Recommended Treatment Options for Depression in Patients on the Bipolar Spectrum

	Name	Pearls
No Risk of Mania	**Lamotrigine (50–200 mg daily)**	Treats bipolar depression, but failed trials in unipolar.
	Lithium (serum levels 0.4–0.6 for depression, 0.8–1.2 for mania)	Treats bipolar depression as monotherapy; augments antidepressants in unipolar depression.
	Atypical antipsychotics (dose in low range)	For bipolar depression: cariprazine, lurasidone, olanzapine/fluoxetine combination, quetiapine. For unipolar depression (as antidepressant augmentation): aripiprazole, brexpiprazole, cariprazine, lurasidone, olanzapine/fluoxetine combination, quetiapine, risperidone, ziprasidone.
	Omega-3 fatty acids (1000–3000 mg range)	Moderate effect size for unipolar and bipolar depression, but only when EPA ≥ 1.5 times the DHA amount.
	N-acetylcysteine (2,000 mg daily)	Treats subsyndromal bipolar (but not unipolar) depression. May take 6 months to see benefits, but those benefits go away within a week of discontinuation.
	Ramelteon (8 mg qhs)	Nightly dosing of this non-sedating hypnotic reduced the frequency of bipolar depression in two small trials.
Low Risk of Mania	**Pramipexole (0.75–2 mg qhs)**	Effective for unipolar, bipolar, and treatment-resistant depression in 5 small controlled trials. Lacks weight gain, cognitive, or sexual side effects. Rarely, causes compulsivity syndromes (eg, gambling) and, at higher doses, mild hallucinations.
	Modafinil (up to 200 mg qam) and armodafinil (up to 250 mg qam)	Treats residual fatigue in unipolar depression and both mood and fatigue in bipolar depression. Though efficacy studies have mixed results, patients appreciate these options as they tend to improve cognition and overall functioning.
	Bupropion (150–450 mg range)	The risk of antidepressant-induced mania, from low to high, is: bupropion < SSRIs < SNRIs < tricyclics. Start bupropion low (75 mg), raise slowly (by 75 mg/week), and use with a mood stabilizer to reduce the risk further.
	Light therapy	Large effect size for bipolar and unipolar depression. To reduce risk of mania, use at midday (12 pm–2 pm), start at 15 min/day, and raise by 15 min/week to a target time of 1 hour/day. Check cet.org for effective products (eg, Carex brand).
	ECT and TMS	ECT is effective in treatment-resistant bipolar and unipolar depression with a larger effect size than TMS. Studies of TMS in bipolar depression are promising but preliminary.

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