Clinical Guidelines

Pharmacologic Treatment of Schizophrenia

Updated May 1, 2023

Community Behavioral Health
A DIVISION OF DBHIDS | CBHPHILLY.ORG

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TABLE OF CONTENTS

1. BACKGROUND

Schizophrenia is considered one of the most severe and detrimental mental health conditions, especially if untreated. Symptoms of schizophrenia tend to result in social isolation, stigma, and unemployment within patients. One in a hundred people will develop schizophrenia and distribution is seen equally between genders. The age of onset is typically in early adulthood in the early twenties[1].

Symptoms of schizophrenia can be categorized as positive, negative, or cognitive impairments. Certain symptoms of schizophrenia can resemble other diagnoses such as schizoaffective disorder, depressive disorder with psychotic features, and bipolar disorder with psychotic features. Patients who are diagnosed with schizophrenia may also have dual diagnoses of anxiety, depression, panic, or obsessive-compulsive disorders. Due to the nature of schizophrenia, many patients lack awareness of their illness and have high rates of medication nonadherence, symptom relapse, poor psychosocial function, poor hygiene, and overall negative health outcomes. Patients may also develop comorbid substance use disorders secondary to schizophrenia[2]. Patients with schizophrenia are two to three times more likely to die earlier than the general population due to physical conditions and infectious diseases[3].

The cause of schizophrenia is not clear. There are general hypotheses that correlate the disease with genetic and environmental factors. However, there are many care options available for patients who have schizophrenia. Options include medication, psychoeducation, family interventions, cognitive behavioral therapy, and psychosocial rehabilitation. One or multiple of these can be integrated into a patient's specific care plan.

2. PURPOSE

Community Behavioral Health (CBH) is committed to working with our provider partners to continuously improve the quality of behavioral health care for our shared population. Whenever possible, this is best accomplished by the implementation of evidence-based practices, as well as those informed by nationally recognized treatment guidelines, while respecting the need for individualized treatment and recovery planning. These guidelines will be maintained and updated collaboratively with providers and system stakeholders to reflect evolving evidence-based practices or changes in national guidelines.

The following are medication prescribing standards, adapted for the CBH Network from national treatment guidelines. They are intended to guide providers in aligning their practices with the best available scientific evidence to help members with schizophrenia access state-of-the-art care.

To assess quality of care, CBH will be collecting several standardized metrics. These metrics come either from the Healthcare Effectiveness Data and Information Set (HEDIS) set of measures, used by most major healthcare organizations for quality improvement, or are measures of clear clinical priority in our network. While CBH will be

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[1] *Jauhar S, Johnstone M, McKenna PJ. Schizophrenia. The Lancet (2022 Feb 4);399(10323)*

[2] *Lähteenvuo M, Batalla A, Luykx JJ, Mittendorfer-Rutz E, Tanskanen A, Tiihonen J, Taipale H. Morbidity and mortality in schizophrenia with comorbid substance use disorders. Acta Psychiatrica Scand. 2021 Jul;144(1):42-49. doi: 10.1111/acps.13291. Epub 2021 Mar 8. PMID: 33650123; PMCID: PMC8359349.*

[3] *Department of Behavioral Health and Intellectual disAbility Services (DBHIDS), Philadelphia Behavioral Health Practice Guidelines.*

collecting specific data related only to guidelines that have been issued to the network thus far, the use of empirical guidelines and practice parameters is encouraged in all prescribing.

CBH expects providers to follow these guidelines in addition to all other relevant CBH, state, and federal regulations and standards, including CBH prescribing Bulletins (e.g., **DBHIDS/CBH Bulletin 07-07: Screening for and Treatment of the Components of Metabolic Syndrome**), the **Network Inclusion Criteria (NIC) Standards of Excellence**, and the Department of Behavioral Health and Intellectual disAbility Services (DBHIDS) **Practice Guidelines for Resiliency and Recovery-Oriented Treatment**.

Note further that the following are guidelines for the pharmacologic treatment of schizophrenia. CBH and DBHIDS encourage a biopsychosocial and recovery-based approach to treatment; in each case, these guidelines for medication treatment should be but one part of a robust, multidisciplinary treatment approach that involves high-quality psychosocial treatment, collaboration with physical health providers, and inclusion of families and other supports.

CBH has updated its guidelines for the treatment of schizophrenia to reflect the **published evidence-based practice parameters of the American Psychiatric Association issued in 2021**. CBH encourages its network providers to remain current with the state of evidence-based practice parameters and to incorporate these into the clinical care offered. These guidelines reflect the best scientific evidence available to guide treatment delivery and should be considered the standard of care in the CBH Network.

3. PRACTICE GUIDELINES (SUMMARIZED AND ADAPTED FROM THE APA GUIDELINES)

3.1. Screening and Referral

Every individual should have as thorough an initial evaluation as their clinical status allows, including complete psychiatric and general medical histories and physical and mental status examinations. Interviews with family members or other persons knowledgeable about the individual should be conducted routinely (unless the individual refuses to grant permission) especially since some members with psychosis are unable to provide a reliable history at the first interview. The initial psychiatric evaluation should include the following:

- History of present illness
- Psychiatric history, including hospitalizations, prior psychiatric diagnoses and treatments
- Substance use history
- Medical history
- Family and social history
- Examination, including mental status examination and suicidal intent

Family inclusion, to the extent possible, is a vital part of care adherent to DBHIDS recovery principles. Specific goals for care should be discussed with the patient, along with the patient's family, if applicable.

3.2. Safety/Risk Assessment

Antipsychotic medications are considered first line agents for treatment of schizophrenia. These medications have an adverse effect profile that requires risk versus benefit considerations. First generation antipsychotic medications may cause muscle-related adverse effects such as bradykinesia, akathisia, tremor, dystonia, parkinsonism, tardive dyskinesia, and rigidity. Second generation antipsychotic medications may cause similar movement disorders, but it is not as likely as with the first-generation class. Second generation antipsychotics have a higher risk of metabolic adverse effects. Any changes in blood pressure, weight, hemoglobin A1C and lipids should be noted. Additionally, patients should be evaluated on their risk for suicide at each visit.

3.3. Harm Reduction

For patients with schizophrenia and comorbid substance use disorder, harm reduction strategies should be considered to mitigate risks associated with substance use that could worsen outcomes. Co-occurring substance use disorder and schizophrenia is associated with high rates of hospitalization and mortality.

3.4. Assessment

Measurement of body weight and vital signs (heart rate, blood pressure, temperature) is also required and will serve as a baseline measurement to ensure that medication prescribed is consistent with **DBHIDS/CBH Bulletin 07-07** regarding the appropriate monitoring for adverse metabolic effects of antipsychotic medications.

Ongoing evaluation of substance use should be documented to ensure the negative effects of substance use are not limiting recovery. This evaluation should involve an assessment of tobacco use given the high rate of tobacco use in people with schizophrenia, the related adverse health outcomes, and in some cases the effect that tobacco smoking may have on antipsychotic blood levels. Tobacco has an interaction with antipsychotic medications in that it may lower serum levels of the drug which could lead to untreated symptoms[4].

3.5. Cultural and Social Determinants of Health

Schizophrenia falls within the top 15 leading causes of disability worldwide. Patients with schizophrenia often have other physical health conditions and/or co-occurring mental or behavioral health conditions. Financial costs that are associated with schizophrenia tend to be higher than those with other conditions. This makes it difficult for patients to receive care, especially given that the nature of the disease may prevent patients from employment. Costs associated with schizophrenia can be categorized as direct and indirect. According to the **World Health Organization**, indirect costs include loss of productivity, criminal justice involvement, and social services, amongst others.

3.6. Diagnosis

Diagnosis of schizophrenia should be made in accordance with DSM-5 criteria. The DSM-5 criteria for schizophrenia states that two or more active-phase symptoms must be present for a period of at least one month. Of the active-phase symptoms, one must be delusions, hallucinations, or disorganized speech. The patient must also show a decreased level of functioning in daily activities related to work, relationships, or self-care. Continuous signs must be evident for at least

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[4] *Kennedy WK, Jann MW, Kutscher EC. Clinically Significant Drug Interactions with Atypical Antipsychotics. CNS Drugs (2013);27:1021-1048.*

6 months, with one month of active-phase symptoms. Lastly, a comprehensive differential diagnosis is needed to rule out other conditions in which a patient may present with similar symptoms[5].

The American Psychiatric Association (APA) Practice Guidelines for the Treatment of Patients with Schizophrenia recommend that an initial psychiatric evaluation includes history of pertinent illness, psychiatric history, substance use history, medical history, family history, personal and social history, and examination including mental status examination. The guidelines mention that upon initial presentation, neurosyphilis, Huntington's disease, Wilson's disease and anti N-methyl-D-aspartate (NMDA) receptor encephalitis are conditions that can mimic schizophrenia symptoms. A thorough history allows clinicians to better understand how to treat schizophrenia, along with any co-occurring mental conditions.

3.7. Laboratory Testing

Initial medical evaluation should include a Complete Blood Count (CBC); measurements of blood electrolytes, glucose, cholesterol, and triglycerides; tests of liver, renal, and thyroid function; a syphilis test, along with other STIs, with consent; and, when indicated and permissible, determination of HIV status and a test for Hepatitis C. Routine evaluation of substance use with a toxicology screen should also be part of the medical evaluation. A pregnancy test should be strongly considered for individuals with childbearing potential. In individuals for whom the clinical picture is unclear or where there are abnormal findings from a routine examination, more detailed studies (e.g., Magnetic Resonance Imaging (MRI) scan or Computed Tomography (CT) scan) should be considered. Members' files should include documentation of all components of evaluation completed; providers should obtain documentation of evaluation completed by outside providers when applicable.

3.8. Treatment

The goals of treatment for schizophrenia include targeting symptoms, preventing relapse, and increase overall functioning of the patient for reintegration into society. While pharmacotherapy is an effective mainstay of disease management, residual symptoms may persist. Therefore, the combination of nonpharmacological interventions, such as psychotherapy, should also be incorporated in care. Additionally, treatment plans should include a determination of the most optimal setting of care, such as partial hospital, intensive outpatient, psychosocial rehabilitation, Clubhouse models, etc.

Pharmacologic treatment with an FDA-approved antipsychotic medication should be initiated promptly upon diagnosis of schizophrenia due to the association between acute psychotic exacerbations and emotional distress, disruption to the individual's life, and substantial risk of dangerous behaviors to self, others, or property. Considerations should be made for instances where medication may interfere with diagnostic assessment. Except in cases of emergency, a full-informed consent process must take place.

The selection of an antipsychotic medication should be guided by the member's previous experience with antipsychotics, including the degree of symptom response, side effects, and preferred route of medication administration. While most members prefer oral medication, the experience of recurrent relapses related to nonadherence should prompt a discussion of long-acting injectable antipsychotic medication.

[5] ***Substance Abuse and Mental Health Services Administration. Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health***

In cases of treatment resistance (defined as symptoms that fail to respond to two adequate trials of traditional antipsychotic medications[6]), serious consideration to an appropriately monitored trial of clozapine should be given. Providers should be familiar with clozapine prescribing guidelines and regulations (see the **clozapine Risk Evaluation and Mitigation Strategy (REMS) program**) or be able to collaborate with a clozapine-prescribing provider.

Adjunctive medications are also commonly prescribed for comorbid conditions. Benzodiazepines may be used to treat catatonia as well as to manage both anxiety and agitation acutely until the antipsychotic has had time to be therapeutically effective (primarily in individual settings). Antidepressants can be considered for treating comorbid major depression or obsessive-compulsive disorder. Mood stabilizers and beta-blockers may be considered for reducing the severity of recurrent hostility and aggression. However, these medications are not recommended as primary treatments for schizophrenia, or even as routinely prescribed "adjuncts" absent clear indications. Careful attention must be paid to potential drug interactions, especially those related to metabolism by cytochrome P450 enzymes. Anticholinergic medications should be considered for treatment-emergent movement side effects (e.g., dystonia) if dose modification or medication change is not advisable.

3.9. Monitoring of Treatment

The most common contributors to symptom relapse are antipsychotic medication nonadherence, substance use, and stressful life events, although relapses are not uncommon because of the natural course of the illness, despite continuing treatment. If nonadherence is suspected, reasons for it should be evaluated and considered in the treatment plan.

Providers should consider adherence scales such as the Drug Attitude Inventory (DAI-10 and DAI30), the Personal Evaluations of Transitions in Treatment (PETiT), **Medication Adherence Rating Scale** (MARS), or Clinician Rating Scale (CRS).[7]

Strategies to improve adherence that are deemed most rigorously backed by research from the Expert Consensus Guidelines on Adherence include:[8]

- Symptom and side effect monitoring
- Social work targeting logistical problems (e.g., assistance with community resource navigation)
- Medication monitoring/environmental supports

Additional strategies include but are not limited to:

- Consideration of long-acting antipsychotics

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[6] Kane JM, Honigfeld G, Singer J. Clozapine for the treatment resistant schizophrenic: a double-blind comparison versus chlorpromazine/benztropine. Arch Gen Psychiatry. 1988;45:789–96.

*[7] Questionnaires and supporting information available at **http://www.easacommunity.org/files/Medication%20Adherence%20Scale.pdf**.*

[8] Velligan, D. I., Weiden, P. J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., & Docherty, J. P. (2010). Strategies for addressing adherence problems in individuals with serious and persistent mental illness: recommendations from the expert consensus guidelines. Journal of Psychiatric Practice®, 16(5), 306-324.

- Cognitive Behavioral Therapy (CBT)
- Devoting more time in the therapeutic encounter to specifically address adherence
- Shared decision-making approaches

A comprehensive treatment/recovery plan that emphasizes avoiding hospitalization, treatment interruptions, medical illness, substance use, and other barriers to recovery must be developed and individualized to reflect individual recovery goals, consistent with both APA guidelines and the DBHIDS NIC Standards for Excellence. Additionally, the patient should be provided a list of resources for psychiatric rehabilitation programs within the community. Ongoing collateral contact with important people in the member's life should occur (with member's consent).

Once stabilized on medication, ongoing evaluations should assess maintenance of progress towards recovery goals, effective treatment of increased symptoms or relapses, and monitoring of adverse treatment effects. Relapses are often precipitated by psychosocial stressors. Ongoing evaluations must be comprehensive in this regard (i.e., not limited to "medication management").

Monitoring for the adverse metabolic effects of antipsychotic medications should occur according to **DBHIDS/CBH Bulletin 07-07**. Ongoing evaluations for Extrapyramidal Side Effects (EPSE) should be documented regularly (the use of a standardized instrument, such as the Abnormal Involuntary Movement Scale (AIMS)[9] is preferred). Monitoring for EPSE should occur at each visit using a screen tool, such as AIMS, to be utilized no less than every 6 months. The risk of tardive dyskinesia should, of course, form part of any informed consent discussion related to antipsychotic medications, even those considered "atypical." Monitoring for other adverse effects, such as hyperprolactinemia should be completed according to the prescribing information for each individual agent. See Appendix 5.4. for Lab Monitoring recommendations.

3.10. Coordination of Care/Linkages

Given the burden of physical health challenges faced by persons with schizophrenia and the physical health effects of many medication treatments, collaboration with physical health providers, and documentation of such collaboration, is imperative.

3.11. Aftercare Planning/Discharge

Whether prescribed in oral or long-acting injectable form, the member's ability to obtain the medication through their pharmacy benefit provider must be considered: many members may begin a medication in the hospital, only to find that the medication is not routinely covered upon discharge. Efforts must be made to eliminate the occurrence of such predictable interruptions in treatment. CBH has **LAI resources** to identify best practices when transitioning a patient from an inpatient setting to outpatient, with medication related transitions of care.

[9] *Guy W. ECDEU Assessment Manual for Psychopharmacology: Revised (DHEW publication number ADM 76-338). Rockville, MD, US Department of Health, Education and Welfare, Public Health Service, Alcohol, Drug Abuse and Mental Health Administration, NIMH Psychopharmacology Research Branch, Division of Extramural Research Programs, 1976: 534–7*

4. MONITORING

CBH encourages providers to maintain robust internal quality management programs to ensure treatment of CBH members adheres to these and other applicable guidelines. In addition to "as needed" reviews of records when quality issues arise, CBH will be tracking and sharing three main performance metrics with providers, all of which are standard National Committee for Quality Assurance (NCQA) HEDIS measures:

1. **SAA: Adherence to Antipsychotic Medications for Individuals with Schizophrenia**
2. **SSD: Diabetes Screening for People with Schizophrenia or Bipolar Disorder Who Are Using Antipsychotic Medications**
3. **SMD: Diabetes Monitoring for People with Diabetes and Schizophrenia**: Assesses adults 18–64 years of age with schizophrenia and diabetes who had both an LDL-C test and an HbA1c test during the measurement year.

In addition, providers must maintain documentation of all evaluations and interventions described in these guidelines, whether delivered by the provider or an outside practitioner. CBH and the **DBHIDS Network Improvement and Accountability Collaborative (NIAC)** will continue to monitor treatment provided to ensure that care is consistent with the **DBHIDS Network Inclusion Criteria (NIC) Standards of Excellence**.

5. APPENDICES

5.1. References

- **Department of Behavioral Health and Mental Retardation Services (DBHIDS) Bulletin 07-07: Screening for and Treatment of the Components of Metabolic Syndrome, November 1, 2007.**
- **Department of Behavioral Health and Intellectual disAbility Services (DBHIDS), Network Inclusion Criteria, 2019.**
- **Department of Behavioral Health and Intellectual disAbility Services (DBHIDS), Philadelphia Behavioral Health Practice Guidelines.**
- Kane JM, Honigfeld G, Singer J. Clozapine for the treatment resistant schizophrenic: a double-blind comparison versus chlorpromazine/benztropine. Arch Gen Psychiatry. 1988;45:789–96.
- Questionnaires and supporting information available at **http://www.easacommunity.org/files/Medication%20Adherence%20Scale.pdf**
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- World Health Organization [**https://www.who.int/news-room/fact-sheets/detail/schizophrenia#:~:text=Schizophrenia%20affects%20approximately%2024%20million,as%20many%20other%20mental%20disorders**]
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- APA Guidelines [**https://psychiatryonline.org/doi/epdf/10.1176/appi.books.9780890424841**]
- Substance Abuse and Mental Health Services Administration. Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health [Internet]. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2016 Jun. Table 3.22, DSM-IV to DSM-5 Schizophrenia Comparison. Available from: **https://www.ncbi.nlm.nih.gov/books/NBK519704/table/ch3.t22/**

5.2. Special Populations: Patients of Childbearing Potential

Patients who are pregnant or breastfeeding should consult with their provider regarding the plan of care that optimizes outcomes for both the patient and the infant. Prior to conception, during pregnancy, or while breastfeeding, it is important for the patient to collaborate with providers to identify the risk versus benefit of untreated illness and the potential for negative fetal or neonatal effects. Symptoms should be managed in the patient using the lowest effective dose during pregnancy. Long-term effects of breastfeeding while taking antipsychotic medications are not well established. Patients who want to continue breastfeeding while being treated with psychotropic medications should review the care plan with their provider utilizing shared decision making.

5.3. Access to Treatment Toolkit

- https://cbhphilly.org/cbh-providers/available-services/lai-antipsych/
- https://cbhphilly.org/wp-content/uploads/2022/04/CBH_LAI-Resources_2022-04-26.pdf

5.4. Lab Monitoring Recommendations

Parameter	*Suggested Frequency*
Personal and Family History (Obesity, Diabetes, Dyslipidemia, Hypertension, Coronary Heart Disease)	Annually
Height, Weight, BMI	Every 4 weeks for the first 12 weeks, then every 3 months
Waist Circumference	Annually
Blood Pressure, Pulse, Fasting Blood Glucose, Lipid Profile	12 weeks, then annually

After baseline metabolic parameters are obtained, the suggested frequency of metabolic lab monitoring for patients who take antipsychotic medications may change.

5.5 Member Resources

- CBH Antipsychotic Medication Guide
- CBH Guía Sobre los Medicamentos Antipsicóticos
- Taking Medications for Your Behavioral Health Conditions
- Diabetes Care for Members with Behavioral Health Conditions
- Diabetes Screening for Members with Behavioral Health Conditions Who Take Medications
- Diabetes Monitoring for Members with Behavioral Health Conditions Who Take Medications