U.S. Department of Veterans Affairs

A Quick Reference Guide (2017)

Prescription Stimulants

Re-evaluating use of Prescription Stimulants for Adult Attention-Deficit/Hyperactivity Disorder (ADHD)

Attention Healthcare Provider:

These recommendations are intended for re-evaluating prescription stimulant use in patients with attention-deficit / hyperactivity disorder.
Individual patient-specific characteristics should be considered when determining appropriate therapy.

Table of Contents

Key Messages for Re-evaluating Use of Prescription Stimulants

1. Before diagnosing ADHD, assess for and manage other co-morbidities that may be mimicking or causing ADHD-like symptoms
2. Rule out medication and social factors as causes of ADHD-like symptoms
3. Ensure the patient meets DSM-5 criteria for ADHD prior to offering treatment
4. Assess Veterans who are currently on stimulants to assure that the benefits of the medication outweigh the risks

Common contributors to and causes of ADHD-like symptoms [1-4]

Cognitive disorders	• Mild cognitive impairment • Traumatic brain injury • Dementia
Toxic/metabolic/infectious	• Nutritional deficiency (e.g. thiamine) • Heavy metal toxicity • Infection (e.g. urinary tract infection)
Psychiatric conditions	• Depression • Anxiety • Post-traumatic stress disorder (PTSD) • Substance use disorder (SUD) • Bipolar disorder
Other	• Parkinson's disease • Developmental disorder • Sleep apnea • Thyroid disease • Hepatic disease
Medications	• Steroids • Caffeine and nutritional supplements • Nicotine • Central nervous system (CNS) sedating medications (e.g. opioids, benzodiazepines, antipsychotics, anticholinergics) • Anticonvulsants

DSM-5 criteria for ADHD*[5]

Persistent pattern of (A) inattention and/or (B) hyperactivity-impulsivity that interferes with functioning or development, as characterized by A or B; several symptoms prior to age 12 years; several symptoms in ≥ 2 settings; symptoms do not occur only during the course of another disorder and are not better explained by another mental disorder

A: Inattention 5 or more of the following persisting for ≥ 6 months that have a negative impact directly on social and academic/occupational activities	**B: Hyperactivity and Impulsivity** 5 or more of the following persisting for ≥ 6 months that have a negative impact directly on social and academic/occupational activities
1. Fails to give close attention to details or makes careless mistakes	1. Leaves seat in situations when remaining seated is expected
2. Difficulty sustaining attention in tasks	2. Fidgets with or taps hands/feet or squirms in seat
3. Does not seem to listen when spoken to directly	3. Feels restless
4. Does not follow through on instructions and fails to finish tasks	4. Unable to engage in leisure activities quietly
5. Difficulty organizing tasks and activities	5. Often "on the go" as if "driven by a motor"
6. Avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort	6. Blurts out an answer before a question has been completed
7. Often loses things necessary for tasks or activities	7. Often talks excessively
8. Easily distracted by extraneous stimuli	8. Has difficulty waiting his or her turn
9. Forgetful in daily activities	9. Often interrupts or intrudes on others

*For full DSM-5 criteria please see DSM-5; criteria listed here apply to those 17 years old and older

FDA-approved Stimulant Medications for ADHD and Recommended Dosing*** [6-8]

Generic Name	Brand Name	Starting Dose	Max Dose mg/day
Methylphenidate osmotic release oral system (OROS)	Concerta®	18 mg or 36 mg	72 mg
Dexmethylphenidate XR	Focalin XR®	10 mg	40 mg
Methylphenidate	Metadate CD®	20 mg	60 mg
Methylphenidate CD	Medate ER®	20 mg	60 mg
Methylphenidate IR	Ritalin®	5 mg BID	60 mg
Methylphenidate ER	Ritalin SR®	5 mg BID	60 mg
Methylphenidate LA	Ritalin LA®	20 mg	60 mg
Mixed amphetamine salts	Adderall IR®	5 mg once or twice daily	40 mg
Mixed amphetamine salts-XR	Adderall XR®	20mg	20 mg**
Dextroamphetamine	Dexadrine®	5 mg once or twice daily	40 mg
Lisdexamfetamine	Vynase®	30mg	70 mg

*Once daily dosing unless otherwise stated; Mixed Amphetamine Salts = amphetamine/dextroamphetamine;
**Higher doses have been used but have not been shown to be more effective; IR = immediate release; ER = extended release; LA = long acting; XR = extended release;
***Please see VA National Formulary for current list of formulary medications (https://www.pbm.va.gov/PBM/NationalFormulary.asp)

Adverse Effects of Stimulant Medications in the Adult Population*[6,7,9]

		Mixed amphetamine salts	Methylphenidate	Lisdexamfetamine
Cardiovascular effects	Increased blood pressure	X**	X	+
	Tachycardia	++	++	++
	Palpitations	++	+	-
Neurologic Effects	Headache	++++	++++	-
	Insomnia	++++	+++	++++
	Anxiety	++	++	++
	Dizziness	++	X	X
	Tremor/Twitching	++	+	+
Psychiatric Effects	Aggressive behavior	-	+	-
	Angry/Irritable	++	+++	+
	Nervousness	+++	+	-
	Restlessness	-	+	+
	Emotional lability	++	+	-

*Frequencies reported as available; **= Avg 2-4 mmHg systolic blood pressure; Mixed amphetamine salts frequencies reported for XR formulation only; += 1-3%; ++= 4-9%; +++= 10-15%; ++++= 16% or more; X=exact % unavailable

Adverse Effects of Stimulant Medications in the Adult Population* [6,7,9] continued

		Mixed amphetamine salts	Methylphenidate	Lisdexamfetamine
Dermatologic Effects	Diaphoresis	++	++	-
Endocrine/Metabolic Effects	Weight loss	+++	++	-
Gastrointestinal Effects	Abdominal pain	+++	X	+
	Appetite loss	++++	++++	++++
	Nausea	++	+++	++
	Vomiting	++	+++	+
	Indigestion/Dyspepsia	++	+	-
	Xerostomia	++++	+++	++++
Respiratory	Nasal Congestion	-	X	-
	Nasopharyngitis	-	X	-

*Frequencies reported as available
**= Avg 2-4 mmHg systolic blood pressure
Mixed amphetamine salts frequencies reported for XR formulation only;
+= 1-3%; ++= 4-9%; +++= 10-15%; ++++= 16% or more
X=exact % unavailable

Non-stimulant medications for Adult ADHD*[8-12]

	FDA approved	Place in therapy	Clinical pearls
Atomoxetine	Yes	Consider in patients with comorbid substance use disorder and/or anxiety and ADHD Consider in patients who can't tolerate or don't respond to stimulants	Delayed therapeutic benefits (weeks-months) Low abuse potential CYP450 2D6 interactions possible
Buproprion	No	Generally considered 3rd line after stimulants and atomoxetine	Delayed therapeutic benefits (1-2 months) May cause central nervous system stimulation, dose-related increased risk of seizures
Clonidine ER Guanfacine ER (alpha 2 agonists)	No	Can be considered in patients who have failed other ADHD treatment options or who require treatment for comorbid conditions Paucity of evidence to support use in adults with ADHD	Delayed therapeutic benefits (1-2 weeks) Clonidine - adverse effects (sedation, bradycardia, hypotension) limit use Guanfacine - less CNS depression and hypotensive activity than clonidine Avoid abrupt discontinuation

*Please see VA National Formulary for current list of formulary medications (https://www.pbm.va.gov/PBM/NationalFormulary.asp)

Non-stimulant medication dosing for Adult ADHD*[8-12]

	Initial dose	Max dose	Dose adjustment
Atomoxetine	40 mg/day, increased after minimum of 3 days to ~80 mg/day	100 mg/day	For patients receiving strong CYP2D6 inhibitors (e.g. paroxetine, fluoxetine) or patients known to be CYP2D6 poor metabolizers: • Initial: 40 mg/day; if tolerating therapy but inadequate response may increase after ≥ 4 weeks to 80 mg/day Hepatic impairment: • Moderate impairment: (Child-Pugh class B): All doses should be reduced to 50% of normal • Severe impairment: (Child-Pugh class C): All doses should be reduced to 25% of normal
Buproprion	Sustained Release: 100 mg once daily in the morning; increase weekly to achieve desired treatment goals Extended release: 150 mg once daily in the morning for 1 week; increase to 300 mg once daily for 3 weeks	Sustained Release: 200 mg twice daily Extended Release: 450 mg once daily	Renal Impairment: Use with caution; labeling suggests a reduction in dose and/or frequency be considered but no specific dosing recommendations provided Hepatic Impairment: • Mild impairment (Child-Pugh class A): Use with caution; reduction in dose and/or frequency but no specific dosing recommendations • Moderate to severe impairment, including severe hepatic cirrhosis (Child-Pugh class B-C): Use with extreme caution; lower max doses required

*Please see VA National Formulary for current list of formulary medications (https://www.pbm.va.gov/PBM/NationalFormulary.asp)

References

1. Goodman, D.W., et al., Clinical Presentation, Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder (ADHD) in Older Adults: A Review of the Evidence and its Implications for Clinical Care. Drugs Aging, 2016. 33(1): p. 27-36.
2. Paris, J., V. Bhat, and B. Thombs, Is Adult Attention-Deficit Hyperactivity Disorder Being Overdiagnosed? Can J Psychiatry, 2015. 60(7): p. 324-8.
3. Youssef, N.A., et al., Is obstructive sleep apnea associated with ADHD? Ann Clin Psychiatry, 2011. 23(3): p. 213-24.
4. Asherson, P., et al., Adult attention-deficit hyperactivity disorder: key conceptual issues. Lancet Psychiatry, 2016. 3(6): p. 568-78.
5. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
6. Drug Information Handbook for Psychiatry. 7th ed. 2009: Lexi-Comp.
7. Association, A.P., The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia. 2016, American Psychiatric Associatio: American Psychiatric Association 1000 Wilson Boulevard Arlington, VA 22209-3901.

8. Parikh AR, B.S., Adult ADHD: Pharmacologic treatment in the DSM-5 era. Current Psychiatry, 2016. 15(10): p. 18-25.

9. Up-to-Date. Waltham, MA. (Accessed October 2016).

10. Asherson, P., et al., Efficacy of atomoxetine in adults with attention deficit hyperactivity disorder: an integrated analysis of the complete database of multicenter placebo-controlled trials. J Psychopharmacol, 2014. 28(9): p. 837-46.

11. Childress, A.C., A critical appraisal of atomoxetine in the management of ADHD. Ther Clin Risk Manag, 2016. 12: p. 27-39.

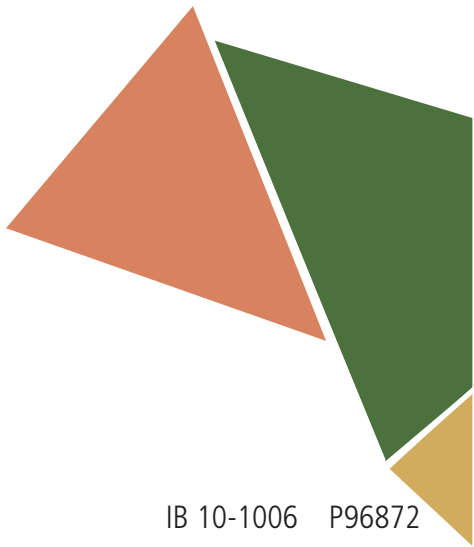
12. Briars, L. and T. Todd, A Review of Pharmacological Management of Attention-Deficit/Hyperactivity Disorder. J Pediatr Pharmacol Ther, 2016. 21(3): p. 192-206.

U.S. Department of Veterans Affairs

This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing SharePoint.

VA PBM Academic Detailing Service Email Group:
PharmacyAcademicDetailingProgram@va.gov

VA PBM Academic Detailing Service SharePoint Site:
https://vaww.portal2.va.gov/sites/ad



July 2017

IB 10-1006 P96872