MRI; ARIA monitoring per label (MRI schedule); multidisciplinary coordination

EU authorization does not guarantee uniform access; national HTA/reimbursement decisions determine availability. CHMP = Committee for Medicinal Products for Human Use; EC = European Commission; FDA = U.S. Food and Drug Administration

Key Trial-Driven Practice Differences

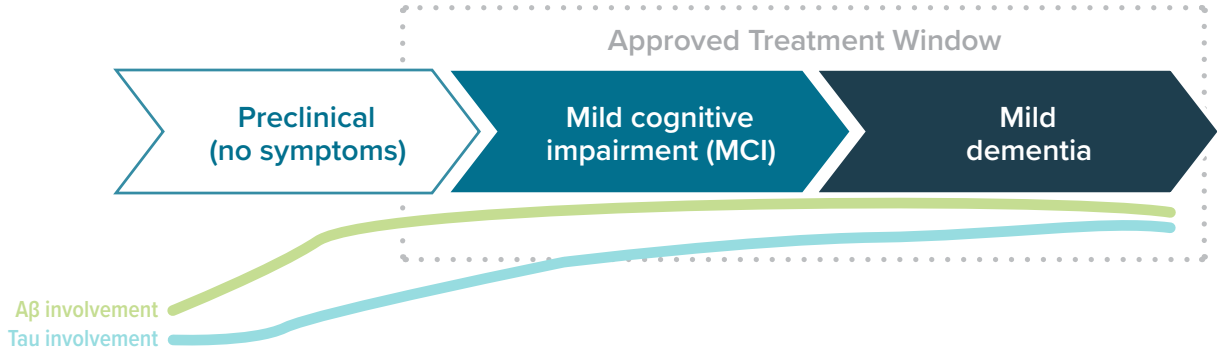
Lecanemab	Donanemab
Fixed dosing schedule	Treat-to-clear strategy
Continues regardless of amyloid reduction	Discontinued after amyloid clearance confirmed by PET
No tau-based selection	Trial finding: differential treatment effect by baseline tau burden

In TRAILBLAZER-ALZ 2, participants with higher tau burden showed smaller treatment effects, consistent with later-stage disease biology.

Decoding the ATT Landscape

Mechanisms, Evidence, and the Evolving Role of Pharmacy

Timing of ATTs in AD



Practice Context for Pharmacists

- Both agents have demonstrated slowing of disease progression across cognitive and functional domains
- Earlier treatment initiation is associated with greater observed benefit
- Real-world extrapolation needed: only 5–8% of U.S. adults meet strict trial criteria
- Patient selection should consider MRI eligibility, comorbidities, APOE ε4 status, and logistical capacity

Safety & Monitoring

KEY SAFETY CONSIDERATIONS:

- The most significant safety risks with amyloid-targeting therapies are ARIA-E (edema/effusion) and ARIA-H (hemorrhage)
- ARIA risk is higher in APOE ε4 carriers
- MRI monitoring is required to detect ARIA, which may occur before symptoms develop

References

1. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21.
2. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease. *JAMA*. 2023;330(6):512-527.
3. Pittock RR, Aakre JA, Castillo AM, et al. Eligibility for anti-amyloid treatment in a population-based study. *Neurology*. 2023;101(19):e1837-e1849.
4. Jack CR Jr, Knopman DS, Jagust WJ, et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *Lancet Neurol*. 2013;12(2):207–216.

KEY **TAKEAWAYS**

1. ATTs = disease-modifying, not symptomatic therapies
2. Approved agents differ in amyloid target and mechanism, and are not interchangeable
3. Treatment is intended for early symptomatic disease (MCI → mild dementia)
4. ARIA risk and MRI readiness are central to safe implementation
5. Pharmacists play a critical role in appropriate selection and multidisciplinary coordination