

Table 4. Pharmacologic Approaches for Impulsivity

Medication/relevant FDA indication	Mechanism of action	Typical dose	Indication/ evidence	Common side effects	Serious reactions	Caution/other information
Antidepressants						
Fluoxetine MDD, OCD, bipolar depression	SSRI	20 mg/d; typically 20–80 mg/d, max 120 mg/d in OCD	Off-label: primary impulsive aggression, PTSD, impulsive aggression First line but mixed results with ICDs	Insomnia, headache, nausea, sexual side effects, weight gain	Bleeding (especially GI bleeding), hyponatremia/SIADH, serotonin syndrome, fractures	2D6 inhibitor; black box for suicidality aged <24 y; long half life
Atomoxetine ADHD	SNRI	Child: <70 kg: 0.5 mg/kg/d in 2 divided doses; max 100 mg/d >70 kg: follow adult dosing Adult: 40 mg/d, max 100 mg/d	Off-label: impulsivity due to ADHD, binge-eating disorder	Sedation, fatigue, nausea, increase in blood pressure, insomnia, dizziness, anxiety, agitation, anticholinergic side effects, sexual dysfunction, dysmenorrhea	Hyper/hypotension, increased heart rate and risk of cardiac adverse events, orthostasis, suicidality, chemical hepatitis	Minimum trial 6–8 wk though improvement can continue for 8–12 wk; can be combined with stimulants
Desipramine MDD	TCA	Child: 25 mg at bedtime; max 100 mg/d Adult: 25–50 mg/d; max 300 mg/d	Off-label: impulsivity due to ADHD	Dry mouth, blurred vision, weight gain, sexual dysfunction, constipation, urinary retention, headache, dizziness, somnolence	Arrhythmia, cardiac conduction abnormalities (AV block), seizures	Check ECG before initiation and at each dose increase; black box for suicidality in those aged <24 y; increased lethality in overdose compared to other medication classes
Bupropion MDD, seasonal affective disorder, smoking cessation	NDRI	Child: IR >8 y: 37.5 mg twice/d; max 400 mg/d SR >11 y: 2 mg/kg/d; max 3 mg/kg/d or 150 mg XL >12 y: 150 mg/d; max 400 mg/d Adult and geriatric: IR: 100 mg twice/d; max 450 mg/d in 3–4 divided doses SR: 150 mg/d; max 200 mg twice/d XL: 150 mg/d; max 450 mg/d	Off-label: ADHD, bipolar depression	Agitation, dry mouth, insomnia, nausea, headache, weight loss	Lowers seizure threshold	Black box for suicidality in those aged <24 y; avoid in eating disorders, alcohol use disorders, or epilepsy
Antipsychotics						
Aripiprazole BPAD, MDD, schizophrenia, irritability in autism	Partial D <sub>2</sub> agonist, partial 5-HT <sub>1A</sub> agonist, 5-HT <sub>2A</sub> antagonist	Child: 1–2.5 mg/d; up to 15 mg/d Adult: 10–15 mg/d; max 30 mg/d Geriatric: 2–5 mg once/d, up to 15 mg/d	Off-label: dementia, OCD, Tourette syndrome, conduct disorder, aggression in autism	Akathisia, anxiety, insomnia, tremors, somnolence, weight gain, headache	Can cause more impulsive behaviors such as pathologic gambling and impulse control disorders so use with caution in impulse control disorders; NMS	Minimal risk of hyperprolactinemia, favorable side effect profile, can be combined with clozapine for rational polypharmacy; black box warning with dementia; requires metabolic monitoring
Risperidone Schizophrenia, BPAD, irritability in autism	D2, 5-HT <sub>2A</sub> , α <sub>1</sub> , α <sub>2</sub> , H <sub>1</sub> antagonist	Child: 0.25–0.5 mg daily depending on weight; max 2–3 mg/d Adult: 2 mg daily in 1–2 divided doses; max 6 mg/d Geriatric: 0.5 mg twice/d; max 6 mg daily	Off-label: Tourette syndrome, ODD, conduct disorder, behavioral symptoms of dementia, aggression in autism	Somnolence, orthostatic hypotension, weight gain	Hyperprolactinemia, EPS (typically at >4 mg daily)	Requires metabolic monitoring; black box warning for increased mortality in older adults
Olanzapine Schizophrenia, BPAD, MDD, schizophrenia, irritability in autism	5-HT <sub>2A</sub> , D <sub>2</sub> , H <sub>1</sub> , M <sub>1</sub> , α <sub>1</sub> , 5-HT <sub>2C</sub> antagonist	Child: 1.25–5 mg; max 20 mg/d Adult: 2.5–10 mg daily; max 20 mg/d Geriatric: 2.5 mg/d; max 10 mg	Off-label: Tourette syndrome, OCD, trichotillomania, gambling	Significant weight gain, hyperglycemia, dyslipidemia, somnolence, dry mouth, constipation	Drug reaction with eosinophilia and systemic symptoms (DRESS)	Cigarette smoking may increase clearance by 40%; black box warning for increased mortality in older adults
Quetiapine Schizophrenia, bipolar mania, bipolar depression	5-HT <sub>2A</sub> , D <sub>2</sub> , H <sub>1</sub> , α <sub>1</sub> antagonist, 5-HT <sub>1A</sub> agonist	Child: IR: 25 mg twice/d; max 800 mg/d XR: 50 mg/d; max 800 mg/d Adult: IR: 100–200 mg/d; max 800–1,200 mg daily XR: 300 mg/d; max 800–1,200 mg daily Geriatric: 25 mg at bedtime; max 300 mg/d	Off-label: Parkinson psychosis, behavioral symptoms of dementia	Dizziness, sedation, weight gain, constipation, hypotension	Orthostatic hypotension, possibly cataract formation	Requires metabolic monitoring; black box warning for increased mortality in older adults
Clozapine Treatment-resistant schizophrenia, suicidal behavior in schizophrenia or schizoaffective disorder	D <sub>1,4</sub> , 5-HT <sub>2A</sub> , 5-HT <sub>2C</sub> antagonist	Adult: 12.5–25 mg/d; 300 mg by the end of 2 wk; max 900 mg/d Geriatric: 6.25 mg/d, max 50 mg/d	Off-label: dementia, Parkinson psychosis, treatment-resistant bipolar disorder, autism, developmental disability	Orthostasis, weight gain, sedation, sialorrhea, tachycardia	Agranulocytosis, myocarditis, GI hypomotility, NMS, QTc prolongation	Dose requirements higher in smokers; if a patient stops smoking, reduce the dose by 60%–70%; must be tapered; requires frequent blood draws; can lower seizure threshold
Ziprasidone Agitation/aggression in psychotic disorders, substance use, or medical causes	Possibly D <sub>2</sub> , 5-HT <sub>2A</sub> , α <sub>1</sub> , 5-HT <sub>1D</sub> , 5-HT <sub>2C</sub> antagonist, 5-HT <sub>1A</sub> agonist	Child >35 kg: 20 mg/d; max 160 mg Adult: 40 mg twice/d with meal; max 80 mg twice/d	Off-label: delirium in the ICU, delusional infestation, treatment-resistant depression	Sedation, akathisia, dizziness, rash	QTc prolongation, bradycardia, DRESS	Need to be taken with 500-calorie food bolus; requires metabolic monitoring; black box warning for increased mortality in older adults
Pimozide Tourette syndrome	Blocks D <sub>2</sub> receptors in the nigrostriatal pathway	Child: 0.5 mg–1 mg/d; dose range 2–8 mg/d Adult: 1–2 mg/d; max 10 mg/d	Off-label: skin picking	Constipation, akathisia, akinesia, drowsiness	ECG abnormalities	If therapy requires >4 mg/d, CYP2D6 genotyping should be performed; baseline ECG should be performed
Antiepileptics and anticonvulsants						
Carbamazepine Bipolar disorder, focal seizures, and generalized onset seizures	Blocks voltage-gated sodium channels, inhibits glutamate release	Adult: 100–400 mg/d, max 1,600 mg/d For primary impulsive aggression, 450 mg/d is initial target dose with low-subtherapeutic drug levels	Off-label: primary impulsive aggression, intermittent explosive disorder	Dizziness, sedation, nausea, headache, rash	Myelosuppression, hepatitis, jaundice, SJS/TEN, angioedema, SIADH	Monitor drug level (mean 4.3 ug/mL), CBC with differential, sodium, LFTs, HLA-B*57:01 in people of Asian descent; teratogenic; self-inducer, enzyme inducer and inhibitor of many common medications (OCs, antibiotics, psychotropics)
Oxcarbazepine Focal seizures	Unknown; thought to be blocking voltage-gated sodium channels, stabilizing neuronal membranes, decreasing propagation of synaptic impulses; modulates activity of calcium channels	300 mg twice/d; max 2,400 mg/d	Off-label: BPAD, primary impulsive aggression, intermittent explosive disorder	Headache, ataxia, dizziness, nausea, vomiting, drowsiness	SJS/TEN, anaphylaxis, angioedema, hyponatremia	Better tolerated than CBZ and is not teratogenic; reduce efficacy of OCs by up to 50%; moderate enzyme inducer; check HLA-B*57:01 in people of Asian descent before starting
Valproic acid Bipolar disorder, focal seizures, and generalized onset seizures	Inhibits voltage-gated sodium channels, increases GABA activity, inhibits GABA transaminase, modulates calcium channels	Adult: 250 mg 3 times/d; increase by 250–500 mg to target serum level 20–30 mg/kg in 1–4 divided doses for rapid symptom control Geriatric: 125–250 mg 3 times/d; increase by 125–250 mg to target serum level	Off-label: primary impulsive aggression, bipolar depression, intermittent explosive disorder, aggression in brain injury and dementia	Teratogenic in pregnancy, thrombocytopenia, PCOS, weight gain, somnolence, tremor, hair loss, nausea, fatigue, dizziness	Hepatotoxicity, pancreatitis	Effective for aggression at mean level of 39.2 ug/mL; teratogenic, so need baseline pregnancy test; monitor: CBC, weight, PT/PTT, LFTs, glucose, lipids, and check drug level 3 days after dose change; check level, CBC, LFTs every 6 mo
Lamotrigine Bipolar disorder, focal seizures, generalized onset seizures	Inhibits glutamate release, inhibits voltage-gated sodium channels	Child and geriatric: 25 mg/d × 2 wk, 50 mg/d × 2 wk, 100 mg/d; max 200 mg/d Adult: 25 mg/d × 2 wk, 50 mg/d × 2 wk, 100 mg/d × 1 wk, then 200 mg/d; max 400 mg/d	Off-label: aggression, treatment-resistant depression, intermittent explosive disorder, PTSD, impulsivity in borderline eating disorders	Dizziness, headache, rash	SJS/TEN, angioedema	High risk of SJS in pediatrics
Topiramate Migraine, seizures	Blocks voltage-gated sodium channels, enhances GABA activity, glutamate antagonist, carbonic anhydrase inhibitor	Child: 6–12 y, <20 kg: 15 mg/d; max range 2–3 mg/kg/d >12 y: 25 mg/d; max 100 mg/d Adult: 25 mg/d; max 200 mg twice/d	Off-label: alcohol use disorder, antipsychotic-induced weight gain, binge eating disorder, cocaine use	Somnolence, fatigue, dizziness, memory difficulties, confusion, ataxia, paresthesias, nausea, anorexia, weight loss, change in taste perception	Metabolic acidosis, renal stones, osteomalacia, rare activation of suicidality, secondary angle-closure glaucoma, hyperammonemia, hyperthermia, oligohidrosis (children)	No benefit over placebo for gambling
Alpha-2 agonists						
Clonidine ADHD	Stimulates α <sub>2</sub> adrenoreceptors and supports neuronal inhibition by hyperpolarizing nerves, resulting in reduced sympathetic outflow from the CNS	Child: 0.05–0.1 mg nightly, max 0.2–0.4 mg/d depending on weight Adult and geriatric: 0.1 mg/d, increase by 0.1 mg and divided doses; max 0.4 mg/d	Off-label: ICU sedation, opioid withdrawal, agitation in autism, ADHD, Tourette syndrome	Sedation, dizziness, dry mouth, depression, anxiety, nausea, hypotension	Sinus bradycardia, AV block, hypertensive encephalopathy during withdrawal	Requires taper; comes in transdermal formulation
Guanfacine ADHD	Selective α <sub>2A</sub> adrenergic receptor agonist, which reduces sympathetic activity on the heart and circulatory system	Child: 1 mg nightly; max 3–7 mg/d depending on formulation Adult: 1 mg nightly; max 4 mg/d	Off-label: OCD, ADHD	Sedation, weakness, dizziness, dry mouth, constipation	Hypotension, syncope, sinus bradycardia	Less likely to cause hypotension than clonidine
Anxiolytics						
Buspirone GAD	Serotonin 5-HT <sub>1A</sub> receptor partial agonist	Child: 5 mg/d; range, 7.5–30 mg twice/d Adult and geriatric: 10 mg/d in 2–3 divided doses; max 60 mg/d	Off-label: depression augmentation	Dizziness, lightheadedness, drowsiness, nausea, headache, jitteriness	None	Absorption increases 2x with food so be consistent if taking with or without food; can improve impulsivity
Alprazolam GAD, short-term anxiety, panic disorder	Short-acting benzodiazepine	Child: 0.005–0.02 mg/kg 3 times/d; max 4 mg/d Adult: 0.25 mg 3–4x/d; max 8 mg/d Geriatric: 0.25 mg 2–3x/d and titrate slowly	Off-label: GABAergic withdrawal	Somnolence	Anterograde amnesia, paradoxical reaction	Risk of dependence; risk when used with opioids; avoid in geriatric; withdrawal syndrome
Lorazepam Anxiety, procedural anxiety/sedation	Short to intermediate-acting benzodiazepine	Child: 0.25–2 mg 2–3 times/d; max 2 mg/dose Adult and geriatric: 0.5–1 mg twice/d; max 6–10 mg/d Agitation: 1–4 mg IV every 3–10 min until symptom control achieved	Often given parenterally with an antipsychotic in acute agitation Off-label: agitation, stimulant intoxication, GABAergic withdrawal, NMS, serotonin syndrome	Somnolence, ataxia	Anterograde amnesia, paradoxical reaction, increased fall risk, respiratory depression	Risk of dependence; risk when used with opioids; avoid in geriatric; withdrawal syndrome; propylene glycol toxicity when used >10 mg/d IV
Beta blockers						
Propranolol	Nonselective β-adrenoreceptor blocker; blocks β <sub>1</sub> and β <sub>2</sub> adrenergic stimulation	Adult and geriatric: IR: 10 mg twice/d, max 120 mg/d ER: 20 mg/d; max 80 mg/d Performance anxiety: 10–20 mg 30–60 min prior to activity; max 40 mg 3 times/d	Off-label: anxiety, agitation due to primary psychotic disorder, autism, developmental delay, performance anxiety	Dizziness, fatigue, bradycardia, hypotension	May mask clinical signs of hypoglycemia and hyperthyroidism	May exacerbate asthma, COPD, CHF; requires taper
Glutamatergic antagonists						
Memantine Alzheimer disease (moderate-severe)	NMDA receptor blockade leading to reduced glutamate excitotoxicity, neuroprotection	Adult: 10 mg/d; max 20 mg/d For dementia: start at 5 mg/d	Off-label: skin picking, alcohol use disorder, gambling, kleptomania, ADHD	Confusion, dizziness, drowsiness, headache	Falling, seizures, agitation, delusions, hallucinations	No benefit for nicotine dependence
N-acetylcysteine APAP toxicity	Antioxidant; increases glutathione synthesis	Adult: 600 mg/d; max 2,400 mg/d	Off-label: trichotillomania, OCD, cannabis dependence, gambling disorder, skin picking	GI upset, body odor	Avoid with nitroglycerin due to hypotension; may slow clotting so avoid with blood thinners	Available over the counter
Antimanic agents						
Lithium Bipolar disorder	Unknown; alters cation transport across cell membranes; influences the reuptake of serotonin and norepinephrine; inhibits second messenger systems, neuroprotective effects	Child: 600–900 mg in 2–3 divided doses; max 1,200 mg/d based on level Adult: 600–900 mg/d in 2–3 divided doses based on chosen formulation; max 900–1800 mg/d based on level Geriatric: adult dosing but start low and go slow	Efficacy in bipolar disorder is partly due to reduction in impulsivity Off-label: MDD, postpartum psychosis, primary impulsive aggression, gambling	Gastrointestinal upset, tremor, thirst/polydipsia, hypothyroidism, acne, leukocytosis	Nephrogenic diabetes insipidus, dysrhythmia, bradycardia	Monitor: lithium level, thyroid-stimulating hormone, basic metabolic panel at initiation, then 1–2 mo, then every 6–12 mo; check level after every dose change and when adding a medication that alters metabolism such as NSAIDs, ACEI, HCTZ; levels altered by dietary sodium intake
Opioid antagonists						
Naltrexone Alcohol use disorder, opioid use disorder	Inhibit dopamine release in the nucleus accumbens through disinhibition of GABA input to dopamine neurons in the ventral tegmental area	Child: 25 mg/d; max 100 mg/d Adult: 50 mg/d; max 100 mg/d	Off-label: gambling, compulsive sexual behavior, kleptomania Inconsistent evidence with binge eating, trichotillomania, and substance use	Headache, nausea, vomiting, somnolence, anorexia	Hepatocellular injury, eosinophilic pneumonia	Check LFT prior to administration-contraindicated with elevations 3x upper limit of normal
Stimulants						
Methylphenidate ADHD	NDRI; increases dopaminergic and noradrenergic activities in the prefrontal cortex	Dosing varies based on formulation and brand Child: IR: 2.5–5 mg twice/d; max 60 mg/d XR: 18 mg/d; max 72 mg/d Adult and geriatric: IR: 10–20 mg/d in 2 doses; max 60 mg/d Intermediate acting: 10 mg twice/d; max 60 mg/d XR: 18–36 mg/d; max 72 mg/d	May reduce aggression in patients with ADHD as impulsivity and acting out are symptoms	Hypertension, decreased appetite, anxiety, irritability	Acute MI, sudden cardiac death, growth suppression, priapism, new-onset psychosis or exacerbation of psychotic or manic symptoms	May increase impulsive behaviors such as skin picking, gambling, and trichotillomania in patients without ADHD
Amphetamine salts ADHD	Promotes the release of dopamine and norepinephrine from the presynaptic nerve	Child: <6 y: 20–30 mg/d; max 70 mg/d Adult: 30 mg/d; max 70 mg/d	May reduce aggression in patients with ADHD as impulsivity and acting out are known symptoms	Hypertension, decreased appetite, anxiety, irritability	Acute MI, sudden cardiac death, growth suppression, new-onset psychosis, serotonin syndrome	May increase aggression and anger in patients without ADHD; risk of misuse
Lisdexamfetamine ADHD, binge-eating disorder	Converts to dextroamphetamine, which increases the levels of dopamine and norepinephrine	Child: <6 y: 20–30 mg/d; max 70 mg/d Adult: 30 mg/d; max 70 mg/d	Can treat ADHD Special indication for binge-eating disorder	Decreased appetite, xerostomia, abdominal pain	Acute MI, sudden cardiac death, growth suppression, new-onset psychosis, serotonin syndrome	Risk of abuse

Abbreviations: ACEI = angiotensin-converting enzyme inhibitors, ADHD = attention-deficit/hyperactivity disorder, CBC = complete blood count, ECG = electrocardiogram, GABA = γ-aminobutyric acid, GI = gastrointestinal, HCTZ = hydrochlorothiazide, IV = intravenous, LFT = liver function test, MDD = major depressive disorder, MI = myocardial infarction, NDRI = norepinephrine-dopamine reuptake inhibitor, NSAID = nonsteroidal anti-inflammatory drugs, PCOS = polycystic ovary syndrome, PTSD = posttraumatic stress disorder, SJS/TEN = Stevens-Johnson syndrome/toxic epidermal necrolysis, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.