PSYCHOSTIMULANT & ADHD-Related AGENTS

A. FDA approved indications (Documentation Required) See Table 1

1. Attention Deficit/Hyperactivity Disorder (ADHD)
2. Narcolepsy (Except Dexmethylphenidate preparations**)**
3. Binge Eating Disorder (Lisdexamfetamine)

B. Non-FDA approved, commonly used indications (Documentation Required)

1. Fatigue due to medical conditions (Rule out sleep apnea first)
2. Obesity (mixed salt amphetamines)
3. Refractory depression (methylphenidate)
4. Apathy due to medical conditions (Brain injury, Trauma, HIV)

C. Minimal documentation (Documentation Required)

1. All standard outpatient & inpatient requirements
2. In children/adolescents: Family history, developmental history, school behavior, collateral information obtained from sources such as teachers, parents, care takers, special school placement if any and other providers, and/or Psychometric assessment scores.
3. In Adults:
   A. History of ADHD diagnosis or symptoms
   B. Any past treatment in childhood/adolescence including treatment response.
   C. In patients who report symptoms of ADHD (including during childhood), verification is required by obtaining collateral information or psychometric testing or rating scales prior to initiating treatment.
   D. Detailed Substance Use history
   E. In patients who report symptoms of ADHD, always consider addressing the co-morbid condition which may mimic the symptoms of ADHD.
   F. All adults with ADHD should receive an adequate trial with a non-controlled FDA approved medication as first line treatment or document failure to previous "adequate trial" with a non-controlled medication.
   G. In patients with substance use, stimulant medications may be provided in accordance to Section P of medication practice guideline, Guidelines for Prescribing Controlled Psychotropic Medications to Patients with Substance Use.
   H. Impairment in functionality due to ADHD in at least 2 settings
   I. Document rationale if early fills needed
   K. If family member(s) has h/o substance misuse, document steps taken to avoid misuse
   J. CURES:

   Review of cures report is required prior to initiation of any controlled psychotropic medication, and again at intervals no longer than 4 months throughout treatment or whenever misuse of the medications suspected, including when it's used more frequently or at higher dose than prescribed without provider consultation.

DOCUMENT YOUR OBSERVATION IN THE PROGRESS NOTE.

D. Maximum dosage - See Medication Summary for MDD, or Table 1

E. Duration

1. For Outpatient: Document rationale when making any medication change.
2. For Inpatient: Document rationale when making more than 3 changes in any 7-day period.

F. Polypharmacy* (Documentation Required)

1. Adequate medication doses should be used over a sufficient period of time to obtain desired results before introducing polypharmacy.
2. If using >1 same class psychostimulant agent is necessary, provide clear supportive rationale for adding the second agent. Refer to section E2 for duration of use.

G. Standard laboratory and examination requirements (Documentation Required)

1. For inpatient: Basic laboratory studies on admission
2. For outpatient:
    a. Children and Adolescents
        - Height, weight, blood pressure and pulse at baseline, every 6 months, and after dose adjustment
        - Stunting of growth in long-term administration in patients between 7-10 years of age: 2cms less height, 2.7kg less weight due to 3 years of continuous stimulant use without any breaks, no growth rebound is noted). Recommend using medication breaks over the weekends to avoid stunting growth).
    b. Adult
        - Weight, blood pressure, and pulse at baseline and every 6 months, and after dose adjustment
    c. For all age groups
        i. Obtain cardiovascular history of patient and family prior to initiating a stimulant trial.
        ii. Patients with preexisting heart disease or symptoms suggesting significant cardiovascular disease should be referred for consultation with a pediatrician, internist and/or cardiologist for clearance prior to a stimulant trial. If stimulants are initiated, then the patient should also be followed by the pediatrician, internist and/or cardiologist during the course of treatment.
        iii. Patient h/o seizures and TBI
        iv. Urine toxicology screen as per the Controlled Medication Guidelines and as clinically indicated.

H. Black Box Warnings – See Table 2

I. Warnings & Precautions

1. Hypersensitivity to drug/class/component
2. MAO-Inhibitors - during or within 14 days following the administration of MOAIs (atomoxetine, psychostimulants)
3. Pregnancy
4. Severe anorexia
5. Hyperactivity due to depression and anxiety or any other psychiatric disorders
6. CAD, Advanced arteriosclerosis
7. Age less than 6 years (less than 3 years with dextroamphetamine)
8. Presence of motor tics or Tourette's syndrome (Stimulants may be considered after obtaining proper consult as stimulants may or may not worsen Tics)
9. Family history of motor tics or Tourette's syndrome (methylphenidate)
10. Caution if substance abuse present
11. Caution if Hypertension
12. Caution if Renal impairment
13. Caution if Glaucoma (atomoxetine)
14. Caution if Hyperthyroidism (mixed salt amphetamines)
15. Caution if Seizure disorder
16. Criteria specific to adults:
    - Psychostimulants are to be initiated as treatment for an adult by outpatient psychiatrists only.
    - Documentation of ADHD diagnosis as set by DSM
    - Initiation of treatment with amphetamines or methylphenidate in an adult with Attention Deficit Disorder requires prior trials of at least one antidepressant and/or Atomoxetine.
17. Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.
18. Stimulants can cause modest increase in the average blood pressure (about 2-4 mmHg) and average heart rate (about 3-6 bpm) and some individuals may have larger increases. All patients should be monitored for larger changes in heart rate and blood pressure.

19. Methylphenidate may cause leukopenia and/or anemia. Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

J. Drug Interactions (Please see Epocrates or PI or appropriate resources for more details)

1. Drugs with levels (or clinical effects) that can be significantly increased by amphetamines: especially MAO inhibitors, tricyclics, sympathomimetic drugs (including OTC products), phenobarbital, phenytoin, other anticonvulsants, warfarin, meperidine
2. Drugs with effects that can be reduced or blocked by amphetamines: antipsychotics, antihistamines, antihypertensives, adrenergic blockers

K. Adverse Events (Document Assessment of following): (Please refer to PIs or appropriate resources i.e. Epocrates for more details)

Serious Side Effects:

- Dependency, abuse
- Psychosis
- Mania
- Aggressive behavior
- Stevens-Johnson syndrome
- Sudden death
- Cardiovascular events (MI, Stroke, HTN, tachycardia)
- Seizure
- Priapism
- Peripheral vasculopathy
- Rhabdomyolysis
- Precipitation of involuntary motor tics or even full-blown Tourette's syndrome (stimulants may be used in Tourette's syndrome and stimulants may or may not worsen tics).
- W/D symptoms if abrupt DC (prolonged, high dose use)
- Stunting of growth in long-term administration

Common Side Effects:

- Anorexia
- Weight loss
- Xerostomia
- Insomnia
- Headache
- Abdominal pain
- Irritability/restlessness/agitation
- Emotional lability
- Anxiety, depression
- Dizziness
- Nervousness
- Diaphoresis
- Nausea/Vomiting/Constipation
- Motor/phonic tic exacerbation
- Palpitation/tachycardia (esp. w/mixed amphetamine salts), dysrhythmia, increased BP
- Visual disturbance
- Restlessness
- Somnolence
- Libido changes

L. Other agents used Off Label for the Treatment of ADHD

1. Antidepressants
    - Bupropion (Wellbutrin)
    - Imipramine (Tofranil)
    - Nortriptyline (Pamelor)
2. α_2 Adrenergic agonist
    - Clonidine (Catapres)
    - Guanfacine (Tenex)

Attachments

Table 1 FDA approved Indications and Maximum Dose
Table 2 Black Box Warnings

References:

1. Lichtenstein P and et al, Medication for Attention Deficit-Hyperactivity Disorder and Criminality, NEJM 367;21, 2006-2014
2. Psychiatry Online, April 19, 2013, DOI: 10.1176/appi.pn.2013.4a6: ADHD related\Expert Discusses Problems of Comorbid ADHD Substance Use Disorder in Adolescents
3. City and County of San Francisco, Department of Public Health, Community behavioral health services: Pharmacotherapy for Adult Attention Deficit/Hyperactivity Disorder
4. National Institute for Health and Clinical Excellence (NICE clinical guideline 72), Attention deficit hyperactivity disorder: September 2008 last modified: March 2013 (guidance.nice.org.uk/cg72).
5. APA Psychiatric News, Expert Discusses Problems of Comorbid ADHD Substance Use Disorder in Adolescents
6. Epocrates.com
7. Micromedix.com
8. PIs for various drugs

PSYCHOSTIMULANTS & OTHER ADHD RELATED AGENTS

Table 1: FDA-Approved Indications and Maximum Daily Dose (Bolded RXs are Non-Formulary at SCVH&HS)

Generic Name	Brand Name	Maximum Daily Dosage		ADHD	Narcolepsy
		Adult	Adolescent & Children		
Amphetamine Preparations					
Short-Acting					
Amphetamine/ D. Amphetamine	Adderall	40 mg (ADHD) 60mg(Narcolepsy)	40 mg (>3yo, ADHD) 60 mg (≥6 yo, Narcolepsy)	X	X
Dextroamphetamine	Dexedrine, **Dextrostat**	60 mg	40mg >6yo, ADHD 60mg>6yo, Narcolepsy	X	X
Methamphetamine	**Desoxyn**	25 mg	25 mg (≥ 6 yo)	X	
Long-Acting					
Amphetamine/ D. Amphetamine	Adderall XR[1]	60 mg	30 mg (6-12 yo); 40 mg (13-17 yo)	X	
Dextroamphetamine	**Dexedrine spansule**	60 mg	40 mg (≥ 6, ADHD) 60 mg (≥ 6 yo, dose to optimal response, Narcolepsy)	X	X
Lisdexamfetamine	**Vyvanse**	70 mg	70 mg (≥ 6 yo)	X	
Amphetamine Related					
Modafinil	**Provigil**	400 mg	non-FDA approved		X
α2-Adrenergic Agonist					
Guanfacine ER	**Intuniv**	Dosing NA	.12mg/kg up to 4mg	X	
Methylphenidate Preparations					
Short Acting					
Dexmethylphenidate	**Focalin**	20 mg	20 mg (≥ 6 yo)	X	
Methylphenidate	**Methylin**	60 mg	60 mg (> 6 yo)	X	X
Methylphenidate	Ritalin	60 mg	60 mg (> 6 yo)	X	X
Intermediate-Acting					
Methylphenidate	**Metadate ER[2]**	60 mg	60 mg (> 6 yo)	X	X
Methylphenidate	Ritalin SR[2]	60 mg	60 mg (> 6 yo)	X	X
Methylphenidate	**Metadate CD[3]**	60 mg	60 mg (> 6 yo)	X	X
Methylphenidate	**Ritalin LA[4]**	60 mg	60 mg (> 6 yo)	X	X
Long Acting					
Dexmethylphenidate	**Focalin XR[5]**	40 mg	30 mg (≥ 6 yo)	X	
Methylphenidate	Concerta[6]	72 mg	54 mg (6-12 yo); 72 (>13 yo)	X	X
Methylphenidate	**Daytrana**	30mg/9h patch	30 mg/9h patch (>6 yo)	X	
Methylphenidate	**Jornay PM[7]**	**100mg**	**100mg (≥6yo)**	**X**	
Selective Norepinephrine Reuptake Inhibitor					
Atomoxetine	Strattera	100 mg	1.4 mg/kg (>6yo, ≤ 70kg); 100 mg (>6yo, > 70kg)	X	

References: P.Is., Epocrates, Micromedix, AACP Practice Parameters for the Assessment and Treatment of ADHD 7-07

Comments:

1. Adderall XR caps contain D & L salts in the ratio of 3:1 & Tmax is about 7 hours vs. 3 hours for the IR. Food prolongs Tmax by 2.5hrs
2. Metadate ER & Rtalin SR are extended release with Tmax of 4.7hrs (1.3-8.2 hrs vs. 1.9 hours (0.2-4.4hrs) for IR, Food can inc. Cmax.
3. Metadate CD contains 30% IR component & 70% ER beads resulting in an early peak About 1.5 hrs & 2nd peak about 4.5 hrs post dose. High fat meal delays early peak by 1 hr, inc. Cmax by 30% & AUC by about 17%.
4. Ritalin LA produces a bi-modal plasma conc. (i.e. 2 distinct peaks approximately 4 hours apart) in children & adults 1.5-3 hours and 4.5 to 6 hours. High fat breakfast in adults results in a longer lag time to absorption & variable delays to reach the 1st and 2nd peak concentration.
5. Focalin XR uses Spheroidal Oral Drug Absorption System & each capsule contains 50% IR & 50% delayed rel. beads resulting in 2 peaks 4 hours apart. High fat breakfast in adults results in a longer lag time to absorption & variable delays to reach the 1st and 2nd peak concentration.
6. Concerta tabs consist of a semipermeable membrane with an immediate release drug overcoat and an osmotic pressure controlled trilayer core. The tablet shell is eliminated in the stool. The delivery system results in an initial max conc. In 1 hr & gradual increase in conc. Over the next 5-9 hrs and the peak conc. Between 6 and 10 hours.
7. Jornay PM ER caps contain beads with 2 coatings (outer delayed release & inner extended rel.). Given pm & Tmax in 14hours.Do not substitute mg to mg form other methylphenidate products.

Table 2: Black Box Warnings

	Black Box Warning
Amphetamines	Amphetamine has a high potential for abuse. Administration of amphetamines for prolonged periods of time may lead to drug dependence and must be avoided. Particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic use or distribution to other, and the drugs should be prescribed or dispensed sparingly.
	Misuse of Amphetamines may cause sudden death and serious cardiovascular adverse events.
Strattera	Strattera increases suicidal ideation in short term studies in children and adolescent with ADHD. Anyone considering the use of Strattera in a child or adolescent must balance the risk with the clinical need. Co-morbidities occurring with ADHD may be associated with an increase in the risk with suicidal ideation and/or behavior. Patients who are started on therapy should be monitored closely for suicidality (suicidal thinking and behavior), clinical worsening, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber.
Methylphenidate	Methylphenidate should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during withdrawal from abusive use, since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that my require follow-up.