Medications for bipolar disorder

Acute mania, bipolar depression, and maintenance. Different medications win in each phase, and the choice for one phase has to keep the others in mind. Reviewed against current guidelines as of June 8, 2026.

Bipolar treatment is three separate problems: acute mania, bipolar depression, and long-term maintenance. Companion to the full guide at psychiatryrx.org/guides/medications-for-bipolar-disorder/.

First-line options by phase

Drug	Class	Notes
Lithium	Mood stabilizer	Mania and maintenance. Target 0.8 to 1.2 mEq/L acute, 0.6 to 0.8 maintenance. Reduces suicide risk.
Valproate (divalproex)	Mood stabilizer	Mania and maintenance. Level 50 to 125 mcg/mL. Favored for mixed features and rapid cycling. Teratogenic.
Lamotrigine	Mood stabilizer	Maintenance for depression prevention. Slow titration for rash risk. Weak for acute mania.
Quetiapine	Atypical	Mania, bipolar depression (300 mg), and maintenance. Sedating.
Lurasidone	Atypical	Bipolar depression, monotherapy or adjunct. Metabolically kinder. Requires 350 kcal with dose.
Cariprazine	Atypical	Mania, bipolar depression (1.5 to 3 mg), and mixed features. Long half-life.
Aripiprazole	Atypical	Mania and maintenance. LAI available. Metabolically kinder.
Olanzapine, olanzapine-fluoxetine	Atypical	Mania and bipolar depression (Symbyax). Effective but heavy on weight and metabolism.
Risperidone, asenapine, ziprasidone	Atypical	Mania. LAI options for risperidone. Ziprasidone needs food (500 kcal).

Second-line and augmentation

Drug	Class	When to consider
Carbamazepine	Mood stabilizer	Mania when first-line has failed. Strong CYP3A4 inducer. Hematologic risks.
Oxcarbazepine	Mood stabilizer	Fewer interactions than carbamazepine, weaker bipolar evidence.
Topiramate	Anticonvulsant	Weight-neutral adjunct. Thin evidence for mood stabilization alone.
Adjunctive bupropion or SSRI	Antidepressant	Bipolar depression refractory to first-line, always with a stabilizer on board.
Clozapine	Atypical	Refractory mania, especially with psychotic features.
ECT	Neuromodulation	Highly effective for severe bipolar depression, psychotic features, or suicidal ideation.
Ketamine, esketamine	NMDA antagonist	Off-label in bipolar depression, always with a stabilizer on board.

LAI atypical (aripiprazole, paliperidone, risperidone)	Atypical	Maintenance when adherence is a chronic problem.

Special considerations

- Pregnancy: lithium is the least teratogenic effective mood stabilizer. Fetal echo 16 to 20 weeks. Valproate is off the table in anyone of reproductive potential unless every alternative has failed. Lamotrigine clearance rises 30 to 60 percent in pregnancy, so it needs dose adjustment during and after.
- Older adults: lithium levels rise as renal function drops. Target 0.4 to 0.6 mEq/L is often enough. Atypicals carry the mortality boxed warning in dementia.
- Renal and hepatic: lithium is renal, so kidney function matters. Valproate and carbamazepine are hepatic and can raise LFTs. Baseline and periodic labs are standard.
- Substance use: valproate is often favored over lithium because it forgives missed doses and dehydration better. Stimulants can precipitate mania.
- Comorbid anxiety in bipolar: quetiapine or lurasidone can cover both. Avoid antidepressant monotherapy.

What tips the choice

Acute mania: lithium or valproate plus an atypical for fastest control. Acute bipolar depression: quetiapine, lurasidone, cariprazine, or olanzapine-fluoxetine, with a background stabilizer. Maintenance with mostly manic history: lithium or valproate. Maintenance with mostly depressive history: lamotrigine plus something covering mania. Rapid cycling or mixed features: valproate or lamotrigine, avoid antidepressants. Suicidality: lithium if tolerable, since it's the only mood stabilizer with anti-suicide evidence. Reproductive potential: avoid valproate. Poor adherence: LAI atypical. Metabolic risk: lurasidone, aripiprazole, or cariprazine over olanzapine or quetiapine.

Watchouts

- Antidepressant monotherapy without a mood stabilizer can trigger mania or accelerate cycling. Always pair with a stabilizer.
- Lamotrigine rash: serious rash risk is highest in the first weeks. Any rash needs prompt evaluation. Miss more than 5 days and titration has to restart.
- Lithium has a narrow therapeutic index. Toxicity climbs with dehydration, NSAIDs, ACE inhibitors, ARBs, and thiazides. Teach patients to hold during significant vomiting or diarrhea.
- Valproate: teratogenic, hepatotoxic. Ammonia can rise independently of LFTs. Avoid in pregnancy potential.
- Carbamazepine: hematologic monitoring, autoinducer, drops levels of most 3A4 substrates including OCPs.
- Abrupt lithium discontinuation carries a real risk of manic relapse. Response to lithium may be reduced if restarted after stopping.

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