Psychotropic Medication Audit Criteria and Guidelines

Aripiprazole (Abilify®, Abilify® Maintena™, Aristada®)
Asenapine (Saphris®)
Brexpiprazole (Rexulti®)
Cariprazine (Vraylar®)
Iloperidone (Fanapt®)
Lumateperone (Caplyta®)
Lurasidone (Latuda®)
Olanzapine (Zyprexa®, Zyprexa® Relprevv™)
Paliperidone (Invega®, Invega Sustenna®, Invega Trinza®)
Quetiapine (Seroquel®)
Risperidone (Risperdal®, Risperdal Consta®)
Ziprasidone (Geodon®)

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Indications

This document lists only FDA-approved indications from the product labeling. The PEFC acknowledges that there are off-label indications for use that have supporting evidence for efficacy. If a medication is prescribed for an off-label indication, documentation in the patient chart is recommended.

- Aripiprazole: bipolar I disorder; irritability associated with Autistic Disorder; major depressive disorder, adjunct; schizophrenia; Tourette's disorder
- Asenapine: bipolar I disorder; schizophrenia
- Brexpiprazole: major depressive disorder, in combination with antidepressants; schizophrenia
- Cariprazine: bipolar I disorder, acute mixed or manic episodes; depressed bipolar I disorder; schizophrenia
- Iloperidone: schizophrenia
- Lumateperone: depressive episodes in bipolar I or II disorder, monotherapy or in combination with lithium or valproate; schizophrenia
- Lurasidone: depressive episodes in bipolar I disorder, monotherapy or in combination with lithium or valproate; schizophrenia
- Olanzapine: agitation, acute; bipolar I disorder, acute mixed or manic episodes, maintenance therapy; depressive episodes in bipolar I disorder, in

combination with fluoxetine; major depressive disorder, treatment-resistant, in combination with fluoxetine; schizophrenia;
- Paliperidone: schizoaffective disorder; schizophrenia
- Quetiapine: bipolar disorder, depressive episodes; bipolar I disorder, acute manic or mixed episodes; bipolar I disorder, maintenance, in combination with lithium or valproate; major depressive disorder, adjunct; schizophrenia; bipolar I disorder
- Risperidone: bipolar I disorder, acute manic or mixed episodes, monotherapy or in combination with lithium or valproate; irritability associated with Autistic Disorder; schizophrenia
- Ziprasidone: agitation, acute; bipolar I disorder, acute manic or mixed episodes, monotherapy; bipolar I disorder, maintenance, in combination with lithium or valproate; schizophrenia

Black Box Warning

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo.
- Aripiprazole, quetiapine: Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies.

Contraindications

- Hypersensitivity to agent or any components of the product
- Asenapine: severe hepatic impairment (Child-Pugh C)
- Lurasidone: coadministration with strong CYP3A4 inducers or inhibitors
- Ziprasidone: known history of QT prolongation, including congenital long QT syndrome; concomitant administration with other drugs that cause QT prolongation; uncompensated heart failure; recent acute myocardial infarction

Warnings and Precautions

- Blood dyscrasias including neutropenia, leukopenia, and agranulocytosis
- Body temperature regulation
- Cerebrovascular adverse events (stroke, transient ischemic attack) in elderly patients with dementia-related psychosis
- Cognitive and motor impairment
- Dementia-related psychosis
- Metabolic changes (hyperglycemia, dyslipidemia, weight gain)
- Esophageal dysmotility and aspiration
- Tardive dyskinesia
- Falls
- Neuroleptic malignant syndrome (NMS)

- Orthostatic hypotension
- Seizures
- Aripiprazole: impulse control impairment; suicidal thoughts and behaviors in children, adolescents, and young adults; suicide
- Asenapine: hyperprolactinemia; hypersensitivity reactions; QT interval prolongation
- Brexpiprazole: impulse control impairment
- Cariprazine: late-occurring adverse reactions
- Iloperidone: QT interval prolongation; hyperprolactinemia; priapism; suicide
- Lurasidone: hyperprolactinemia; activation of mania/hypomania; neurological adverse reactions with patients with Parkinson's Disease or Dementia with Lewy Bodies
- Olanzapine: anticholinergic effects; drug reaction with eosinophilia and systemic symptoms (DRESS); hyperprolactinemia; suicide
- Paliperidone: QT interval prolongation; hyperprolactinemia; gastrointestinal obstructive symptoms; priapism
- Quetiapine: increases in blood pressure (children and adolescents; QT prolongation; hyperprolactinemia; hypothyroidism; anticholinergic effects; cataracts; increased risk of suicidal thinking and behavior in children, adolescents, and young adults; may precipitate a mixed\manic episode; discontinuation syndrome
- Risperidone: hyperprolactinemia; priapism; patients with phenylketonuria
- Ziprasidone: QT prolongation; rash; severe cutaneous adverse reactions, including DRESS and SJS; hyperprolactinemia; priapism; suicide

Adverse Reactions

Side Effects Which Require Medical Attention

- Anticholinergic effects
- Hypotension, orthostatic hypotension
- Hypertension, increased systolic and/or diastolic blood pressure
- Hyperpyrexia
- Muscle rigidity
- Autonomic instability (irregular pulse or blood pressure, tachycardia, and diaphoresis)
- Nausea
- Vomiting
- Constipation
- Visual changes
- Dizziness
- Somnolence/altered mental status
- Extrapyramidal side effects (akathisia, dystonia, parkinsonism)
- Tardive dyskinesia
- Amenorrhea

- Galactorrhea
- Gynecomastia
- Agranulocytosis
- Leukopenia
- Nasal congestion
- Hyperglycemia
- Clinically significant weight gain
- Hypercholesterolemia or hyperlipidemia
- ECG changes (QTc > 500 msec)
- Cataracts (quetiapine)
- Seizures
- Rash
- Priapism
- Suicidal thoughts and behaviors

Drug Interactions of Major Significance

- Concomitant use of drugs that prolong QTc interval
- Concomitant use of CNS depressants
- Concomitant use of anticholinergic drugs
- Concomitant use of drugs that may lower blood pressure
- Concomitant use of drugs that cause EPS
- Concomitant use with lithium may enhance the neurotoxic effect of antipsychotic agents
- May diminish the therapeutic effect of anti-Parkinson agents
- May diminish the stimulatory effect of amphetamines
- May diminish the therapeutic effect of antidiabetic agents
- Concomitant use with strong inhibitors or inducers of Cytochrome 450. The following are the major metabolic pathways for the atypical antipsychotics:
  - Aripiprazole: CYP 2D6 and 3A4
  - Asenapine: CYP 1A2 and UGT1A4 (direct glucuronidation)
  - Brexpiprazole: CYP3A4 and 2D6
  - Cariprazine: CYP3A4 and 2D6
  - Iloperidone: CYP 3A4 and 2D6
  - Lumateperone: CYP 3A4 and UGT (glucuronidation)
  - Lurasidone: CYP 3A4
  - Olanzapine: CYP 1A2 and 2D6 (minor)
  - Paliperidone: (non-hepatic, primarily renal elimination)
  - Quetiapine: CYP 3A4
  - Risperidone: CYP 2D6 and 3A4 (minor)
  - Ziprasidone: aldehyde oxidase, 3A4 and 1A2 (minor)

See: Indiana Univ Drug Interaction Table

See: Lexicomp, Micromedex for more information

Special Populations

- Pediatrics/Adolescents
  - Aripiprazole, asenapine, lurasidone, olanzapine, quetiapine, risperidone, paliperidone, and ziprasidone: See "Psychotropic Medication Utilization Parameters for Children and Youth in Texas Public Behavioral Health (6th Version)" for specific details.
  - Brexpiprazole, cariprazine, and iloperidone: Reviewed but not included/ recommended by the Psychotropic Medication Utilization Parameters for Children and Youth in Texas Public Behavioral Health (6th Version)
  - Lumateperone: Safety and effectiveness not established in pediatric patients
- Geriatric
  - Elderly patients have an increased risk of adverse effects to antipsychotics. Consider increased risk relative to the small beneficial effect in the treatment of dementia-related psychosis and behavioral disorders.
  - Usually require lower dose and more gradual dose titrations
- Renal
  - Brexpiprazole: maximum dose adjusted for moderate to severe or ESRD (CrCl less than 60 mL/min)
  - Cariprazine: not recommended in severe (CrCl less than 30 mL/min)
  - Lurasidone: dose adjustment indicated in moderate to severe (CrCl less than 50 mL/min)
  - Paliperidone: dose adjustment indicated in mild to moderate to severe (CrCl 10 to <80 mL/min); not recommended in severe (CrCl <10 mL/min)
  - Risperidone: initial dose may be adjusted in renal impairment
- Hepatic
  - Asenapine: contraindicated in severe (Child-Pugh C)
  - Brexpiprazole: maximum dose adjusted for moderate to severe (Child-Pugh score 7 or greater)
  - Cariprazine: not recommended in severe (Child-Pugh score 10 to 15)
  - Iloperidone: not recommended in severe hepatic impairment, dose reduction may be required in moderate
  - Lumateperone: not recommended in moderate or severe (Child-Pugh B or C)
  - Lurasidone: dose adjustment indicated in moderate to severe (Child-Pugh score 7 to 15)
  - Quetiapine: dose adjustment may be indicated in hepatic impairment
  - Risperidone: initial dose may be adjusted in hepatic impairment

- Hemodialysis
  - No dosage adjustments provided in the manufacturer's labeling
- Pregnancy and Breastfeeding
  - Review product-specific labeling. Consider risks/benefits in reviewing medication-specific labeling

Patient Monitoring Parameters

Baseline Tests:

- Pregnancy test (females of childbearing potential)
- Waist circumference and BMI (weight in lbs x 703)/height^2 in inches
- FPG or HbA1c
- Fasting lipid panel within 30 days of initiation if not done within last year
- EPS evaluation (exam for rigidity, tremor, akathisia)
- TD assessment
- ECG at baseline or as soon as scheduling allows, and patient is able to cooperate
- Magnesium prior to initiating iloperidone and ziprasidone
- CBC
- CMP
- TSH

Ongoing:

- Bowel function- note at least weekly
- Pregnancy test (females) as clinically indicated
- BMI and waist circumference monthly for 6 months then quarterly when dose is stable
- FPG or HbA1c repeat 3–4 months after starting then at least annually
- Fasting lipid panel 3-4 months after initiating a new antipsychotic and at least annually if lipid levels are in normal range; repeat every 6 months if LDL is > 130 mg/dL
- EPS evaluation weekly after initiation & dose increases, continue 2 weeks after last increase
- TD assessment every 3 months and as clinically indicated
- ECG as clinically indicated
- Serum potassium and magnesium periodically for iloperidone and ziprasidone if at risk of electrolyte disturbance
- CBC as clinically indicated
- CMP including renal and liver function annually
- TSH as clinically indicated
- Inquiry for symptomatic prolactin elevation yearly (quarterly during 1st year for antipsychotics associated with increased prolactin)

- Prolactin level annually if symptoms of prolactin elevation (e.g. gynecomastia, amenorrhea)
- Vision questionnaire and ocular evaluation yearly, ocular evaluation every 2 years if $\leq$ 40 years old
- Determine if metabolic syndrome criteria (3 of the 5 criteria) are met 3-4 months after initiating a new antipsychotic medication and at least annually thereafter
- Olanzapine PAMOATE injection requires continuous observation for sedation/delirium at least 3 hrs after injection

Dosing

- See HHSC Psychiatric Drug Formulary for dosage guidelines.
- Exceptions to maximum dosage must be justified as per medication rule.