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]

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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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