Bipolar Disorder (Acute Mania or Mixed Episodes) in Children and Adolescents Ages 6 to 17 Years Old

Level 0

Comprehensive assessment. Use systematic interview covering mania and depression symptoms, as well as other associated and comorbid problems (e.g., psychosis, behavioral problems, ADHD symptoms, substance misuse). Obtain a family history of psychopathology including depression and mania. Information from teachers and other outside informants is useful to document pattern and course of symptoms.

- Classic bipolar disorder has distinct episodes representing a clear change from usual behavior; DSM-5 symptoms consist of manic symptoms: elevated and/or irritable mood and increased energy occurring most of the day, every day; co-occurring symptoms include grandiosity, decreased need for sleep, rapid speech, and flight of ideas (no current validity under age 6).
- Episodes of mania should be distinct from baseline ADHD symptoms. If truly comorbid, mania should be treated and stabilized before treating ADHD.
- If the diagnosis of mania cannot be distinguished from ADHD, and especially combined ADHD and Oppositional Defiant Disorder, ADHD should be treated first with discussion with family members about advantages and disadvantages. Refer to ADHD guidelines on page 18.
- If rage outbursts are the primary focus of treatment, track the frequency, intensity, number and duration of episodes. Rule out Disruptive Mood Dysregulation Disorder (DMDD).
- If DMDD is present, refer to those recommendations on page 45; otherwise, treat the primary disorder first and then treat the aggression. Refer to the aggression treatment guidelines on page 29.

Level 1

For manic/mixed episodes, monotherapy with one of the following FDA approved agents (approved for youth between the ages of 10-17):

- Aripiprazole
- Risperidone
- Quetiapine
- Asenapine

For classic mania in adolescents:

- Lithium, (FDA approved for ages 12 to 17 years)

For youth with bipolar depression:

- Lurasidone (FDA approved for ages 10 to 17 years)

Bipolar Disorder (Acute Mania or Mixed Episodes) in Children and Adolescents Ages 6 to 17 Years Old *(continued)*

Level 2

For acute mania or mixed episodes, if there is partial response to a single atypical antipsychotic, augment with lithium

If monotherapy with atypical antipsychotic listed in Level 1 is not effective:

- **2a.** Switch to monotherapy with another antipsychotic listed in Level 1 or olanzapine.
- **2b.** Switch to lithium.

For bipolar depression, if lurasidone not effective, switch to olanzapine/fluoxetine combination.

Level 3

Re-assess the diagnosis. Refer to specialist.

For acute mania or mixed episodes, monotherapy with antipsychotic (except clozapine) not listed in Level 1 or 2, or combination of antipsychotic with mood stabilizer [lithium, or valproid acid (VPA)/divalproex if lithium failed].

For bipolar depression, based on adult evidence, consider lamotrigine.

Level 4

Consider clozapine or ECT in adolescents.

Not Recommended: Two antipsychotics concurrently (except during cross-tapering).

Dosing Recommendations for Atypical Antipsychotics in Bipolar Disorder in Children and Adolescents Ages 6 to 17 Years Old

Clinicians should realize that data below age 10 for treating mania and mixed states are limited and caution in using pharmacological treatment below age 10 is warranted.

Table 10.

Dosing Recommendations for Atypical Antipsychotics and Mood Stabilizers in Bipolar Disorder			
Drug Name	**Starting Dose**	**Maximum Dose**	**FDA Approved Age Range**
Bipolar Mania			
Aripiprazole	2–5 mg/day	30 mg/day	10–17 years old
Asenapine	2.5 mg sublingual (SL) twice a day. After 3 days, may increase to 5 mg SL twice daily, and after an additional 3 days up to 10 mg SL twice a day, as needed and as tolerated. Avoid food and liquids for at least 10 minutes before and after administration.	10 mg twice a day	10–17 years old
Lamotrigine	12.5 mg/day	150 mg/day (<50 kg weight) 200 mg/day (>50 kg weight)	Not approved in children or adolescents for bipolar disorder.
Lithium	300–600 mg/day Goal for acute mania: Blood level 0.8–1.2 mEq/L Goal for maintenance: Blood level 0.6–1 mEq/L	Dose determined by blood level. Max trough blood level should be 1.2 mEq/L	12–17 years old
Olanzapine	2.5–5 mg once daily. Titrate weekly by 2.5–5 mg increments.	20 mg/day	13–17 years old
Quetiapine	Children: 12.5 mg bid Adolescents: 25 mg bid	Children: 400 mg/day Adolescents: 600 mg/day	10–17 years old
Risperidone	Children: 0.25 mg/day Adolescents: 0.5–1 mg bid	Children: 4 mg/day Adolescents: 6 mg/day	10–17 years old
Valproate	10–15 mg/kg/day in divided doses Goal: 80–125 mcg/mL	Dose determined by blood level. Max blood level should be 125 mcg/mL.	Not approved in children or adolescents for bipolar disorder.
Bipolar Depression			
Lamotrigine	12.5 mg/day	150 mg/day (<50 kg weight) 200 mg/day (>50 kg weight)	Not approved in children or adolescents for bipolar disorder.
Lurasidone	20 mg/day	80 mg/day	10–17 years old
Olanzapine/ Fluoxetine	3 mg/25 mg once daily	12 mg/50 mg once daily	10–17 years old

Dosing Recommendations for Atypical Antipsychotics in Bipolar Disorder in Children and Adolescents Ages 6 to 17 Years Old

Table 10 *(continued)*.

Dosing Recommendations for Atypical Antipsychotics and Mood Stabilizers in Bipolar Disorder			
Drug Name	**Starting Dose**	**Maximum Dose**	**FDA Approved Age Range**
Mixed Episodes			
Aripiprazole	2–5 mg/day	30 mg/day	10–17 years old
Asenapine	2.5 mg sublingual (SL) twice a day. After 3 days, may increase to 5 mg SL twice daily, and after an additional 3 days up to 10 mg SL twice a day, as needed and as tolerated. Avoid food and liquids for at least 10 minutes before and after administration.	10 mg twice a day	10–17 years old
Olanzapine	2.5–5 mg once daily. Titrate weekly by 2.5–5 mg increments.	20 mg/day	13–17 years old
Chlorpromazine	Children: 25–50 mg/day Adolescents: 25–100 mg/day	Children (under 12): 200 mg/day Adolescents: 500 mg/day	Not approved for pediatric mania
Risperidone	Children: 0.25 mg/day Adolescents: 0.5–1 mg bid	Children: 4 mg/day Adolescents: 6 mg/day	10–17 years old
Maintenance			
Aripiprazole	2-5 mg/day	30 mg/day	10–17 years old
Lithium	300–600 mg/day Goal for acute mania: Blood level 0.8–1.2 mEq/L Goal for maintenance: Blood level 0.6–1 mEq/L	Dose determined by blood level. Max trough blood level should be 1.2 mEq/L	12–17 years old
Valproate	10–15 mg/kg/day in divided doses Goal: 80–125 mcg/mL	Dose determined by blood level. Max blood level should be 125 mcg/mL.	Not approved in children or adolescents for bipolar disorder.

**Medications are listed in alphabetical order.*

Dosing Recommendations for Atypical Antipsychotics in Bipolar Disorder in Children and Adolescents Ages 6 to 17 Years Old

Monitoring

- Refer to *Principles of Practice* on page 8.

Minimizing side effects when switching psychotherapeutic medications

- Start low. Go slow. Stop slowly. Avoid abrupt stopping, starting, and/or switching to reduce risk of rebound and withdrawal phenomena.
- Do not switch until the primary disorder has been treated according to target disorder guidelines at adequate dose and duration.
- Only stop and/or switch abruptly if a serious adverse effect necessitates it (i.e., severe neutropenia, agranulocytosis, diabetic ketoacidosis, neuroleptic malignant syndrome, acute pancreatitis, lithium toxicity, Stevens-Johnson syndrome, etc.).
- Slow switch using cross-titration is the preferred method; an even slower switch can be done using the plateau-cross titration method, with therapeutic dose overlap of medications (when switching to a less sedating cholinergic medication, or one with a much longer half-life).
- If time permits, do not reduce the first medication by more than 25–50% per 5 half-lives.

Additional considerations

- When switching medications, the more different the binding affinity for the same receptor (between the two drugs), the greater risk for side effects and rebound and withdrawal phenomena (especially sedating: anti-cholinergic, dopaminergic).
- The more different the half-life of the medications with the same physiological effect (desired or undesired), the greater the risk for withdrawal and rebound phenomena. Withdrawal and rebound phenomena are most likely when discontinuing from a short half-life medication.
- Withdrawal and rebound phenomena are most likely to occur when switching from a strongly antihistaminergic (sedating) or anti-cholinergic medication (e.g., clozapine, olanzapine, quetiapine), to a less strongly binding medication (e.g., haloperidol, molindone, paliperidone, aripiprazole, ziprasidone); or from a strongly binding anti-dopaminergic medication [i.e., first-generation antipsychotics (FGA AP) such as risperidone, paliperidone] to a less strongly binding antipsychotic (e.g., clozapine, quetiapine); or a full antagonist to a partial agonist (e.g., aripiprazole).
- Insufficient efficacy or increased side effects may occur during a switch when medications metabolized by cytochrome P450 liver enzymes are paired with a medication that affects that same enzyme.
- Never discontinue lithium or clozapine abruptly to avoid potentially severe rebound of mania or psychosis.
- Quetiapine and mirtazapine can lead to more sedation at lower doses (below 250–300 mg for quetiapine and below 15 mg for mirtazapine) because of its high affinity for histamine receptors. This is offset by increased alpha-adrenergic activity at higher doses, which counteracts this sedative effect at lower doses.

For a full list of references, visit ***http://medicaidmentalhealth.org/***.