Florida Best Practice Medication Guidelines for Treatment of Acute Bipolar Depression

Adjunctive Psychosocial Treatments (as indicated)

- Cognitive Behavior Therapy
- Family-focused therapy
- Interpersonal and Social Rhythm Therapy

Level 0: Comprehensive Assessment

- Careful differential diagnostic evaluation
- Suicidality and aggression
- Psychiatric, substance abuse and physical co-morbidities
- Measurement-based care
- Collaborative treatment decision-making
- Psychosocial assessment

Level 1: Established efficacy, but limited tolerability*

- Quetiapine monotherapy
- Olanzapine + fluoxetine

Level 2: Established tolerability, but limited efficacy**

- Lamotrigine monotherapy
- (Lithium or valproate) + (lamotrigine, SSRI or Bupropion)

**Tolerability limitations include sedation and weight gain*
***Efficacy limitations include negative randomized controlled trials and meta-analyses*

Level 3: *If Levels 1 and 2 ineffective or not tolerated**

- Electroconvulsive Therapy (ECT)
- Transcranial Magnetic Stimulation (TMS)
- SGA + (lithium, valproate, lamotrigine, SSRI or Bupropion)
- Antimanic therapy + (SNRI, modafanil, pramipexole, MAOI, TCA, thyroid, stimulant)
- Carbamazepine
- Adjunctive inositol, eicosapentaenoic acid (EPA)

** Consideration merited due to clinical need, despite even greater efficacy/tolerability limitations than level 1 and 2 treatments*

Number of iterations at each level and adjunctive treatment(s) to be determined by clinician judgment/patient needs

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Measurement-based care:

- Treatment targets need to be precisely defined
- Use of rating scales recommended
- Effectiveness and safety/tolerability of medication treatment must be systematically assessed

Recommended rating scales:

- 16-item Quick Inventory of Depression Symptoms (public domain) www.ids-qids.org/translations/english/QIDS-SREnglish2page.pdf
- Montgomery Asberg Depression Rating Scale (public domain) www.opapc.com/images/pdfs/MADRS.pdf
- Patient Health Questionnaire-9 (public domain) http://www.phqscreeners.com/pdfs/02_PHQ-9/English.pdf
- Young Mania Rating Scale (public domain) http://www.askdrjones.com/wp-content/uploads/patientforms/YMRS%202.pdf

References:

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2. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2009. ***Bipolar Disorders*** 2009:11:225-255.
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4. Ketter TA. Handbook of Diagnosis and Treatment of Bipolar Disorder. Washington, DC: ***American Psychiatric Publishing Inc.,*** 2010.
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Mood Stabilizers – Recommendations for Bipolar Disorders

Medication	Dosage	Comments
Lithium	In acute mania: 0.8 – 1.2 mEq/L (1200-2400 mg/d)	Initial titration for tolerability – start 600-900 mg/d, increase 300 mg/day every 5 days. Check levels 5 days after initiation/dose change. Check levels frequently if clinical toxicity. Monitor renal and thyroid functions. Lower doses/levels may be necessary in non-manic compared to manic patients. For maintenance, some patients require 0.8 to 1.2 mEq/L, others can be maintained with lower levels, but not below 0.6 mEq/L in elderly, start with lower lithium dose, titrate more slowly, and require lower serum lithium levels.
Valproate	In acute mania: 85 -125 µg/mL (5-60 mg/kg/d; 1000-2500 mg/d)	Initial loading may be tolerated, but some patients need initial titration for tolerability. Check levels 48 hrs after initiation and adjust dose accordingly. Side effects (esp. gastrointestinal) more evident above 100µg/mL. More eratogenic than other mood stabilizers. Lower doses/levels may be necessary in non-manic compared to manic patients.
Carbamazepine	In acute mania: 200 – 1600 mg/d (6-12 µg/mL)	Initial titration for tolerability due to hepatic auto-induction – start 200-400 mg/d, increase 200 mg/d every 3 days. Lower doses/levels may be necessary in non-manic compared to manic patients. Monitor for blood dsycrasias and serious rash. Screen Asians for HLA-B*1502 (serious rash risk indicator). Decreases serum levels of multiple other drugs.
Lamotrigine	In bipolar maintenance 100 – 400 mg/d	Initial titration to reduce risk of serious rash (Stevens-Johnson syndrome), start 25 (12.5 with valproate) mg/d after 2 and 4 weeks and weekly thereafter. Initial target dose 200 mg/d, but final doses may be 100-400 mg/d. May be used in some patients with acute bipolar depression (despite acute efficacy limitation) due to good tolerability and depression prevention efficacy.

Mood Stabilizers – Recommendations for Bipolar Disorders

Second Generation Antipsychotics & Antidepressants – Recommendations for Bipolar Disorder

Medication	Dosage	Comments
Second Generation Antipsychotics (SGA)	In acute mania: -Aripiprazole: 15-30 mg/d -Asenapine: 10-20 mg/d -Olanzapine: 6-20 mg/d -Quetiapine: 400-800 mg/d -Risperidone: 2-6 mg/d -Ziprasidone: 80-160 mg/d - Clozapine: 60-400 mg/d (if treatment resistant)	Initial titration may be necessary for tolerability. Lower doses may be necessary in non-manic patients (e.g. quetiapine 300 mg/day or lower to attenuate sedation). Ziprasidone should be taken with food. Asenapine is sublingual. Monitor for side effects, including sedation (esp. with quetiapine and clozapine), weight gain (esp. with olanzapine and clozapine), akathisia (esp. with aripiprazole and ziprasidone), and EPS (esp. with risperidone). Monitor weight and BMI at each visit and laboratory metabolic indices at baseline, 3 months and yearly thereafter.
Antidepressants	In acute bipolar depression: -Bupropion: 300-450 mg/d -Citalopram: 20-40 mg/d -Escitalopram: 10-20 mg/d -Fluoxetine: 20-80 mg/d -Paroxetine: 20-50 mg/d -Sertraline: 50-200 mg/d	May be used in combination with antimanic drugs in some patients with acute bipolar depression, but should not be prescribed as monotherapy in patients with bipolar I disorder due to manic switch risk. SNRIs and TCAs have greater manic switch risk. Increased suicidality risk in pediatric and young adult patients. Utility in bipolar depression prevention is controversial.