

	Drug Class	Indications	Drug Name	Warnings	Behaviors
Antidepressants	Selective Serotonin Reuptake Inhibitors (SSRIs)	Depression Off-label: panic disorder; SAD; OCD; PTSD	Citalopram (Celexa)*	<ul style="list-style-type: none"> ● Black Box Warning: <u>All antidepressants increase the risk in suicidal thinking and behavior (suicidality)</u> in children, adolescents, and young adults in the treatment of major depressive disorder. Although there is a reduction in risk in patients 65 years and older, monitor patients of all ages for <i>any</i> clinical worsening, suicidality, or changes in behavior. ● Beers' Criteria: <ul style="list-style-type: none"> ○ SSRIs and SNRIs may cause LOW sodium levels or cardiac changes (increased blood pressure or heart conduction). Use with caution in elderly. ○ Bupropion: Not recommended in patients with epilepsy. ● Serotonin Syndrome (except Bupropion): Agitated, confused, abnormal, fast heart rate; "seeing or hearing things that are not there," more stiffness, tremors 	<ul style="list-style-type: none"> ● Fatigue ● Loss of energy ● Sad expression ● Loss of interest in activities (including self-care) ● Crying ● Increased thoughts about wanting to die or "take their own life" ● Acting recklessly ● Refusal of food, care, or medications ● Inability to sleep ● Anxious, worrying ● Changes in appetite ● Nervousness ● Negative statements (guilt, worthlessness, hopelessness)
		Depression; GAD Off-label: panic disorder; SAD; OCD; PTSD	Escitalopram (Lexapro)		
		Depression; panic disorder; OCD Off-label: PTSD	Fluoxetine (Prozac)		
		OCD Off-label: depression; panic disorder; SAD; PTSD	Fluvoxamine (Luvox)		
		Depression; GAD; panic disorder; SAD; OCD; PTSD	Paroxetine (Paxil, Pexeva, Paxil CR)		
		Depression; panic disorder; SAD; OCD; PTSD Off-label: GAD	Sertraline (Zoloft)		
		Depression	Vilazodone (Viibryd)*		
	Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	Depression	Desvenlafaxine (Pristiq)*		
		Depression; GAD	Duloxetine (Cymbalta)		
		Depression	Levomilnacipran HCl (Fetzima)*		
			Milnacipran HCl (Savella)*		
		Depression; GAD; panic disorder; SAD; PTSD	Venlafaxine (Effexor, Effexor ER)		
	Tricyclic Antidepressants (TCAs)	Depression Off-label: PTSD	Amitriptyline (Elavil)		
		Depression	Amoxapine		
		OCD Off-label: Depression; panic disorder	Clomipramine (Anafranil)		
		Depression; insomnia	Doxepin (Silenor)		
		Depression	Nortriptyline (Pamelor)		
			Protriptyline HCl (Vivactil)*		
			Trimipramine maleate (Surmontil)*		
	Tetracyclic Antidepressants	Depression	Maprotiline HCl*		
			Mirtazapine (Remeron, Remeron SolTab)		

	Serotonin Reuptake Inhibitor	Depression Off-label: PTSD	Nefazodone HCl*	<ul style="list-style-type: none"> • Hypertensive Crisis (MAOIs only): N/V, neck stiffness, radiating occipital headaches, palpitations, sweating, clammy skin, fever 	
		Depression Off-label: insomnia	Trazodone HCl		
	Serotonin Reuptake Inhibitor; 5-HT1A receptor agonist; 5-HT3 receptor antagonist	Depression	Vortioxetine (Brintellix)*		
		Monoamine Oxidase Inhibitors (MAOIs)	Isocarboxazid (Marplan)*		
			Phenelzine sulfate (Nardil)* Tranylcypromine (Parnate)*		
Dopamine Reuptake Inhibitor	Depression; SAD	Bupropion (Aplenzin, Forfibo XL, Wellbutrin, Wellbutrin SR, Wellbutrin XL)			
Antipsychotics	1 st Generation, Typical	Schizophrenia; psychosis Off-label: Psychosis associated with Alzheimer's	Chlorpromazine	<ul style="list-style-type: none"> • Black Box Warning: Elderly patients with dementia-related psychosis treated with <u>all antipsychotic drugs</u> are at an <u>increased risk of death</u> via cardiac causes (heart failure, sudden death, stroke, CVA) or infections (pneumonia). • Black box warning(Clozapine): <ul style="list-style-type: none"> ○ <u>Life-threatening agranulocytosis</u> risk. Require ANC $\geq 2000/\text{mm}^3$ and WBC $\geq 3500/\text{mm}^3$ to use agent. Monitor ANC and WBC prior to and during treatment. Discontinue and do not rechallenge if ANC $< 1000/\text{mm}^3$ or WBC $< 2000/\text{mm}^3$. <u>Clozapine Registry enrollment needed.</u> ○ <u>Orthostatic hypotension, bradycardia, syncope, and</u> 	<ul style="list-style-type: none"> • <u>Delusions:</u> fixed false beliefs • <u>Hallucinations:</u> visual, auditory, tactile • <u>Paranoia:</u> Delusion with excessive irrational fear/anxiety • Yelling, anger outbursts • Physical resistance to care • <u>Flight of ideas:</u> Thoughts jump from one to another • <u>Catatonia:</u> Social withdrawal, lack of motivation, flat affect, poor attention • Neglect of self-care • Abnormal postures
			Fluphenazine*		
			Haloperidol (Haldol)		
			Perphenazine*		
		Severe motor and phonic tics in patients with Tourette's disorder Off-label: Psychosis	Pimozide (Orap)*		
		Schizophrenia; psychosis Off-label: Psychosis associated with Alzheimer's	Prochlorperazine*		
	Thioridazine HCl*				
	2 nd Generation, Atypical	Bipolar I; depression; schizophrenia Off-label: Psychosis associated with Alzheimer's	Trifluoperazine HCl*		
			Aripiprazole (Abilify)		
			Bipolar I, schizophrenia		
Treatment resistant schizophrenia; suicidal behavior in schizophrenia			Clozapine (Clozaril)*		
Schizophrenia	Schizophrenia	lloperidone (Fanapt)*			
Schizophrenia; depression associated with bipolar I	Schizophrenia; depression associated with bipolar I	Lurasidone (Latuda)*			

2 nd Generation, Atypical	Bipolar I (maintenance or acute mania); schizophrenia	Olanzapine (Zyprexa, Zydis ODT, Relprevv injection)	<p><u>cardiac arrest</u> in patients at risk for these events with Clozapine. Risk is highest during initial titration period especially with rapid dose increases.</p> <p>○ <u>Myocarditis and myopathy risk</u> increased with Clozapine.</p> <ul style="list-style-type: none"> ● Black box warning (Olanzapine injection): Sedation (coma) and delirium (agitation, anxiety, confusion, disorientation) can occur. ● Beers' Criteria: Increased risk of death, falls and fractures; and LOW sodium levels. Avoid use for behavioral problems of dementia unless non-drug options have failed and patient is a threat to self or others. ● Neuroleptic Malignant Syndrome: Rigid limbs, cannot move, sweating excessively, confused, disorientated, gasping for air, fecal & urinary incontinent.
	Schizophrenia	Paliperidone (Invega, Invega Sustenna)*	
	Bipolar I (acute mania & depression); schizophrenia; depression (XR only)	Quetiapine (Seroquel, Seroquel XR)	
	Bipolar I; schizophrenia	Risperidone (Risperdal, Risperdal Consta, Risperdal M-Tab)	
	Bipolar I; schizoprehenia Off-label: Psychosis associated with Alzheimer's	Ziprasidone (Geodon)*	

Anti-Anxiety Drugs	Benzodiazepines	GAD, panic disorder; short-term relief of anxiety	Alprazolam (Xanax)	<ul style="list-style-type: none"> • Beers' Criteria: <u>All benzodiazepines</u> increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in elderly. Avoid using in elderly for insomnia, agitation, or delirium. May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe GAD, procedural anesthesia, or end-of-life care. 	<ul style="list-style-type: none"> • Crying • Fearful • Nervousness • <u>Restlessness:</u> Fidgeting, pulling, tapping • Inability to relax • Tachycardia • Palpitations • Calling out • Poor concentration on tasks • Irritable, anger outbursts
		GAD; EtOH withdrawal	Chlorazepate dipotassium (Tranxene-T)		
		Short-term relief of anxiety; EtOH withdrawal	Chlordiazepoxide HCl		
		Panic disorder; SAD Off-label: Adjunct in schizophrenia	Clonazepam (Klonopin)		
		Anxiety; EtOH withdrawal Off-label: Panic disorder	Diazepam (Valium)		
		Short-term relief of anxiety; panic disorder	Lorazepam (Ativan)		
		Short-term relief of anxiety; EtOH withdrawal	Oxazepam*		
5-HT1A & 5-HT2 receptor Agonists	GAD, SAD	Buspirone (Buspar)	<ul style="list-style-type: none"> • Avoid abrupt withdrawal (trouble sleeping, fever, seizures, irritability) 		
Histamine-1 (H1) Receptor Antagonists	GAD	Hydroxyzine (Vistaril)	<ul style="list-style-type: none"> • Beers' Criteria: <u>All first-generation antihistamines</u> are highly <u>anticholinergic</u>; CrCL reduced with advanced age, and tolerance develops when used as hypnotic; greater risk of toxicity: confusion, dry mouth, constipation, and other anticholinergic effects. 		
Sedatives/Hypnotics	Histamine-1 (H1) Receptor Antagonists	Insomnia	Diphenhydramine (Benadryl)	<ul style="list-style-type: none"> • Beers' Criteria: <u>All benzodiazepines</u> increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in the elderly • See below for Caution for all sedatives/hypnotics 	<ul style="list-style-type: none"> • Inability to fall asleep • Frequent nocturnal awakenings • Awakening early in the morning • Difficulty of sleep maintenance
		Benzodiazepines	Insomnia		
	Flurazepam HCl*				
	Quazepam (Doral)*				
	Temazepam (Restoril)				
Melatonin Receptor Agonists	Insomnia	Ramelteon (Rozerem)*			
		Non-24-hour sleep-wake disorder (periods of good sleep & bad sleep)	Tasimelteon (Hetlioz)*		

	Non-benzodiazepine Agents for Insomnia	Insomnia; difficulty of sleep onset; sleep maintenance	Eszopiclone (Lunesta)*	<ul style="list-style-type: none"> • Beers' Criteria: <u>Non-benzodiazepines</u> increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in elderly. Avoid using >90 days in elderly for insomnia. • Caution: All <u>hypnotics or sedatives</u> may lead to abnormal thinking and behavior changes (decreased inhibition, aggression, bizarre behavior, agitation, hallucinations, depersonalization). 			
		Insomnia	Zaleplon (Sonata)*				
		<u>Ambien, Edluar, Zolpimist:</u> Insomnia; difficulty of sleep onset <u>Ambien CR:</u> Insomnia; difficulty of sleep onset; sleep maintenance <u>Intermezzo:</u> "As needed" treatment of middle-of-the-night insomnia with ≥4 hours of sleep time remaining	Zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist)				
CNS Stimulants	C-II CNS Stimulants	ADHD; narcolepsy	Amphetamine/ Dextroamphetamine (Adderall, Adderall XR)*	<ul style="list-style-type: none"> • Black box warning (C-II CNS stimulants): <ul style="list-style-type: none"> ○ Associated with <u>serious cardiovascular events</u> e.g. sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems (sudden death, stroke and MI in adults). ○ <u>Abuse potential</u> with prolonged drug use. • Beers' Criteria: Avoid Methylphenidate in treatment of insomnia in the elderly. 	<ul style="list-style-type: none"> • Excessive daytime sleepiness • Constant sleepiness • Paroxysms of falling asleep without warning (sleep attacks) • <u>Cataplexy:</u> brief and sudden loss of muscle tone • <u>Hypnagogic hallucinations:</u> Seeing and hearing things prior to sleep onset • Trouble sleeping at night • <u>Sleep paralysis:</u> Inability to move upon awakening • Tendency to take multiple naps during the day 		
		ADHD	Dexmethylphenidate HCl (Focalin, Focalin XR)*				
		ADHD; narcolepsy	Dextroamphetamine sulfate (Dexedrine, ProCentra, Zenzedi)*				
		ADHD	Lisdexamfetamine dimesylate (Vyvanse)*				
		ADHD	Methamphetamine HCl (Desoxyn)*				
		ADHD; narcolepsy (except Concerta, Daytrana, Metadate CD, Ritalin LA, and Quillivant XR)	Methylphenidate HCl (Concerta, Daytrana [patch], Metadate CD, Methadate ER, Methylin, Quillivant XR [suspension], Ritalin, Ritalin LA, Ritalin SR)				

	C-IV CNS Stimulants	Narcolepsy; shift work sleep disorder (SWSD); adjunctive therapy for obstructive sleep apnea/hypopnea syndrome (OSAHS)	Armodafinil (Nuvigil)* Modafinil (Provigil)*	<ul style="list-style-type: none"> • Caution: May induce mixed/manic episode in psychosis or bipolar disorders. May exacerbate symptoms of behavior and thought disorder in psychotic patients; new onset psychosis or mania may occur with stimulant use; observe for symptoms of aggression, hostility, or suicidal ideation. 	
Mood Stabilizers	Anticonvulsants	<u>Equetro</u> : Acute mania or mixed episodes associated with bipolar I	Carbamazepine (Carbatrol, Epitol, Equetro, Tegretol, Tegretol XR)	<ul style="list-style-type: none"> • Black box warning (Carbamazepine): <ul style="list-style-type: none"> ○ <u>Increased risk of anemia and agranulocytosis.</u> Monitor CBC with differential and platelets prior to and during treatment. Discontinue if BMS occurs. ○ <u>Severe, fatal skin reactions (TENS, SJS)</u> can occur especially in Asian patients with variant HLA-B*1502 allele. Screen prior to treatment. If (+), <u>do not</u> start agent. • Black box warning (Lamotrigine): <u>Severe, fatal rashes (SJS, TENS, angioedema)</u>. Increased risk with concomitant Valproic acid – titrate with recommended doses. • Black box warning (Valproic acid, Valproate sodium, Divalproex): <u>Pancreatitis and hepatic failure</u> • See below for Beers' Criteria on anticonvulsants 	<ul style="list-style-type: none"> • Irritable • Anger outbursts • Yelling/threatening • Impulsive behavior • Refusal of care • Sad, depressed mood • <u>Grandiosity:</u> Increased self-esteem • Poor attention • <u>Delusions:</u> Fixed false beliefs • <u>Flight of ideas:</u> Thoughts jump from one to another • Restless • <u>Hallucinations:</u> visual, auditory, tactile
		Maintenance therapy for bipolar I	Lamotrigine (Lamictal, Lamictal XR)		
		Off-label: Bipolar I	Oxcarbazepine (Trileptal, Oxtellar XR)		
		Off-label: Bipolar I (adjunctive)	Topiramate (Topamax, Topamax Sprinkle, Topiragen, Trokendi XR)		
		<u>Depakote, Depakote ER, Stavzor:</u> Mania associated with bipolar disorder	Valproic Acid, Valproate Sodium, Divalproex sodium (Depacon, Depakene, Depakote, Depakote Sprinkles, Depakote ER)		

	Element, Antimanic Agent	Maintenance therapy for mania in bipolar I	Lithium carbonate (Lithobid, Eskalith) Lithium citrate (Cibalith-S)	<ul style="list-style-type: none"> • Black box warning (Lithium): <u>Lithium toxicity is related to serum concentrations and may occur at therapeutic doses.</u> Monitor levels, fluid intake, and salt intake regularly. • Beers' Criteria: Increased risk of ataxia, falls, and fractures; and LOW sodium levels may occur with anticonvulsants. Avoid unless needed for seizures or mood disorders. 	
Psychotherapeutic Combinations	Benzodiazepine/ TCA	Treatment resistant moderate to severe depression	Chlordiazepoxide/Amitriptyline (Limbitrol)*	<ul style="list-style-type: none"> • Black Box Warning: For antidepressants, <u>increased risk in suicidal thinking and behavior (suicidality).</u> For antipsychotics, <u>increased risk of death</u> via cardiac causes (heart failure, sudden death, stroke, CVA) or infections (pneumonia) in dementia-related psychosis. • Beers' Criteria: All benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in the elderly. Avoid using any of these agents in elderly patients for insomnia, agitation, or delirium. 	<ul style="list-style-type: none"> • See behaviors under <u>"Antidepressants"</u> • See behaviors for <u>"Antipsychotics"</u>
	Antipsychotic/ SSRI	Treatment-resistant depression; depressive episodes associated with bipolar I disorder	Olanzapine/Fluoxetine (Symbyax)*		
	Antipsychotic/ TCA	Anxiety; depression; schizophrenia with depression	Perphenazine/Amitriptyline (Etrafon, Etrafon-A, Triavil)*		

* Refers to non-formulary drugs in the Valley Care Health System. CVA = cerebrovascular accident, GAD = generalized anxiety disorder, SAD = social anxiety disorder, PD = panic disorder, OCD = obsessive compulsive disorder, PTSD = post-traumatic stress disorder, BMS = bone marrow suppression, TENS = toxic epidermal necrolysis, SJS = Stevens - Johnson syndrome

**Cannot use antipsychotics or benzodiazepines for the treatment of "agitation."

References

1. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2012.
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