Schizophrenia

GUIDELINE HIERARCHY

CPGs are updated every two years or as necessary due to updates made to guidelines or recommendations by the American Psychiatric Association (APA). When there are differing opinions noted by national organizations, WellCare will default to the member's benefit structure as deemed by state contracts and Medicaid / Medicare regulations. If there is no specific language pertaining to the topic of Schizophrenia, WellCare will default (in order) to the following:

- National Committee for Quality Assurance (NCQA);
- United States Preventive Services Task Force (USPSTF), National Quality Strategy (NQS), Agency for Healthcare Research and Quality (AHRQ);
- Specialty associations, colleges, societies, etc. (e.g., American Academy of Family Physicians, American Congress of Obstetricians and Gynecologists, American Cancer Society, etc.).

Links to websites within the CPGs are provided for the convenience of Providers. Listings do not imply endorsement by WellCare of the information contained on these websites. NOTE: All links are current and accessible at the time of MPC approval.

WellCare aligns with the APA on the topic of Schizophrenia. The following are highlights from their guidelines.

AMERICAN PSYCHIATRIC ASSOCIATION (APA)

WellCare adheres to the American Psychiatric Association (2002) *Practice Guideline for the Treatment of Patients with Bipolar Disorder, Second Edition.* WellCare adheres to the 2005 *Guideline Watch* – the document contains an update of the 2002 guideline. The text of both can be found at http://psychiatryonline.org/guidelines

OVERVIEW

Schizophrenia is a brain disorder is thought to be the expression of a group of genetically distinct conditions. The hallmark symptom is psychosis (e.g., experiencing auditory hallucinations [voices] and delusions [fixed false beliefs]). Additional symptoms may be divided into the following 4 domains:

- **Positive symptoms.** Psychotic symptoms, such as hallucinations, which are usually auditory; delusions; and disorganized speech and behavior
- **Negative symptoms.** Decrease in emotional range, poverty of speech, and loss of interests and drive; the person with schizophrenia has tremendous inertia
- **Cognitive symptoms.** Neurocognitive deficits (eg, deficits in working memory and attention and in executive functions, such as the ability to organize and abstract); patients also find it difficult to understand nuances and subtleties of interpersonal cues and relationships
- **Mood symptoms.** Member may seem cheerful or sad in a way that is difficult to understand; may be depressed.

Impaired cognition or a disturbance in information processing is a less vivid symptom that interferes with day-to-day life. People with schizophrenia have lower rates of employment, marriage, and independent living compared with other people. Schizophrenia is a clinical diagnosis. It must be differentiated from other psychiatric and medical illnesses, as well as from disorders such as heavy metal toxicity, adverse effects of drugs, and vitamin deficiencies. Treatment of schizophrenia requires an integration of medical, psychological, and psychosocial inputs. The bulk of care occurs in an outpatient setting and is best carried out by a multidisciplinary team. Psychosocial rehabilitation is an essential part of

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treatment. Antipsychotic medications (or neuroleptic medications or major tranquilizers) may diminish the positive symptoms of schizophrenia and prevent relapses however they are also associated with a number of adverse effects.[1]

Diagnostic Criteria

Schizophrenia is not associated with any characteristic laboratory results. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5), to meet the criteria for diagnosis of schizophrenia, the member must have experienced at least 2 of the following symptoms*:[2]

- Delusions
- Hallucinations
- Disorganized speech
- Disorganized or catatonic behavior
- Negative symptoms

* At least 1 of the symptoms must be the presence of delusions, hallucinations, or disorganized speech.

Continuous signs of the disturbance must persist for at least 6 months, during which the member must experience at least 1 month of active symptoms (or less if successfully treated), with social or occupational deterioration problems occurring over a significant amount of time. These problems must not be attributable to another condition.

The American Psychiatric Association (APA) removed schizophrenia subtypes from the DSM-5 because they did not appear to be helpful for providing better-targeted treatment or predicting treatment response.

Management of Schizophrenia

In 1951, Laborit and Huguenard administered chlorpromazine to patients for its potential anesthetic effects during surgery. Shortly thereafter, Hamon et al. and Delay et al. extended the use of this treatment in psychiatric patients and serendipitously uncovered its antipsychotic activity. Between 1954 and 1975, about 15 antipsychotic drugs were introduced in the United States and about 40 throughout the world. These medications, termed conventional antipsychotics, are also referred to as first generation antipsychotics, typical antipsychotics, major tranquilizers and/or classic neuroleptics. Conventional antipsychotics are most often utilized in the treatment of psychotic disorders (schizophrenia, acute psychosis, psychotic depression) and behavioral disturbances, but have also been utilized off-label for a variety of psychiatric illnesses (e.g., Tourette's disorder, depression with anxiety). They can also be used on or off-label (depending on medication) for nausea/vomiting and hiccups.[3,4]

Conventional antipsychotics are classified as either high or low potency in reference to their activity at the dopamine-2 receptor. High potency antipsychotics are more likely to cause adverse effects such as extrapyramidal symptoms (EPS) and hyperprolactinemia, while low potency antipsychotics are more likely to cause dry mouth, constipation, orthostatic hypotension, weight gain and sedation. Conventional antipsychotics were utilized for many years as first line in the treatment for schizophrenia and other psychotic disorders, until the introduction of clozapine in the United States (1990) opened the era of "atypical" antipsychotic drugs. Atypical antipsychotics became the mainstay for the treatment of numerous psychiatric disorders as they were theoretically thought to be more efficacious (particularly for negative symptoms) and better tolerated (less serious side effects). Current literature suggests the need for individualized treatment and the utility of first generation antipsychotics as viable options in treatment. Schizophrenia is a psychiatric diagnosis that describes a mental disorder characterized by impairments in the perception or expression of reality and by significant social or occupational dysfunction. A person experiencing schizophrenia is typically characterized as demonstrating disorganized thinking, and as experiencing delusions or hallucinations, in particular auditory hallucinations. With the possible exception of clozapine for patients with treatment-resistant symptoms, antipsychotics generally have similar efficacy in treating the positive symptoms of schizophrenia. To date, there is no definitive evidence that one second-generation antipsychotic will have superior efficacy compared with another, although in an individual patient there may be clinically meaningful differences in response.[3,4]

Antipsychotic medications diminish the positive symptoms of schizophrenia and prevent relapses. There is no clear antipsychotic drug of choice for schizophrenia. Clozapine is the most effective medication but is not recommended as first-line therapy due to a rare but serious complication, agranulocytosis. Psychosocial treatment is essential. The best-studied psychosocial treatments are social skills training, cognitive-behavioral therapy, cognitive remediation, cognitive enhancement training, and social cognition training. Psychosocial treatments are currently oriented according to the recovery model. According to this model, the goals of treatment for a person with schizophrenia are as follows:[2]

- To have few or stable symptoms
- Not to be hospitalized
- To manage his or her own funds and medications
- To be either working or in school at least half-time

Prevalence

The onset of schizophrenia usually occurs between the late teens and the mid-30s. For males, the peak age of onset for the first psychotic episode is in the early to middle 20s; for females, it is in the late 20s. The first 5-10 years of the illness can be stormy, but this initial period is usually followed by decades of relative stability (though a return to baseline is unusual). Positive symptoms are more likely to remit than are cognitive and negative symptoms. The prevalence of schizophrenia is about the same in men and women. The onset of schizophrenia is later in women than in men, and the clinical manifestations are less severe. This may be because of the anti-dopaminergic influence of estrogen. Although some variation by race or ethnicity has been reported, no racial differences in the prevalence of schizophrenia have been positively identified. The lifetime prevalence of schizophrenia has generally been estimated to be approximately 1% worldwide; other research found a lifetime risk of 4.0 per 1000 population.[1]

PROFESSIONAL ORGANIZATIONS

WellCare adheres to the 2004 practice guideline from the American Psychiatric Association[2]. The document can be accessed at http://psychiatryonline.org/guidelines. A 2009 update highlights key research studies published since 2004:

- With regard to pharmacotherapy, there have been several important randomized trials of antipsychotics.
  - *For chronic schizophrenia,* trials include the National Institute of Mental Health (NIMH) Clinical Antipsychotic Trial for Intervention Effectiveness (CATIE) and the United Kingdom–funded Cost Utility of the Latest Antipsychotics in Schizophrenia (CUtLASS).
  - *For first-episode schizophrenia,* there are two industry-funded trials, the European First Episode Schizophrenia Trial (EUFEST)—funded by AstraZeneca, Pfizer, and Sanofi-Aventis—and the Comparison of Atypicals for First Episode Schizophrenia (CAFE)—funded by AstraZeneca. For early-onset schizophrenia, there is one trial, the NIMH-funded Treatment of Early-Onset Schizophrenia Spectrum Disorders (TEOSS).
- These trials point to a reconsideration of treatment with the antipsychotics perphenazine and molindone and by extension other first-generation antipsychotics, with the possible exception of haloperidol, for which some trials have shown greater rates of extrapyramidal side effects or less favorable clinical response (2). In addition, a recent population-based cohort study (3) that encompassed 11 years of follow-up showed decreased rates of mortality with perphenazine as compared with other first- and second-generation antipsychotic agents; only clozapine use was associated with lower rates of overall mortality.
- In addition, randomized controlled trials have demonstrated the safety and efficacy of a new antipsychotic, paliperidone, leading to its approval by the U.S. Food and Drug Administration (FDA). Several controlled clinical trials have investigated treatments to prevent or treat antipsychotic-related weight gain and metabolic changes. Additionally, there have been promising clinical trials of bupropion and behavioral interventions to reduce smoking in schizophrenia patients.
- With regard to psychosocial treatments, new studies lend some additional support to the treatments recommended in the 2004 guideline. In addition, combinations of treatments have begun to be tested to enhance supported employment and social skills training. An evidence base has developed for interventions for obesity and for smoking cessation. There also has been continued study of cognitive remediation and peer support and peer-delivered services, which have the potential to play a useful role in recovery.

In addition, WellCare adheres to the American Psychiatric Association (2002) *Practice Guideline for the Treatment of Patients with Bipolar Disorder, Second Edition*. WellCare adheres to the 2005 Guideline Watch – the document contains an update of the 2002 guideline. The text of both can be found at http://psychiatryonline.org/guidelines.

SPECIAL CONSIDERATIONS

The FDA has added a warning to the labeling of the antipsychotic ziprasidone and its generic versions on the risk of DRESS (drug reaction with eosinophilia and systemic syndromes), a rare but potentially fatal skin reaction. Ziprasidone is used to treat schizophrenia and bipolar I disorder. The warning, for the capsule, oral suspension, and injection formulations, is based on reports of six patients who developed signs and symptoms of DRESS 11 to 30 days after initiation of ziprasidone treatment.[2]

MEMBER EDUCATION

The nature of schizophrenia makes it a potentially difficult illness for members to understand. Nevertheless, teaching the member to understand the importance of medication compliance and of abstinence from alcohol and other drugs of abuse is important. Education may improve adherence to medication and help the member cope with the illness. People with schizophrenia have also championed self-help recovery-based approaches to care, with an emphasis on developing the personal strengths and resilience needed to combat this illness. Because other illnesses are common in schizophrenia, education about the importance of a healthy lifestyle and regular health care is helpful. Counseling with respect to sexuality, pregnancy, and sexually transmitted diseases is important for these members. The following resources may also be helpful to members:[1]

- **Mayo Clinic** - http://www.mayoclinic.org/diseases-conditions/schizophrenia/basics/definition/con-20021077
- **National Alliance on Mental Illness (NAMI)** – http://www.nami.org/
- **National Institute of Mental Health -** http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml
- **Medline Plus -** http://www.nlm.nih.gov/medlineplus/schizophrenia.html

MEASURES OF COMPLIANCE

The following items are monitored for compliance by WellCare:

- SZ1 - Compliance with treatment plan addressed
- SZ2 - Suicide risk assessment completed
- SZ3 - Post discharge family involvement and follow up attempted.

CMS has not published any measures for this topic. NCQA has published the following measures for this topic:

Follow-Up After Hospitalization for Mental Illness. Members who are hospitalized due to a mental health diagnosis should follow up with a mental health practitioner:

- 7-Day Follow-Up should include an outpatient visit, intensive outpatient visit or partial hospitalization with a mental health practitioner within 7 days after discharge.
- 30 Day Follow-Up should include an outpatient visit, intensive outpatient visit or partial hospitalization with a mental health practitioner within 30 days after discharge.

Adherence to Antipsychotic Medications for Individuals with Schizophrenia. Members 18 to 64 years of age with schizophrenia should remain on an antipsychotic medication for at least 80% of their treatment period.

Cardiovascular Monitoring for People with Cardiovascular Disease and Schizophrenia. Members 18 to 64 years of age with schizophrenia and cardiovascular disease should have an LDL-C test annually.

Diabetes Screening for People with Schizophrenia or Bipolar Disorder who are Using Antipsychotic Medications. Members 18 to 64 years of age with schizophrenia or bipolar disorder who were dispensed an antipsychotic medication should have an annual diabetes screening.

Diabetes Monitoring for People with Diabetes and Schizophrenia. Members 18 to 64 years of age with schizophrenia and diabetes should have an annual LDL-C test and HbA1c test.

RELATED CLINICAL PRACTICE GUIDELINES

In addition to the information contained in this document, please reference the following CPGs: *Diabetes in Adults:* HS 1009, *Persons with Substance Use Disorders*: HS 1031, and *Substance Use Disorders*: HS 1031.

REFERENCES

1. Frankenburg, FR. Schizophrenia. *MedScape* http://emedicine.medscape.com/article/288259-overview. Published Dec 22, 2014. Accessed July 31, 2015.
2. Practice guideline for the treatment of patients with schizophrenia (2nd ed.). American Psychiatric Association Web site. http://psychiatryonline.org/guidelines. Published 2004. Accessed March 1, 2016.
3. Shen WW. A history of antipsychotic drug development. Compr Psychiatry. 1999 Nov-Dec;40(6):407-14.
4. Department of Psychiatry, Saint Louis University, School of Medicine, MO 63104-1016, USA. Comprehensive Psychiatry (Impact Factor: 2.26). 11/1999; 40(6):407-14. DOI: 10.1016/S0010-440X(99)90082-2.
5. Practice guideline for the treatment of patients with bipolar disorder (2nd ed.). American Psychiatric Association Web site. http://psychiatryonline.org/guidelines. Published 2002. Accessed March 1, 2016.

LEGAL DISCLAIMER

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

Date	History and Revisions by the Medical Policy Committee
3/3/2016	• Approved by MPC. Inclusion of APA reference and CPG Hierarchy.
8/6/2015, 3/5/2015	• Approved by MPC. Added items from Care Management Training; included Measures of Compliance.
1/9/2014, 12/1/2011	• Approved by MPC. No changes.
12/1/2010	• Approved by MPC.