Antipsychotic Utilization in a Pediatric Population

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Disclosures

- Dr. Ehret is a consultant for Saladex Biomedical. She serves as the Pharmacist Expert for SMI Adviser and is the Director for the State of Maryland Office of Pharmacy Services Peer Review Program.

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Objectives

- Describe current practice guidelines regarding the use of antipsychotic medications in a pediatric population
- Outline adverse effects associated with the use of antipsychotic medication in a pediatric population
- Discuss when to initiate an antipsychotic medication in a pediatric population

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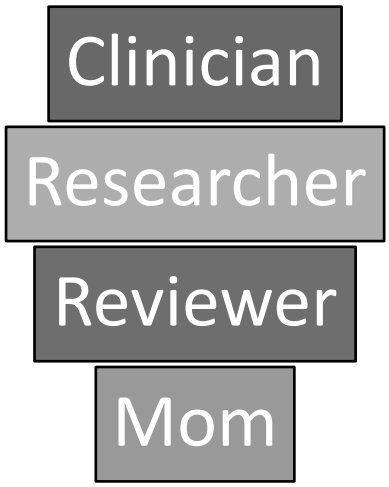
My Perspective



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The Approach

- Common case vignettes
- Tips
- Guidance
- Resources

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Case 1

- 7 year old child with ADHD, PTSD, DMDD, MDD and unspecified anxiety. Provider has only seen child once.
- Current medications: Clonidine XR 1 mg daily
- Child referred to therapy
- Request for: Risperidone 0.5 mg daily
- Target symptoms: Aggression, assault, impulsivity, insomnia, irritability, mood instability

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Poll Question

- Is Risperidone appropriate for this patient?
  - Yes
  - No
  - I need more information

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Antipsychotics in Pediatric Patients

Increasing in use since 1990

- Residential care > group homes > foster care > general population
- Publicly vs. privately insured

Most frequently prescribed

- Risperidone: 42.1%
- Aripiprazole: 28%
- Quetiapine: 19.2%
- Olanzapine: 4.4%

Most frequent target symptom: aggression

J Child Adolesc Psychopharmacol 2021;31:350-7
J Child Adolesc Psychopharmacol 2021;3:381-6
Front Psychiatry 2021;12:623681:ecollection 2021

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Prescribing Patterns

Age (Years)	Stimulant (%)	Antidepressant (%)	Antipsychotic (%)
3-5	0.5	0.2	0.2
6-12	4.6	1	0.8
13-18	3.7	2.8	1.2
19-24	1.6	4	0.8

- Highest prescribing among general psychiatry or child psychiatry for all age groups except stimulants
- Females prescribed antidepressants more than males as age increased
- Males aged 6-18 years prescribed antipsychotics and stimulants more than females

J Child Adolesc Psychopharamcol 2018;28:158-65

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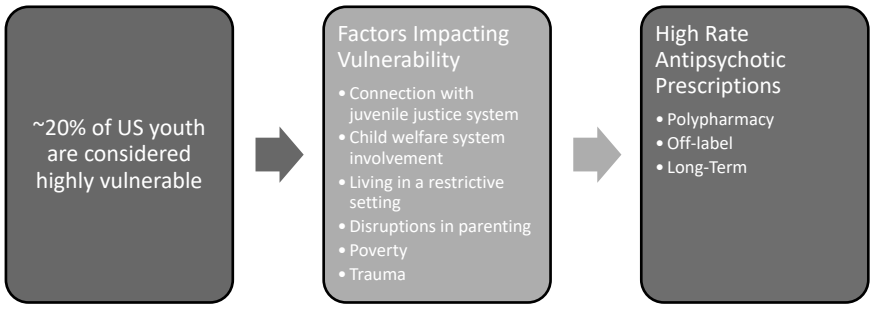
Who is at Risk?



Expert Opin Pharmacother 2018;19:547-60

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What are we trying to do accomplish with ANTIPSYCHOTIC medication?

Achievable Therapeutic Objectives

- Enable the patient to control him/herself
- Relieve signs and symptoms which are troubling or disabling to the patient
- Improve the patient's ability for self-care

Antipsychotics don't control behavior

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Psychiatric medication doesn't help

Developmental Issues:

- Learning disabilities (e.g. reading disability)
- Developmental delay (e.g. speech/language)
- Physical health (e.g. poorly controlled asthma)

Environmental Issues:

- School (e.g. frequent school changes)
- Family (e.g. parental illness or financial stressors)
- Community (e.g. bullying or violence exposure)

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Over Prescribing

- Lack of Access to Mental Health Services
- Expansion of FDA-approved indications
- Off-label use
- Shorter hospitalizations
- Difficulty obtaining acute care hospitalizations
- Lack of shared decision making
- Need for quick response to manage behavior
- Advertising

Psychiatr Serv 1016;67:339-41

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Tip #1:

Consider both the diagnosis and target symptoms.

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Pediatric Approved Antipsychotics

Antipsychotic	Irritability due to autism	Bipolar I	Schizophrenia
Aripiprazole (Abilify)*	X	X	X
Risperidone (Risperdal)	X	X	X
Olanzapine (Zyprexa)		X	X
Quetiapine (Seroquel)		X	X
Asenapine (Saphris)		X	
Paliperidone (Invega)			X
Lurasidone (Latuda)**		X	X

*Also has indication for treatment of Tourette's Disorder
**Indication for bipolar depression

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Assess Problem Behaviors

Timeline: episodic versus chronic

Settings: home, school, community

Impact: relationships, grades, safety

Context: stressors, changes

Emotion: irritability, anxiety

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Case 2

- 15 year old with depression and hallucinations
- Current medication: Quetiapine 75 mg daily, Clonidine 0.1 mg XR 2 daily, Escitalopram 20 mg daily, bupropion 100 SR daily, trazodone 50 mg daily
- Request for: Olanzapine 2.5 mg daily
- Target Symptom: Hallucinations

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Poll Question

- Which recommendation is the best to provide for this patient?
  - Approve the olanzapine in combination with quetiapine
  - Decline the olanzapine, increase the quetiapine

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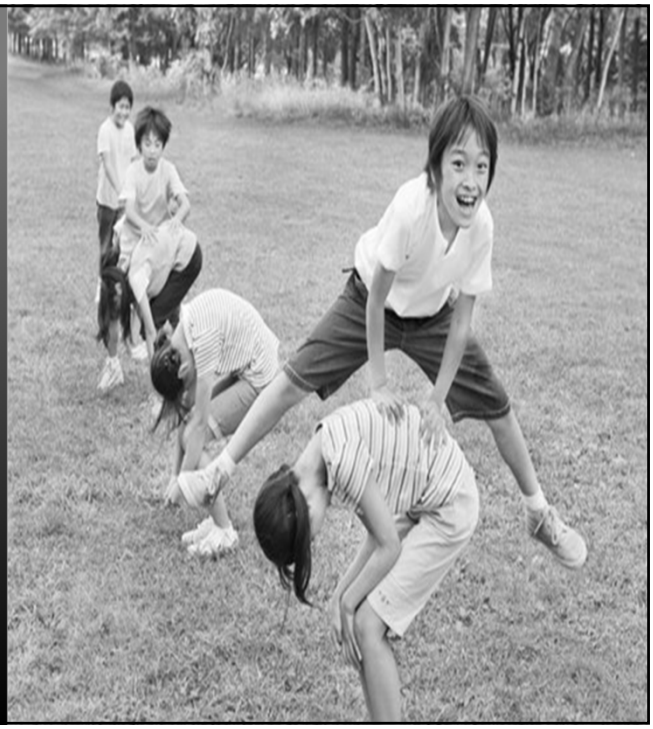
Tip #2

Try not to "leapfrog" over evidence-based treatments



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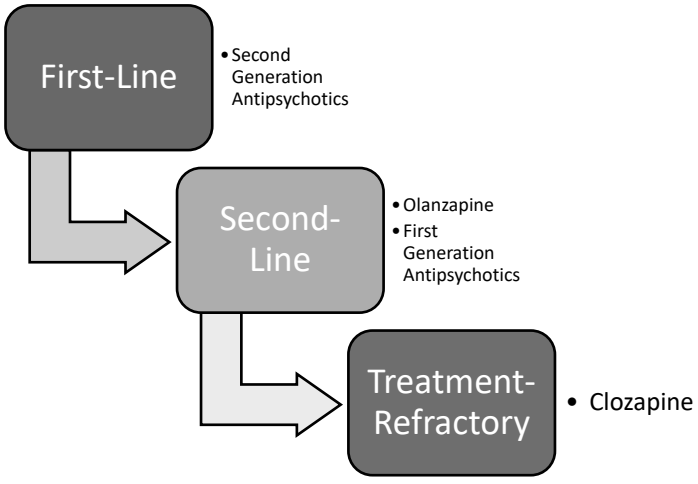
Schizophrenia Treatment Guidelines



J Am Acad Child Adolesc Psychiatry 2013;52:976-90.

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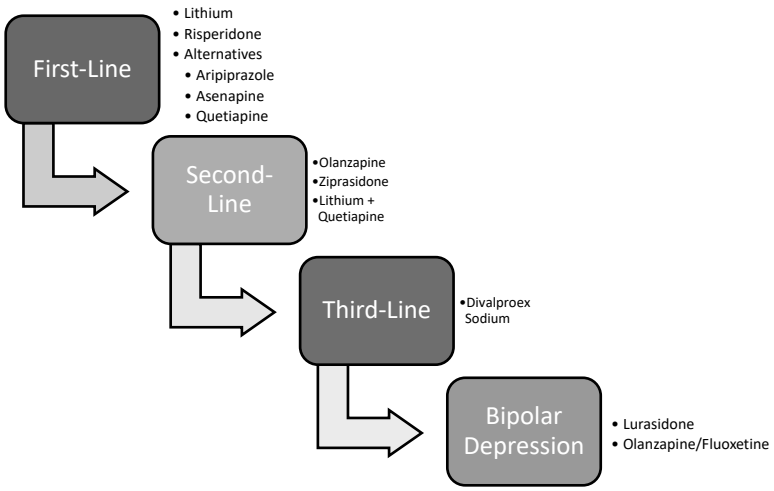
Bipolar Disorder Treatment Guidelines



Bipolar Disord 2018;20:97-170

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Where else are Antipsychotics Recommended?

- Tourette's Disorder
  - Second and third line options
- Autism
  - Risperidone and aripiprazole for irritability

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Long-Acting Injectable Antipsychotic Medications- Pediatrics

- No prospective studies; majority case reports and case series
- Most reported LAI: Risperidal Consta, Invega Sustenna, Abilify Maintena
- Decrease in severity of symptoms and lower remission rates
- Possible decrease in AEs
- Barriers to administration
  - Providers knowledge
  - Clinic administration
  - Patient and guardian acceptance of LAI treatment
  - Insurance approval

J Child Adolesc Psychopharmacol 2022;32:312-27
Pediatric Drugs 2023;25:135-49

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Case 3

- 14 year old with psychotic disorder NOS
- AIMS: 5
  - Lip Movement: 1
  - Upper Arm: 3
  - Lower Leg: 2
- CC: Tremors are not getting better
- Current Medications: Paliperidone 1.5 mg twice daily, benztropine 1 mg twice daily, lorazepam 1 mg three times daily
- Request: Paliperidone 1.5 mg AM, 3 mg PM
- Target Symptoms: Hyperactivity, impulsivity

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Poll Question

- Should the dose of Paliperidone be increased?
  - Yes
  - No
  - I don't know what an AIMS score is

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Tip #3:

Safety first

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How do Antipsychotic Medications Differ?

- Side effect profile
- Efficacy
- Drug interactions
- Pharmacokinetics
- Dosage forms
- Regimen

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Adverse Effects

Evidence	•Short-term studies currently available •Need for long-term studies on brain development
Common Adverse Effects	•Somnolence/sedation •Gastrointestinal distress •Weight gain
Other Effects	•Metabolic Parameters- lipids, glucose, insulin resistance •Hormonal effects- prolactin •QTc Prolongation •NMS
Extrapyramidal Symptoms	•Decreased with SGA vs. FGA •Increased incidence in children and adolescents compared to adults

Psychiatr Serv 2016;67:339-41

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Receptor Binding and Adverse Effects

	H_1	H_2	H_3	M_1	M_3	α_1	α_{2A}	α_{2B}	α_{2C}
Haloperidol		+				++	+	+	+
Aripiprazole	++					++	++	++	++
Asenapine	+++	+++				+++	+++	+++ +	+++
Lurasidone						++	++		+++
Olanzapine	+++	++	+	++	++	++	+	++	+++
Paliperidone	++	+				+++	+++	+++	+++
Quetiapine	+++			+	+	++	+	+	++
Risperidone	+++	+				+++	++	++	+++

Current Neuropharmacol 2018;16:1210-23

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Common Adverse Effect: Obesity

- Visible adverse effect: weight gain
- May not notice: Increased cholesterol, blood sugar
- Blood work and weight monitoring will improve early detection of problems
- Medication monitoring programs track side effect issues

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Metabolic Side Effects

Antipsychotic	Weight Gain	Glucose Abnormalities	Hyperlipidemia
Aripiprazole	Low	Low	Low
Asenapine	Moderate	Moderate	Moderate
Brexipiprazole	Low	Low	Moderate
Cariprazine	Moderate	Moderate	Low
Clozapine	High	High	High
Haloperidol	Low	Low	Low
Iloperidone	Moderate	Moderate	Moderate
Lumateperone	Low	Low	Low
Lurasidone	Low	Moderate	Moderate
Olanzapine	High	High	High
Paliperidone	Moderate	Low	Moderate
Quetiapine	Moderate	Moderate	High
Risperidone	Moderate	Moderate	Low
Ziprasidone	Low	Low	Low

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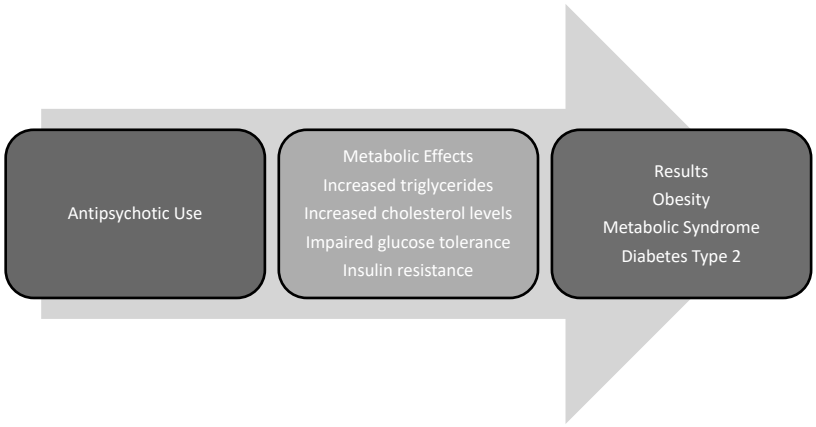
Metabolic Side Effects- Pediatrics



*Antipsychotics chronically prescribed: cardiometabolic risk accumulates

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Monitoring Metabolic Adverse Effects

	Baseline	4 Weeks	8 Weeks	12 Weeks	6 Months	Annually
Weight/ BMI	X	X	X	X	X	X
Fasting Plasma Glucose/ HgA1c	X			X	X	X
Lipids	X			X	X	X
Blood Pressure	X			X	X	X

J Psychopharmacol 2016;30:717-48
J Clin Psychopharmacol 2021;41:13-18

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Physical Morbidity and Mortality

- Sedentary lifestyle
- Obesity
- Cardiovascular diseases
- Obstetric complications
- Altered pain sensitivity

*Lower rate of health care services utilization and medical treatment

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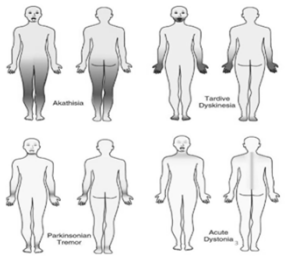
Movement Disorders

Acute Akathisia	•Complaints of restlessness •Excessive fidgety movements •Typically develop within a few weeks or starting medication or raising dose
Acute Dystonia	•Severe muscle spasms of the eyes, head, neck, limbs, or trunk •Severe arching of the back or laryngospasm may occur •Symptoms typically emerge within a few days of starting medication or raising dose
Parkinsonism	•Tremor •Muscular rigidity •Akinesia •Bradykinesia •Symptoms onset typically occurs within a few weeks to months of starting antipsychotic or raising dose
Tardive Dyskinesia	• Involuntary, hyperkinetic, repetitive choreoarthetoid movements • Most commonly observed in the orofacial region • Movements in extremities/trunk may also occur



CNS Spectrums 2015;20:4-14

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Movement Disorders in Pediatrics

- Risk increased with duration of antipsychotic treatment:
  - 3% at 6-12 months
  - 10% at 1-2 years
  - 14% at more than 2 years

Wonodi I, et al. Mov. Disord. 2007;22:1777-1782

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Movement Disorders in Pediatrics

- 118 pediatric patients with psychiatric illness; 5-18 years treated for 6 or more months with antipsychotics
- >80% of antipsychotic prescriptions were for youth with no psychotic symptoms (mood disorders; ADHD)
- 9% showed TD

Wonodi I, et al. Mov. Disord. 2007;22:1777-1782

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Monitoring for Movement Disorders

Disorder	Monitoring Recommendations
Acute Dystonic Reaction	Simpson-Angus Extrapyramidal Symptom Scale Extrapyramidal Symptom Rating Scale Observation and patient report at each visit
Parkinsonism	Simpson-Angus Extrapyramidal Symptom Scale Extrapyramidal Symptom Rating Scale Observation and patient report at each visit
Akathisia	Barnes Akathisia Rating Scale Ask patient about this side effect and suicidal thoughts/plans at each visit
Tardive Dyskinesia	Abnormal Involuntary Movement Scale (AIMS) or Dyskinesia Identification System-Condensed User Scale (DISCUS) at baseline and at least every 6 months/12 months

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AIMS Rating Scale

Patient Name:	Date:	None	Minimal, may be extreme normal	Mild	Moderate	Severe
Facial and Oral Movements						
1. Muscles of Facial Expression e.g., movements of forehead, eyebrows, periorbital area, cheeks; Include frowning, blinking, smiling, grimacing		0	1	2	3	4
2. Lips and Perioral Area e.g., puckering, pouting, smacking		0	1	2	3	4
3. Jaw e.g., biting, clenching, chewing, mouth opening, lateral movement		0	1	2	3	4
4. Tongue Rate only increases in movement both in and out of mouth, NOT inability to sustain movement		0	1	2	3	4
Extremity Movements						
5. Upper (arms, wrists, hands, fingers) Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).		0	1	2	3	4
6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot		0	1	2	3	4
Trunk Movements						
7. Neck, shoulders, hips e.g., rocking, twisting, squirming, pelvic gyrations		0	1	2	3	4
Global Judgments						
8. Severity of abnormal movements		0	1	2	3	4
9. Incapacitation due to abnormal movements		0	1	2	3	4
10. Patient's awareness of abnormal movements (rate only patient's report) 0 = not aware; 1 = aware, no distress; 2 = aware, mild distress; 3 = aware, moderate distress; 4 = aware, severe distress		0	1	2	3	4
Dental Status						
11. Current problems with teeth and/or dentures?		No	Yes			

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Safety of Long-Acting Injectable Antipsychotic Medications

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Case 4

- 16 year old with Bipolar Disorder and intellectual disability
- Current Medication: Olanzapine 10 mg daily
- Request: Zyprexa Relprevv LAI
  - Will have PCP administer injection and then patient will come to psychiatry provider office for the 3 hour monitoring

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Poll Question

- Does this plan meet the requirements of the REMS for Zyprexa Relprevv?
  - Yes
  - No
  - I have no idea

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Tip #4:

Have a consultation plan for outliers

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Injection Sites/Volume of Injection

Medication	Site	Volume of Injection
Fluphenazine	Typically IM, with deltoid or gluteal injections possible	0.5-2 mL
Haloperidol	Deltoid or gluteal IM	3 mL max

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Injection Sites/Volume of Injection

Medication	Site	Volume of Injection
Abilify Maintena	Deltoid or Gluteal IM	0.8-2 mL
Abilify Asimtufii	Gluteal IM	3.2-2.4 mL
Aristada	441 mg: Deltoid or Gluteal IM Higher doses: Gluteal IM	1.6-3.9 mL
Aristada Initio	Deltoid or Gluteal IM	2.4 mL
Invega Sustenna	Loading dose: Deltoid IM Maintenance Dose: Deltoid or Gluteal IM	0.25-1.5 mL
Invega Trinza	Deltoid or Gluteal IM	0.875-2.625 mL
Invega Hafyera	Gluteal IM	3.5-5 mL

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Injection Sites/Volume of Injection

Medication	Site	Volume of Injection
Risperdal Consta	Deltoid or Gluteal IM	2 mL
Perseris	Abdomen or back of upper arm subcutaneously	0.6-0.8 mL
Rykindo	Gluteal IM	2 mL
Uzedy	Abdomen or back of upper arm subcutaneously	0.14-0.7 mL
Zyprexa Relprevv	Gluteal IM	1-2.7 mL

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Safety Concerns

- Needle Size
  - Consideration of body mass
  - Adult studies versus pediatric patients
- Preparation
  - Training to avoid errors
- Oral overlap
- Long-term data not available in pediatric patients

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Zyprexa Relprevv

- REMS: Potential for development of Post-Injection Delirium/Sedation Syndrome (PDSS)
  - Signs and symptoms consistent with olanzapine overdose, in particular sedation and/or delirium
  - Must be administered in registered healthcare facility with ready access to emergency response services
    - Continuously observe patient for at least 3 hours
    - After 3 hours, confirm patient is alert, oriented, and absent of any signs/symptoms of PDSS
    - Must have ride to next location

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Resources

- Movement Disorder Training
  - The AIMS Assessment and Tardive Dyskinesia
- Psychotropic Long-Acting Injectable (LAI) Training Program
  - Psychotropic LAI Training Program

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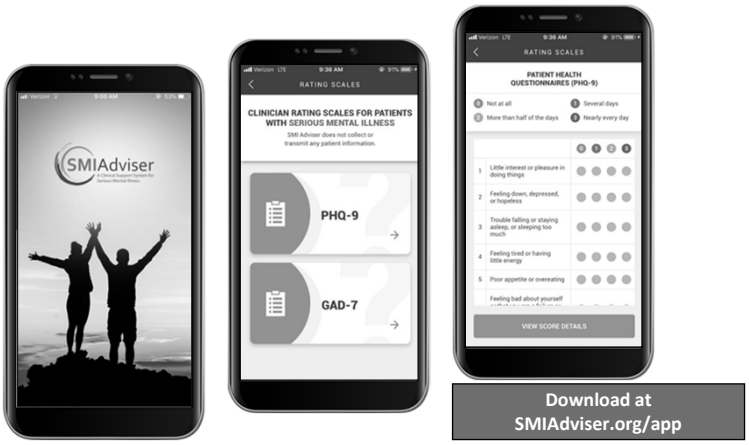
SMI ADVISER APP



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Conclusions

- Verify indications and target symptoms
- Most common adverse effects: hypotension, increased appetite, weight gain, and sedation
- Changes in glucose and lipids
- Treatment plans should be based on treatment guidelines

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Questions

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