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Inclusion Strategies for Adults with Down Syndrome and Access To New Anti-amyloid DMTs

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Disclosures

- No conflicts.
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What are the key issues?

With the emergence of the novel anti-amyloid medications, what are the concerns related to adults with neuroatypical conditions and especially the impact upon DS-AD?

- **Equity in clinical trials**
  - Absence of any participation in extant clinical trials and thus assurances of efficacy of the medications and safety for their use
- **Prescribing criteria issues**
  - Current language in drug formularies does not provide inclusion for adults with neuroatypical condition
- **Dx for eligibility**
  - Inadequate inclusion of specialty tests for dx of AD in adults with neuroatypical conditions or recognition of potential variations in testing criteria

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Why equity for Down syndrome?

Adults with Down syndrome are at high risk of Alzheimer's disease (and diagnosed with DS-AD)

New AD disease modifying treatments have potential to help adults with Down syndrome who meet eligibility criteria

Prescribing criteria either deny access or neglect to acknowledge access options for adults with Down syndrome

Once safety determined there should be no barriers to equal access

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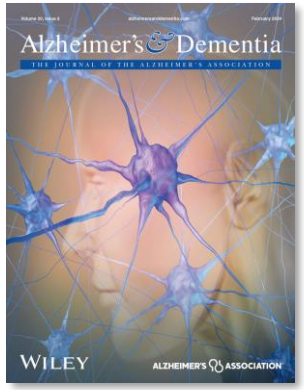
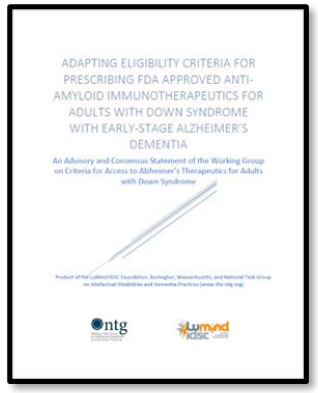
Adapting prescribing criteria for amyloid-targeted antibodies for adults with Down syndrome



https://doi.org/10.1002/alz.13778



Patients with DS/ID are **implicitly not covered** by the prior authorization criteria for AD DMTs, potentially depriving them of access to a beneficial treatment

An international **expert panel convened** and recommended modified prescriber criteria, ensuring their suitability for DS/ID patients once the drugs are deemed safe for use with this group

Many patients with DS/ID show **younger age dementia onset** and **floor effects on AD diagnostic assessments**, compared to adults with sporadic AD.

Recommendations to extant prescribing criteria include:

- **lowering the age** of eligibility (<50)
- **using alternative measures** for diagnosis and neurocognitive decline relevant to DS/ID (specialized DS/ID instruments)
- **broadening latitude** in presentation due to lifelong cognitive limitations (recognizing behavioral variants)
- **raising clinician proficiencies** in diagnosing dementia in adults with DS/ID (continuing education)

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https://lumindidsc.org/wp-content/uploads/2023/06/Working-Group-DS-AD-Eligibility-Criteria-May-30-2023.pdf

What did we do to advocate for equity?

- Identified barriers to equitable access in language of state drug formularies
- Organized a response by convening an expert panel to identify equivalencies to existing language
- Worked with advocacy organizations, governmental authorities, and the medical sphere to alert them to this problem
- Arrived at consensus on equivalencies for determination of presence of Alzheimer's dementia, appropriate tests, and functional impairments
- Distributed report and published findings in professional journal

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Where AD-DMTs are available

- Academab **(Aduhelm™)** had limited use in the USA and was withdrawn from use by Biogen in January 2024.
- Lecanemab (**Leqembi™)** has been approved (Eisai)
  - In the **USA** for general use and its payments are covered for all enrollees in Medicare (CMS, 2023)
  - In **Japan** approved by the Ministry of Health, Labor, and Welfare (MHLW) for adults enrolled in its National Health Insurance program (Igarashi et al., 2023; Japan Times, 2023); also approved for use in **South Korea** by the Ministry of Food and Drug Safety (Pharma Tech, 2024).
  - In **China** approved by the National Medical Products Administration (Biogen, 2023); also approved for use in **Hong Kong** by the Department of Health (Pharma Tech, 2024)
  - In **Great Britain** approved by the Medicines and Healthcare Products Regulatory Agency (MHRA, 2024), but not approved by National Institute for Health and Care Excellence [NICE] for payment within the NHS (okay if private pay) (Financial Times, 2024)
  - In the **United Arab Emirates** approved by the Ministry of Health and Prevention (Biogen, 2024)
  - In **Israel**, it is being used on a trial basis at hospitals (Biogen, 2024; Jerusalem Post, 2024)
- Status in other countries and regions
  - **In the EU**, rejected for approval by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (BioArtic, 2023)
  - **In Canada**, under review by Health Canada (Watt et al., 2023)
- Donanemab (**Kisunla™**) received approval in 2024 in the USA (Eli Lilly, 2024) and Japan (USNews, 2024), and is pending approval in other countries (McKie, 2023)

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Issues related to Down syndrome

- Lack of participation in clinical trials
- Concerns over safety – brain bleed, amyloid-related imaging abnormalities (ARIAs)
- Untried adaptation to infusion processes and PET/MRIs
- Unknown factors in determining eligibility for prescribing
- Undetermined value to administration earlier when high amyloid load is identified
- Absence of international consensus on practice guideline on applicability and administration of DMTs
- Undetermined long-range value in affecting behavior (while reducing amyloid)

Challenges

- In our work we have not found significant awareness, except in the US, for assuring equity in access to AD DMTs and new medication processes.
- Need issue statements from international and regional advocacy groups in the ID, Down syndrome, and Alzheimer's space.
- Need positive prescriptive statements from national medical associations.

What can be done to advocate for equity?

- Track language in prescribing criteria to assure inclusion of Down syndrome
- Promote equity in upcoming clinical trials
- Share alerts to Pharm re: ensuring no barriers are inherent in clinical materials distributed to prescribers
- Consult with medical associations over enhancing practitioner knowledge about DS-AD
- Prepare constituencies (DS/ID families, associations, etc.) to better understand potential value of access to AD DMTs
- Provide materials to countries where AD DMTs are not yet approved so equity can be on table and DS/ID organizations can advocate for inclusion

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Last words

- Advocate for inclusion of adults with intellectual disability/Down syndrome in clinical trials
- Assure investment in trials that produce outcomes for adults with Down syndrome
- Work proactively to have policies of national bodies approving or overseeing use of the AD DMTs to be neutral or not exclusionary
- Aid professional organizations to mount education of prescribers on assessing/ diagnosing adequately AD in adults with neuroatypical conditions, including Down syndrome/intellectual disability
- Provide counsel to families and persons affected as to the risk/benefits of seeking out AD DMTs

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