Prescribing guideline recommendations for second-generation antipsychotics

Second-Generation Antipsychotic (SGA) Medications	
Aripiprazole **(Abilify®)**	Lurasidone **(Latuda®)**
Asenapine **(Saphris®)**	Olanzapine **(Zyprexa®)**
Brexpiprazole **(Rexulti®)**	Paliperidone **(Invega®)**
Cariprazine **(Vraylar®)**	Quetiapine **(Seroquel®)**
Clozapine **(Clozaril®)**	Risperidone **(Risperdal®)**
Iloperidone **(Fanapt®)**	Ziprasidone **(Geodon®)**
Lumateperone **(Caplyta®)**	Xanomeline/trospium **(Cobenfy®)**

- Selection of antipsychotics should be based on individual risk factors for each patient. Factors include *previous response, side effect profiles, family history, co-morbid conditions, medical vulnerabilities, tolerances* and *patient preference/expectations*.[1]

- American Psychological Association (APA) guidelines do not give a preference to first- or second-generation antipsychotics, as there is limited head-to-head supporting clinical trial data.
    - Factors related to the medication choice are the available drug formulations and dosing schedule, as well as drug-drug interactions and metabolism. It is imperative to review the medications a patient may be taking for any drug or disease state interactions.

- Guidelines emphasize utilizing the most appropriate medication per individual patient.

- Consider Clozapine for those with treatment-resistant schizophrenia and/or if the risk for suicide attempts or aggressive behavior remains elevated despite other treatments.

- Determining optimal dosing is challenging, as patients may take between 24 weeks to show an initial response and even longer periods to show an optimal response. Monitor the patient's clinical status for 2-4 weeks at a therapeutic dose before considering a change of therapy.

- Consider long-acting injectable (LAI) antipsychotics if there is a history of medication nonadherence. Patients diagnosed with schizophrenia who take a long-acting antipsychotic versus those taking an oral antipsychotic see a reduced rate of hospitalizations and emergency

room visits, along with an increased adherence to medication management. LAIs have expanded utilization with poor or uncertain adherence to first episodes, maintenance, and acute exacerbation.[2]

- Second-generation antipsychotics can have significant metabolic side effects; these effects vary between the different drugs and require consistent monitoring.

- The Food and Drug Administration (FDA) recommends the following metabolic screening measures for monitoring patients using second-generation antipsychotics. These guidelines may be modified with changes in medication and/or as clinically indicated.[3]

Recommended Metabolic Monitoring				
Measure	**Baseline**	**12 weeks**	**4 months after initiation**	**Annually (or as clinically indicated)**
Weight/body mass index	X	X	X	X
Fasting blood glucose/A1C	X	X	X	X
Fasting lipid profile	X	X	X	X

- The FDA has established black box warnings for the use of all antipsychotic medications, both first- and second-generation antipsychotics, due to increased mortality in elderly patients with dementia-related psychosis.[4,5]

These guidelines are not intended to replace a practitioner's clinical judgment. They are designed to provide information and to assist practitioners with decisions regarding care. The guidelines are not intended to define a standard of care or exclusive course of treatment. Healthcare practitioners using these guidelines are responsible for considering their patient's particular situation in evaluating the appropriateness of these guidelines.

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[1] Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. *Am J Psychiatry*. 2020;177(9):868-872. doi:10.1176/appi.ajp.2020.177901

[2] Lin D, Thompson-Leduc P, Ghelerter I, Nguyen H, Lafeuille MH, Benson C, Mavros P, Lefebvre P. Real-World Evidence of the Clinical and Economic Impact of Long-Acting Injectable Versus Oral Antipsychotics Among Patients with Schizophrenia in the United States: A Systematic Review and Meta-Analysis. CNS Drugs. 2021 May;35(5):469-481. doi: 10.1007/s40263-021-00815-y. Epub 2021 Apr 28.

[3] FDA Press Release September 2024, FDA Approves Drug with New Mechanism of Action for Treatment of Schizophrenia | FDA

[4] Rubino A, Sanon M, Ganz ML, et al. Association of the US Food and Drug Administration Antipsychotic Drug Boxed Warning With Medication Use and Health Outcomes in Elderly Patients With Dementia. JAMA Netw Open. 2020;3(4):e203630. doi:10.1001/jamanetworkopen.2020.3630

[5] Bui TNT, Au RT, Janetzki JL, McMillan SS, Hotham E, Suppiah V. Metabolic Monitoring for Adults Living with a Serious Mental Illness on a Second-Generation Antipsychotic Agent: A Scoping Review. *Adm Policy Ment Health*. 2025;52(2):289-317. doi:10.1007/s10488-024-01408-9