Treatment of Hyperactive, Impulsive, and Inattentive Symptoms in the Context of ASD and ID

Youth with ASD and ID experience symptoms of hyperactivity, impulsivity, and inattention (ADHD) at higher rates than their neurotypical peers. Children and adolescents can benefit from the same evidence-based treatments used to treat ADHD uncomplicated by ASD.

Level 0 - Comprehensive Assessment:

See *Principles of Practice*. In addition, give special consideration to:

- Developmental history and cognitive assessment (neuropsychological or educational)
- ADHD symptom history
- Parent and teacher rating scales (e.g., Vanderbilt Assessment Scales, Conners Parent and Teacher Rating Scales)*
  Note: Conners Parent and Teacher Rating Scales are not in the public domain.
- Teacher behavior reports
- Involvement in community resources
- Physical examination (e.g., if history of staring spells or focal neurological signs: EEG, MRI).
- Safety concerns related to significant impulsivity (e.g., bolting away, darting across roads, excessive climbing).

Level 1 - Methylphenidate or guanfacine monotherapy.

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 and ID compared to normally developing youth with ADHD. Methylphenidate or guanfacine yield benefit in about 50% of children in the ASD and ID population for hyperactivity. Close monitoring is recommended, and lower dosing than expected may be required for tolerability.
- **Methylphenidate is favored over guanfacine for treatment of inattention without hyperactivity.**
  - Obtain resting blood pressure and heart rate at baseline and follow-up visits.
  - ECG is recommended if the child has evidence of cardiac disease or known family history of sudden death. Consult a pediatric cardiologist before initiating treatment.
  - Continue to increase dose until ADHD symptoms are adequately controlled, maximun recommended dosing is reached, or treatment-limiting side effects emerge.

Refer to Tables 3-7 on pages 23-29 for dosing recommendations.

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Level 2 - Combination therapy with methylphenidate and guanfacine OR atomoxetine:

- **2a.** If partial response to monotherapy (i.e., methylphenidate or guanfacine alone), consider combination therapy with methylphenidate and guanfacine.
- **2b.** Atomoxetine
  - Obtain resting blood pressure and heart rate at baseline and follow-up visits.
  - Consider ECG if there is evidence of cardiac disease or known family history of sudden death. Consult a pediatric cardiologist.
  - Consider liver function tests if on other medications or history of hepatic dysfunction.

Refer to Tables 3-7 on pages 23-29 for dosing recommendations.

Level 3 - Reassess and consult specialist.

- Refer to child and adolescent psychiatrist for consultation, or to another pediatric specialist (pediatric neurologist or developmental pediatrician) if indicated.
- Although limited evidence exists in the ASD/ID population, may consider use of an amphetamine preparation.
- Reassess psychosocial interventions that may enhance the efficacy of treatment. Psychosocial interventions such as parent management training may enhance the efficacy and acceptability of treatment.

Refer to Tables 3-7 on pages 23-29 for dosing recommendations.

Not recommended:

- Combination of two alpha-2 agonists (i.e., clonidine and guanfacine)

Treatment of Hyperactive, Impulsive, and Inattentive Symptoms in the Context of ASD and ID *(continued)*

Table 3.

ADHD Medication Treatment for Children under Age 6	
Drug Name	**Starting Dose Recommendation**
Methylphenidate and Amphetamine preparations	
Immediate-Release	
Methylphenidate[1]: Immediate-release: Ritalin®, Methylin®, Methylin® Chewable Tablets, Methylin® Oral Solution	1.25 mg tid – titrate as needed to doses not exceeding 1 mg/kg/day. *Recommendations extrapolated from the Preschool ADHD Treatment Study (PATS).*
Amphetamine[2]: Immediate-release: Mixed amphetamine salts (Adderall®), D-amphetamine (Dexedrine®, Dextrostat®, ProCentra® Oral Solution, Zenzedi®). D- & L-amphetamine (Evekeo®)	2.5 mg/day – titrate as needed to doses not exceeding 0.5 mg/kg/day. *Amphetamine target dose is generally one-half to two-thirds of methylphenidate dose.*
Selective norepinephrine inhibitor	
Atomoxetine (Strattera®)[3]	10 mg/day – titrate as needed to doses not to exceed 1.4 mg/kg/day. *Recommendations extrapolated from the Kratochvil et al. 2011 study.*
Alpha-2 Agonists4	
Alpha-2 Agonists[4]: **Clonidine** (Catapres®, KAPVAY®) **Guanfacine** (Tenex®, Intuniv®)	Starting dose not to exceed: 0.05 mg/day *(immediate-release clonidine, Catapres®)* 0.1 mg/day (*extended-release clonidine, KAPVAY®)* 0.5 mg/day *(immediate-release guanfacine, Tenex®)* 1 mg/day (*extended-release guanfacine, Intuniv ®)* **Monitor carefully for excessive sedation, increased irritability.** *Recommendations based on expert opinion.*

Notes:

[1] No FDA indication for children younger than 6 years old; based on Preschool ADHD Treatment Study results (Greenhill et al., 2006).

[2] FDA indication for ADHD treatment of children 3-5 years old, but no clinical trial study results available.

[3] No FDA indication for children younger than 6 years old; based on Kratochvil et al., 2011.

[4] No FDA indication for ADHD except guanfacine extended-release (Intuniv®) and clonidine extended-release (KAPAVY®) in children 6 years and older; no clinical trial study results available for alpha-2 agonist use for ADHD in children below age 6 years old. There is no new data on extended-release stimulants in preschoolers, but the 2007 American Academy of Child and Adolescent Psychiatry guideline algorithm included extended-release formulations to address compliance concerns (Pliszka et al., 2007).

Continue titration until symptoms are adequately controlled, treatment-limiting side effects emerge, or maximum recommended daily dose is reached.

Table 4.

FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: Methylphenidate Preparations				
Generic Class/ Brand Name	**Typical Starting Dose**	**FDA Max Dose/Day**	**Off-Label Max Dose/Day**	**Comments**
Methylphenidate preparations				
Immediate-Release				Immediate-release stimulants are often used as initial treatment in children (<16 kg), but have disadvantage of bid – tid dosing to control symptoms throughout the day.
Focalin® (dexmethylphenidate hcl tablet)	2.5 mg bid	20 mg	50 mg	
Methylin® (methylphenidate hcl tablet)	5 mg bid	60 mg	>50 kg: 100 mg	
Methylin® Solution (methylphenidate hcl oral solution)	5 mg bid	60 mg	>50 kg: 100 mg	
Methylin® Chewable (methylphenidate hcl chewable tablet)	5 mg bid	60 mg	>50 kg: 100 mg	
Ritalin® (methylphenidate hcl tablet)	5 mg bid	60 mg	>50 kg: 100 mg	
Intermediate-Release				Longer acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep.
Metadate ER® (methylphenidate hcl extended-release tablets)	10 mg qam	60 mg	>50 kg: 100 mg	
Metadate CD® (methlypheidate hcl extended-release capsule)	20 mg qam	60 mg	>50 kg: 100 mg	
Methylin ER® (methylphenidate hcl extended-release tablet)	10 mg qam	60 mg	>50 kg: 100 mg	
Ritalin LA® (methylphenidate hcl extended-release tablet)	20 mg qam	60 mg	>50 kg: 100 mg	

Table 4 *(continued)*.

FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: Methylphenidate Preparations				
Generic Class/ Brand Name	**Typical Starting Dose**	**FDA Max Dose/Day**	**Off-Label Max Dose/Day**	**Comments**
Methylphenidate preparations *(continued)*				
Extended-Release				Aptensio XR®,Metadate CD®, Ritalin LA®, and Focalin XR® capsules may be opened and sprinkled on soft food for immediate consumption. Beads should not be crushed or chewed. Concerta® should not be crushed, chewed, or broken. Swallow whole with liquids. Non-absorbable tablet shell does not dissolve and may be seen in stool. This is normal. Qillivant XR® is an extended-release once-daily suspension. QuilliChew ER® can be broken in half.
Aptensio XR® (methylphenidate hcl extended-release capsule)	Begin with 10 mg qam then titrate by 10 mg at weekly intervals	60 mg	>50 kg: 100 mg	
Concerta® (methylphenidate extended-release tablet)	18 mg qam	72 mg	>50 kg: 108 mg	
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	Not yet known	
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: 100 mg	
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: 100 mg	

Notes:
Ritalin LA 60 mg (specific brand and dose) and Ritalin SR were discontinued for reasons other than safety and effectiveness. Ritalin LA brand drug is still available in 10 mg, 20 mg, 30 mg, and 40 mg capsules (i.e., doses other than 60 mg). The generic methylphenidate extended-release capsule is available in all doses, including 60 mg.

Continue titration until symptoms are adequately controlled, treatment-limiting side effects emerge, or maximum recommended daily dose is reached.

Table 5.

FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: Amphetamine Preparations				
Generic Class/ Brand Name	**Typical Starting Dose**	**FDA Max Dose/Day**	**Off-Label Max Dose/Day**	**Comments**
Amphetamine preparations				
Immediate-Release				Immediate-release stimulants are often used as initial treatment in children (<16 kg) but have disadvantage of bid – tid dosing to control symptoms throughout the day. Note that all amphethmine immediate-release products have the same dosing recommendations.
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	

Table 5 *(continued)*.

FDA Approved ADHD Medications in Children and Adolescents Ages 6 to 17 Years Old: Amphetamine Preparations				
Generic Class/ Brand Name	**Typical Starting Dose**	**FDA Max Dose/Day**	**Off-Label Max Dose/Day**	**Comments**
Amphetamine preparations *(continued)*				
Extended-Release				Extended-release stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep. Adderall XR® capsule may be opened and sprinkled on soft foods. Vyvanse® capsule can be opened and mixed with yogurt, water, or orange juice. For Dyanavel XR® do not substitute for other amphetamine products on mg-per-mg basis. For Adzenys®, do not substitute for other amphetamine products on mg-per-mg basis. For children and adolescents on Adderall XR®, specific starting doses corresponding to Adderall XR® doses are recommended, ranging from 3.1 mg of Adzenys® (for those on 5mg of Adderall XR®) to 18.8 mg of Adzenys® (for those on 30mg Adderall XR®).
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	

***Note:* Continue titration until symptoms are adequately controlled, treatment-limiting side effects emerge, or maximum recommended daily dose is reached.**

Table 6.

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**	**FDA Max Dose/Day**	**Off-Label Max Dose/Day**	**Comments**
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.	Not a Schedule II medication. Consider if active substance abuse or severe side effects of stimulants (mood lability, tics). Give qam or divided doses bid (for effects on late evening behavior). Do not open capsule; must be swallowed whole. Monitor closely for suicidal thinking and behavior, clinical worsening, or unusual changes in behavior.
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)	Not a Schedule II medication. Sedation, somnolence, and fatigue are common and tend to decline over time. Consider baseline electrocardiogram (EKG) before starting. Tablets should not be crushed, chewed, or broken before swallowing because this will increase the rate of release.
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	Do not administer with high fat meals due to increased exposure. May not see effects for 4-6 weeks. Review personal and family cardiovascular history. Do not abruptly discontinue. Taper the daily dose of guanfacine ER by no more than 1 mg, and that of clonidine ER by no more than 0.1 mg every 3 to 7 days to avoid rebound hypertension.

Table 7.

ADHD Medications NOT FDA APPROVED in Children and Adolescents Ages 6 to 17 Years Old			
Generic Class/ Brand Name	**Typical Starting Dose**	**Max Dose/Day**	**Comments**
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	The following applies to both alpha-2 adrenergic agonists: - May be used alone or as adjuvant to another medication class for ADHD. - Do not combine different alpha-2-adrenergic agents with each other - Effective for inattention, impulsivity and hyperactivity; modulating mood level; tics worsening from stimulants; sleep disturbances. Clonidine dosing is 1/10 guanfacine dosing. Clonidine and clonidine ER are more sedating than guanfacine preparations. Consider starting at bedtime to generate tolerance to sedating effects.
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	May not see effects for 4-6 weeks. Review personal and family cardiovascular history. Consider pre-treatment EKG, if warranted by history. Taper the daily dose of guanfacine by no more than 1 mg every 3 to 7 days to avoid rebound hypertension.

***Note:** Extended-release formulations of clonidine (Kapvay®) and guanfacine (Intuniv®) are FDA-approved ADHD medications in children and adolescents 6-17 years old, but short-acting formulations of clonidine (Catapres®) and guanfacine (Tenex®) are not FDA-approved for ADHD.*

Continue titration until symptoms are adequately controlled, treatment-limiting side effects emerge, or maximum recommended daily dose is reached.