Prescribing guidelines 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®)**	

- Practitioners should base selection of antipsychotic 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*.[i] 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.
- Clozapine should be considered for those with treatment-resistant schizophrenia and/or if the risk for suicide attempts or aggressive behavior remains elevated despite other treatments.
- Guidelines do not indicate a preference for either first- or second-generation antipsychotics as the research does not support such an approach but focuses on utilizing the most appropriate medication per individual patient.
- Determining optimal dosing is challenging as patients may take between 2-4 weeks to show an initial response and even longer periods to show an optimal response. Monitoring the patient's clinical status for 2-4 weeks at a therapeutic dose is warranted before considering a change of therapy.
- Long-acting injectable (LAIs) antipsychotics should be considered 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.[ii]

- Second-generation antipsychotics can have significant metabolic side effects; these effects vary between the different drugs and require consistent monitoring.
- The FDA recommends the following screening measures for monitoring patients using second-generation antipsychotics. These guidelines may be modified with changes in medication and/or as clinically indicated.[iii]

Monitoring Patients on Second-Generation Antipsychotic Medications						
Measure	**Baseline**	**4 weeks**	**8 weeks**	**12 weeks**	**Quarterly**	**Annually (or as clinically indicated)**
Personal/Family History	X					X
Weight/body mass index	X	X	X	X	X	X
Waist Circumference	X					X
Blood Pressure	X			X	X	X
Fasting Blood Glucose	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.[iv,v]
- The FDA has included Abilify®, Seroquel®, Seroquel XR®, Latuda®, and Rexulti® in its additional black box warning for increased risk of suicidal thinking and behavior in patients, age 24 years and younger since these agents have indications to be used as adjunct therapy to antidepressants for the treatment of major depression and/or bipolar depression.

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. Health care practitioners using these guidelines are responsible for considering their patient's particular situation in evaluating the appropriateness of these guidelines.

[i] DeJongh BM. Clinical pearls for the monitoring and treatment of antipsychotic induced metabolic syndrome. Ment Health Clin. 2021 Nov 8;11(6):311-319. doi: 10.9740/mhc.2021.11.311. PMID: 34824956; PMCID: PMC8582768

[ii] 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. Erratum in: CNS Drugs. 2021 Aug;35(8):923. PMID: 33909272; PMCID: PMC8144083.

[iii] DeJongh BM. Clinical pearls for the monitoring and treatment of antipsychotic induced metabolic syndrome. Ment Health Clin. 2021 Nov 8;11(6):311-319. doi: 10.9740/mhc.2021.11.311. PMID: 34824956; PMCID: PMC8582768

[iv] 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

[v] 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