Screening, Referral and Treatment for Attention Deficit and Hyperactivity Disorder (ADHD) – Adult – Ambulatory Clinical Practice Guideline

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Release Date: October 2014

Next Review Date: October 2016
Executive Summary
Guideline Overview
This document has been developed to assist in identifying, treating, and monitoring adult patients with potential or diagnosed ADHD.

Key Practice Recommendations
1. Assess symptoms and functional impairment
2. Complete physical exam and consider comorbid or alternative diagnoses
3. Establish ADHD diagnosis using DSM-5 diagnostic criteria
4. Provide behavioral and/or pharmacotherapy
5. Perform periodic follow-up to confirm treatment efficacy and absence of side effects

Companion Documents
1. Adult ADHD Algorithm
2. Adult ADHD Medication Algorithm
3. Adult Medication Charts

External Resources
1. Wisconsin Prescription Drug Monitoring Program (PDMP)
2. Wisconsin Uniform Controlled Substances Act

Scope
Disease/Condition(s):
Attention deficit and hyperactivity disorder (ADHD)

Clinical Specialty:
Family Medicine, Neurology, Pediatrics, Psychiatry, and Psychology

Intended Users:
Primary Care Physicians, Advanced Practice Providers, Psychiatrists, Psychologists

CPG objective(s):
To provide evidence-based recommendations for the effective diagnosis and treatment of adult patients with ADHD.

Target Population:
Adult patients (age 18 years or older).

Methodology
Methods Used to Collect/Select the Evidence: Evidence was selected using hand searches of published literature and electronic databases.
Methods Used to Assess the Quality and Strength of the Evidence and Recommendations: Recommendations developed during the workgroup meetings used the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1) to establish evidence grades for each piece of literature and/or recommendation.

Rating Scheme for the Strength of the Evidence and Recommendations: See Appendix A.

Methods Used to Formulate the Recommendations: Recommendations developed by external organizations were adopted while others were developed via group consensus through discussion of the literature evidence and expert experiences.

Introduction
Attention Deficit Hyperactivity Disorder, originally thought to occur just in childhood, is now widely understood as persisting into adulthood. Between 50 to 65 percent of adults diagnosed with childhood ADHD will continue to have symptoms of inattention, distractibility and impulsivity causing functional impairment as adults. In addition, adults who were never diagnosed as children may present with a complicated array of behavioral, legal and functional problems requesting diagnosis and treatment.

This guideline is designed to provide primary care clinicians with a structure, tools and referral criteria for diagnosis and treatment of adults 18 and over with symptoms typical of ADHD.
Recommendations

Adult ADHD Algorithm (ages 18 years or older)

Suspect ADHD
Self-referral, suggestion of family, friend, employer, or therapist, or previous child or adult diagnosis
Symptoms include: inattention, restlessness, forgetfulness, poor executive functioning, disorganization, impulsive behaviors, poor planning, increased risk of driving and other accidents, family and relationship difficulties

First Visit
1. Assess current symptoms using brief validated tool
2. Establish a childhood history of ADHD symptoms and impact on historical childhood functioning (especially academic difficulty)
3. Assess for functional impairment at home, work, or school and in relationships
4. Assess for mimicking and coexisting psychiatric disorders (especially anxiety and depression)
5. Perform thorough screening for substance abuse
6. Evaluate for medical cause of symptoms

Gather Information
1. Request past medical records, report cards, complete family history
2. Request missing childhood and developmental history
3. Encourage scheduling of second visit with informant who can provide corroboration for symptoms and dysfunction
4. Request informant information behavioral checklist

Second Visit
1. Review/interview for corroboration of childhood symptoms and dysfunction (parent, relative, report cards, medical history)
2. Review childhood history including medical, psychiatric, developmental, and academics
3. Review family psychiatric history
4. Interview for corroboration of current symptoms and dysfunction (spouse/partner, employer, reliable friend) and/or review completed behavioral checklist

Corroborate Diagnosis
1. Confirmation of childhood symptoms and impairment
2. Evidence of current dysfunction
3. Meets DSM-5 criteria

Treatment
1. Education of patient and family
2. Psychological support (support groups, counseling, coaching for time management and task organization)
3. Medications
4. Consider vocational and/or educational accommodation

Follow-up
1. Review target symptoms and occupational/academic behavior/performance
2. Review impressions of informants
3. Monitor for drug adverse effects/toxicity or signs of abuse/diversion
4. Adjust therapy as needed
5. Follow-up monthly until functionality improved, then every 3-6 months

Consider Referral
1. Extreme dysfunction
2. Suicidal or homicidal
3. Substance abuse or dependence
4. Psychosis
5. Extreme psychosocial stressors
6. Previous treatment failures
7. Atypical presentation

See Medication Algorithm and Chart(s)
1. PRESENTATION AND SCREENING

Adults with potential ADHD may present with a self-diagnosis, at the suggestion of a family member, friend, employer or therapist or with other behavioral or psychological problems. (Class I, LOE B) There may or may not be a previous childhood or adult diagnosis of ADHD.

Adult ADHD is commonly characterized by poor executive functioning. Indicators of ADHD and screening symptoms include:

- Inattention
- Restlessness
- Forgetfulness
- Disorganization
- Impulsive behaviors/often impatient
- Poor planning
- Increased risk of driving and other accidents
- Family and relationship difficulties
- Difficulties with parenting

High risk behaviors, failed relationships, legal difficulties, substance abuse and recurrent job loss are common. Physical hyperactivity diminishes in severity with age, but inattentive symptoms become more prominent and may be perceived as incompetence. Some adults compensate by finding a spouse / partner who organizes them or a job which is very active, highly absorbing or stimulating.

2. CLINICAL ASSESSMENT

Evaluation of adults presenting with ADHD symptoms typically requires at least two visits. As well as allowing for a thorough evaluation, two visits allows the clinician to assess motivation for follow up, persistence of symptoms and dysfunction and likelihood for alternative diagnoses. The following components of a complete evaluation are considered during both visits (Class I, LOE C):

- review and corroboration of current symptoms and dysfunction
- determination of a childhood onset
- evaluation for comorbid and /or mimicking psychiatric problems, medical disorders or substance abuse.

First Visit

A. Review Current Symptoms and Functional Impairment (Class I, LOE C)

- DSM-5 diagnostic criteria for ADHD should be used and followed. A validated adult ADHD assessment tool (such as the Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist) may be used to adjunctively evaluate an adult patient.
- Adults may present with distractibility, impulsiveness and poor executive functioning. A variety of psychiatric or lifestyle conditions need to be considered when these symptoms are present.
B. Establish Onset *(Class I, LOE C)*
- ADHD is a neurodevelopmental disorder that may persist into adulthood.
- In order to meet diagnostic criteria, symptoms and functional impairment need to have been present in patients prior to age 12.

C. Perform Medical Evaluation *(Class I, LOE C)*
- Screen for medical, psychiatric or substance abuse issues which could explain or exacerbate symptoms of ADHD. *(Class I, LOE C)*
- Screen for medical and psychological conditions which would influence choice of medication. When considering a stimulant in an adult with risk factors for cardiac disease, the provider should consider a cardiovascular evaluation before initiating therapy. *(Class I, LOE C)*
- Establish baseline vital signs: weight, blood pressure, pulse. *(Class I, LOE C)*
- Laboratory testing should be limited to areas of concern. *(Class I, LOE C)*

D. Evaluate for Psychiatric or Lifestyle Conditions
- Adults may present with distractibility, impulsiveness and poor executive functioning. A variety of psychiatric or lifestyle conditions need to be considered when these symptoms are present. *(Class I, LOE C)*

GATHER ADDITIONAL INFORMATION

A. Corroborate Childhood Onset and Impairment
Childhood history can be gathered by review of medical records, review of report cards or other academic materials, and interview with parents or close family member either in person or via a phone call. High activity patterns, difficult temperament, and frequent accidents or risk taking behavior are common childhood characteristics. Review of academic background should reveal areas of impairment or concern. Look for drop outs, failures, learning disability, special evaluations or classes, suspensions / expulsions, and focused problems in areas such as reading, writing, penmanship or math. *(Class I, LOE C)*

Review of report cards often indicates behavior problems, lack of expected achievement, incomplete work, or inadequate effort. If there is no objective evidence of childhood symptoms and impairment, the diagnosis of adult ADHD should be reconsidered.

B. Review Family Psychiatric History
It is common to have a positive family psychiatric history. Inquire particularly about learning disabilities, behavior problems, legal difficulties, ADHD, and substance abuse. *(Class I, LOE B)*

CONSIDER COMORBID OR ALTERNATIVE PSYCHIATRIC DIAGNOSIS *(Class I, LOE B)*
Psychiatric disorders can cause inattentive symptoms or can influence the course of treatment. Presence of another psychiatric diagnosis does not preclude a diagnosis of
adult ADHD but it does make diagnosis and treatment more confusing. Significant physical, verbal or emotional abuse / neglect can contribute to symptoms characteristic of ADHD. Depression, Post-Traumatic Stress Disorder (PTSD), bipolar disorder, anxiety disorder, personality disorders, substance abuse and other psychiatric disorders should be considered as a part of the evaluation.

Patients whose psychiatric status is unclear should be referred to a mental health provider. Patients with active substance abuse should be referred to a substance use treatment program. Consider evaluation for drug-seeking behavior with multiple pharmacies or prescribing providers using the Wisconsin Prescription Drug Monitoring Program.

It is important to identify comorbid disorders because they can mimic ADHD.
   a. Comorbid or alternative psychiatric conditions should be addressed prior to starting treatment for ADHD.
   b. Certain medical conditions (liver disease, seizures, hypertension, glaucoma) are relative contraindications to certain ADHD medications.

**CONSIDER REFERRAL (Class I, LOE C)**
Referral to psychiatrists and additional providers is always at the discretion of the provider. There are several presentations and co-conditions for which referral is recommended:
   1. Extreme dysfunction
   2. Suicidality or homicidality
   3. Substance abuse or dependence
   4. Psychosis
   5. Extreme psychosocial stressors
   6. Previous treatment failures
   7. Atypical presentation – if presentation as brand new symptoms this is not ADHD, even if not diagnosed as a child the symptoms must concur

**3. ESTABLISH DIAGNOSIS**
To diagnose ADHD, the clinician should determine that DSM-5 criteria have been met. (Class I, LOE B)

**DSM-5 Diagnostic Criteria**

A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:
   
   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. **For older**
adolescents and adults (age 17 and older), at least five symptoms are required.

a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).

b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).

c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).

d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).

e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   **Note:** The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

   a. Often fidgets with or taps hands or feet or squirms in seat.

   b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).

   c. Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.)

   d. Often unable to play or engage in leisure activities quietly.
e. Is often “on the go,” acting as if “driven by a motor” (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).

f. Often talks excessively.

g. Often blurts out an answer before a question has been completed (e.g., completes people’s sentences; cannot wait for turn in conversation).

h. Often has difficulty waiting his or her turn (e.g., while waiting in line).

i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people’s things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.

C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

<table>
<thead>
<tr>
<th>DSM-5 Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specify whether:</td>
</tr>
<tr>
<td><strong>Combined presentation:</strong> If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.</td>
</tr>
<tr>
<td><strong>Predominantly inattentive presentation:</strong> If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.</td>
</tr>
<tr>
<td><strong>Predominately hyperactive/impulsive presentation:</strong> If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.</td>
</tr>
</tbody>
</table>

Specify if:

| In partial remission: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning. |

Specify current severity:

| Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning. |
| Moderate: Symptoms or functional impairment between “mild” and “severe” are present. |
| Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning. |

4. PROVIDE TREATMENT
   *(Class I, LOE C unless otherwise indicated)*
   1. Provide or offer referral regarding ADHD symptom management, and psycho-education or effective coping strategies for both the patient and family.
2. Follow medication treatment protocol and medication chart (Appendix B and Appendix C). (Class I, LOE A) Specific patient needs or wishes should be considered and therapy should be individualized.

3. Little data is available on the use of therapeutic stimulants in pregnancy, but currently they are not associated with major congenital malformations. Risks of discontinuation of therapy should be considered (e.g., driving, vocational responsibilities) along with the benefits for each individual patient. (Class IIb, LOE C)

4. Long term benefit should be assessed for each patient, especially those who continue treatment from a childhood diagnosis. A trial discontinuation of therapy can be considered as children age into adulthood to assess ongoing benefit of therapy.

5. In situations where there is increased risk of substance abuse or diversion, non stimulant preparations or slow release stimulants are preferred and can be used to initiate treatment. When crushed, slow release stimulants resemble immediate release preparations in terms of onset and effect.

6. Adults with ADHD who are also parents may benefit from therapy to assist them with parenting skills.

7. Consider vocational and/or educational accommodation.

8. For patients at high risk of substance abuse, consider establishing a drug contract or conducting periodic drug screens.


5. COMPLETE FOLLOW-UP CARE

Adults with a new diagnosis, uncontrolled symptoms or change in medication should be seen within 30 days by a clinician who can assess for side effects and adjust medication if needed. Monthly contacts or visits should be routine until functionality is significantly improved. Once functionality is improved, follow-up appointments every 3 to 6 months are recommended. Informants should be included, as available, in follow-up sessions. (Class I, LOE C)

At each follow-up visit (Class I, LOE C):

1. Review should specifically include diurnal variation in symptoms, as this informs recommendations for change in timing/formulation of the medications prescribed.


3. Monitor for adherence to therapy, drug side effects/toxicity or signs of abuse/diversion. Also monitor vital signs to assess for increases in blood pressure and pulse.

4. Review impressions of informants.

5. Adjust therapy as needed.

Medications must be prescribed in accordance with Wisconsin Chapter 961 for controlled substances:

1. Prescription must be written for legitimate medical indication.

2. Sign/date prescription on date of issue with:
   a. Patient full name/address.
b. Drug name, strength, dosage form, quantity, directions for use.

3. Up to 3 monthly prescriptions may be given to patients.
   a. The date of issue (date of prescription is written) must be on all three
      prescriptions.
   b. The prescriber writes “fill on or after XX/XX/XXXX” for two prescriptions to be
      filled at a later date.
   c. A prescription for a CII controlled substance cannot be dispensed more than
      60 days after the date of issue on the prescription order.

Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and

treatment of patients. This Clinical Practice Guideline outlines the preferred approach

for most patients. It is not intended to replace a clinician’s judgment or to establish a

protocol for all patients. It is understood that some patients will not fit the clinical

condition contemplated by a guideline and that a guideline will rarely establish the only

appropriate approach to a problem.

References
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4. Greenhill, Laurence, Pliszka, Steven, et al., Practice Parameter for the Use of Stimulant
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Deficit/Hyperactivity Disorder Persistence into Adulthood: Results from the National
6. Kessler, Ronald; Adler, Lenard; et al, The World Health Organization Adult ADHD Self-
Report Scale (ASRS): a Short Screening Scale for Use in the General Population.
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7. McGough, James J and Russell Barkley, Diagnostic Controversies in Adult Attention Deficit
8. Montano, Brendan, Diagnosis and Treatment of ADHD in Adults in Primary Care. J Clin
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11. Meijer WM, Faber A, van den Ban E, and Tobi H. Current Issues Around the
of attention deficit/hyperactivity disorder in adolescents in transition to adult services and in


Appendix A

Figure 1. AHA/ACC Modified GRADE Grading Scheme

<table>
<thead>
<tr>
<th>CLASS I</th>
<th>CLASS IIA</th>
<th>CLASS IIb</th>
<th>CLASS III: No Benefit or CLASS III: Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Benefit ≥ Risk</td>
<td>Procedure/Treatment should be performed/administered</td>
</tr>
<tr>
<td>Procedure/Treatment should be performed/administered</td>
<td>Additional studies with focused objectives needed</td>
<td>Additional studies with broad objectives needed; additional registry data would be helpful</td>
<td>Procedure/Treatment may be considered</td>
</tr>
</tbody>
</table>

**SIZE OF TREATMENT EFFECT**

**LEVEL A**
- Multiple populations evaluated
- Data derived from multiple randomized clinical trials or meta-analyses
- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses

**LEVEL B**
- Limited populations evaluated
- Data derived from a single randomized trial or nonrandomized studies
- Recommendation that procedure or treatment is useful/effective
- Evidence from single randomized trial or nonrandomized studies

**LEVEL C**
- Very limited populations evaluated
- Only consensus opinion of experts, case studies, or standard of care
- Recommendation that procedure or treatment is useful/effective
- Only converging expert opinion, case studies, or standard of care

**CON: PB**
- No Benefit
- Helpful
- Harmful

**CON: PT**
- Not
- Proven
- Treat Harmful to Patients
Appendix B

Adult ADHD Medication Algorithm

Diagnosis of definite or probably adult ADHD made

Treat/refer co-morbid disorder first.

Co-morbid psychiatric or substance abuse disorder?

Treat/refer co-morbid disorder first. NO

At increased risk for substance abuse/diversion?

Stimulant or non-stimulant medication

Non-stimulant medication or slow-release stimulant medication

If stimulant chosen, consider drug contract and/or periodic drug screens.

Improved symptoms/function on monthly follow-up?

Adjust dose or try alternative medication.

If repeated adjustments of medication are not successful, reconsider diagnosis, and consider referral to psychiatry.

Continue medication with 3-6 month follow-up

Last revised/reviewed: 10/2014
ADHD- Adult – Ambulatory Guideline
Appendix C

Medications for Treatment of Attention-Deficit/Hyperactivity Disorder

GENERAL CONSIDERATIONS FOR STIMULANTS

- Consider cardiac risk factors before initiating therapy
- Use cautiously if history of tics
- Give with/after food and swallow whole with liquids
- Longer-acting stimulants may have greater problematic effects on evening appetite and sleep
- Use cautiously if history of substance abuse or diversion concern
- Monitor patient weight and vital signs
- Pellet/beaded capsule formulation may be opened and sprinkled on soft food
- Nonabsorbable tablet shell may be seen in stool (Concerta)
- Consider cardiovascular evaluation before initiating therapy

<table>
<thead>
<tr>
<th>Methylphenidate Products</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Names</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>methylphenidate tab** (Ritalin)</td>
</tr>
<tr>
<td>methylphenidate ^* (Methylin) (equivalent to Ritalin)</td>
</tr>
<tr>
<td>methylphenidate SR tab** (Ritalin SR) Medadate ER and generics rated AB equivalent</td>
</tr>
<tr>
<td>methylphenidate^* (Methylin ER) (equivalent to Ritalin SR)</td>
</tr>
<tr>
<td>Methylphenidate tab** (Metadate ER)</td>
</tr>
<tr>
<td>dexamethasone ** (Focalin) cap</td>
</tr>
<tr>
<td>Product Names</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>methylphenidate(^\dagger) (Metadate CD) cap (bimodal release with 30% immediate release and 70% delayed release)</td>
</tr>
<tr>
<td>methylphenidate ER(^\dagger)(^\ddagger) (Ritalin LA) cap (bimodal release with 50% rapid onset and 50% delayed release)</td>
</tr>
<tr>
<td>dexmethylphenidate(^\dagger)(^\ddagger) (Focalin XR) (bimodal release with 50% immediate release and 50% delayed release)</td>
</tr>
<tr>
<td>methylphenidate (^\dagger) (Daytrana) patch apply to hip for 9 hours</td>
</tr>
<tr>
<td>Methylphenidate(^\dagger)(^\ddagger) (Concerta) tab (bimodal release with immediate onset and delayed release)</td>
</tr>
</tbody>
</table>

\(^\dagger\) FDA approved for treatment of ADHD, \(^\ast\) Generic product, \(^\ddagger\)Oral long acting methylphenidate products have immediate release and extended release components.
<table>
<thead>
<tr>
<th>Product Names</th>
<th>Strengths Available</th>
<th>Duration of action</th>
<th>Usual Dosing (titrate every 7 days, unless otherwise noted)</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short acting</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Dextroamphetamine*</td>
<td>5, 10 mg tablet 1 mg/mL solution</td>
<td>4-6 hours</td>
<td>2.5-15 mg two to three times Daily Titrations 5 mg/week</td>
<td>FDA: 40 mg Off label: 60 mg (&gt;50 kg)</td>
</tr>
<tr>
<td><strong>Intermediate acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextroamphetamine capsule SR§</td>
<td>5, 10, 15 mg capsule</td>
<td>6-8 hours</td>
<td>5-15mg 2 times twice daily Titrations 5 mg</td>
<td>FDA: 40 mg Off label: 60 mg (&gt;50 kg)</td>
</tr>
<tr>
<td>Amphetamine mixed salts tab combo</td>
<td>5, 7.5, 10, 12.5, 15, 20, 30 mg tab</td>
<td>5-8 hours</td>
<td>52.5-30mg 1-2 times once or twice daily Titrations 2.5-5 mg once or twice daily</td>
<td>FDA: 40 mg Off label: 40 mg (≤ 50kg), 60 mg (&gt;50 kg)</td>
</tr>
<tr>
<td><strong>Long acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphetamine mixed salts capsule^</td>
<td>5, 10, 15, 20, 25, 30 capsule</td>
<td>10 hours</td>
<td>10-30mg once daily Titrations 5-10 mg</td>
<td>FDA: 30 mg Off-label: 30 mg (≤ 50kg), 60 mg (&gt;50 kg)</td>
</tr>
<tr>
<td>Lisdexamfetamine (Vyvanse) capsule^</td>
<td>20, 30, 40, 50, 60, 70 mg capsule</td>
<td>10-12 hours</td>
<td>20-70mg once daily Titrations 10-20 mg daily</td>
<td>FDA: 70 mg</td>
</tr>
</tbody>
</table>

^ FDA approved for treatment of ADHD, * Generic product, § Oral long acting methylphenidate products have immediate release and extended release components.
### GENERAL CONSIDERATIONS FOR NON-STIMULANTS

- May be used in cases of history of tics worsening from stimulants
- Avoid bupropion if history of seizure or eating disorders
- Monitor closely for behavioral side effects including suicidal ideation with atomoxetine, tricyclics, and bupropion as identified in FDA Black Box warning for anti-depressants
- Give with/after food and swallow whole with liquids
- Medication of choice if concern about abuse or diversion
- Consider cardiovascular risk factors before initiating tricyclic therapy and evaluate further if needed
- Consider initiation with lower doses to improve tolerability
- Guanfacine and clonidine may be used as adjunctive therapy with stimulants.

<table>
<thead>
<tr>
<th>Non-Stimulant Products</th>
<th>Product Names</th>
<th>Strengths Available</th>
<th>Duration of Action</th>
<th>Usual Dosing</th>
<th>Maximum Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td>nortriptyline* (Pamelor, Aventyl)</td>
<td>10, 25, 50, 75 mg capsule 10 mg/5 mL solution</td>
<td>8-24 hours</td>
<td>0.5 mg/kg/day (May divide dose to 2-3 times daily)</td>
<td>2 mg/kg or 100 mg (whichever is lowest)</td>
</tr>
<tr>
<td></td>
<td>bupropion* (Wellbutrin)</td>
<td>75, 100 mg tab</td>
<td>4-5 hours</td>
<td>3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest) Divide into 2 or 3 daily doses</td>
<td>6 mg/kg/day (or 300 mg Whichever is lowest) Divide into 2 or 3 daily doses</td>
</tr>
<tr>
<td></td>
<td>bupropion SR* (Wellbutrin SR)</td>
<td>100, 150, 200 mg tab</td>
<td>12 hours</td>
<td>3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest) Divide into 2 daily doses.</td>
<td>6 mg/kg/day (or 300 mg whichever is lowest) Divide into 2 daily doses.</td>
</tr>
<tr>
<td></td>
<td>bupropion XL* (Wellbutrin XL)</td>
<td>150, 300 mg tab</td>
<td>24 hours</td>
<td>3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest)</td>
<td>6 mg/kg/day (or 300 mg whichever is lowest)</td>
</tr>
<tr>
<td><strong>Alpha-agonists</strong></td>
<td>clonidine tab ER^ (Kapvay)</td>
<td>0.1, 0.2 mg tab</td>
<td>At least 10-12 hours</td>
<td>0.1-0.4 mg/day Titration: 0.1 mg every 7 days</td>
<td>0.4 mg/day</td>
</tr>
<tr>
<td></td>
<td>clonidine* (Catapres)</td>
<td>0.1, 0.2, 0.3 mg tab</td>
<td>At least 4-6 hours</td>
<td>0.05 mg at bedtime; 01 mg (≥ 45 kg) Titrate by 0.05 mg (&lt;45 kg) or 0.1 mg (≥ 45 kg) increments to twice daily, three times daily, four times daily</td>
<td>0.4 mg (&gt;45 kg)</td>
</tr>
<tr>
<td><strong>Product Names</strong></td>
<td><strong>Strengths Available</strong></td>
<td><strong>Duration of Action</strong></td>
<td><strong>Usual Dosing</strong></td>
<td><strong>Maximum Dosing</strong></td>
<td></td>
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<tr>
<td><strong>Alpha-agonists</strong></td>
<td>guanfacine* (Tenex)</td>
<td>1, 2 mg tab</td>
<td>6-8 hours</td>
<td>0.5 mg at bedtime (&lt;45 kg), 1 mg at bedtime (≥ 45 kg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>guanfacine tab ER^* (Intuniv)</td>
<td>1, 2, 3, 4 mg tabs</td>
<td>At least 10-12 hours</td>
<td>0.05-0.12 mg/kg daily (or 1-4 mg once daily)</td>
<td></td>
</tr>
<tr>
<td><strong>Norepinephrine reuptake inhibitor</strong></td>
<td>atomoxetine^ (Strattera) capsule</td>
<td>10, 18, 25, 40, 60, 80, 100 mg capsule</td>
<td>At least 10-12 hours</td>
<td>Initial dose 40 mg/day After ≥ 3 days (increase to 80 mg daily)</td>
<td></td>
</tr>
</tbody>
</table>

*Generic product  
^ FDA Approved

**Potential Harms:** Side Effects of Pharmacotherapy

- **Stimulants:** The most common side effects include appetite decrease, weight loss, insomnia, or headache. Less common side effects include tics and emotional lability/irritability, liver toxicity, hypertension, cardiac arrhythmia and psychosis.
- **Atomoxetine:** Side effects of atomoxetine that occurred more often than those with placebo include gastrointestinal distress, sedation, and decreased appetite.
- The U.S. Food and Drug Administration (FDA) and its Pediatric Advisory Committee have reviewed data regarding psychiatric adverse events to medications for the treatment of attention deficit/hyperactivity disorder (ADHD). For each agent examined (all stimulants, atomoxetine, and modafinil), there were reports of rare events of psychotic symptoms, specifically involving visual and tactile hallucinations of insects. Symptoms of aggression, suicidality (but no completed suicides), and cardiovascular issues were also reported.
- **Bupropion** may cause mild insomnia or loss of appetite. The highest recommended dose of bupropion is 450 mg. Higher doses may increase the risk of seizure.
- **Tricyclic Antidepressants (TCAs)** such as nortriptyline - frequently cause anticholinergic side effects such as dry mouth, sedation, constipation, changes in vision, or tachycardia. Among the TCAs, desipramine should be used with extreme caution in children and adolescents because there have been reports of sudden death. For TCAs electrocardiography should be considered for patients at risk and be performed at baseline and after each dose increase. Once the patient is on a stable dose of the TCA, a plasma level should be obtained to ensure the level is not in the toxic range.
- **Alpha-agonists:** Side effects of alpha-agonists include sedation, dizziness, and possible hypotension. Abrupt discontinuations of alpha-agonist are to be avoided.
- **Combinations of Medications:** There have been four deaths reported to the FDA of children taking a combination of methylphenidate and clonidine, but there were many atypical aspects of these cases.