BIPOLAR DEPRESSION: PHARMACOLOGICAL TREATMENTS

1st Line Medications:

QUETIAPINE (SEROQUEL): High Efficacy, High Side Effects, NNT = 5-6

**Dosing Information:** The typical titration schedule for Seroquel in bipolar depression is as follows: Day 1, 50 mg qhs; Day 2, 100 mg qhs; Day 3, 200 mg qhs; and Day 4, 300 mg qhs. The target dosage is 300 mg qhs. This titration schedule can be slowed down because of side effects, especially sedation. For mixed and manic states the medication should be initiated in bid doses totaling 100 mg/day on Day 1, increased to 400 mg/day on Day 4 with further increments of up to 100 mg/day in bid divided doses (usual max: 600 mg in mania). Typically more of the dose is given at HS.

**General Information:** Seroquel is FDA approved for depressive episodes associated with bipolar disorder, acute manic episodes associated with bipolar I disorder as either monotherapy or adjunct therapy to lithium or Depakote, maintenance treatment of bipolar I disorder as adjunct therapy to lithium or Depakote, and for the treatment of schizophrenia. T½: 6 hr. Off-label uses include anxiety (particularly in patients with a history of substance use at 12.5 mg to 25 mg PRN tid or qid) and insomnia. Careful consideration of risk vs. benefit is required in off label use because of long-term risk of TD and metabolic side effects. Available in a long acting form: Seroquel XR.

**Black Box Warnings:** (1) Increased risk of death related to psychosis and behavioral problems in elderly patients with dementia (1.6-1.7 fold), (2) Increased initial risk of suicidality when used for treatment of depression (in patients less than 24).

**Common Side Effects:** orthostatic hypotension, constipation, dyspepsia, dizziness, dry mouth, somnolence, elevated liver enzymes, fatigue, pain, and rash. EPS is uncommon and Seroquel is second only to Clozaril in having the least amount of EPS. Metabolic side effects are moderate.

**Monitoring:** needed for metabolic side effects (fasting glucose and lipids, checked on initiation and q 6 months). Long-term potential of TD probably lowest in the group of atypical antipsychotics and much decreased compared to typicals.

**Coverage:** Seroquel is very expensive but is a formulary drug for GAU patients.

LITHIUM: Moderate efficacy, moderate side effects, NNT (at higher doses): 8-9

**Dosing Information:** **Start:** 150 – 300 mg bid to tid with doses up to 1200 – 1500 mg daily and higher based on renal function and drug levels (0.6 - 1.2 meq/L). Use lower part of the range for maintenance and higher part of range for acute episodes. Also available as extended release typically given in the same initial total daily dosages at night.

**Drug Levels:** Checked 5 days after starting the medication or increasing the dosage. The blood is typically drawn for a drug level before the morning dosage of lithium.

**General Information:** Lithium is FDA approved for bipolar disorder, acute episodes and for maintenance. There is a strong anti-suicidal effect of this drug. It is much less effective in patients with rapid cycling, mixed episodes, or PTSD.

**Black Box Warnings:** toxicity and the need to check levels. Lithium has some efficacy for treating bipolar depression. There is a risk of teratogenesis during first trimester of pregnancy (Epstein’s anomaly of heart—need to inform women of childbearing age of this risk).

**Common Side Effects:** diarrhea, nausea, tremor, and increase frequency of urination. Sedation, weight gain (less than Depakote) and mild cognitive impairment seen. Need to be cautious about concurrent medications that can affect renal clearance including NSAIDS and HTN medications.

**Monitoring:** Prior to starting this medication will want to do basic metabolic panel and TSH.

**Coverage:** $, F (lithium carbonate & citrate), $, NF (Lithobid, Eskalith).
LAMOTRIGINE (LAMICTAL): Low efficacy, low side effects, NNT ~13

**Dosing Information:** **Start:** 25 mg daily for weeks 1 and 2, then 50 mg daily for weeks 3 and 4, then 100 mg qday for week 5, and finally 200 mg qday for week 6+ (the usual target dose). Dosage will need to be adjusted up for patients taking enzyme-inducing drugs such as Tegretol or oral contraceptives and down for drugs such as Depakote. Starter packs are available. **Serum drug levels are not measured as no therapeutic range has been established for Lamictal unlike Tegretol and Depakote.**

**General Information:** Lamictal is FDA approved for maintenance treatment of bipolar I disorder. It is more effective in keeping patient from moving into a depressed state vs. a manic state. May work more effectively with patients with more severe symptoms.

**Black Box Warnings:** for serious, life-threatening rashes requiring hospitalization and discontinuation of treatment (Stevens Johnson syndrome @ approx. 1: 1000 to 2000). The risk of rash may also be increased by co-administration of lamotrigine with Depakote (valproic acid) exceeding the recommended initial dose of lamotrigine, or exceeding the recommended dose escalation for lamotrigine. Nearly all cases of life-threatening rashes associated with lamotrigine have occurred within 2 to 8 weeks of treatment initiation. Lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug related.

**Common Side Effects:** GI upset, ataxia, dizziness, headache, and somnolence. Patients on Lamictal typically don’t have weight gain, or cognitive deficits.

**Coverage:** The drug is expensive but is in the formulary.