ANTIPSYCHOTICS AGENTS – ATYPICAL

A. FDA approved indications For Adults

1. Schizophrenia - treatment-resistant (Clozapine)
2. Reduction in risk of recurrent suicidal behavior in Schizophrenia or Schizoaffective Disorder (Clozapine)
3. Bipolar Disorder: depressive or acute manic episodes (Quetiapine IR/XR)
4. Bipolar Disorder: depressive episodes (Olanzapine/Fluoxetine, Quetiapine IR/XR)
5. Bipolar Disorder Maintenance:
   • Monotherapy: Aripiprazole, Olanzapine, Risperidone and Risperdal Consta
   • Adjunctive treatments: Lithium, Depakote, Quetiapine IR/XR, Zipsidone, and Quetiapine
6. Agitation with Schizophrenia or Bipolar Disorder: IM Formulations (Aripiprazole, Olanzapine, Zipsidone for Schizophrenia ONLY)
7. Treatment of agitation in Schizophrenia: Aripiprazole and Olanzapine
8. MDD Adjunctive treatment: Aripiprazole and Quetiapine XR
9. Treatment Resistant Depression (Symbyax)
10. Schizoaffective Disorder (Invega)

B. FDA approved indications For Children/Adolescents

1. Schizophrenia in children and adolescents 13-17y.o. (Aripiprazole, Risperidone, Quetiapine IR, Olanzapine)
2. Bipolar disorder: acute manic/mixed episodes 10-17 y.o. (Aripiprazole, Risperidone, quetiapine, Olanzapine)
3. Bipolar Disorder: depressive episodes (Olanzapine/Fluoxetine, Quetiapine IR/XR, Olanzapine)
4. Treatment of irritability associated with Autistic Disorder, including symptoms of aggression towards others, deliberate self-injuriousness; temper tantrums, and quickly changing moods
   • 5-16 y.o. (Risperidone)
   • 6-17 y.o (Aripiprazole)
C. Non-FDA approved common uses:

Required
1. Psychotic Depression
2. Augmentation in Anxiety Disorders, Sleep Disorder
3. Pervasive Developmental Disorders, behavioral disturbances, and Autism
4. Augmentation in Tic disorders and Tourette’s Syndrome
5. Substance-induced Psychosis
6. Specific Movement Disorders e.g. Huntington’s Chorea and Parkinson’s Disease
7. Personality Disorder symptoms
8. Severe agitation and aggressive outbursts in children and adolescents

Documentation Required

C. Minimal Documentation
1. All standard outpatient & inpatient requirements

Documentation Required

D. Dosing Information
(Refer to Medication Maximum Daily Dose (MDD) and Tables 1&2)

1. “As needed” dosing of Antipsychotics:
   - Should be minimized, given lack of evidence for efficacy
   - Documentation should include rationale for using antipsychotics instead of standard, alternative treatments.

2. Use of Quetiapine for sleep disturbance: In the absence of mood or psychotic symptoms, the use of Quetiapine <150mg for >60 days is discouraged and requires documentation of specific rationale. Documentation should include: list of prior trials of pharmacological and non-pharmacological agents and the outcome, implementation of healthy sleep hygiene and must document discussion of risk vs. benefit in context of metabolic syndrome.

3. Applicable to Abilify Maintenna ONLY:
   - Prior to starting Abilify Maintena, Aripiprazole naïve patients require two weeks of oral Aripiprazole to establish tolerability.
• After the first ABILIFY MAINTENA injection, continue with oral aripiprazole or other antipsychotics for two weeks to maintain therapeutic antipsychotic concentration during initiation of therapy.

• Dosage adjustment needed for 2D6 poor metabolizer and/or with 3A4 inhibitors (see PI for details).

4. Applicable to Aripiprazole Lauroxil (Aristada)

• For patients naïve to aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment with Aristada.

• In conjunction with the first Aristada injection, administer treatment with oral aripiprazole for 21 consecutive days.

• 10mg qday oral Aripiprazole is equivalent to 441mg qmonth, 15mg qday equal to 662mg and 20mg qday equal to 882mg. 441 & 662mg may be administered monthly and 882mg may be administered monthly or q6weeks.

•Dosage adjustments are required for 1. Known CYP2D6 poor metabolizers and 2. For patients taking CYP3A4 inhibitors, CYP2D6 inhibitors, or CYP3A4 inducers (See PI for more details).

• For patients with both strong CYP3A4 and strong CYP2D, avoid 662mg and 882mg doses of Aristada.

5. Applicable to Invega Sustenna ONLY:

• For patients who have never taken oral Paliperidone or oral or injectable risperidone, it is recommended to establish tolerability with oral Paliperidone or oral risperidone prior to initiating treatment with Invega Sustenna®.
• Upon initiation of therapy with Invega Sustenna®, cross coverage with oral Paliperidone or Risperidone is not necessary.

6. Applicable to Risperdal Consta ONLY:

• For patients who have never taken oral Risperidone, it is recommended to establish tolerability with oral Risperidone prior to initiating treatment with Risperdal Consta®.

• Oral Risperidone (or another antipsychotic medication) should be given with the first injection of Risperidal Consta® and continued for 3 weeks (and then discontinued) to ensure that adequate therapeutic plasma concentrations are maintained prior to the main release phase of risperidone from the injection site.

Documentation Required E. Duration of Use/Medication Changes

• Inpatient and Outpatient: Document rational for all dosage or medication changes in each progress note.

Documentation Required F. Polypharmacy

1. Documentation regarding failed monotherapy must include specifics such as: dosage, duration of therapy and the clinical response (see purpose section of medication guideline for patients that are currently on polypharmacy i.e. at the time of transfer).

2. Use of more than one antipsychotic agent beyond the 90 days cross titration period requires the following documentation:

• That a risk/benefit analysis was performed and discussed with the patient
• The rationale for not attempting to taper or discontinue the poly pharmacy regimen every 6 month period

G. Drug Interactions

(Refer to Epocrates.com or http://www.uptodate.com/contents/second-generation-antipsychotic-medications-pharmacology-administration-and-side-effects#H191680213)
H. Black Box Warnings

(Refer to Table 4)

1. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

2. ARIPIPRAZOLE, QUETIAPINE, SYMBYAX, LATUDA ONLY
   - Children, adolescents, and young adults up to age 24 taking antidepressants for Major Depressive Disorder (MDD) and other psychiatric disorders are at increased risk of suicidal thinking and behavior.

3. CLOZAPINE ONLY
   - Because of a significant risk of agranulocytosis, a potential life threatening adverse effect, Clozapine should be reserved for the use in (1) treatment of severely ill patients with schizophrenia who failed to show an acceptable response to adequate courses of standard antipsychotic drug treatment, or (2) for reducing the risk of recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder who are judged to be at risk for reexperiencing suicidal behavior.
   - Seizure has been associated with the use of Clozapine. Dose seems to be an important predictor of seizure, with a greater likelihood at higher Clozapine doses.
   - Analysis of post marketing safety databases suggested that Clozapine is associated with an increased risk of fatal myocarditis, especially during, but not limited to, the first month of therapy.
   - Orthostatic hypotension, with or without syncope, can occur with Clozapine treatment. Rarely, collapse can be profound, and be accompanied by respiratory and/or cardiac arrest. Orthostatic hypotension is more likely to occur in initial titration in association with rapid dose escalation.

4. ZYPREXA RELPREV
   a. Post-Injection Delirium/Sedation Syndrome-Adverse event with signs and symptoms consistent with Olanzapine overdose, in particular, sedation (including coma) and/or delirium, have been reported following injections of ZYPREXA RELPREV, ZYPREXA RELPREVV must be administered in a registered healthcare facility with
ready access to emergency response services. After each injection, patients must be observed at the healthcare facility by a healthcare professional for at least 3 hours. Because of this risk, ZYPREXA RELPREVV is available only through a restricted distribution program called ZYPREXA RELPREVV Patient Care Program and requires prescriber, healthcare facility, patient, and pharmacy enrollment.

Documentation required

I. **Standard laboratory and examination requirements**

(Refer to Table 3)

1. For Inpatient: Basic laboratory studies on admission
2. For Outpatient: (See Atypical Antipsychotic Lab Monitoring)

   Upon initiation of treatment, unless recent studies obtained elsewhere are documented, the following baseline studies are required:
   - Blood pressure
   - Weight and/or body mass index calculation (BMI). Consider baseline waist/hip ratio measurement
   - Fasting glucose
   - Fasting lipid panel
   - Complete blood count (CBC) (Per the guideline for Clozapine)

   There is an increased risk of myelosuppression with all antipsychotic agents especially in patients who are concomitantly on other myelosuppressive drugs i.e. CBZ and VPA. It is recommended to monitor more closely by ordering more frequent CBC with differentials.

3. *If signs/symptoms of tardive dyskinesia are noted, AIMS examination is required at least annually.*

4. **Applicable to Quetiapine only:**
   - Consider eye examination for cataracts at initiation of treatment or shortly thereafter and at 6 month intervals during chronic treatment

5. **Applicable to Clozapine only (Refer to Prescriber Information):**
   - Complete baseline prior to start date
-CBC with differential. However, only ANC needs to be monitored & reported to REM to rule out neutropenia.

- For general population i.e. those without benign ethnic neutropenia (BEN), interrupt treatment if neutropenia is suspected to be clozapine-induced for ANC less than 1,000 cells per microliter and 500 cells per microliter for those with BEN.

- Although re-challenging patients with clozapine-induced severe neutropenia is not recommended, patients may now be re-challenged if the prescriber determines that the risk of psychiatric illness is greater than the risk of recurrent severe neutropenia (refer to FDA safety bulletin for more details).

- Substantial drops in ANC do not require action unless the patient experiences neutropenia. 
https://www.fda.gov/drugs/drugsafety/ucm461853.htm

- Vital signs: BP, pulse and weight
- Consultation with a neurologist for patients with a history of seizures or intracranial disease

- During Clozapine treatment
  - ANC monitoring weekly from initiation to 6 months. Then every 2 weeks from 6 to 12 months and monthly after 12 months.

6. Consider additional or more frequent monitoring whenever there is a change in patient’s mental or physical status.

J. Pregnancy and Lactation (Refer to Table 4)

K. Absolute contraindications (Applicable to Clozapine only)

1. History of previous hypersensitivity of Clozapine or any other component of this drug
2. History of agranulocytosis
3. History of clozapine-induced severe granulocytopenia or agranulocytosis
4. Myeloproliferative disorder
5. Uncontrolled epilepsy
6. Severe CNS depression or comatose state
7. Concomitant use with other agents having a well-known potential to cause agranulocytosis or suppress bone marrow function
8. Initial WBC count less than 4000/mm$^3$
9. Initial granulocyte count less than 1500/mm$^3$

Documentation Required

L. Relative contraindications (Applicable to all atypical)
1. Recent myocardial infarction (within 6 weeks)
2. If baseline ECG indicates a QTc interval > 420 ms, caution using Geodon (consider cardiology consultation)

3. Applicable to Clozapine only:
   - Untreated hypertension or tachycardia
   - History of orthostatic hypotension
   - History of any serious physical illness in the prior month
   - Any agent with significant potential for bone marrow suppression or agranulocytosis, e.g. Carbamazepine
   - History of poor follow-through with frequent mandatory lab testing
   - Pregnancy category: B

M. Precautions: (Refer to Table 4 for Black Box Warnings and Pregnancy Categories)
1. Use with caution in:
   - The elderly, in the presence of cardiovascular disease and seizure disorders
   - In patients with: Suspected hepatic disorder (monitor clinically and measure transaminase periodically)
   - In patients with: Narrow angle glaucoma, Prostatic hypertrophy (May result in urinary retention)
   - Elderly patients with dementia related psychosis: increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) reported with Olanzapine, Aripiprazole and Risperidone.

2. Monitor if QT interval exceed 420 ms and discontinue drug if patient is symptomatic or if QT interval exceed
500 ms. Do not use ziprasidone in patients with a history of QTc prolongation, recent myocardial infarction, uncompensated heart failure, or in combination with drugs known to prolong the QTc interval. Patients with hypokalemia or hypomagnesemia may also be at risk.

3. Cigarette smoking is reported to induce the metabolism and decrease the plasma level of Clozaril and Zyprexa.

4. Agitation, aggression, delirium, worsening of psychosis, diaphoresis and abnormal movements associated with rapid Clozapine or Quetiapine withdrawal (suggested to taper clozapine by 25-100mg / week and quetiapine by 50-200 mg / week)

5. Confusion, disturbed concentration, disorientation (more common with high doses or in the elderly)

6. Lower seizure threshold

7. Orthostatic Hypotension

8. Weight gain is common with most second generation antipsychotics. Long term data is limited with Ziprasidone or Aripiprazole, moderate risk is seen with Quetiapine and risperidone, and high risk is seen with Clozapine and olanzapine. Weight gain may predispose to coronary artery disease, hyperglycemia, and obstructive sleep apnea

9. Metabolic syndrome, also called insulin resistance syndrome, consists of disturbed glucose metabolism, obesity, hyperlipidemia, and hypertension

10. Neuroleptic malignant syndrome – rare disorder characterized by muscular rigidity, tachycardia, hyperthermia, altered consciousness, autonomic dysfunction, and increase in CPK—can occur with any class of antipsychotic agent, at any dose, and at anytime (increased risk in hot weather). Other risk factors include polypharmacy, organic brain syndromes, mood disorders, dehydration, low serum sodium, exhaustion, and agitation
11. Lens change can occur after chronic use of quetiapine (reported incidence of 0.005%)

12. Pregnancy category and Nursing mother (See Table 3)

13. Applicable to Clozapine only:
   - Cardiomyopathy, signs and symptoms include exertional dyspnea, fatigue, orthopnea, paroxysmal nocturnal dyspnea, and peripheral edema
   - Fever should be evaluated to rule out the possibility of an underlying infectious process or the development of agranulocytosis
   - Pulmonary embolism, consider in those present with deep vein thrombosis, acute dyspnea, chest pain, or with other respiratory signs and symptoms
   - Hepatitis
   - Anticholinergic toxicity: eye, gastrointestinal, and prostate
   - Caution use in patients with renal or cardiac diseases

14. Applicable to Asenapine ONLY: The use of Saphris® (Asenapine Maleate) has been associated with serious type 1 hypersensitivity reactions which may include anaphylaxis, angioedema, low blood pressure, rapid heart rate, swollen tongue, difficulty breathing, wheezing, or rash. In several cases, these reactions occurred after the first dose. Healthcare professionals are encouraged to counsel patients who are receiving the drug about how to recognize the signs and symptoms of a serious allergic reaction.

15. Applicable to Aripiprazole ONLY: Compulsive or Uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with Aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). Such urges were reported to have stopped after dosage reduction or discontinuation (http://www.fda.gov/Drugs/DrugSafety/ucm498662.htm).

16. Applicable to Olanzapine ONLY: Olanzapine has been linked to a severe condition known as Drug
Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS may start as a rash that can spread to all parts of the body. It can include fever, swollen lymph nodes, and a swollen face. It causes a higher-than-normal eosinophil count that can cause inflammation or swelling. DRESS can result in injury to organs, including the liver, kidneys, lungs, heart, or pancreas and can lead to death. DRESSS is a potentially fatal drug reaction with a mortality rate of up to 10%. The FDA recommends that physicians immediately stop treatment with Olanzapine if DRESSS is suspected and consider systemic corticosteroids. (Please see the FDA Advisory for more details http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm500123.htm

17. Leukopenia, Neutropenia and Agranulocytosis have been reported with all antipsychotics.

Attachments:
Table 1: FDA-Approved Indications & Applicable Daily Dosing For Adults
Table 2: FDA-Approved Indications & Applicable Daily Dosing For Children/Adolescents
Table 3: Formulations & Dosing Requirements
Table 4: Laboratory Monitoring
Table 5: Black Box Warnings, Pregnancy Categories, Nursing Mother
Table 6: Adverse Effect Profile
Refer to appendix for standardized treatment algorithms including Texas Medication Algorithm.
Refer to appendix for American Diabetic Association Guidelines for use of atypical antipsychotics.
Medication Practice Guideline Appendix section is available online @ www.sccmhd.org
Rev. 6-2012

References:
2. WWW.Epocrates.com
3. WWW.MicorMedix.com
4. FDA Package Insert for each respective Atypical Antipsychotic medication
**Table 1: FDA-Approved Indications & Applicable Daily Dosing in mg Unless Specified For Adults**

<table>
<thead>
<tr>
<th>FDA Approved Indications</th>
<th>Agitation with schizophrenia (IM)</th>
<th>Agitation with schizophrenia or bipolar disorder (IM)</th>
<th>Bipolar Disorder maniac</th>
<th>Bipolar Disorder: depressive</th>
<th>Schizophrenia</th>
<th>SAD</th>
<th>MDD, adjunct</th>
<th>Treatment Resistant Depression</th>
<th>Schizophrenia: Treatment-Resistant Depression</th>
<th>Schizophrenia/SAD: Reduction in Risk of Recurrent Suicidal Behavior</th>
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<tr>
<td>Aripiprazole (Abilify) b</td>
<td>9.75-30</td>
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<td>10-30</td>
<td>2-15</td>
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<tr>
<td>Aripiprazole Lauroxil (Aristada)</td>
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<td>441-882 qmonth or 882 q6wks</td>
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<td>Aripiprazole (Abilify Maintena)</td>
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<td>460mg IM qmonth</td>
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<td>Asenapine (Saphris)</td>
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<td>10-20</td>
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<td>Brexpiprazole (Rexulti)</td>
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<td>1-4</td>
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<td>Iloperidone (Fanapt)</td>
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<td>12-24</td>
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<td>Lurasidone (Latuda)</td>
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<td>20-120</td>
<td>40-160</td>
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<tr>
<td><strong>Olanzapine (Zyprexa) + Zydis</strong></td>
<td>10-30</td>
<td>5-20</td>
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<td>Olanzapine (Relprev IM) c</td>
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<td>210 q2wks to 405 q4wks</td>
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<tr>
<td>Olanzapine&amp; Fluoxetine (Symbyax)</td>
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<td>3/25 to 18/75</td>
<td>3/25 to 18/75</td>
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<td>Paliperidone (Invega)</td>
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<td>6-12</td>
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<td>Paliperidone palmitate (Sustenna IM)</td>
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<td>39-234 q4wks</td>
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<td>Paliperidone palmitate (Invega Trinza IM)</td>
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<td>273-819 q3months</td>
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<td>Quetiapine (Seroquel/IR)</td>
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<td>50-800</td>
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<td>Quetiapine (Seroquel/XR)</td>
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<td>50-300</td>
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<td>Risperidone (Risperdal)</td>
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<td>2-6</td>
<td>1-16</td>
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<td>Risperidone (Risperdal Consta IM) d</td>
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<td>12.5-50 q2wks</td>
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<td>Ziprasidone (Geodon)</td>
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<td>10-40</td>
<td>40-160</td>
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</tbody>
</table>

*Bolded agents reflect formulary status at SCVHHS.*

**Notes:**

a Reference: Prescribing Information (PI), Epocrates, Micromedex

b Abilfy is considered non-formulary on SCVHHS Formulary Effective 12/01/2011.

c Zyprexa Relprev: Due to the need for rigorous monitoring, SCCMH department does not support the use of Relprev in its outpatient programs.

d When initiating tx, overlap with oral Risperidone or other antipsychotics x3 weeks.
Table 2: FDA-Approved Indications & Applicable Daily Dosing in mg Unless Specified for Children/Adolescents

<table>
<thead>
<tr>
<th>FDA Approved Indications b</th>
<th>Bipolar Disorder: both depressive/acute manic episodes</th>
<th>Bipolar Disorder: acute manic/mixed episodes</th>
<th>Bipolar Disorder: depressive episodes</th>
<th>Schizophrenia</th>
<th>Irritability with autistic disorder a</th>
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</thead>
<tbody>
<tr>
<td>Aripiprazole (Abilify) c</td>
<td>2-30 child/adol 10-17yo</td>
<td>2-30 child/adol 10-17yo</td>
<td>2-30 child/adol 13-17yo</td>
<td>2-15 child/adol 6-17yo</td>
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<tr>
<td>Olanzapine (Zyprexa) + Zydis</td>
<td>2.5-20 child/adol 13-17yo</td>
<td>5-20 child/adol 10-17 yo</td>
<td>2.5-20 child/adol 13-17yo</td>
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<tr>
<td>Olanzapine&amp; Fluoxetine (Symbyax)</td>
<td>3/25 to 18/75</td>
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<tr>
<td>Quetiapine (Seroquel/IR)</td>
<td>50-600 child/adol 10-17yo</td>
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<td>50-800 child/adol 13-17 yo</td>
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<tr>
<td>Quetiapine (Seroquel/XR)</td>
<td>50-800 child/adol 10-17yo</td>
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<td>Risperidone (Risperdal)</td>
<td>0.5-6 child/adol&gt;10yo</td>
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<td>1-6 child/adol 13-17yo</td>
<td>0.5-1 child/adol 5-16yo</td>
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</tbody>
</table>

Bolded agents reflect formulary status at SCVHHS.

a Irritability includes symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods.
b Reference: Prescribing Information (PI), Epocrates, Micromedex
c Abilfy is considered non-formulary on SCVH&HS Formulary Effective 12/01/2011.
d Zyprexa Relprev: Due to the need for rigorous monitoring, SCCMH department does not support the use of Relprev in its outpatient program.
<table>
<thead>
<tr>
<th>Formulations</th>
<th>Dosing Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tablet or capsule (mg)</strong></td>
<td><strong>Oral solution</strong></td>
</tr>
<tr>
<td>Aripiprazole (Abilify)</td>
<td>2,5,10,15,20,30</td>
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<tr>
<td>Aripiprazole Lauroxil (Aristada)</td>
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<tr>
<td>Aripiprazole (Abilify Maintena)</td>
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<tr>
<td>Asenapine (Saphris)</td>
<td>5,10 SL</td>
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<tr>
<td>Brexiprazole (Rixulti)</td>
<td>0.25, 0.5, 1, 2, 3,4 mg</td>
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<td><strong>Clozapine (Clozaril)</strong></td>
<td>25, 50, 100, 200</td>
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<td>Iloperidone (Fanapt)</td>
<td>1,2,4,6,8,10,12</td>
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<tr>
<td>Lurasidone (Latuda)</td>
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<td><strong>Olanzapine (Zyprexa, Relprevv IM)</strong></td>
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</tr>
<tr>
<td>Olanzapine&amp; Fluoxetine (Symbyax)</td>
<td>3/25,6/25,6/50,12/25,</td>
</tr>
<tr>
<td><strong>Paliperidone (Invega, Sustenna IM, Paliperidone (Invega Trinza)</strong></td>
<td>1.5,3,6,9 ER</td>
</tr>
<tr>
<td>Quetiapine (Seroquel IR, XR)</td>
<td>25,50,100,200,300, 400,50XR,150XR,20 0XR, 300XR,400XR</td>
</tr>
<tr>
<td>Risperidone (Risperdal, Risperdal Consta IM)</td>
<td>.25,.5,1, 2,3,4</td>
</tr>
<tr>
<td>Ziprasidone (Geodon)</td>
<td>20,40,60, 80</td>
</tr>
</tbody>
</table>

**Bolded agents reflect formulary status at SCVHHS.**

* Bipolar Disorder Depression is administered once daily at bedtime.
* Lurasidone (Latuda) should be take with food, at least 350 calories.
* Quetiapine (Seroquel) XR should be taken without food or a light meal (approx 300 cal)
* Ziprasidone (Geodon) – The absorption of Geodon is increased 2-fold in the presence of food (>500 calories)

References: Epocrates, Precribing Information, Micromedex
Table 4: Laboratory Monitoring Requirements

<table>
<thead>
<tr>
<th>Table 1 – Metabolic monitoring parameters based on American Diabetes Association/American Psychiatric Association consensus guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Medical history*</td>
</tr>
<tr>
<td>Weight (BMI)</td>
</tr>
<tr>
<td>Waist circumference</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Fasting glucose/hemoglobin A₁c</td>
</tr>
<tr>
<td>Fasting lipids</td>
</tr>
</tbody>
</table>

* Personal and family history of obesity, diabetes, hypertension, and cardiovascular disease.

Revised by ADA in 2010

Reference:

http://www.psychiatrictimes.com/metabolic-disorders/metabolic-monitoring-patients-antipsychotic-medications/page/0/3
### Table 5: Black Box Warnings, Pregnancy Categories, Nursing Mother

<table>
<thead>
<tr>
<th>Black Box Warning</th>
<th>Pregnancy Category (PC); Nursing Mother (NM)</th>
</tr>
</thead>
</table>
| **Aripiprazole**   | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
2. Increased Suicidality risk in children and adolescent up to age 24  
PC: C  
NM: not know if excreted in milk, do not breast feed |
| **Asenapine**      | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: C  
NM: not know if excreted in milk, do not breast feed |
| **Brexirazole** (Rixulti) | Increase mortality in elderly patients w/ dementia-related psychosis  
2. Increased Suicidality risk in children and adolescent up to age 24  
Evidence has demonstrated fetal abnormalities or risks. Use alternative agents. Harmful effects during breastfeeding cannot be ruled out |
| **Clozapine**      | 1. Agranulocytosis;  
2. Seizures  
3. Myocarditis  
4. Other adverse cardiovascular and respiratory effects, including orthostatic hypotension, collapse, respiratory and/or cardiac arrest;  
5. Increase mortality in elderly w/ dementia-related psychosis  
PC: B  
NM: excreted in milk, do not breast feed |
| **Iloperidone**    | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: C  
NM: not know if excreted in milk, do not breast feed |
| **Lurasidone**     | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: B  
NM: not know if excreted in milk, do not breast feed |
| **Olanzapine**     | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: C  
NM: excreted in milk, do not breast feed |
| **Olanzapine IM**  | 1. Patients are at risk for severe sedation (including coma) and/or delirium after each injection and must be observed for at least 3 hours in a registered facility with ready access to emergency response services. Because of this risk, Zyrexa Relprevv is available only through restricted distribution program called Zyrexa Relprevv Patient Care Program, and requires prescriber, healthcare facility, patient, and pharmacy enrollment.  
PC: C  
NM: excreted in milk, do not breast feed |
| **Olanzapine& Fluoxetine** | 1. Increased mortality in elderly patients w/ dementia-related psychosis  
2. Increased Suicidality risk in children and adolescent up to age 24  
PC: C  
NM: excreted in milk, do not breast feed |
| **Paliperidone**   | 1. Increased mortality in elderly patients with Dementia-related psychosis  
PC: C  
NM: excreted in milk, do not breast feed |
| **Quetiapine**     | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
2. Increased Suicidality risk in children and adolescent up to age 24  
PC: C  
NM: excreted in milk, do not breast feed |
| **Risperidone**    | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: C  
NM: excreted in milk, do not breast feed |
| **Ziprasidone**    | 1. Increase mortality in elderly patients w/ dementia-related psychosis  
PC: C  
NM: not know if excreted in milk, do not breast feed |

Bolded agents reflect formulary status at SCVMC
### Table 6: Selected adverse effects of antipsychotic medications for schizophrenia

<table>
<thead>
<tr>
<th></th>
<th>Weight gain/diabetes mellitus</th>
<th>Hypercholesterolemia</th>
<th>EPS/TD</th>
<th>Prolactin elevation</th>
<th>Sedation</th>
<th>Anticholinergic side effects</th>
<th>Orthostatic hypotension</th>
<th>QTc prolongation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First generation agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
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<td>+</td>
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<tr>
<td>Fluphenazine</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>–/+</td>
<td>–</td>
<td>ND</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>–/+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Loxapine</td>
<td>++</td>
<td>ND</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>–</td>
<td>ND</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>++</td>
<td>ND</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>–</td>
<td>ND</td>
</tr>
<tr>
<td>Pimozide</td>
<td>+</td>
<td>ND</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Thioridazine*</td>
<td>++</td>
<td>ND</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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<td>Thiothixene</td>
<td>++</td>
<td>ND</td>
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<tr>
<td>Trifluoperazine</td>
<td>++</td>
<td>ND</td>
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<td>++</td>
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<td>+</td>
<td>+</td>
<td>ND</td>
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<tr>
<td><strong>Second generation agents</strong></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–/+</td>
</tr>
<tr>
<td>Asenapine</td>
<td>++</td>
<td>–</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>–</td>
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<td>+</td>
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<tr>
<td>Brexpiprazole®</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–/+</td>
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<td>–/+</td>
<td>–/+</td>
</tr>
<tr>
<td>Cariprazine®</td>
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<td>–/+</td>
<td>++</td>
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<td>+</td>
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<td>–/+</td>
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<tr>
<td>Medicine</td>
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<tr>
<td>Clozapine</td>
<td>±</td>
<td>±</td>
<td>–/+</td>
<td>–/+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Iloperidone</td>
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<td>Lurasidone</td>
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<td>–/+</td>
<td>++</td>
<td>–</td>
<td>+</td>
<td>–/+</td>
</tr>
<tr>
<td>Olanzapine</td>
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<td>+</td>
<td>++</td>
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<td>Paliperidone</td>
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<td>+++</td>
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<td>–</td>
<td>++</td>
<td>±</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+++</td>
<td>+++</td>
<td>–/+</td>
<td>–/+</td>
<td>++</td>
<td>++</td>
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<td>Risperidone</td>
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<td>Ziprasidone</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

Adverse effects may be dose dependent.

EPS: extrapyramidal symptoms; TD: tardive dyskinesia; ND: no data.

* Thioridazine is also associated with dose-dependent retinitis pigmentosa. Refer to text.

¶ Based upon limited experience.

Δ Clozapine also causes granulocytopenia or agranulocytosis in approximately 1 percent of patients requiring regular blood cell count monitoring. Clozapine has been associated with excess risk of myocarditis and venous thromboembolic events including fatal pulmonary embolism. These issues are addressed in the UpToDate topic review of guidelines for prescribing clozapine section on adverse effects.

References:
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