

EVIDENCE-BASED MEDICATION USE FOR TARGET SYMPTOMS IN CHILDREN & ADOLESCENTS WITH AUTISM SPECTRUM DISORDER



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Autism Spectrum Disorder (ASD): Overview of Treatment with Medications

This presentation will provide a targeted overview of evidence-based use of medications for a range of severe behavioral health symptoms and diagnoses often seen in children and adolescents with ASD.

TARGET SYMPTOMS

With ASD we don't treat the "disorder," medications are sometimes indicated to address accompanying symptoms.

BUT...

If you identify a disorder comorbid with the ASD, follow the evidence-based guideline for that disorder.



**Response to medication does NOT
help differentiate the diagnosis.**

Medication Use for Target Symptoms in Children & Adolescents with ASD

- ➔ Aggression: Irritability, Self-Injury, Aggressive Behavior & Explosive Outbursts
- ➔ Hyperactive, Impulsive & Inattentive Symptoms
- ➔ Sleep Disturbances
- ➔ Restricted, Repetitive Behaviors
- ➔ Medication Optimization /Deprescribing

Levels of Evidence

A = Meta-analysis of RCTs or 2 RCTs or more

B = Small RCT or more than 1 open label study

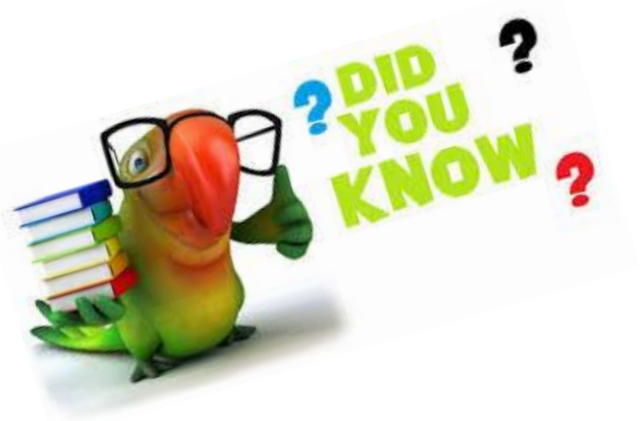
C = Open label or case series; extrapolation from adult studies

D = Pediatric trials assessing tolerability; Expert opinions based on non-systematic reviews of results or mechanistic studies

E = Anecdotal



Medication Treatment of **Hyperactive, Impulsive & Inattentive Symptoms** in the Context of ASD



There are differences in the treatment of hyperactivity/impulsivity/inattention in children with ADHD vs ASD



METHYLPHENIDATE* OR GUANFACINE* MONOTHERAPY

Hyperactive,
Impulsive &
Inattentive
Symptoms in
the Context
of ASD

- If child has significant symptoms, consider methylphenidate or guanfacine as a first line medication
- Use methylphenidate or guanfacine (both immediate-release and extended-release) with caution since adverse behavioral effects may be higher in youth with ASD & ID compared to normally developing youth with ADHD
- Close monitoring is recommended and lower dosing than expected may be required for tolerability
- Methylphenidate or guanfacine yield benefit in about 50% of children in the ASD & ID population





METHYLPHENIDATE* OR GUANFACINE* MONOTHERAPY

Hyperactive,
Impulsive &
Inattentive
Symptoms in
the Context
of ASD

- Combination therapy with Methylphenidate* + Guanfacine* OR Atomoxetine*

2a. If partial response to monotherapy (ie, methylphenidate* or guanfacine* alone), consider combination therapy with methylphenidate* and guanfacine*

OR

2b. Atomoxetine* monotherapy





REASSESS & CONSULT SPECIALIST

Hyperactive,
Impulsive &
Inattentive
Symptoms in
the Context
of ASD

- Refer for consultation to child and adolescent psychiatrist, developmental-behavioral pediatrician or pediatric neurologist if indicated
- Although limited evidence exists in the ASD/ID population, may consider use of an amphetamine preparation
- Psychosocial intervention is not as effective for core ADHD symptoms as medication, though parent management training may enhance the efficacy and acceptability of treatment



NOT RECOMMENDED

- Combination of two alpha-2 agonists (ie, clonidine* and guanfacine*)
- Use of antipsychotics for ADHD symptoms or as sedatives



Hyperactive, Impulsive & Inattentive Symptoms in the Context of ASD

The Bottom Line

1

Monotherapy with methylphenidate* or guanfacine*

2

2a. If partial response to monotherapy (i.e., methylphenidate* or guanfacine* alone), consider combination therapy with methylphenidate and guanfacine

OR

2b. Atomoxetine* monotherapy

3

Diagnostic review and/or consultation
May consider use of an amphetamine* preparation





Remember...

If you identify a disorder comorbid with the ASD, follow the evidence-based guideline for that disorder



Medication Treatment of Aggression: Irritability, Self-Injury, Aggressive Behavior & Explosive Outbursts in the Context of ASD



CLONIDINE* OR GUANFACINE* MONOTHERAPY

Irritability,
Self-Injury,
Aggressive
Behavior &
Explosive
Outbursts in
the Context
of ASD

- For mild – moderate aggression
- Consider an alpha-2 agonist (i.e., clonidine* or guanfacine*) although limited evidence exists, the side effects compared to antipsychotics medications are potentially less severe





RISPERIDONE OR ARIPIPRAZOLE MONOTHERAPY

Irritability,
Self-Injury,
Aggressive
Behavior &
Explosive
Outbursts in
the Context
of ASD

- For severe aggression
- Consider risperidone or aripiprazole for severe irritability, including aggression, self-injury, and significant mood lability
- ASD: Risperidone or aripiprazole is recommended. If monotherapy with one of these agents is ineffective, switch to the other agent
- ID*: Risperidone is recommended





REASSESS & CONSULT SPECIALIST

Irritability,
Self-Injury,
Aggressive
Behavior &
Explosive
Outbursts in
the Context of
ASD

- If no response or treatment-limiting side effects emerge with risperidone and aripiprazole monotherapy, reassess and refer to a specialist (child and adolescent psychiatrist, pediatric neurologist, or developmental pediatrician)
- Consider use of alternative antipsychotics* based on side-effect profiles
- Consider stopping the medication to evaluate need for continued use
- Need to continue monitoring for adverse metabolic effects



Aggression: Irritability, Self-Injury, Aggressive Behavior & Explosive Outbursts in the Context of ASD

The Bottom Line

1

Mild to moderate aggression
Consider an alpha-2 agonist (ie., clonidine* or guanfacine*)

2

Moderate to severe aggression
Consider treatment with risperidone or aripiprazole.
If monotherapy with one of these agents is ineffective, switch to the other agent.

3

Reassess and consult specialist
Consider use of alternative antipsychotics* based on side-effect profiles



Medication Treatment of Sleep Disturbances in the Context of ASD

There are no prescription medications FDA cleared for the treatment of insomnia in youth.



Select Medications for Insomnia

- Melatonin
- Alpha-2 Agonists:
 - Clonidine, Guanfacine
- Antihistamines:
 - Diphenhydramine, Doxylamine, Hydroxyzine
- Antidepressants:
 - Trazodone, Mirtazapine, Doxepin, Amitriptyline
- Benzodiazepines
- Zolpidem
- Ramelteon



Deciding if you are targeting sleep latency (time to fall asleep) or total sleep duration may help guide your decision.

Melatonin

Level of Evidence A

11 RCTs and 5 open label studies of in children with ASD/ID have demonstrated significant benefit

- It's not approved for use as a children's sleep aid.
- Evidence suggests that melatonin may be effective for the short-term treatment of sleep disorders in children and adolescents with ASD.

Clonidine*

Level of Evidence C

No controlled studies in children with ASD/ID with sleep disturbance; 2 positive retrospective reviews in youth with ASD; 1 positive retrospective review in youth with ADHD; 1 in youth in general population

- It's not approved for the treatment of insomnia.
- No trials with clonidine ER* or guanfacine*/guanfacine ER*



Other Select Medications for Insomnia

| Name | Level of Evidence | Comments | Dosing Guidance |
|------------------|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| Atomoxetine* | C | Small literature that exists seems to demonstrate <u>not</u> effective. One RCT (N=54) in children diagnosed with ASD+ADHD was negative (Hollway et al, 2018) | No specific dosing guidelines available |
| Benzodiazepines* | D | No controlled or open label studies of BZs in children with ASD/ID | No specific dosing guidelines available |
| Diphenhydramine | D | It's not approved for use as a children's sleep aid. No controlled or open label studies of diphenhydramine in children with ASD/ID. 3 controlled studies in non-ASD/ID children with sleep disturbance; results were mixed: No significant differences – Merentstein et al (2006) & Paul et al (2004) Significant Differences - Russo et al (1976). | Teens 16 years and above: <ul style="list-style-type: none"> • Begin 12.5-25 mg qHS. • Maximum daily dose of 50-100 mg |
| Doxylamine* | E | No controlled or open label studies in children with ASD/ID | Children 12 and older: <ul style="list-style-type: none"> • Begin 12.5 to 25 mg qHS • Maximum daily dose of 50 mg |
| Eszopiclone* | C | Small literature that exists seems to demonstrate <u>not</u> effective. No controlled or open label studies in children with ASD/ID. One RCT (N=486) in children diagnosed with ADHD was negative (Sangal et al, 2014) | No specific dosing guidelines available |
| Mirtazapine* | E | No controlled studies in children with ASD/ID. One open label study in children diagnosed with developmental disorders was negative (Posey et al, 2001) | No specific dosing guidelines available |
| Ramelteon* | D | No controlled or open label studies in children with ASD/ID. Two small case series (N=5) suggests benefit (Kawabe et al, 2014; Stigler et al, 2011). | No specific dosing guidelines available |
| Trazodone* | E | No controlled or open label studies in children with ASD/ID | No specific dosing guidelines available |
| Zolpidem* | C | Small literature that exists seems to demonstrate <u>not</u> effective. No controlled or open label studies in children with ASD/ID. One RCT, one open label, one open series in non-ASD youth were all negative. | Use not recommended |



MELATONIN MONOTHERAPY

level

1

Sleep
Disturbances
in the
Context of
ASD

- Dosing guidance:
 - Begin 1-3 mg at bedtime
 - If no significant improvement in sleep after one week, increase by 1-3 mg each week until:
 - ☑ satisfactory improvement OR
 - ☑ treatment-limiting side effects have emerged OR
 - ☑ a total daily dose of 10 mg has been reached
- 1-10 mg at bedtime
- Administer 30 - 60 minutes prior to bedtime
- Parents should select a product with the USP Verified Mark or other 3rd party independent testing to allow for safer use.



- Dosing guidance:
 - Begin (0.1 mg) ½ to 1 tab at bedtime; increase by that amount weekly to 0.2 to 0.3 mg at bedtime
 - If no significant improvement in sleep after one week, begin increasing by ½ tab each week at qHS until:
 - ☑ there has been a satisfactory improvement in the sleep disturbance OR
 - ☑ treatment-limiting side effects have emerged OR
 - ☑ a total daily dose of 0.3 mg has been reached.
- Clonidine* 0.025 - 0.3mg qHS



NOT RECOMMENDED

- Use of antipsychotics* for sleep disturbances due to potential for metabolic & other side effects



Sleep Disturbances in the Context of ASD

The Bottom Line

1

Monotherapy with melatonin

2

Monotherapy with clonidine*

3

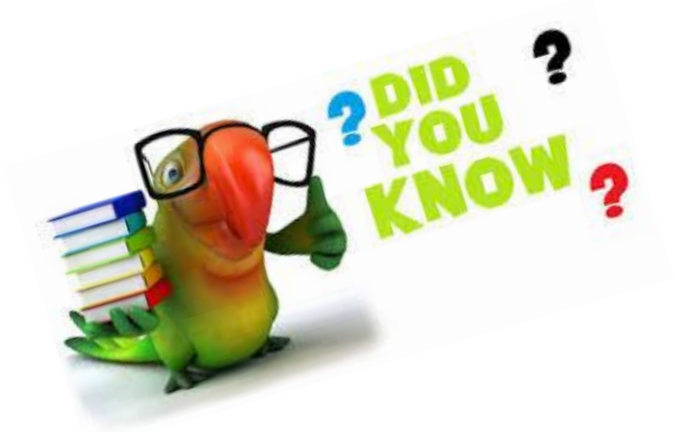
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Medication Treatment of Restricted, Repetitive Behaviors in the Context of ASD

Restricted, Repetitive Behaviors look like OCD but are NOT OCD



Medication Treatment of Restricted, Repetitive Behaviors in the Context of ASD

What We Know...

- Limited or no evidence exists for recommendation of medications in this domain.
- Restricted, repetitive behaviors (RRBs) should not be a target of treatment unless severely interfering with the individual's level of functioning in daily activities or causing significant distress.
- Parent/family education is recommended.

Medication Treatment of Restricted, Repetitive Behaviors in the Context of ASD

What We Know...

- Caution is recommended when attempting to reduce these behaviors, as they may be helpful for self-regulation of anxiety, agitation, and/or frustration.
- In some cases, restricted interests can be an asset.
- CBT and/or Applied Behavior Analysis (ABA) may be the most beneficial treatments and should be adapted to the individual's language and cognitive abilities

Medication Treatment of Restricted, Repetitive Behaviors in the Context of ASD

What We Know...

- Despite the lack of high-quality evidence that SSRIs are directly beneficial for repetitive behaviors and rigidity in children with ASD, they may be indirectly helpful by reducing anxiety.

Medications for RRBs

| Antidepressants | Evidence |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| Fluoxetine | 1 small RCT (n=44) showed fluoxetine was beneficial in reducing repetitive behaviors and 2 RCTs (n=304 total) were not clinically significant |
| Citalopram | 1 RCT (n= 149) citalopram was ineffective |
| Escitalopram | No RCTs; minimal evidence to suggest the effectiveness of escitalopram in youth with ASD |
| Sertraline | No RCTs in adults or children. 2 open-label trials in adults with ASD have noted improvements in repetitive behaviors. |
| Fluvoxamine | 1 unpublished RCT in children reported limited efficacy |
| Other Meds | |
| Risperidone | 1 RCT (n=101) revealed improvement in CY-BOCs |
| Buspirone | 1 RCT (n=166) revealed mixed results with improvement in RRBs at lower doses |
| Divalproex | 1 small RCT (n=13) showed improvement in RRBs |



Medications for RRBs

- Evidence is limited and mixed.
- General consensus --little support for the routine use of medications to treat restricted/repetitive behaviors in ASD

Restricted, Repetitive Behaviors in the Context of ASD

The Bottom Line

1

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2

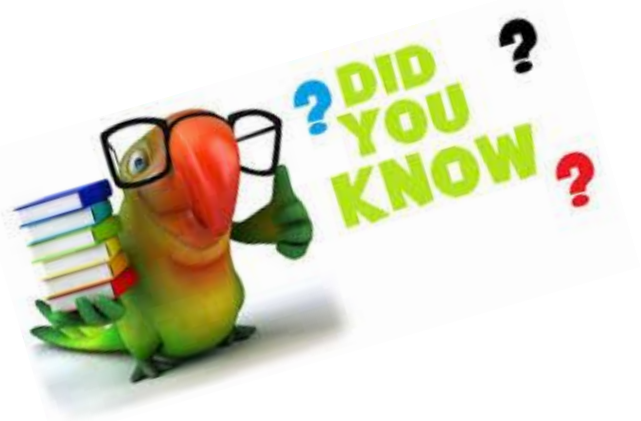
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Medication Optimization ("Deprescribing")

What is Deprescribing?

- ⇒ A structured approach to identifying and discontinuing medications when existing or potential harms outweigh existing or potential benefits.
- ⇒ Deprescribing  Medication cessation
- ⇒ The goal is to use the minimum effective dose and lowest number of medications necessary to manage symptoms and maintain functioning.



The term *medication optimization* may better reflect the broader context in which prescribing decisions in this population are made.

Background

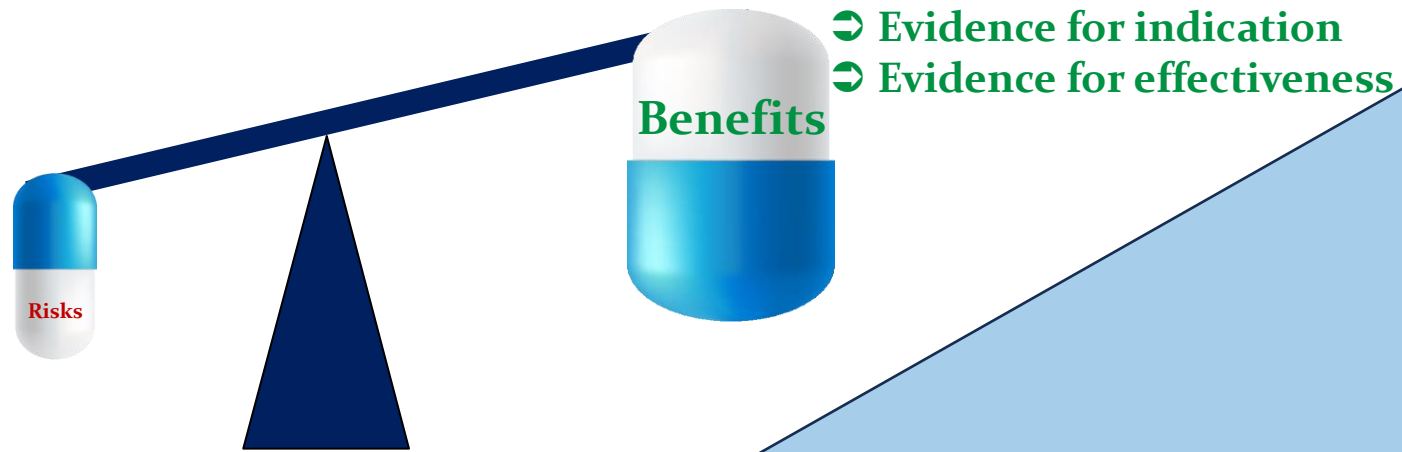
- Clinical experience suggests that reducing or stopping psychotropic medication is not always straightforward.
- Some are reluctant to consider changes to med regimens that might have been unchanged for years and where it has become difficult to determine the positive or negative impact of treatment.
- Incomplete notes or staff changes may result in knowledge of the original indication for medication or previous attempts to discontinue medication being forgotten.

Background

Possible mechanisms for failure of antipsychotic reduction:

- Subjective interpretation of behavioral symptoms by caregivers and family (misattributions)
- Some people with ASD & ID might benefit from antipsychotic treatment
- Misinterpretation of withdrawal symptoms as recurrence of the original target/challenging behavior

Weigh your risks vs benefits



Principles of Good Deprescribing

- Be clear about the reasons for de-prescribing psychotropic medication.
- **Begin with a comprehensive assessment:**
 - Consider the patient's med history before deprescribing.
 - Consider other factors that might alter the benefits and risks of deprescribing.
 - Document clearly, accurately & in detailed fashion the reason(s) for deprescribing.

Principles of Good Deprescribing

Begin with a comprehensive assessment...

- Consider the patient's/families ideas, concerns and expectations.
- Communicate all deprescribing decisions and the justifications to appropriate personnel/individuals involved.
- Adhere to evidence-based guidelines and local formularies where appropriate. Use caution where the population with ASD & ID have not been considered in the guideline/formulary development process.

Principles of Good Deprescribing

Identify meds that could be discontinued or reduced:

- Ensure all medicines are effective, safe, cost-effective, in appropriate form and individualized for the patient.
- Start with medications:
 - Without a clear indication.
 - If after assessment, it remains unclear what symptoms the medication was targeting.
 - With the least evidence of efficacy for the symptoms the medication is prescribed to treat.

Principles of Good Deprescribing

Plan for medication reduction & cessation:

- Determine the frequency of visits and monitor for adverse effects or potential relapse.
- Consider the level of risk if symptoms were to relapse, including risk of hospitalization and safety risk from suicidal or homicidal behavior.
- Develop a crisis or safety plan.

Principles of Good Deprescribing

Plan for medication reduction & cessation...

- Make one change at a time. Allow adequate time for adjustment to dose reduction, which is related medication half-life.
- Avoid times of crisis; choose a time anticipated to have low incidence of significant stressors.
- De-prescribe psychotropic medications within the limitations of your knowledge, skills and experience of individuals with ASD & ID and the target/presenting behaviors.

Questions/Comments?



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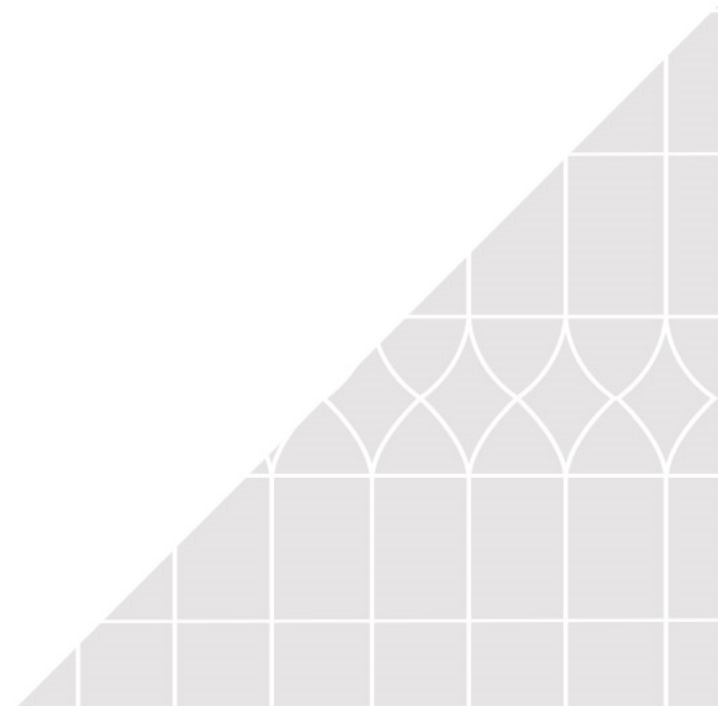
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MEDICATION TABLES



Medications for the Treatment of **Hyperactive, Impulsive & Inattentive** Symptoms in the Context of ASD & ID

Dosing Guide Under age 6

| ADHD Medication Treatment for Children under Age 6 | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Drug Name | Starting Dose Recommendation |
| Methylphenidate and Amphetamine Preparations | |
| Immediate-Release | |
| *Methylphenidate: Ritalin [®] , Methylin [®] , Methylin [®] Chewable Tablets, Methylin [®] Oral Solution | 1.25 mg/day |
| *Amphetamine: Adderall [®] , Dexedrine [®] , Dextrostat [®] , ProCentra [®] Oral Solution, Zenzedi [®] , Evekeo [®] | 2.5 mg/day |
| Selective norepinephrine inhibitor | |
| *Atomoxetine: Strattera [®] | 10mg/day |
| Alpha-2 Agonists⁴ | |
| Immediate-Release | |
| *Clonidine: Catapres [®] | 0.05mg/day |
| *Guanfacine: Tenex [®] | 0.5mg/day |
| Extended-Release | |
| *Guanfacine: Intuniv [®] | 1mg mg/day |
| *Clonidine: KAPVAY [®] | 0.1mg/day |



* Adapted from 2019 Autism Spectrum Disorder & Intellectual Developmental Disorder: Florida Best Practice Psychotherapeutic Medication Recommendations for Target Symptoms in Children & Adols

Medications for the Treatment of **Hyperactive, Impulsive & Inattentive** Symptoms in the Context of ASD & ID: Dosing Guide 6-17 yo

| FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: | | | |
|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------|-------------------------|
| Methylphenidate Preparations | | | |
| Brand Name/Generic Class | Typical Starting Dose | FDA Max Dose/Day | Off-Label Max Dose/Day* |
| Methylphenidate preparations | | | |
| Immediate-Release | | | |
| Focalin® (dexmethylphenidate HCL tablet) | 2.5mg | 20mg | 50mg |
| Methylin® (methylphenidate HCL tablet) | 5 mg bid | 60 mg | >50 kg: 100mg |
| Methylin® Solution (methylphenidate HCL oral solution) | 5 mg bid | 60 mg | >50 kg: 100mg |
| Methylin® Chewable (methylphenidate HCL chewable tablet) | 5 mg bid | 60 mg | >50 kg: 100mg |
| Ritalin® (methylphenidate HCL tablet) | 5 mg bid | 60 mg | >50 kg: 100mg |
| Intermediate-Release | | | |
| Metadate ER® (methylphenidate HCL extended-release tablets) | 10 mg qam | 60 mg | >50 kg: 100mg |
| Metadate CD® (methylphenidate HCL extended-release capsule) | 20 mg qam | 60 mg | >50 kg: 100mg |
| Methylin ER® (methylphenidate HCL extended-release tablet) | 10 mg qam | 60 mg | >50 kg: 100mg |
| Ritalin LA® (methylphenidate HCL extended-release tablet) | 20 mg qam | 60 mg | >50 kg: 100mg |
| Extended-Release | | | |
| Aptensio XR® (methylphenidate HCL extended-release capsule) | Begin with 10 mg qam then titrate by 10 mg at weekly intervals | 60mg | >50 kg: 100mg |
| Concerta® (methylphenidate extended-release tablet) | 18 mg qam | 72 mg | >50 kg: 108mg |
| Cotempla XR-ODT® (methylphenidate extended-release orally disintegrating tablet) | 17.3 mg qam | 51.8 mg | 51.8 mg |
| Daytrana® patch (methylphenidate transdermal system) | Begin with 10 mg patch daily, then titrate up by patch strength 5 mg qam | 30 mg | 50 mg |
| Focalin XR® (dexmethylphenidate HCL extended-release capsule) | 5 mg qam | 30 mg | 50 mg |
| Quillivant XR® (methylphenidate HCL extended-release oral suspension) | Begin with 20 mg qam, then titrate up by 10 mg to 20 mg at weekly intervals | 60 mg | >50 kg: 100mg |
| QuilliChew ER® (methylphenidate HCL extended-release chewable tablet) | Begin with 20 mg qam then titrate in increments of 10 mg, 15 mg or 20 mg at weekly intervals | 60 mg | >50 kg: 100mg |

Medications for the Treatment of Hyperactive, Impulsive & Inattentive Symptoms in the Context of ASD & ID:

Dosing Guide 6-17yo

| FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: Amphetamine Preparations | | | |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------|-------------------------|
| Brand Name/Generic Class | Typical Starting Dose | FDA Max Dose/Day | Off-Label Max Dose/Day* |
| Amphetamine preparations | | | |
| Immediate-Release | | | |
| Adderall® (amphetamine mixed salts tablet) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Dexedrine® (dextroamphetamine immediate-release tablet) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Dextrostat® (dextroamphetamine immediate-release tablet) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Evekeo® (d- and l-amphetamine tablet) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Procentra Oral Solution® (d-amphetamine oral solution) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Zenzedi® (d-amphetamine tablet) | 5 mg daily – bid | 40 mg | >50 kg: 60 mg |
| Extended-Release | | | |
| Dexedrine Spansule® (dextroamphetamine sulfate extended -release capsule) | 5–10 mg daily to twice per day | 40 mg | Not yet known |
| Adderall XR® (amphetamine extended-release mixed salts capsule) | 10 mg daily | 6–12 years: 30 mg 13–17 years: 20 mg | >50 kg: 60 mg |
| Vyvanse® (lisdexamfetamine capsule) | 20–30 mg daily | 70 mg | Not yet known |
| Dyanavel XR® 2.5mg/mL (amphetamine extended-release oral suspension) | 2.5 to 5 mg daily | 20 mg | Not yet known |
| Adzenys XR-ODT® (amphetamine extended-release orally disintegrating tablet) | 6.3 mg qam unless switched from Adderall XR (Refer to conversion schedule) | 6–12 years: 18.8 mg 13–17 years: 12.5 mg | Not yet known |

Medications for the Treatment of Hyperactive, Impulsive & Inattentive Symptoms in the Context of ASD & ID: Dosing Guide 6-17 yo

FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: SNRIs and Alpha-Adrenergic Agonists

| Generic Class/ Brand Name | Typical Starting Dose | Max Dose/Day | Off-Label Max Dose/Day |
|----------------------------------------------------|---------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Selective norepinephrine reuptake inhibitor | | | |
| Strattera® (atomoxetine) | Start at 10 mg/day and increase by 10 mg/week | Lesser of 1.4 mg/kg or 100 mg | No off-label recommendation. |
| Alpha- adrenergic agonists | | | |
| Intuniv® (guanfacine ER) | 1 mg daily then titrate up by 1 mg increments once per week | Lesser of 0.12 mg/ kg or 4 mg daily (6-12 years) 7 mg daily (13-17 years) | Lesser of 0.17 mg/kg or 4 mg daily (6-12 years) 7 mg daily (13-17 years) |
| KAPVAY® (clonidine ER) | 0.1 mg/day at bedtime | 0.4 mg/day in divided dose of 0.2 mg bid | 0.4 mg/day |
| Alpha- adrenergic agonists | | | |
| Catapres® (clonidine*) | 0.05 mg nightly; titrate in 0.05 mg increments two times per day, three times per day, or four times per day. | 27–40.5 kg: 0.2 mg; 40.5–45 kg: 0.3 mg; >45 kg: 0.4 mg | N/A |
| Tenex® (guanfacine*) | 0.5 mg nightly; titrate in 0.5 mg increments two times per day, three times per day, or four times per day. | 27–40.5 kg: 2 mg; 40.5.–45 kg: 3 mg; >45 kg: 4 mg | N/A |



Medications Used to Treat:

Aggression, Irritability, Self-Injury, Aggressive Behavior & Explosive Outbursts in ASD

| Dosing Recommendations 6 Yrs and Older | | | | |
|-----------------------------------------------|----------------------|--------------------------|-------------------------------------------------|-----------------------------|
| Medication | Starting Dose | Titration | Maximum Dose | Discontinuation |
| Risperidone (Risperdal®) | 0.25mg at bedtime | 0.25 mg/ week | Child (6-12): 2 mg Adolescent (13-17) 4 mg | 0.25 mg – 0.5 mg/ 3 days |
| Aripiprazole (Abilify®) | 2mg/day | 2 – 2.5 mg/ 1-2 weeks | Child (6-12): 15 mg Adolescent (13-17) 15 mg | 0.25 mg – 0.5 mg/ 3 days |

Medications for Pediatric Sleep Disturbances in the Context of ASD

| Medication | Starting Dose | Titration | Max Daily Dose | Discontinuation |
|------------|-------------------------|-------------------------------------------------|----------------|---------------------------|
| Melatonin | 1-3 mg q hs | If necessary, based on response and body weight | 10 mg | As clinically appropriate |
| Clonidine* | 0.05 mg q hs/ 1 week | 0.05 mg/ week | 0.3 mg | 0.05 mg/3 days |

Note: Continue titration until symptoms are adequately controlled, treatment-limiting side effects emerge or max daily dose is reached. Melatonin is considered a dietary supplement.

*NOT FDA-Approved for treatment of insomnia in children and adolescents.