

Position Statement on Long-Acting Injectable Antipsychotics in Early Psychotic Illness: A Call for Further Research and Enhanced Education

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Issue:

Rationale: Schizophrenia is associated with a 13-15 year reduction in life expectancy and lifelong disability. Early intervention programs for psychosis improve longitudinal outcomes, but both dropout of early intervention care and medication non-adherence are common early in the course of psychotic illness. The critical early intervention period of the first 2 years of psychotic illness also has the highest risk of premature death due to suicide and other unnatural causes in schizophrenia. There is an urgent public health need to prioritize preventive strategies to reduce morbidity and premature mortality within the first 2 years of psychotic illness. Emerging evidence suggests use of long-acting injectable (LAIA) treatment in the early psychosis period may be a promising approach to reduce premature mortality and improve long-term outcomes by reducing the risk of relapse. Here, we highlight critical areas for further research and the need to prioritize education on LAIAs to improve access and enhance patient autonomy.

I. Priority areas for future research on LAIAs: Recent meta-analytic evidence suggests LAIA treatment may be superior to oral antipsychotics in reducing psychiatric hospitalizations, risk of relapse, and all-cause mortality in schizophrenia. LAIAs are associated with a greater mortality benefit when initiated early in the course of psychotic illness compared to multi-episode illness, suggesting that early LAIA initiation may be a promising strategy to improve outcomes in patients at heightened risk of premature mortality. However, the majority of research on LAIA treatment to date is on adults with chronic multi-episode schizophrenia. Many trials on LAIA also exclude individuals with comorbid substance use diagnoses, which limits generalizability to many adolescent and young adult populations. Given the potential prognostic benefits associated with early LAIA initiation, there is a crucial need for further research to better understand the role of LAIA treatment following the first episode of psychosis.

LAIA utilization varies widely across the United States, with research estimating statewide variation in prescription rates ranging from 4-22%. Many patients living in rural areas and other areas traditionally underserved by healthcare face structural barriers to LAIA treatment due to the need for in-person visits. Further, only a minority of outpatient psychiatric practices offer LAIA treatment, in part due to the infrastructure needed (e.g., refrigeration, sharps disposal, nursing support). To reduce barriers to LAIA treatment, additional research on the feasibility, effectiveness, and cost of community-based strategies (e.g., visiting nurses and community pharmacists) is needed to reduce disparities and inequities in access to LAIA treatment.

I. Need for education on LAIAs in residency training: Clinician knowledge-related deficits on LAIA use remains a leading drive of underuse of LAIA treatment. As noted in the 2020 APA Practice Guideline for the Treatment of Patients with Schizophrenia, LAIA treatment is indicated for patients who prefer to take a long-acting formulation over daily oral medications. LAIAs are associated with several patient-centered advantages, such as the convenience of not having to take

daily medication and increased discretion in shared living environments (e.g., college dormitories) compared to oral antipsychotics. However, research suggests that it is common for clinicians to only offer LAIA treatment to patients with confirmed or suspected non-adherence to antipsychotic treatment. Including LAIAs in shared decision-making discussions with patients based on perceived medication adherence may ultimately limit patient autonomy, as patients who may prefer LAIA over oral antipsychotics due to favorable lifestyle benefits may not be aware of this treatment option. Variations in clinician knowledge and comfortability with LAIA treatment also perpetuate disparities in access to treatment. Residency programs should ensure pharmacology curricula include longitudinal education on LAIA and that residents have the opportunity to initiate and manage LAIA treatment under supervision in clinical training. Further, residents should receive didactic training on the importance of shared-decision making and other strategies to enhance patient autonomy in treatment planning related to antipsychotics.

APA Position:

A. The APA recommends further research on the acceptability, tolerability, and effectiveness of LAIA treatment in early psychotic illness.

Rationale: Emerging evidence suggests that LAIA treatment may be a promising preventive tool to reduce the risk of adverse outcomes in the early psychosis period. However, the majority of prior work comparing LAIA to oral antipsychotics is in adult patients with multi-episode illness. There is a crucial need for further research to better understand the heterogeneity of the treatment effect of LAIA treatment to define the role of LAIA treatment in early psychosis. Additionally, there is limited research to date on the use of LAIA treatment in adolescent populations following the first episode of psychosis.

B. The APA supports and highlights the need for the following to expand access to LAIA treatment in schizophrenia:

1. Residency programs should integrate training on the indications, contraindications, and management of LAIA treatment longitudinally in residency psychopharmacology curricula

Rationale: Psychiatry residency programs should ensure all residents have both didactic and applied educational opportunities focused on LAIA treatment in their curricula. Didactic LAIA education should include a comprehensive overview of LAIA dosing, indications (e.g., including use as a preventive tool), contraindications, alternatives, and patient-centered risks and benefits of LAIA compared to oral antipsychotic treatment. Education on LAIAs in psychiatry residency should also include the importance of shared decision-making and integrating patient preference in treatment planning.

2. Further research on community-based strategies to expand access to LAIA treatment

Rationale: Research on community-based models to reduce structural barriers to LAIA treatment, such as outpatient pharmacist-physician collaborative models, is needed to reduce disparities and inequities in access to LAIA treatment and to promote patient recovery. Further research on patient engagement approaches related to the early initiation of LAIAs would also inform strategies to enhance patient agency in shared decision-making discussions in early psychotic illness.

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