

## Medications for Attention-deficit/hyperactivity Disorder (ADHD)

The mechanism by which both stimulant and non-stimulant medications work for ADHD appears to be by modulation of dopamine (DA) and norepinephrine (NE) systems.

Both stimulants and atomoxetine commonly cause anorexia, abdominal pain, and irritability. Headaches are also a common adverse effect of stimulants. In general, while stimulants appear to cause insomnia, atomoxetine and the other non-stimulants cause drowsiness, sedation, or fatigue. Additionally, clonidine and guanfacine commonly cause dry mouth. Initial drug selection depends on drug-specific and patient-specific factors. Both categories of medications are effective in reducing core ADHD symptoms, however the body of evidence supporting stimulants is larger and the effect size is larger as compared to non-stimulants.

DRUG CATEGORY	MEDICATIONS	COMMON SIDE EFFECTS	MONITORING PARAMETERS	ADDITIONAL COMMENTS
<b>CNS STIMULANTS</b>				
Amphetamines	<ul style="list-style-type: none"> <li>▪ Amphetamine (IR, ODT, XR-ODT, XR-liq)*</li> <li>▪ Dextroamphetamine/Amphetamine (IR, ER)</li> <li>▪ Dextroamphetamine (IR, ER, Liq)</li> <li>▪ Lisdexamfetamine (IR, chew)</li> <li>▪ Methamphetamine (IR)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Cardiovascular:</b> elevated blood pressure, tachycardia, palpitations</li> <li>▪ <b>CNS:</b> headache, insomnia</li> <li>▪ <b>Endocrine:</b> weight loss, slowing of growth rate in children</li> <li>▪ <b>GI:</b> decreased appetite, xerostomia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Targeted cardiac history and cardiac exam: monitor heart rate and blood pressure, consider ECG</li> <li>▪ Height, weight, and growth rate in children</li> <li>▪ CNS activity</li> <li>▪ Behavioral changes</li> </ul>	<p><b>Black Box Warnings:</b></p> <ul style="list-style-type: none"> <li>▪ Amphetamines have a high potential for abuse and dependence</li> <li>▪ Misuse of amphetamines may cause sudden death and serious cardiovascular adverse reactions</li> </ul>
Methylphenidates	<ul style="list-style-type: none"> <li>▪ Dexmethylphenidate (IR, ER)</li> <li>▪ Methylphenidate (IR, ER, chew, XR-chew, XR-ODT, Liq, XR-liq, patch)</li> </ul>	<ul style="list-style-type: none"> <li>▪ May lower the convulsive threshold in patients with a history of seizures</li> <li>▪ May exacerbate anxiety</li> </ul>	<ul style="list-style-type: none"> <li>▪ Signs of peripheral vasculopathy</li> <li>▪ Assess for risk of abuse or addiction</li> </ul>	
<b>NON-CNS STIMULANTS</b>				
Selective Norepinephrine Reuptake Inhibitor (SNRI)	Atomoxetine (IR)	<ul style="list-style-type: none"> <li>▪ <b>Cardiovascular:</b> elevated blood pressure and tachycardia</li> <li>▪ <b>CNS:</b> drowsiness, fatigue, headache, insomnia</li> <li>▪ <b>GI:</b> abdominal pain, xerostomia, decreased appetite, nausea, vomiting</li> <li>▪ <b>GU:</b> erectile dysfunction</li> <li>▪ <b>Dermatologic:</b> hyperhidrosis</li> </ul>	<ul style="list-style-type: none"> <li>▪ Targeted cardiac history and cardiac exam; monitor heart rate and blood pressure, consider ECG</li> <li>▪ Height, weight, and growth rate in children</li> <li>▪ Behavioral changes</li> </ul>	<p><b>Black Box Warning:</b></p> <ul style="list-style-type: none"> <li>▪ Increased risk of suicidal ideation in children and adolescents</li> </ul>
Centrally Acting Alpha <sub>2</sub> Agonists	<ul style="list-style-type: none"> <li>▪ Clonidine (ER)</li> <li>▪ Guanfacine (ER)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Cardiovascular:</b> hypotension</li> <li>▪ <b>CNS:</b> drowsiness, fatigue, headache, sedation,</li> <li>▪ <b>GI:</b> constipation, xerostomia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Targeted cardiac history and cardiac exam; monitor heart rate and blood pressure, consider ECG</li> </ul>	<ul style="list-style-type: none"> <li>▪ Only the extended-release forms of these medications are indicated for ADHD</li> </ul>
<b>SELECT MEDICATIONS USED OFF-LABEL FOR ADHD</b>				
Norepinephrine/Dopamine Reuptake Inhibitor (NDRI)	Bupropion (IR, ER)	<ul style="list-style-type: none"> <li>▪ <b>Cardiovascular:</b> tachycardia</li> <li>▪ <b>CNS:</b> agitation, anxiety, headache, insomnia</li> <li>▪ <b>Endocrine:</b> weight loss</li> <li>▪ <b>GI:</b> nausea, constipation, xerostomia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Targeted cardiac history and cardiac exam; monitor heart rate and blood pressure, consider ECG</li> <li>▪ Weight and BMI</li> </ul>	<ul style="list-style-type: none"> <li>▪ Data from a meta-analysis of controlled trials support the use of bupropion in the treatment of ADHD in adults</li> <li>▪ There is evidence supporting its use in the setting of ADHD and comorbid depression, as well as comorbid bipolar disorder as an adjunct to mood stabilizers</li> <li>▪ Contraindicated in history of seizures, bulimia, and/or anorexia</li> <li>▪ Contraindicated with MAOIs</li> </ul> <p><b>Black Box Warning:</b></p> <ul style="list-style-type: none"> <li>▪ Increased risk of suicidal ideation in children and adolescents</li> </ul>

\*Dosage forms available: IR = Immediate Release Oral Formulation, ER= Extended Release Oral Formulation, Chew= Chewable Tablet, XR-chew= Extended Release Chewable Tablet, ODT= Orally Disintegrating Tablet, XR-ODT= Extended Release Orally Disintegrating Tablet, Liq= Oral Liquid, XR-liq= Extended Release Oral Liquid, Patch= Patch

### Special Populations:

- Non-stimulants with the exception of *atomoxetine* may be preferred in patients with pre-existing psychotic disorder, bipolar disorder, or depression due to the concern for possible induction of a mixed/manic episode or exacerbation of behavior disturbance and thought disorder symptoms.
- Non-stimulants are preferred in patients with tics or Tourette's syndrome, patients with a history of substance abuse, or patients with anxiety.
- Stimulants and *atomoxetine* are not recommended for use by patients with cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of these drugs.