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

Daniel Castellanos, MD

Founding Associate Dean of GME, DIO & Professor of Psychiatry

Creighton University School of Medicine - Phoenix

Creighton UNIVERSITY School of Medicine

Creighton UNIVERSITY School of Medicine

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 2RCTs or more

B = Small RCT or more than 1 open label study

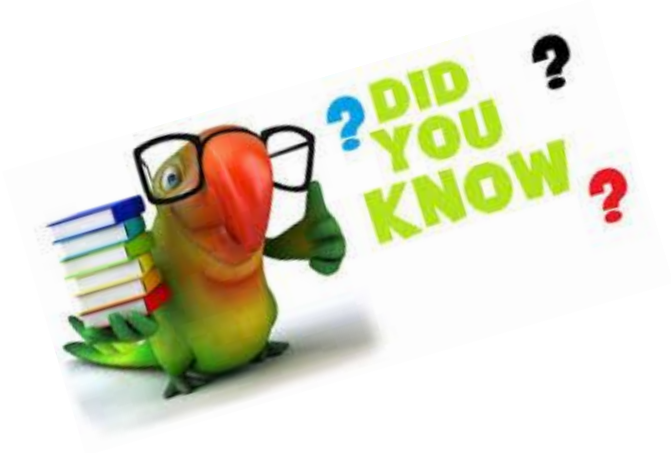
C = Open label or case series; extrapolation from adult studies

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

Creighton
UNIVERSITY
School of Medicine



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

level 1

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

level 2

Hyperactive, Impulsive & Inattentive Symptoms in the Context of ASD

METHYLPHENIDATE* OR GUANFACINE* MONOTHERAPY

- 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

level 3

Hyperactive, Impulsive & Inattentive Symptoms in the Context of ASD

REASSESS & CONSULT SPECIALIST

- 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

- 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

Creighton UNIVERSITY School of Medicine

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

Creighton UNIVERSITY
School of Medicine

level 1

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

CLONIDINE* OR GUANFACINE* MONOTHERAPY

- For <u>mild – moderate</u> 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

level 2

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

RISPERIDONE OR ARIPIPRAZOLE MONOTHERAPY

- For <u>severe</u> 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

level 3

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

REASSESS & CONSULT SPECIALIST

- 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

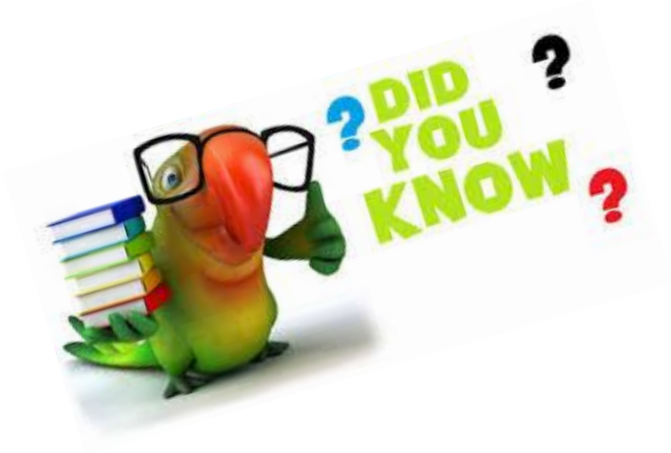
Reassess and consult specialist

Consider use of alternative antipsychotics* based on side-effect profiles

Creighton UNIVERSITY School of Medicine

Medication Treatment of **Sleep Disturbances** in the Context of ASD

Creighton
UNIVERSITY
School of Medicine



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*

Creighton UNIVERSITY School of Medicine

Other Select Medications for Insomnia

Name	Level of Evidence	Comments	Dosing Guidance
Atomoxetine*	C	Small literature that exists seems to demonstrate not 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: • 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: • Begin 12.5 to 25 mg qHS • Maximum daily dose of 50 mg
Eszopiclone*	C	Small literature that exists seems to demonstrate not 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 not 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

level 1

Sleep Disturbances in the Context of ASD

MELATONIN MONOTHERAPY

- 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 independ testing to allow for safer use.

Creighton UNIVERSITY School of Medicine

level 2

Sleep Disturbances in the Context of ASD

CLONIDINE* MONOTHERAPY

- 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

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

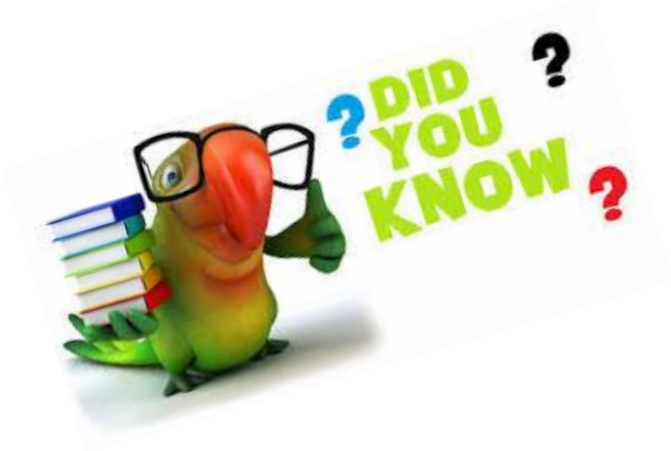
Sleep Disturbances in the Context of ASD
The Bottom Line

1. Monotherapy with melatonin
2. Monotherapy with clonidine*
3. ?

Creighton UNIVERSITY School of Medicine

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

Creighton UNIVERSITY
School of Medicine



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.

Creighton UNIVERSITY School of Medicine

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

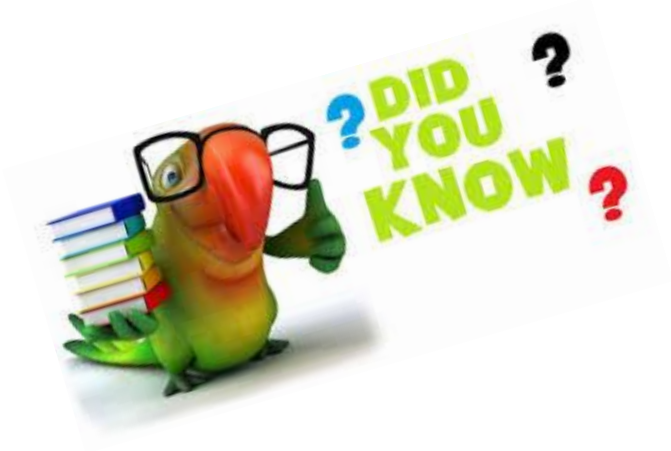
1. ??
2.
3.

Medication Optimization ("Deprescribing")

Creighton UNIVERSITY School of Medicine

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

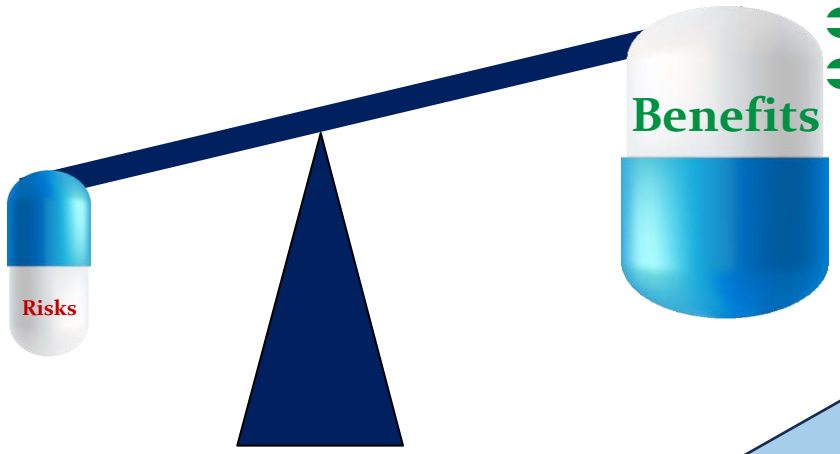
- Clinical experience suggests that reducing or stopping psychotropic medication is not always straightforward.
- Some are reluctant to consider changes to med regimens that might have been unchanged for years and where it has become difficult to dtermine the positive or negative impact of treatment.
- 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:

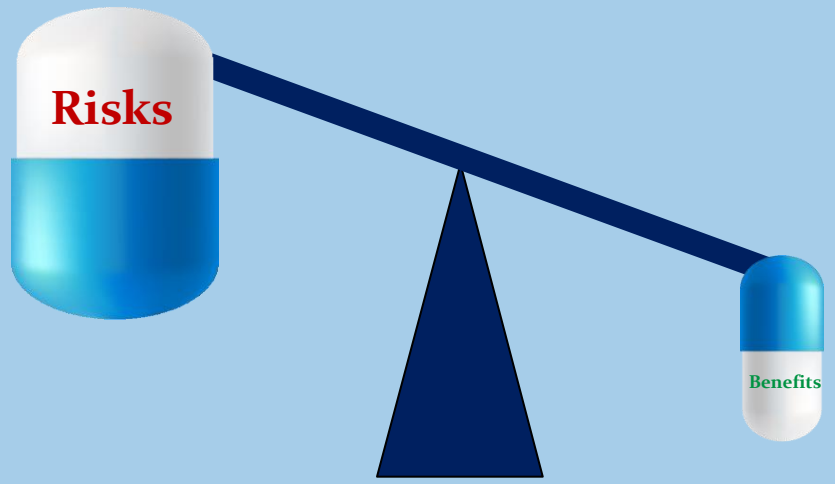
- Subjective interpretation of behavioral symptoms by caregivers and family (misattributions)
- Some people with ASD & ID might benefit from antipsychotic treatment
- Misinterpretation of withdrawal symptoms as recurrence of the original target/challenging behavior

Weigh your risks vs benefits



- Evidence for indication
- Evidence for effectiveness

- Age related effects
- Diagnosis related factors
- Side effects
- Comorbid conditions
- More medications
- Drug interactions



- Age related effects
- Diagnosis related factors
- Side effects
- Comorbid conditions
- More medications
- Drug interactions

- Evidence for indication
- Evidence for effectiveness

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.

Creighton UNIVERSITY School of Medicine

Questions/Comments?

Daniel Castellanos, MD
Founding Associate Dean of Graduate Medical Education
Professor of Psychiatry
Creighton University School of Medicine-Phoenix
Designated Institutional Official

Creighton UNIVERSITY School of Medicine

Select References

- 2019 Autism Spectrum Disorder & Intellectual Developmental Disorder: Florida Best Practice Psychotherapeutic Medication Recommendations for Target Symptoms in Children & Adolescents- Full Set of Guidelines. http://floridabhcenter.org/child-2019-asd-id-pop-guideline.html
- Hyman SL, Levy SE, Myers SM, COUNCIL ON CHILDREN WITH DISABILITIES, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. Pediatrics 2020; 145.
- Sturman N, Deckx L, van Driel ML. Methylphenidate for children and adolescents with autism spectrum disorder. Cochrane Database Syst Rev 2017; 11:CD011144.
- Fung LK, Mahajan R, Nozzolillo A, et al. Pharmacologic Treatment of Severe Irritability and Problem Behaviors in Autism: A Systematic Review and Meta-analysis. Pediatrics 2016; 137 Suppl 2:S124.
- Williamson E, Sathe NA, Andrews JC. Medical therapies for children with autism spectrum disorder--an update. Comparative Effectiveness Review No. 189. Agency for Healthcare Research and Quality, Rockville, MD May 2017. Available at: https://effectivehealthcare.ahrq.gov/topics/asd-medical/research-2017 (Accessed on April 05, 2018).
- Howes OD, Rogdaki M, Findon JL, et al. Autism spectrum disorder: Consensus guidelines on assessment, treatment and research from the British Association for Psychopharmacology. J Psychopharmacol 2018; 32:3.
- Williams Buckley A, Hirtz D, Oskoui M, et al. Practice guideline: Treatment for insomnia and disrupted sleep behavior in children and adolescents with autism spectrum disorder: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2020; 94:392.

Creighton UNIVERSITY School of Medicine

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

Creighton UNIVERSITY School of Medicine

* 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® (methlypheidate 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.