

# Schizophrenia in Children and Adolescents

## Level 0

### ***Comprehensive assessment***

- ◆ Diagnosis based on:
  - ◇ Symptom presentation
  - ◇ Mental status examination findings (e.g., responding to internal stimuli, bizarre beliefs, disorganized speech)
  - ◇ Course of illness, especially a decline in function or failure to progress
- ◆ Assess potential confounding factors, including any history of significant developmental problems, mood disorders, trauma, or substance abuse.

### ***Helpful clinical tools include:***

Structured diagnostic interviews

- ◆ Kiddie-SADS-Present and Lifetime Version (K-SADS-PL)

Symptom interviews

- ◆ Brief Psychiatric Rating Scale for Children (BPRS-C)
- ◆ Positive and Negative Syndrome Scale (PANSS-6)

Links to clinical tools listed above are available at <https://floridabhcenter.org/>.



## Level 1

Monotherapy with an antipsychotic agent FDA-approved to treat schizophrenia in adolescents:

- ◆ Aripiprazole, lurasidone, risperidone, quetiapine, (ages 13 years and older)
- ◆ Paliperidone (ages 12 years and older)
- ◆ Haloperidol (age 3 years and older), perphenazine, thiothixene (ages 12 years and older)

First-line medication choice is based on side effect profile, patient/family preference and cost.

For all antipsychotic trials, monitor side effects systematically, including:

- ◆ Extrapyramidal side effects, including Parkinsonism, akathisia and tardive dyskinesia
- ◆ Metabolic monitoring per ADA guidelines

*Note: Adjunctive agents may be indicated to treat/prevent EPS or metabolic side effects.*

If there is no appreciable symptom improvement (less than minimally improved on the CGI) after two weeks at a therapeutic dose, consider changing to a different agent (see Level 2).

A therapeutic trial is generally defined as 4 to 6 weeks with doses up to FDA-approved dosages in adults (with allowances for children < 13 years of age), as tolerated.

Youth with schizophrenia and their families also need intensive support and case management services, including:

- ◆ Psychoeducational therapies addressing treatment options
- ◆ Safety planning
- ◆ Relapse prevention and adherence challenges
- ◆ Special education and/or vocational programs
- ◆ Resiliency training
- ◆ Refer to first-episode psychosis specialty program if available.





### **Helpful links:**


- ◆ NAVIGATE program: NAVIGATE is a comprehensive program that provides early and effective treatment to individuals who have experienced a first episode psychosis. For more information, visit <https://navigateconsultants.org/>.
- ◆ National Institute of Mental Health Recovery After an Initial Schizophrenia Episode (RAISE) Resource page: <https://www.nimh.nih.gov/health/topics/schizophrenia/raise/raise-resources-for-patients-and-families>

### **Notes:**

1. For those presenting with catatonia and schizophrenia, strongly consider consultation with a child and adolescent psychiatrist. For those presenting with catatonia not responding to antipsychotic monotherapy, short-term augmentation with high dose benzodiazepines is recommended in an acute care setting. ECT should be considered for those presenting with catatonia and not responding to short-term high dose benzodiazepines.
2. Olanzapine is FDA approved to treat schizophrenia in adolescents (ages 13 years and older). However, given the risk of metabolic side effects, olanzapine is not recommended as a first-line treatment.
3. Although the first-generation neuroleptics, e.g., haloperidol, perphenazine, and thiothixene are FDA approved for use in adolescents, they have not been as well studied as the newer second-generation medications in the pediatric population.

*Above website links were updated at the time of publication.*

	<p><b>Level 2</b></p> <p>Monotherapy with alternative drug FDA-approved to treat schizophrenia in adolescents (from Level 1 above or olanzapine) if the first agent tried is not effective or poorly tolerated.</p> <p>Continue psychosocial interventions.</p>
	<p><b>Level 3</b></p> <p>Monotherapy with alternative drug FDA-approved to treat schizophrenia in adolescents (from Level 1 above or olanzapine), or with an antipsychotic FDA approved for adults, but not approved for children and adolescents.</p> <p><u>Notes:</u></p> <ol style="list-style-type: none"> <li>1. For nonresponse to second generation agents, consider trial of first generation agent.</li> <li>2. Ziprasidone (Findling et al., 2013) and asenapine (Findling et al., 2015) were not found to be statistically superior to placebo for treating adolescent schizophrenia, and therefore are not recommended for treating schizophrenia in this age group.</li> <li>3. Clozapine is reserved for treatment refractory cases (Refer to Level 5).</li> </ol> <p>For patients with treatment failure characterized by ongoing psychotic symptoms exacerbated by non-adherence, psychosocial strategies should be enhanced to address non-adherence, including developing strategies to better monitor medication administration.</p> <p>Treatment with a long-acting depot antipsychotic agent should be considered as clinically appropriate, including in situations of non-adherence.</p> <p>Available long-acting agents include aripiprazole extended-release injectable suspension, paliperidone palmitate, risperidone microspheres, haloperidol decanoate, fluphenazine decanoate. None of these agents are FDA-approved for use under the age of 18 years old.</p> <p><i>Note: Olanzapine pamoate (Zyprexa Relprevv) is a long-acting agent that has been linked with a potentially life-threatening post injection syndrome. Use with children and adolescents is not FDA approved and is NOT recommended. For more information, visit <a href="https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-review-study-sheds-light-two-deaths-associated-injectable">https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-review-study-sheds-light-two-deaths-associated-injectable</a></i></p> <p><i>Above website link was updated at the time of publication.</i></p>
	<p><b>Level 4</b></p> <p>Using a single antipsychotic, adjunctive treatment with a mood stabilizer or an antidepressant may be considered to target comorbid mood symptoms, aggression, or negative symptoms.</p> <p>Continue psychosocial interventions.</p>
	<p><b>Level 5</b></p> <p>Clozapine trial for treatment refractory schizophrenia.</p> <p><u>Notes:</u></p> <ol style="list-style-type: none"> <li>1. Treatment refractory defined as failing at least two therapeutic dose trials of an antipsychotic agent for at least 6 weeks at a therapeutic dose that was adhered to <math>\geq 80\%</math> of the time.</li> <li>2. Clozapine can only be prescribed through the Clozapine Risk Evaluation and Mitigation Strategy (REMS) program, <a href="https://www.newclozapinerems.com/home">https://www.newclozapinerems.com/home</a>.</li> </ol>

	<p><b>Level 6</b></p> <p>For patients that have failed to respond to multiple different antipsychotics, diagnostic reevaluation and consultation are indicated. Electroconvulsive therapy (ECT) may be considered for adolescents with schizophrenia who do not adequately respond to or cannot tolerate antipsychotic medications.</p>
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For a full list of references, visit <https://floridabbcenter.org/>.

**Table 14.**

Dosing Recommendations for Treatment of Schizophrenia in Children and Adolescents			
Medication	Starting Dose	Maximum Dose	FDA Approved Age Range
<b>First-Generation Antipsychotics</b>			
Haloperidol*	3–12 years: 0.05–0.15 mg/kg/day in divided doses two to three times daily  >12 years: 0.5–2 mg/day in divided doses two to three times daily	3–12 years: 0.15 mg/kg/day in divided doses  >12 years: 20 mg/day**	Ages 3 and older
<b>Second-Generation Antipsychotics</b>			
Aripiprazole*	2–5 mg/day	30 mg/day	13–17 years old
Clozapine	Start at 12.5 mg, titrate slowly (max increase of 25 mg every other day during week 1, thereafter if tolerated increase by 25 to 50 mg every other day). Hold dose/reduce dose if benign drug fever or tachycardia that often dissipates over time. Target dose: 250 mg to 450 mg/day in divided doses (lower doses in females and non-smokers).	Maximum dose 600 mg/day in divided doses (900 mg in severe cases if tolerated, but increased seizure risk at doses $\geq$ 600 mg/day).  Target clozapine blood level of 350–450 ng/mL).	Not FDA approved for children and adolescents
Lurasidone	40 mg/day	80 mg/day	13–17 years old
Olanzapine*	2.5–5 mg/day	20 mg/day	13–17 years old
Paliperidone*	3 mg/day	6–12 mg/day***	12–17 years old
Quetiapine	IR: 25 mg twice per day ER: 50 mg once daily	800 mg/day	13–17 years old
Risperidone*	0.5 mg/day	6 mg/day	13–17 years old

\* Medications indicated with an asterisk (\*) are available in long-acting injectable (LAI) formulations. Paliperidone LAI requires trial of oral risperidone prior to initiation of LAI. Most aripiprazole LAI formulations require trial of oral aripiprazole prior to initiation of LAI.

\*\*The FDA maximum for haloperidol is 100 mg/day based on old trials in adults, but doses over 20 mg/day are not generally recommended in children and adolescents unless benefits clearly outweigh risks.

\*\*\*6 mg/day recommended maximum dose in children and adolescents weighing less than 51 kg