Unnecessary Medications, Psychotropic Medications, and Medication Regimen Review Critical Element Pathway

Use for a resident who has potentially unnecessary medications, is prescribed psychotropic medications or has the potential for an adverse outcome to determine whether facility practices are in place to identify, evaluate, and intervene for potential or actual unnecessary medications. Use also to evaluate the medication regimen review (MRR) process.

NOTE: If the resident has a diagnosis of dementia and is receiving any psychotropic medications (including but not limited to antipsychotic medications) the surveyor should refer to the Dementia Care Critical Element Pathway as a guide to determine the facility's compliance at F744.

Review the Following in Advance to Guide Observations and Interviews:

☐ Review the most current comprehensive and most recent quarterly (if the comprehensive isn't the most recent assessment) MDS/CAAs for areas pertinent to the medications ordered such as adverse consequences and behaviors.

☐ Review all medications currently ordered or discontinued going back to the most recent signed recapitulation. Determine if the facility:

✓ **Documents an acceptable clinical indication for use.**
- Medication is prescribed for a diagnosed condition and not being used for convenience or discipline.
- Medication is clinically indicated to manage a resident's symptoms or condition where other causes have been ruled out.
- Signs, symptoms, or related causes are persistent or clinically significant enough (e.g., causing functional decline) to warrant the initiation or continuation of medication therapy.
- Intended or actual benefit is sufficient to justify the potential risk(s) or adverse consequences associated with the medication, dose, and duration.

✓ **Demonstrates use of written protocols or resources to guide antibiotic use.**
- The use of infection assessment tools for antibiotic use for one or more infections (e.g., use of a Situation, Background, Assessment and Recommendation (SBAR) communication tool for UTI assessment, application of the Loeb minimum criteria for initiation of antibiotics).

✓ **Demonstrates monitoring for each medication as appropriate.**
- The following medications pose a high risk for adverse consequences and should be monitored:
  - **Opioids –** assess pain, implement bowel program.
  - **Anticoagulant –** *monitoring for* bleeding/bruising, protime/international normalized ratio (PT/INR), interaction with other medications, lab work, *ensure* communication of lab values, implementation of new orders in response to lab values and/or symptoms.
  - **Diuretics –** edema, potassium level, signs of electrolyte imbalance.
  - **Insulin –** monitoring of blood glucose levels, hemoglobin A1c (HbA1c), and symptoms of hyper/hypoglycemia.
  - **Antibiotics –** interactions with other medications (e.g., warfarin), adverse events (e.g., rash, diarrhea); prescriptions must include documentation of indication, dose, route and duration and be reviewed 2-3 days after antibiotic initiation to assess response and labs, and prescriber should reassess antibiotic selection as appropriate.

  - **All psychotropics –** monitor behavioral expressions or indications of distress.
- Facility staff, along with the pharmacist and prescribing practitioner recognize and evaluate the onset or worsening of signs or symptoms, or a change in condition to determine whether these potentially may be related to the medication regimen; and follow up as necessary upon identifying adverse consequences.
- Facility staff monitor the effectiveness of each medication and make changes to the pharmacological intervention, when necessary.

✓ **Demonstrates appropriate dosing for each medication.**
- Is there documentation of a rationale for any medication that exceeds the manufacturer's recommendations, clinical practice guidelines, evidence-based guidelines or standards of practice?

✓ **Documents duration for each medication.**
- Medications are not used for an excessive duration.

✓ **Documents clinical rationale for continued use for the medications, as required.**
- Tapering when clinically indicated in an effort to discontinue or reduce the dose.
- Concomitant use of two or more medications in the same pharmacological class.
- Potential incompatibilities between medications.

✓ **Demonstrates a system that monitors and addresses the presence of or potential for adverse consequences.**
- A clear clinical rationale from the attending physician/prescribing practitioner for continuing a medication that may be causing an adverse consequence, including risks and benefits.

✓ **Demonstrates a system for and documents gradual dose reduction (GDR) for psychotropic medications *and non-pharmacological approaches*, unless contraindicated.**

✓ **Demonstrates adherence to requirements for as needed (PRN) psychotropic and antipsychotic medications.**
- Residents do not receive PRN psychotropic medications unless necessary to treat a diagnosed specific condition *that is* documented in the record.
- PRN orders for psychotropic medications which **are not** antipsychotic medications are limited to 14 days. The attending physician/prescriber may extend the order beyond 14 days if he or she believes it is appropriate. If the attending physician extends the PRN for the psychotropic medication, the medical record *should* contain a documented rationale and determined duration.
- PRN orders for psychotropic medications which **are** antipsychotic medications are limited to 14 days. A PRN order for an antipsychotic cannot be renewed unless the attending physician/prescriber evaluates the resident to determine if it is appropriate to write a new PRN order for the antipsychotic medication. The evaluation entails direct evaluation of the resident and assessment of the resident's current conditions and progress to determine if the PRN antipsychotic medication is still needed. Attending physician/prescribing practitioner documentation of the evaluation should address:
  - Whether the antipsychotic medication is still needed on a PRN basis?
  - What is the benefit of the medication to the resident?
  - Have the resident's expressions or indications of distress improved as a result of the PRN antipsychotic medication?

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☐ Review the care plan for medications, especially high-risk medications, and individualized approaches to care, including non-pharmacological interventions.

Observations:

☐ Are care planned interventions implemented for medications that pose a high risk for adverse consequences?

☐ What non-pharmacological approaches to care are used? Are they effective?

☐ What pharmacological interventions are used? Why was the medication used and was it effective (e.g., pain is relieved, distress is addressed)?

☐ How does staff respond and interact with the resident?

☐ Does the resident continue to show expressions or indications of distress? If so, how does staff respond?

☐ Are staff using a medication for convenience or discipline? If so, describe. (For concerns related to a medication that involves an inadequate indication for use and evidence shows the medication is also being used for the purpose of discipline or convenience rather than to treat the resident's medical symptoms, surveyors should assess compliance with §483.10(e)(1) and §483.12(a)(2), F605, Right to Be Free From Chemical Restraints.)

☐ Does the resident have psychosocial, behavioral, mental, or physical adverse consequences that may be related to a medication? *Evaluate if the resident experienced psychosocial harm related to a side effect(s) of a medication(s):*

- Anorexia/unplanned weight changes, edema;
- Decline in physical functioning (e.g., mobility or activities of daily living (ADLs));
- Rash, pruritus;
- Bleeding or bruising, spontaneous or unexplained;
- Respiratory changes;
- Bowel dysfunction (e.g., cramping abdominal pain);
- Urinary retention, incontinence;
- Dehydration or swallowing difficulty;
- Falls, dizziness, or headaches;
- Muscle/nonspecific pain or unexplained abnormal movement;
- Psychomotor agitation (restlessness, pacing, hand wringing);
- Psychomotor retardation (slowed speech, thinking, movement);
- Subdued, sedated, lethargic, or withdrawn;
- Insomnia or sleep disturbances;
- Mental status changes;
- Behavioral changes or unusual behavior patterns; or
- Depression, apathy or mood disturbance.

Resident, Family or Resident Representative Interview:

☐ What medications do you get and why do you need to take them?

☐ What are your goals for your medications?

☐ What alternatives to taking some of the medications, including non-pharmacological approaches, has staff told you about?

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- ☐ What information on the risk*s*, benefits and potential side effects of medications were you provided?
- ☐ What changes in your medications have occurred, including gradual dose reductions for psychotropic medications?

  NOTE: Permission given by or a request made by the resident and/or representative does not serve as a sole justification for the medication itself.
- ☐ Do you think the medication has helped (e.g., pain control, improvements in function, decrease in edema, mood)? If not, why?
- ☐ What side effects have you had from the medication (ask about specific medications)? Have you experienced any changes in what you are able to do since starting or changing a medication(s)? Do you have allergies to any medication(s)?
- ☐ Have you participated in discussions and/or care plan meetings about your medications?

Staff Interviews (Nursing Aides, Nurse, Director of Nursing (DON), Social Services):

- ☐ What, when, and to whom do you report changes in the resident's status (e.g., indications of distress or pain)?
- ☐ How do you learn what the resident's daily care needs are?
- ☐ What non-pharmacological approaches are used?
- ☐ What is the clinical indication for the medication?
- ☐ How does the facility monitor the medication?
  - ○ What monitoring tools or systems are used?
  - ○ How did the interdisciplinary team (IDT) determine what should be monitored?
  - ○ For psychotropic medications, how did you determine what behavior to monitor?
  - ○ How do you assure orders for medication monitoring are implemented (e.g., HbA1c, PT/INR)?
  - ○ How do you communicate relevant information regarding medication monitoring for this resident to other team members?
- ☐ How do you assess whether each medication is effective?
- ☐ How does the facility ensure a review of medications for GDRs?
- ☐ If the resident is on a psychotropic medication: When did you attempt to reduce the medication and what were the results?
- ☐ If the practitioner denied a GDR: Did the practitioner provide a *clinical rationale for not performing the* GDR?
- ☐ Why does the resident have *multiple* medications in the same class?
- ☐ How does the IDT determine what dose and duration is clinically indicated?
- ☐ If the amount of any medication exceeds the manufacturer's recommendations, clinical or evidence-based practice guidelines, or standards of practice, what is the rationale?
- ☐ How do you monitor for significant adverse consequences?
- ☐ Has the resident had a change in condition, diet, weight loss, dehydration, or acute illness? If so, what was done to assess the possible complications for these changes due to medications?
- ☐ Has the resident had an adverse reaction? If so, what and how was the adverse reaction addressed?
- ☐ How do you evaluate whether medications should be initiated, continued, reduced, discontinued, or otherwise modified? How often is the evaluation for modification conducted?
- ☐ Are there policies and procedures in place to address issues which include the different steps in the MRR process and steps to take when an identified irregularity requires immediate action?
- ☐ How are medication-related issues communicated to other staff, the attending practitioner or prescribing practitioner, and resident and, if appropriate, resident representative?

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- ☐ How do you monitor staff to ensure they are implementing care planned approaches?
- ☐ What was the rationale for the practitioner's decisions in managing the resident's medications or medication-related concerns?
- ☐ How did you involve the resident in decisions regarding medications?
- ☐ How often is the MRR conducted and are medical charts included in this review?
- ☐ Under what circumstances is the MRR conducted more often than monthly?
- ☐ How is the MRR process conducted for short-stay residents?
- ☐ Has there been a change in the resident's overall function and mood that potentially may indicate unnecessary medications or adverse reactions? If so, describe.
- ☐ If the resident is receiving PRN psychotropic or antipsychotic medication(s): How is this medication monitored and how does the IDT determine if the PRN medication is clinically indicated and ensure the PRN orders are consistent with PRN requirements for psychotropic and antipsychotic medications?
- ☐ Ask about any other related concerns the surveyor has identified.

Pharmacist Interview:

- ☐ Do you perform a monthly MRR (or more frequently if needed)?
- ☐ Do you include each resident's medical record in this monthly review?
- ☐ How do you evaluate PRN medications, specifically PRN psychotropic and antipsychotic medications?
- ☐ What are you reviewing (e.g., adequate indication, dose, continued need, and adverse consequences)?
- ☐ Did you identify and report to the attending physician, medical director, and DON any irregularities with this resident's medication regimen? Did you use a separate, written report?
- ☐ If the pharmacist didn't identify a specific issue, ask why the issue was not identified as an irregularity on the MRR.
- ☐ What is the MRR process for short-stay residents?
- ☐ What protocols to do you have in place (e.g., lab to monitor for adverse events and drug interactions related to use of antibiotics and other high-risk medications)?
- ☐ Are you part of the IDT who reviews this resident's medication?
- ☐ What steps do you take when an irregularity requires immediate action? Are these steps part of facility policy?

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Attending Practitioner, Medical Director, and DON Interviews:

- ☐ Did you receive a written report of irregularities identified during the MRR?
- ☐ Did you make a change in the resident's medication in response to the identified irregularity(ies) or document a rationale if you didn't make a change in the medication regimen?
- ☐ What is the rationale behind why the medication is being used (e.g., antipsychotic for dementia or other high-risk medications)?
- ☐ What other approaches were attempted prior to the use of a psychotropic medication and/or while attempting a GDR?
- ☐ When was a GDR last completed? What was the result?
- ☐ Are you included in the IDT meeting for this resident?

Record Review:

- ☐ Was the underlying cause (medical, environmental, or psychosocial stressors) of the conditions or symptoms requiring the medication identified?
- ☐ If a medication was discontinued, was there evidence *the medication was tapered down gradually*, if applicable (e.g., for psychotropic and antipsychotic medications)?
- ☐ Did the pharmacist conduct an MRR for the resident at least once a month that included a review of the resident's medical record?
- ☐ Did the pharmacist identify and report all medication irregularities to the attending physician, medical director, and DON? Were the irregularities documented on a separate, written report? Were the reports acted upon?
- ☐ Did the attending physician document in the medical record that the irregularity was reviewed? What, if any, action was taken? What rationale was documented if no change was made to the medication regimen?
- ☐ If the resident had a change in condition such as, dehydration or acute illness, was the medication regimen reviewed? Did the pharmacist complete a MRR?
- ☐ Is there evidence of actual or potential adverse events, such as allergic reactions, inadequate monitoring? (Refer to the CMS Adverse Drug Event Trigger Tool).
- ☐ Was there a "significant change" in the resident's condition (i.e., will not resolve itself without intervention by staff or by implementing standard disease-related clinical interventions; impacts more than one area of health; requires IDT review or revision of the care plan)? If so, was a significant change comprehensive assessment conducted within 14 days?
- ☐ Is the MAR accurate, complete and followed according to standards of practice?
- ☐ For antibiotics: Are signs or symptoms of infection documented? Have appropriate diagnostic tests been obtained to inform antibiotic selection and continuation?
- ☐ What is the facility response when monitoring indicates a lack of progress toward the therapeutic goal?
- ☐ What individualized, non-pharmacological approaches were documented, specifically for residents who receive psychotropic medications?
- ☐ Review the facility's policies regarding psychotropic medications and MRR. Are they updated and maintained? Does the policy include timeframes for the steps in the process? Does the policy include the steps the licensed pharmacist must take for a medication irregularity that requires urgent action?

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Critical Elements Decisions:

1. For the **Medication Regimen Review (MRR)**:
   A. Did the licensed pharmacist:
      - Conduct an MRR, at least monthly, that included a review of the resident's medical record;
      - Conduct an MRR more frequently, as needed; and
      - Report irregularities to the attending physician, medical director, and the DON?

   B. Did the attending physician document:
      - Review of identified irregularity(ies);
      - The action, if any, taken;
      - A rationale if no action is taken?

   C. Has the facility developed and implemented MRR policies and procedures?
      - Do they address, at a minimum:
        - Time frames for steps in the MRR process;
        - Steps the pharmacist must take when an irregularity requires urgent action.

   If No to any of the above, cite F756

2. For **Unnecessary Medications**: Did the facility ensure that each resident's medication regimen was free from unnecessary medications? (Note: If the unnecessary medication is a psychotropic medication, cite F758)
   If No, cite F757

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3. For **Psychotropic Medications**, did the facility ensure that:
   - they are used only to treat a specific, diagnosed, and documented condition;
   - a GDR was attempted *and non-pharmacological approaches to care were implemented*, unless clinically contraindicated;
   - PRN use is only if necessary to treat a specific, diagnosed, and documented condition;
   - PRN orders for psychotropic medications which **are not** for antipsychotic medications are limited to 14 days, unless the attending physician/prescribing practitioner documents a rationale to extend the medication;
   - PRN orders which **are** for antipsychotic medications are limited to 14 days, without exception and the attending physician/prescribing practitioner did not renew the order without first evaluating the resident?

   If No to any of the above, cite F758
   NA, the resident was not prescribed psychotropic medications.

4. Did the facility conduct ongoing review for antibiotic stewardship?
   If No, cite F881

5. For newly admitted residents and if applicable based on the concern under investigation, did the facility develop and implement a baseline care plan within 48 hours of admission that included the minimum healthcare information necessary to properly care for the immediate needs of the resident? Did the resident and resident representative receive a written summary of the baseline care plan that he/she was able to understand?
   If No, cite F655
   NA, the resident did not have an admission since the previous survey OR the care or service was not necessary to be included in a baseline care plan.

6. If the condition or risks related to medications were present at the time of the required comprehensive assessment, did the facility comprehensively assess the resident's physical, mental, and psychosocial needs to identify the risks and/or to determine underlying causes, to the extent possible, and the impact upon the resident's function, mood, and cognition?
   If No, cite F636
   NA, condition/risks were identified after completion of the required comprehensive assessment and did not meet the criteria for a significant change MDS OR the resident was recently admitted and the comprehensive assessment was not yet required.

7. If there was a significant change in the resident's status, did the facility complete a significant change assessment within 14 days of determining the status change was significant?
   If No, cite F637
   NA, the initial comprehensive assessment had not yet been completed therefore a significant change in status assessment is not required OR the resident did not have a significant change in status.

8. Did staff who have the skills and qualifications to assess relevant care areas and who are knowledgeable about the resident's status, needs, strengths and areas of decline, accurately complete the resident assessment (i.e., comprehensive, quarterly, significant change in status)?
   If No, cite F641

9. Did the facility develop and implement a comprehensive person-centered care plan that includes measurable objectives and timeframes to meet a resident's medical, nursing, mental, and psychosocial needs and includes the resident's goals, desired outcomes, and preferences?
   If No, cite F656
   NA, the comprehensive assessment was not completed.

10. Did the facility reassess the effectiveness of the approaches and review and revise the resident's care plan (with input from the resident and, if appropriate, the resident representative) to meet the resident's needs?
    If No, cite F657
    NA, the comprehensive assessment was not completed OR the care plan was not developed OR the care plan did not have to be revised.

*11. Do the practitioner's diagnostic practices meet professional standards? **NOTE**: CMS is aware of situations where practitioners have potentially misdiagnosed residents with a condition for which antipsychotics are an approved use (e.g., new diagnosis of schizophrenia) which would then exclude the resident from the long-stay antipsychotic quality measure.*
If No, cite F658

Other Tags, Care Areas (CA), and Tasks (Task) to Consider: Right to be Informed and Participate F552, F553, Notification of Change F580, Chemical Restraints F605, Choices (CA), *Activities (CA)*, Social Services F745, Admission Orders F635, Professional Standards F658, Pain (CA), General Pathway (CA) for Diabetic Management, Dementia Care (CA), ADLs (CA), Urinary Incontinence (CA), Behavioral-Emotional Status (CA), Nutrition (CA), Hydration (CA), Sufficient and Competent Staffing (Task), Physician Services F710, F711, Pharmacy Services F755, *Medical Director F841, Antibiotic Stewardship Program (Infection Control Task)*, *QAPI/QAA* (Task).

TMF Quality Innovation Network

Antipsychotic Medication Reference

User Guide

- Usual dosage ranges represent treatment of schizophrenia in healthy adults unless otherwise indicated. Dosage adjustments are often required based on patient age, renal and hepatic function, etc.
- Side effects/adverse effects are not necessarily listed in order of severity or frequency.
- Not all side effects/adverse effects are represented. Consult full prescribing information for complete list and frequency of side effects.
- Off-label uses identified by one or more references/compendia do not imply appropriate use.
- A Black Box Warning (BBW) provides an alert to serious or life-threatening risks with the use of a medication.

1st Generation Antipsychotics

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Chlorpromazine (Thorazine®): Usual oral dosage range for acute treatment of schizophrenia – 300-1000-mg/day in divided doses[1]	• Management of manifestations of psychotic disorders[2] • Treatment of schizophrenia[2] • Control the manifestations of the manic type of manic-depressive illness[2] • Treatment of severe behavioral problems in children marked by combativeness and/or explosive hyperexcitable behavior[2] • Short-term treatment of hyperactive children who show excessive motor activity with accompanying conduct disorders consisting of some or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability and poor frustration tolerance[2]	Adults and children (6 months to 12 years)[2]	• Behavioral symptoms associated with dementia (elderly); psychosis/agitation associated with dementia[3] • Treatment of migraine in adults (intramuscular/intravenous)[4]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[3] Drowsiness, extrapyramidal symptoms (dystonia, motor restlessness, pseudo-parkinsonism, tardive dyskinesia), neuroleptic malignant syndrome, lowering of seizure threshold, hyperprolactinemia, jaundice, hematologic disorders, agranulocytosis, hypotensive effects, ECG changes, convulsive seizures, allergic reactions, endocrine disorders, autonomic reactions, changes in skin pigmentation, ocular changes, increase in appetite, peripheral edema, lupus-like syndrome, weight changes, and hyperpyrexia[2]
Fluphenazine (Prolixin®): Usual oral dosage range for acute treatment of schizophrenia – 5-20mg/day in divided doses[1]	• Management of manifestations of psychotic disorders[5]	Adults[5]	• Psychosis/agitation associated with dementia[6] • Postherpetic neuralgia • Antiemetic[7] • Chorea of Huntington Disease[6] • Chronic tic disorders[6]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[6] Extrapyramidal symptoms, neuroleptic malignant syndrome, hyperprolactinemia, drowsiness, lethargy, nausea, loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, constipation, hypertension, fluctuations in blood pressure, blurred vision, glaucoma, bladder paralysis, fecal impaction, paralytic ileus, tachycardia, nasal congestion, metabolic and endocrine (weight change, peripheral edema, abnormal lactation, gynecomastia, menstrual irregularities, impotence), allergic reactions, hematologic changes, jaundice, lupus-like syndrome, hypotension severe enough to cause fatal cardiac arrest, altered electrocardiographic and electroencephalographic tracings, altered cerebrospinal fluid proteins, cerebral edema, asthma, laryngeal edema, and angioneurotic edema[5]

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Haloperidol (Haldol®): Usual oral dosage range for treatment of acute schizophrenia – 1-20mg/day in divided doses[1,8]	• Management of manifestations of psychotic disorders[9] • Tourette's syndrome[9]	Adults and children (3-12 years)[9]	• Treatment of nonschizophrenia psychosis • May be used for the emergency sedation of severely agitated or delirious patients • Adjunctive treatment of ethanol dependence • Postoperative nausea and vomiting (alternative therapy) • Psychosis/agitation associated with dementia[8] • Hiccups • Obsessive-compulsive disorder • Prevention of chemotherapy-induced nausea and vomiting • Phencyclidine psychosis (improving phencyclidine-induced aggression, combativeness, and schizophreniform symptoms like hallucinations, delusions and disorganized thinking)[10]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[8] Cardiovascular effects (arrhythmias, QT prolongation, torsades de points, sudden death, tachycardia), tardive dyskinesia, dystonia, neuroleptic malignant syndrome, hyperprolactinemia, extrapyramidal symptoms, hypotension, hypertension, insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, exacerbation of psychotic symptoms including hallucinations and catatonic-like behavioral states, hematologic effects, jaundice, dermatologic reactions, endocrine disorders, gastrointestinal effects, autonomic reactions (dry mouth, blurred vision, urinary retention, diaphoresis), respiratory effects (laryngospasm, bronchospasm), cataracts, retinopathy, and visual disturbances[9]
Loxapine (Loxitane®): Usual oral dosage range for acute treatment of schizophrenia – 30-100mg/day in divided doses[1]	• Treatment of schizophrenia[11] • Agitation associated with schizophrenia or bipolar I disorder[49]	Adults[11]	• Psychosis/agitation associated with dementia[49]	**BBW: Increased mortality in elderly patients with dementia-related psychosis** **BBW: Bronchospasm with inhalation**[49] Tardive dyskinesia, neuroleptic malignant syndrome, hematologic effects, extrapyramidal symptoms, tachycardia, hypotension, hypertension, orthostatic hypotension, lightheadedness, syncope, EKG changes, anticholinergic effects, dermatologic effects, hematologic effects, gastrointestinal side effects, weight gain, weight loss, dyspnea, ptosis, hyperpyrexia, flushing, headache, paresthesia, and polydipsia, galactorrhea, amenorrhea, gynecomastia, and menstrual irregularity[11]
Perphenazine (Trilafon®): Usual oral dosage range for acute treatment of schizophrenia – 16-64mg/day in divided doses[1]	• Treatment of schizophrenia[12] • Control of severe nausea and vomiting[12]	Adults and children ≥ 12 years[12]	• Psychosis/agitation associated with dementia[50]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[50] Tardive dyskinesia, neuroleptic malignant syndrome, hypotension (if pressor needed, use norepinephrine), hyperprolactinemia, extrapyramidal symptoms, convulsive seizures, jaundice, sedation, dry mouth or salivation, nausea, vomiting, diarrhea, anorexia, constipation, obstipation, fecal impaction, urinary retention, frequency or incontinence, bladder paralysis, polyuria, nasal congestion, pallor, myosis, mydriasis, blurred vision, glaucoma, perspiration, hypertension, change in pulse rate, allergic reactions, endocrine effect, cardiovascular effects (tachycardia, bradycardia, ECG changes), hematological effects, and ocular changes[12]
Pimozide (Orap®): Usual oral dosage range for treatment of Tourette's syndrome – 1-10mg/day in divided doses[13]	• Suppression of motor and phonic tics in patients with Tourette's syndrome who have failed to respond satisfactorily to standard treatment[14]	Adults and children ≥ 12 years[14]	• Parasitosis (delusional)[15]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[64] Tardive dyskinesia, sudden death, neuroleptic malignant syndrome, hematologic effects, extrapyramidal symptoms, ECG changes, hyperpyrexia, asthenia, chest pain, periorbital edema, postural hypotension, hypotension, hypertension, tachycardia, palpitations, increased salivation, nausea, vomiting, anorexia, GI distress, loss of libido, weight gain, weight loss, dizziness, tremor, parkinsonism, fainting, and dyskinesia[14]

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Prochlorperazine (Compazine®): Usual oral dosage range for acute treatment of schizophrenia – 50-150mg/day in divided doses[1]	• Treatment of schizophrenia (unsupported)[16] • Short-term treatment of generalized non-psychotic anxiety (unsupported)[16] • Control of severe nausea and vomiting[16]	Adults and children ≥ 20 pounds and ≥ 2 years[16]	• Treatment of intractable, severe migraine[65]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[51] Tardive dyskinesia, neuroleptic malignant syndrome, hypotension, extrapyramidal symptoms, drowsiness, dizziness, amenorrhea, blurred vision, skin reactions, leukopenia, agranulocytosis, and jaundice[16]
Thioridazine (Mellaril®): Usual oral dosage range for acute treatment of schizophrenia – 300-800mg/day in divided doses[1]	• Management of schizophrenic patients who fail to respond adequately to treatment with other antipsychotic drugs[17]	Adults and pediatric patients with schizophrenia who are unresponsive to other agents[17]	• Management of agitation and psychotic events in patients with dementia and Alzheimer's disease[18]	**BBW: Increased mortality in elderly patients with dementia-related psychosis** **BBW: Pro-arrhythmic effects including torsade de pointes**[52,65] Pro-arrhythmic effects (prolongation of QT interval), orthostatic hypotension, neuroleptic malignant syndrome, extrapyramidal symptoms, hyperprolactinemia, drowsiness, nocturnal confusion, lethargy, dry mouth, blurred vision, constipation, nausea, vomiting, diarrhea, dermatitis, skin eruptions, and endocrine effects[17]
Thiothixene (Navane®): Usual oral dosage range for acute treatment of schizophrenia – 6-50mg/day in divided doses[1,19]	• Management of schizophrenia[19]	Adults and children ≥ 12 years[19]	• Nonpsychotic patient, dementia behavior (elderly); psychosis/agitation associated with dementia[20]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[20] Tardive dyskinesia, extrapyramidal symptoms, sudden death, hyperprolactinemia, seizures, hematologic effects, neuroleptic malignant syndrome, hepatic effects, dry mouth, blurred vision, nasal congestion, constipation, increased sweating, increased salivation, tachycardia, hypotension, light-headedness, syncope, drowsiness, restlessness, agitation, insomnia, impotence, allergic reaction, jaundice, endocrine effects, hyperpyrexia, anorexia, nausea, vomiting, diarrhea, increase in appetite and weight, weakness or fatigue, polydipsia, and peripheral edema[19]
Trifluoperazine (Stelazine®): Usual oral dosage range for acute treatment of schizophrenia – 4-40mg/day in divided doses[1]	• Management of schizophrenia[21] • Short-term treatment of generalized non-psychotic anxiety[21]	Adults and children 6-12 years[21]	• Psychosis/agitation associated with dementia[53]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[53] Extrapyramidal symptoms, drowsiness, dizziness, skin reactions, rash, dry mouth, insomnia, amenorrhea, fatigue, muscular weakness, anorexia, lactation, blurred vision, and hematologic effects[21]

2nd Generation (Atypical) Antipsychotics

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Aripiprazole (Abilify®): Usual oral immediate release dosage range for monotherapy for treatment of schizophrenia – 15-30mg/day[22] (see full prescribing information for dosages for other indications)	• Autistic disorder – psychomotor agitation[23] • Bipolar disorder – psychomotor agitation[23] • Bipolar I disorder, adjunctive therapy with lithium or valproate[23] • Bipolar I disorder, monotherapy, manic or mixed episodes[23] • Major depressive disorder, adjunctive treatment in patients receiving antidepressant[23] • Schizophrenia – psychomotor agitation[23] • Schizophrenia[23] • Tourette's syndrome[25]	Can be used in children ages 6 and older; however, recommended ages differ for the various indications[23]	• Cocaine dependence[24] • Restless leg syndrome[24] • Trichotillomania[24] • Psychosis/agitation associated with dementia[25]	**BBW: Increased risk of suicidality in children, adolescents and young adults**[25] **BBW: Increased mortality in elderly patients with dementia-related psychosis**[25] Neuroleptic malignant syndrome, orthostatic hypotension, tardive dyskinesia, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): • Adult schizophrenia: akathisia • Adult (monotherapy) bipolar mania: akathisia, sedation, restlessness, tremor and extrapyramidal disorder • Adult (adjunctive therapy with lithium or valproate) bipolar mania: akathisia, insomnia, and extrapyramidal disorder • Adult major depressive disorder (adjunctive treatment to antidepressant therapy): akathisia, restlessness, insomnia, constipation, fatigue and blurred vision • Adult agitation associated with schizophrenia or bipolar mania: nausea[23]

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Asenapine (Saphris®): Usual oral dosage range for treatment of schizophrenia – 10-20mg/day in divided doses[22]	• Schizophrenia – acute treatment[26] • Schizophrenia – maintenance treatment[26] • Bipolar mania or mixed – monotherapy[26] • Bipolar mania or mixed – as an adjunct to lithium or valproate[26]	Safety and efficacy have not been established in children[26]	• Psychosis/agitation associated with dementia[54]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[54] Neuroleptic malignant syndrome, tardive dyskinesia, cerebrovascular events, QT prolongation, suicide, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): • Schizophrenia: akathisia, oral hypoesthesia, and somnolence • Bipolar Disorder (Monotherapy): somnolence, dizziness, extrapyramidal symptoms other than akathisia, and weight increase • Bipolar Disorder (Adjunctive): somnolence and oral hypoesthesia[26]
Brexpiprazole (Rexulti®): Usual oral dosage range for schizophrenia 1-4mg/day[57] (see full prescribing information for dosages for other indications)	• Major depressive disorder (adjunctive treatment)[57] • Schizophrenia[57]	Safety and effectiveness have not been established in pediatric patients[58]	• Psychosis/agitation related to Alzheimer's dementia[57]	**BBW: Increased mortality in elderly patients with dementia-related psychosis, increased risk of suicidal thoughts in patients ≤ 24 years**[57] Neuroleptic malignant syndrome, tardive dyskinesia, metabolic changes, leukopenia, neutropenia, agranulocytosis, orthostatic hypotension and syncope, seizures, falls[58] Most common adverse reactions were: • MDD: Weight increased and akathisia (≥ 5% and at least twice the rate for placebo) • Schizophrenia: Weight increased (≥ 4% and at least twice the rate for placebo)[58]
Cariprazine (Vraylar®): Usual oral dosage range for schizophrenia 1.5-6mg/day[59] (see full prescribing information for dosages for other indications)	• Schizophrenia • Bipolar I disorder (acute treatment of manic or mixed episodes)[59]	Safety and effectiveness have not been established in pediatric patients[60]	• Psychosis/agitation associated with dementia[59]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[59] Neuroleptic malignant syndrome, tardive dyskinesia, late occurring adverse reactions due to long half-life, metabolic changes, and orthostatic hypotension[60] Most common adverse reactions (incidence ≥ 5% and at least twice the rate of placebo) were: • Schizophrenia: extrapyramidal symptoms and akathisia • Bipolar mania: extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness[60]
Clozapine (Clozaril®, FazaClo® ODT): Usual oral immediate release dosage range for treatment of schizophrenia – 50-500mg/day in divided doses[22]	• Schizophrenia, treatment-resistant[27] • Recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorders[27]	Safety and efficacy has not been established in children[27]	• Parkinson's disease – Psychotic disorder[28] • Schizoaffective disorder[29] • Acute manic episodes associated with bipolar disorder; treatment of refractory bipolar mania[28] • Obsessive-compulsive disorders[28] • May be effective in the treatment of tardive dyskinesia[28] • Treatment resistant psychosis/agitation associated with dementia[28]	**BBW: Increased mortality in elderly patients with dementia-related psychosis** **BBW: Myocarditis, cardiomyopathy, and mitral valve incompetence, seizures, orthostatic hypotension, bradycardia, syncope, and severe neutropenia**[29] Agranulocytosis (mandatory monitoring, fatal if not detected early and therapy interrupted), adverse events observed in incidence of > 5%: • Central nervous system complaints including drowsiness/sedation, dizziness/vertigo, headache and tremor • Autonomic nervous system complaints including salivation, sweating, dry mouth and visual disturbances • Cardiovascular findings including tachycardia, hypotension and syncope • Gastrointestinal complaints including constipation and nausea; fever[27]
Iloperidone (Fanapt®): Usual oral dosage range for treatment of schizophrenia – 2-24mg/day in divided doses[22] (must titrate slowly from a low starting dose to avoid orthostatic hypotension due to alpha-adrenergic blocking properties)	• Schizophrenia[30]	Safety and effectiveness in pediatric patients has not been established[30]	• Psychosis/agitation associated with dementia[55]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[55] Neuroleptic malignant syndrome, QT prolongation, tardive dyskinesia Commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia, and weight increase[30]

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Lurasidone (Latuda®): Usual oral dosage range for treatment of schizophrenia 40-160mg/day[31]	• Schizophrenia[31] • Bipolar depression[56]	Safety and effectiveness in pediatric patients has not been established[31]	• Psychosis/agitation associated with dementia[56]	**BBW: Increased mortality in elderly patients with dementia-related psychosis, increased risk of suicidal thoughts in pediatric and young adult patients**[56] Neuroleptic malignant syndrome, tardive dyskinesia, metabolic changes, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): somnolence, akathisia, nausea and parkinsonism[31]
Olanzapine (Zyprexa®, Zyprexa® Zydis®, Zyprexa® Relprevv®): Usual oral immediate release dosage range for schizophrenia 10-20mg/day[22]	• Agitation – bipolar I disorder[32] • Agitation – schizophrenia[32] • Bipolar I disorder, acute mixed or manic episodes[32] • Bipolar I disorder – adjunct therapy with lithium or valproate[32] • Bipolar I disorder, maintenance therapy[32] • Schizophrenia[32] • Depressed bipolar I disorder[32] • Depression, Treatment-resistant; adjunct[32] • Bipolar disorder, depressed phase[32] • Major depressive disorder (treatment resistant)[32]	Adults and children > 13 years old[32]	• Agitation, acute-dementia[33,34] • Delirium[34] • Obsessive-compulsive disorder – adjunct therapy, treatment resistant[33,35] • Severe major depression with psychotic features[35] • Chronic pain; prevention of chemotherapy-associated delayed nausea or vomiting[34] • Tourette's syndrome[35] • Stuttering[35] • Parasitosis (delusional)[35] • Insomnia (elderly)[35] • Post-traumatic stress disorder[34]	**BBW: Increased mortality in elderly patients with dementia-related psychosis** **BBW: Post-injection delirium/sedation syndrome with Zyprexa Relprevv®**[66] Suicide, neuroleptic malignant syndrome, metabolic changes, commonly observed adverse reactions oral olanzapine (incidence ≥ 5% and at least twice placebo): postural hypotension, constipation, weight gain, dizziness, personality disorder, akathisia, asthenia, dry mouth, dyspepsia, increased appetite, somnolence, and tremor[32]
Olanzapine/fluoxetine (Symbyax®): Usual oral dosage range for bipolar and major depressive disorders 6/25-12/50mg/day[36]	• Bipolar disorder, depressed phase[36] • Major depressive disorder (treatment-resistant)[36]	Safety and effectiveness in children and adolescent patients has not been established[36]		**BBW: Increased mortality in elderly patients with dementia-related psychosis** **BBW: Suicidal thoughts and behaviors**[36] Neuroleptic malignant syndrome, metabolic changes, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): disturbance in attention, dry mouth, fatigue, hypersomnia, increased appetite, peripheral edema, sedation, somnolence, tremor, vision blurred, and weight increased Adverse reactions reported in clinical trials of olanzapine and fluoxetine in combination are generally consistent with treatment-emergent adverse reactions during olanzapine or fluoxetine monotherapy[36]
Paliperidone (Invega®): Usual oral immediate release dosage range for schizophrenia 3-9mg/day **Invega® Sustenna®** 39-234mg/month IM[22]	• Schizoaffective disorder[37] • Schizophrenia[37]	Adults > 18 years old[37]	• Psychosis/agitation related to Alzheimer's dementia[38] • Delusional parasitosis[38]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[38] QT prolongation, neuroleptic malignant syndrome, tardive dyskinesia, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): • Schizophrenia: extrapyramidal symptoms, tachycardia, akathisia • Schizoaffective disorder: extrapyramidal symptoms, somnolence, dyspepsia, constipation, weight increase and nasopharyngitis[37]
Pimavanserin (Nuplazid®): Usual dosage range for Parkinson disease psychosis 34mg/daily[61]	• Parkinson disease psychosis[61]	Safety and effectiveness have not been established in pediatric patients[61]		**BBW: Increased mortality in elderly patients with dementia-related psychosis**[61] QT interval prolongation Most common adverse reactions (≥ 5% and twice the rate of placebo): peripheral edema and confusional state[62]

Drug Name	FDA-Approved Indications	Age Group for Which Approved	Off-Label Uses	Side Effects/Adverse Effects
Quetiapine (Seroquel®, Seroquel® XR): Usual oral immediate release dosage range for schizophrenia 250-500mg/day in divided doses[22]	• Bipolar disorder, depressed phase[39] • Bipolar disorder (maintenance) as an adjunct to lithium or divalproex[39] • Acute treatment of manic episodes associated with bipolar I disorder, as monotherapy[39] • Acute treatment of mania as an adjunct to lithium or divalproex[39] • Schizophrenia[39] • Adjunctive treatment of major depressive disorders in combination with antidepressants (XR formulation only)[41,42]	Adults and children > 13 years old[39]	• Autism[40] • Delirium in critically ill patient[40] • Generalized anxiety disorder[40] • Post-traumatic stress disorder[40] • Delusional parasitosis[40] • Psychosis/agitation associated with dementia[41] • Insomnia, adjunct therapy in elderly[41] • Treatment resistant obsessive-compulsive disorder[33,41] • Alcohol dependence[41] • Psychosis in Parkinson's disease[41] • Trichotillomania[41]	**BBW: Increase mortality in elderly patients with dementia related psychosis** **BBW: Suicidal thoughts and behavior**[40] Neuroleptic malignant syndrome, metabolic changes, QT prolongation, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): somnolence, dry mouth, dizziness, constipation, asthenia, abdominal pain, postural hypotension, pharyngitis, weight gain, lethargy, ALT increased, and dyspesia[39]
Risperidone (Risperdal®): Usual oral immediate release dosage range for schizophrenia 2-8mg/day in divided doses **Risperdal® Consta®** 25-50mg every 2 weeks IM[22]	• Schizophrenia[43] • Autistic disorder – Irritability[43] • Bipolar I disorder – short term of acute manic or mixed episodes, in combination with lithium or valproate[43]	Adults and children > 5 years; however, recommended ages differ for the various indications[43]	• Stuttering[44] • Insomnia (elderly)[44] • Tardive dyskinesias[44] • Psychosis in Parkinson's disease[44] • Management of agitation and psychotic events in patients with dementia and Alzheimer's disease[44] • Tourette's syndrome[44] • Psychosis/agitation associated with dementia[33,44] • Obsessive-compulsive disorder-adjunct therapy[33] • Post-traumatic stress disorder[33,45] • Delirium in the critically ill patient[45] • Major depressive disorder[45]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[45] Neuroleptic malignant syndrome, tardive dyskinesia, metabolic changes, orthostatic hypotension, common adverse reactions in clinical trials (≥ 10%): somnolence, increased appetite, fatigue, insomnia, sedation, parkinsonism, akathisia, vomiting, cough, constipation, nasopharyngitis, drooling, rhinorrhea, dry mouth, abdominal pain-upper, dizziness, nausea, anxiety, headache, nasal congestion, rhinitis, tremor, and rash[43]
Ziprasidone (Geodon®): Usual oral dosage range 40-160mg/day[22]	• Bipolar I disorder, acute manic or mixed episodes, monotherapy[46] • Schizophrenia[46] • Acute agitation in schizophrenic patients[46]	Safety and effectiveness for pediatric patients has not been established[46]	• Psychosis/agitation associated with dementia[47] • Autism[48] • Tourette's syndrome[48] • Major depressive disorder[47]	**BBW: Increased mortality in elderly patients with dementia-related psychosis**[47] Neuroleptic malignant syndrome, tardive dyskinesia, hyperglycemia and diabetes mellitus, rash, commonly observed adverse reactions (incidence ≥ 5% and at least twice placebo): • Somnolence, respiratory tract infection, extrapyramidal symptoms (extrapyramidal syndrome, hypertonia, dystonia, dyskinesia, hypokinesia, tremor, paralysis, and twitching) • None of these adverse reactions occurred individually at an incidence greater than 10% in bipolar mania trials, dizziness (dizziness and lightheadedness), akathisia, abnormal vision, asthenia, vomiting, and headache[46]

REFERENCES

[1]Lehman AF, Kreyenbuhl J, Buchanan RW et al. The Schizophrenia Patient Outcomes Research Team (PORT). Updated Treatment Recommendations 2003. Schizophrenia Bulletin. 2004; 30(2): 193–217. [2]Chlorpromazine [prescribing information]. Indianapolis, IN: Upsher-Smith Laboratories, Inc. [3]Chlorpromazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 8. [4]Chlorpromazine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2012 February. [5]Fluphenazine [prescribing information]. Spring Valley, IN: Par Pharmaceuticals, Inc.; 2005. [6]Fluphenazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 5. [7]Fluphenazine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2012 January. [8]Haloperidol. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [9]Haloperidol [prescribing information]. Morgantown, IN: Mylan Pharmaceuticals Inc.; 2011. [10]Haloperidol. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2010 March. [11]Loxapine [prescribing information]. Philadelphia, IN: Lannett Company Inc.; 2011. [12]Perphenazine [prescribing information]. Huntsville, IN: Qualitest Pharmaceuticals. [13]Pimozide. In Facts & Comparisons Online [Internet Database] Indianapolis, IN: Wolters Kluwer Health. Updated 2011 Sept. [14]Pimozide [prescribing information]. Sellersville, IN: Gate Pharmaceuticals; 2011. [15]Pimozide. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2011 October. [16]Prochlorperazine [prescribing information]. Rockford, IN: UDL Laboratories, Inc. [17]Thioridazine [prescribing information]. Morgantown, IN: Mylan Pharmaceuticals Inc. [18]Thioridazine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2012 January. [19]Thiothixene [prescribing information]. Morgantown, IN: Mylan Pharmaceuticals Inc.; 2011. [20]Thiothixene. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 5. [21]Trifluoperazine [prescribing information]. Morgantown, IN: Mylan Pharmaceuticals Inc.; 2010. [22]Crismon L, Argo TR, Buckley PF. Chapter 76. Schizophrenia. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011. http://www.accesspharmacy.com/content.aspx?aID=7987911. Accessed June 4, 2012. [23]Abilify [prescribing information]. Tokyo, Japan: Otsuka Pharmaceutical Co, Ltd.; 2012. [24]Aripiprazole. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2012 March. [25]Aripiprazole. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 7. [26]Saphris [prescribing information]: Whitehouse Station, NJ: Merck & Co., Inc.; 2011. [27]Clozaril [prescribing information]: East Hanover, NJ: Novartis Pharmaceuticals Co.; 2011. [28]Clozapine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2011 Jan. [29]Clozapine In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 1. [30]Fanapt [prescribing information]: East Hanover, NJ: Novartis Pharmaceuticals Co.; 2011. [31]Latuda [prescribing information]: Marlborough, MA: Sunovion Pharmaceuticals Inc.; 2012. [32]Zyprexa [prescribing information]: Indianapolis, IN: Eli Lilly & Company; 2011. [33]Maglione M, Ruelaz Maher A, Hu J, et al. Off-Label Use of Atypical Antipsychotics: An Update. Comparative Effectiveness Review No. 43. (Prepared by the Southern California Evidence-based Practice Center under Contract No. HHSA290–2007–10062 – 1.) Rockville, MD: Agency for Healthcare Research and Quality. September 2011. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm. [34]Olanzapine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 15. [35]Olanzapine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2010 Aug. [36]Symbyax [prescribing information]: Indianapolis, IN: Eli Lilly & Company; 2012. [37]Invega [prescribing information]: Titusville, NJ: Janssen Pharmaceuticals; 2011. [38]Paliperidone. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [39]Seroquel [prescribing information]: Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2012. [40]Quetiapine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 8. [41]Quetiapine. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2010 March. [42]Seroquel (Quetiapine) XR. [prescribing information]: Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2012. [43]Risperdal [prescribing information]: Titusville, NJ: Ortho-McNeil-Janssen Pharmaceuticals, Inc.; 2011. [44]Risperdone. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2011 Sept. [45]Risperidone. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 8. [46]Geodon [prescribing information]: NY, NY: Roerig, division of Pfizer, Inc.; 2009. [47]Ziprasidone In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [48]Ziprasidone. In: Facts & Comparisons Online [Internet Database]. Indianapolis, IN: Wolters Kluwer Health. Updated 2012 March. [49]Loxapine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [50]Perphenazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 1. [51]Prochlorperazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 8. [52]Prochlorperazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [53]Trifluoperazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 3. [54]Asenapine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 September 8. [55]Iloperidone. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [56]Lurasidone. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [57]Brexpiprazole. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [58]Rexulti (brexpiprazole) [prescribing information]. Rockville, MD: Otsuka America Pharmaceutical; February 2017. [59]Cariprazine. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 31. [60]Vraylar (cariprazine) [prescribing information]. Irvine, CA: Allergan USA Inc.; February 2017. [61]Pimavanserin. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 August 21. [62]Nuplazid (pimavanserin) [prescribing information]. San Diego, CA: Acadia Pharmaceuticals Inc: April 2017. [63]Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. URL: http://www.clinicalpharmacology.com. Updated April 2017. [64]Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. URL: http://www.clinicalpharmacology.com. Updated April 2017. [65]Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. URL: http://www.clinicalpharmacology.com. Updated April 2017. [66]Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. URL: http://www.clinicalpharmacology.com. Updated April 2017.

Monitoring Guidelines and Adverse Effects

Assessments to monitor physical status and detect concomitant physical conditions		
Assessment	**Initial or Baseline**	**Follow-Up**
Vital signs	Pulse, blood pressure, temperature	As clinically indicated, particularly as medication doses are titrated
Hematology	CBC	If clinically indicated, including assessment of patients treated with clozapine
Blood chemistries	Electrolytes, renal function tests (BUN/creatinine ratio), liver function tests, thyroid function tests	Annually and as clinically indicated
Infectious diseases	Test for syphilis, hepatitis C and HIV, if clinically indicated	
Pregnancy	Consider pregnancy test for women of childbearing potential	
Toxicology	Drug toxicology/screen, heavy metal screen, if clinically indicated	Drug toxicology screen, if clinically indicated
Imaging/EEG	EEG, brain imaging (CT or MRI, with MRI being preferred), if clinically indicated	

Practice Guideline for the Treatment of Patients with Schizophrenia Second Edition, American Psychiatric Association, 2010; 1–184

Relative Side-Effect Incidence of Commonly Used Antipsychotics[a,b]						
	Sedation	**EPS**	**Anticholinergic**	**Orthostasis**	**Weight Gain**	**Prolactin**
Aripiprazole	+	+	+	+	+	+
Asenapine	+	++	+/–	++	+	+
Brexpiprazole	+	+	+	+	+	+
Cariprazine	+	++	+/-	+/-	?	?
Chlorpromazine	++++	+++	+++	++++	++	+++
Clozapine	++++	+	++++	++++	++++	+
Fluphenazine	+	++++	+	+	+	++++
Haloperidol	+	++++	+	+	+	++++
Iloperidone	+	+/–	++	+++	++	+
Lurasidone	+	+	+	+	+/–	+/–
Olanzapine	++	++	++	++	++++	+
Paliperidone	+	++	+	++	++	++++
Pimavanserin	+	+	+	++	?	?
Perphenazine	++	++++	++	+	+	++++
Quetiapine	++	+	+	++	++	+
Risperidone	+	++	+	++	++	++++
Thioridazine	++++	+++	++++	++++	+	+++
Thiothixene	+	++++	+	+	+	++++
Ziprasidone	++	++	+	+	+	+

EPS, extrapyramidal side effects; relative side-effect risk: ±, negligible; +, low; ++, moderate; +++, moderately high; ++++, high; ? unknown.

[a]Side effects shown are relative risk based on doses within the recommended therapeutic range.

[b]Individual patient risk varies depending on patient-specific factors.

Adapted from: Pharmacotherapy: A Pathophysiologic Approach. DiPiro J., et al. Copyright 2017. Reproduced with permission from McGraw-Hill Companies, Inc. [Sept. 20, 2017].

Antipsychotic agents. In: Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Updated 2017 June 20.

Second-Generation Antipsychotic Monitoring Guide							
	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Every 5 years
Personal Family History[+]	✓					✓	
Weight & Height (BMI)	✓	✓	✓	✓	✓		
Waist Circumference	✓					✓	
Blood Pressure	✓			✓		✓	
Fasting Plasma Glucose	✓			✓		✓	✓
Fasting Plasma Lipids	✓			✓			✓

[+]Family history of obesity, diabetes, dyslipidemia, hypertension and/or cardiovascular disease

Adapted from American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004; 27(2):596-601.

Definitions, Warnings and Precautions

Definitions of Select Adverse Effects

1. Tardive Dyskinesia: involuntary, repetitive body movements such as lip smacking, tongue protrusion and grimacing
2. Parkinsonism: tremor, decreased bodily movement, rigidity and postural instability
3. Anticholinergic Effects: dry mouth, dry eyes, difficulty urinating, constipation, blurred vision, confusion, memory impairment, drowsiness, nervousness, agitation, rapid heart rate and weakness
4. Extrapyramidal Symptoms (EPS): various movement disorders such as acute, sustained muscle contractions causing twisting and repetitive movements or abnormal postures (dystonic reactions), pseudoparkinsonism, and inability to initiate movement (akinesia) and/or inability to remain motionless (akathisia)

Warnings and Precautions[1]

- Elderly Patients with Dementia-Related Psychosis: increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack, including fatalities).
- Suicide/Suicidality and Antidepressants: increased risk of suicidality in children, adolescents and young adults with major depressive disorder; closely supervise high-risk patients.
- Neuroleptic Malignant Syndrome: manage with immediate discontinuation and close monitoring.
- Tardive Dyskinesia: discontinue if clinically appropriate.
- Metabolic Changes: atypical antipsychotic drugs have been associated with metabolic changes that include hyperglycemia/diabetes mellitus, dyslipidemia and body weight gain.
- Hyperglycemia/Diabetes Mellitus: monitor glucose regularly in patients with, and at risk for, diabetes.
- Dyslipidemia: undesirable alterations in lipid levels have been observed in patients treated with atypical antipsychotics.
- Weight Gain: weight gain has been observed with atypical antipsychotic use; monitor weight.
- Hyperprolactinemia: prolactin elevations occur and persist during chronic administration. Prolactin is a hormone that may cause breast enlargement (gynecomastia) and sexual dysfunction.
- Orthostatic Hypotension: use with caution in patients with known cardiovascular or cerebrovascular disease.

- Leukopenia, Neutropenia and Agranulocytosis has been reported with antipsychotics. Patients with a history of a clinically significant low white blood cell count or a drug-induced leukopenia/neutropenia should have their complete blood count monitored frequently during the first few months of therapy, and discontinuation of drug should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors.
- Seizures/Convulsions: use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.
- Potential for Cognitive and Motor Impairment: use caution when operating machinery.
- QT Prolongation: increases in QT interval; avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval.

Boxed Warning[2]

This type of warning is also called the Black Box Warning (BBW) and alerts to serious or life-threatening risks with the use of a medication.

> "Antipsychotic medications are not approved for the treatment of patients with dementia-related psychoses (see Boxed Warning)."

WARNING[3]

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature.

Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patient is not clear.

[1]Antipsychotic Agents. In: Facts & Comparisons Online [Internet Database], Indianapolis, IN: Wolters Kluwer Health. Updated 2012 Jan.

[2]U.S. Food and Drug Administration; Consumer Health Information; A Guide to Drug Safety Terms at FDA; November 2012

[3]Center for Drug Evaluation and Research; Approval Package for Zyprexa/Olnazapine; Eli Lilly; Approved Aug. 14, 2008.

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