

Risperidone [Risperdal]

FDA Indications:

- **Schizophrenia**, ages 13 and older (oral & long acting IM)
- **Acute mania/mixed mania**, ages 10 and older (oral, mono therapy and adjunct to lithium or valproate)
- **Autism-related irritability**, ages 5-16

Off-label use:

- Early-onset psychosis/schizophrenia
- Behavioral disturbance (irritability, aggression, stereotypies and explosive behavior) and psychotic symptoms associated with a wide range of childhood psychiatric disorders (autism spectrum disorder, intellectual disability, oppositional defiant disorder and conduct disorder)
- Augmentation in refractory OCD
- Self-mutilation and aggressive behavior
- Tic disorders, Tourette's disorder, and trichotillomania

Mechanism of Action:

- Risperidone acts as a **strong antagonist at D2** (reducing positive symptoms, EPSE, prolactin elevation), along with having antagonist properties at alpha-1 (sedation, orthostatic effects), 5-HT_{2A} (reducing negative symptoms, sedation) and 5-HT₇ (pro-cognitive, anxiolytic, antidepressant) receptors
- Has some antagonist effect at H₁ (appetite increase, weight gain, sedation, anxiolytic), M₃ (metabolic effects), alpha-2 (pro-cognitive, antidepressant) and 5-HT_{1A} (pro-cognitive, anxiolytic, antidepressant) receptors
- Theory that rapid dissociation from the D₂ receptor, allowing endogenous dopamine to periodically bind, may be why second generation/atypical antipsychotics are less likely to cause extrapyramidal side effects.

Dosage forms:

- Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg
- Oral solution: 1 mg/mL
- M-tab/oral disintegrating tablets: 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg

Dosing guidelines:

- For psychosis in children and adolescents:
 - Start 0.25 mg BID and increase gradually
 - Suggested daily dose for children: 1-2 mg
 - Suggested daily dose for adolescents: 2.5-4 mg
- Dose titration recommended to minimize orthostatic hypotension

Pharmacology:

- Peak plasma level occurs within 1-1.5 hours (parent compound)
- Elimination half-life: 3-20 hours (parent compound)
- Metabolized by CYP450 2D6, 3A4 and P-gp
- Inhibits CYP450 2D6 and 3A4

Side effects:

- Greater than 30% risk of sexual dysfunction.
- Greater than 10% risk of orthostatic hypotension, drowsiness, sedation, insomnia, agitation, parkinsonism, akathisia, galactorrhea, weight gain, hyperglycemia and hyperlipidemia.
- Greater than 2% risk of anticholinergic effects, EKG abnormalities and photosensitivity.

- Less than 2% risk of dystonic reactions, tachycardia, QTc prolongation >450 msec, blood dyscrasias, hepatic disorder, seizures, rashes, and pigmentation.

Clinical Pearls:

- Before starting:
 - Weigh all patients and monitor weight gain against that expected for normal growth
 - Obtain a baseline personal and family history of diabetes, obesity, dyslipidemia, hypertension, and cardiovascular disease
 - Measure waist circumference, blood pressure, fasting plasma glucose, and fasting lipid profile
- After starting:
 - Measure BMI monthly x3, then quarterly
 - Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications
 - Measure blood pressure, fasting plasma glucose, fasting lipid after three months and then repeat annually
- Abnormal Involuntary Movement Scale (AIMS):
 - Formal assessment for extrapyramidal side effects
 - 14-item questionnaire
 - Should be completed every 3-6 months
- Treat or refer for treatment of any metabolic or weight-related complications. Consider switching to another atypical antipsychotic for patients who gain a significant amount of weight, become hypertensive, develop a metabolic syndrome, or acquire diabetes.

References:

1. Elbe, Dean, et al. *Clinical Handbook of Psychotropic Drugs For Children and Adolescents*. Hogrefe Publishing, 2019.
2. Home Page | Dmh.mo.gov. <https://dmh.mo.gov/media/21821/download>.
3. Stahl, Stephen M., et al. *Stahl's Essential Psychopharmacology: Prescriber's Guide*. Cambridge University Press, 2017.
4. Stahl, Stephen M., et al. *Stahl's Essential Psychopharmacology: Prescriber's Guide Children and Adolescents*. Cambridge University Press, 2018.
5. Title: *Practice Parameter for the Use of Atypical Antipsychotic Medications in Children and Adolescents - AACAP*. https://www.aacap.org/App_Themes/AACAP/docs/practice_parameters/Atypical_Antipsychotic_Medications_Web.pdf.