

## Bipolar I Acute or Mixed Mania - 6-17 Years

**Level 0** Comprehensive assessment. **Narrow phenotype**, classic bipolar grandiosity, hypersexuality, elevated mood, decreased sleep, cycling, flight of ideas (no current validity under age 6). Qualify symptoms using frequency, intensity, number and duration of episodes. Use of rating scales highly encouraged (Young Mania Rating Scale, Child Mania Rating Scale).

**Level 1** Monotherapy with one of these three agents:

- Aripiprazole
- Risperidone
- Quetiapine

- For euphoric mania in adolescents, consider lithium.

**Level 2** Monotherapy with atypical antipsychotic listed in Level 1 AND augmentation with mood stabilizer(s) (lithium, VPA/divalproex), but not two antipsychotics.

**Level 3** Monotherapy with antipsychotic except clozapine not listed in Level 1 or combination with mood stabilizer(s).

**Level 4** Clozapine or ECT.

### Notes:

1. **Not recommended** oxcarbazepine: little consensus to support the use of this agent for acute mania in pediatric patients. The only randomized controlled trial of oxcarbazepine failed to find a difference from placebo; only open treatment data available for carbamazepine in children & adolescents. No evidence for topiramate or lamotrigine as acute antimanic agents.
2. Avoid antidepressants; use with caution with comorbid anxiety or OCD.

# Dosing Recommendations for Atypical Antipsychotics in Children and Adolescents - Bipolar Disorder: Acute or Mixed Mania - 6-17 Years\*

*\*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.*

Drug Name	Starting Dose	Maximum Dose	FDA Approved Age Range
Aripiprazole	2-5 mg/day	30 mg/day	10-17 years
Risperidone	Children: 0.25 mg/day Adolescents: 0.5 - 1 mg BID	Children: 4 mg/day Adolescents: 6 mg/day	10-17 years
Quetiapine	Children: 12.5 mg BID  Adolescents: 25 mg BID	400 mg/day  600 mg/day	10-17 years
Lithium	300 - 600 mg/day <u>Goal: acute mania:</u> 0.8 – 1.2 mE q/L <u>Goal maintenance:</u> 0.6 – 1 mE q/L	1.2 mEq/L	12-17 years
Valproate	10-15 mg/kg/day in divided dose Goal: 80-125 mcg/mL	Dose determined by blood level. Max blood level should be 125 mcg/mL	Not approved
Haloperidol	Children: 0.25 mg - 0.5 mg/day  Adolescents: 0.5 - 1 mg/day	Children: 4 mg/day  Adolescents: 10 mg/day	Not approved for pediatric mania
Chlorpromazine	Children: 25 - 50 mg/day  Adolescents: 25 - 100 mg/day	Children: 200 mg/day (under 12)  Adolescents: 500 mg/day	Not approved for pediatric mania
Olanzapine	2.5 mg to 5 mg once daily Weekly titration by 2.5 to 5 mg increments	20 mg/day	13-17 years

# Bipolar I Acute or Mixed Mania - 6-17 Years, continued

## Minimizing side effects when switching psychotropic medications

- Start low! Go slow! And 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 (esp. 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 rebound and withdrawal 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 (i.e., Clozapine, Olanzapine, Quetiapine), to a less strong binding medication (i.e., haloperidol, molindone, peridone, paliperidone, aripiprazole, Ziprasidone); or from a strongly binding anti-dopaminergic (i.e. FGA AP, Risperidone Paliperidone) to a less strongly binding antipsychotic (i.e., clozapine, quetiapine, clozapine); or a full antagonist, to a partial agonist (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 psychoses.
- Quetiapine and Mirtazapine can lead to more sedation at lower doses (below 250-300 mg for Quetiapine, and below mg for Mirtazapine).