














| ADHD Treatment Chart                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  | 1,2,3,4 CADDRA 2011,5,6,7,8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | © Originally prepared by: Monica Lee; Brent Jensen, Loren Regier BSP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  | www.RxFiles.ca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  | Apr 13                                                                                                                          |  |
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| Generic/TRADE g=generic avail<br>(Strength & forms) Pregnancy <sup>9</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  | Side effects (SE) / Contraindications CI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  | √ = therapeutic use / Comments /<br>Drug Interactions DI/ Monitor M                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  | Initial <sup>4</sup> / Typical Dose <sup>8</sup> (Max mg/day) * Titration <sup>4</sup><br>{Child(up to 40 kg); Adolescent; Adult}                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  | \$  /<br>30 days                               |  |
| <b>PSYCHOSTIMULANTS</b> Response rate ~75%, effect size ~0.9; <b>SHORT-ACTING:</b> (Ritalin, Dexedrine) are less money & flexible for initial Tx, esp in small kids. But, social stigmatization, ↑drug diversion related to in-school dosing, & need school staff support.<br><b>INTERMEDIATE-ACTING:</b> (Ritalin SR, Dexedrine Spansules) may last up to 8 hours. [CADDRA 2011 guidelines generally recommend long-acting agents as 1 <sup>st</sup> line; however expert opinion notes role for individualization of therapy.]<br><b>LONG-ACTING:</b> (Concerta, Biphentin, Adderall XR, Vyvanse) are dosed once-daily & have less fluctuation in serum levels (may ↑ compliance). Less abuse potential. But: may affect evening appetite & sleep, & are more expensive (varying drug plan coverage). Harder to titrate. |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                 |  |
| <b>Amphetamine Mixed Salts</b><br>dextroamphetamine and<br>levoamphetamine salts (3:1)<br><b>ADDERALL XR</b> <br>5, 10, 15, 20, 25, 30mg cap<br>50% immediate release &<br>50% gradual release [MOA:↑ DA,NE]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  | <b>Common:</b> appetite suppression, ↓ weight, insomnia, headache, dry mouth, rebound irritability, nausea/vomiting, constipation/diarrhea, GI upset, dizziness, anxiety, tremor, ↑BP & ↑HR, emotional lability; slow growth<br><b>Infrequent:</b> uncovering tics, sexual dysfunction, tactile & visual hallucinations, psychosis, ↓ seizure threshold<br><b>Serious:</b> sudden death (see Cardiac Risk note below)<br><b>CI:</b> advanced arteriosclerosis, symptomatic CV dx, hyperthyroidism<br>↑BP, hypersensitivity/idiosyncrasy to sympathomimetic amines, glaucoma, agitated states, drug abuse hx, or MAOI use within 14day |  | √ ADHD age ≥ 6yr <sup>(narcolepsy in the USA)</sup><br>May be opened & sprinkled on soft foods<br><b>Duration: 8-12hr (long-acting)</b><br><b>DI:</b> ↑amphetamines effect: acetazolamide, antacid; MAOI & linezolid <sup>↑ effect &amp; ↑BP</sup> ; sympathomimetics <sup>↑HR &amp; BP</sup> , & TCAs <sup>↑ CV effects</sup><br><b>M:</b> ADHD symptoms, behaviour & academic performance; rating scales e.g. SNAP-IV, Conners', CGI; physical exam, patient & family cardiac hx; [ECG only if at risk population <sup>CADDRA 2011</sup> at baseline & consider repeat if pt age <12yr at initial ECG or if change in patient symptoms eg. palpitations/syncope]<br>BP, HR: At Day 0, 1 & 3months then q6-12months<br>Pediatric patients: development, weight & growth                                                                                                                                                                                                                                                                                     |  | <b>Peds:</b> 10mg qam / <b>30mg qam</b> (30 mg/d) Titrate 5-10mg q7d<br>AAP 2011: start 2.5-5mg OD-BID/XR 5mg OD (40mg/d)<br><b>Adolescents:</b><br>10mg qam / <b>30mg qam</b> (20-30 or 50 <sup>CADDRA</sup> mg/d) Titrate 5-10mg q7d<br><b>Adults:</b><br>10mg qam / <b>50mg qam</b> (20-30 or 50 <sup>CADDRA</sup> mg/d) Titrate 5-10mg q7d (doses up to 60mg/d used but no adequate evidence of ↑ benefit)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  | 86 / 123 (123)<br><br>86 / 123 (218)<br><br>86 / 218 (218)                                                                      |  |
| <b>Precautions:</b> amphetamine misuse or if cardiac dx → ↑BP/↑HR, <b>serious CV events</b> or even sudden death; hx of drug dependence→ ↑ abuse; hx seizures/EEG changes→ may ↓seizure threshold; pre-existing psychosis, bipolar or hx of tics or Tourette's <sup>‡</sup> → may worsen disorder                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                 |  |
| <b>Dextroamphetamine</b><br><b>DEXEDRINE</b> 5 <sup>c</sup> mg tab <br><b>DEXEDRINE Spansule</b><br>10, 15mg cap<br>[MOA: blocks re-uptake of DA; increases release of DA and NE]<br>{SK Formulary: max \$20/Rx for age ≤14yrs.}                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  | <b>Common:</b> as in Adderall XR<br><b>Infrequent:</b> as in Adderall XR<br><b>Serious:</b> as in Adderall XR<br><b>CI:</b> as in Adderall XR + patients with motor tics or with a family hx of diagnosis of Tourette's Syndrome <sup>‡</sup><br><b>Precautions:</b> as in Adderall XR + tartrazine (FD&C Yellow No. 5) sensitivity, esp. with aspirin sensitivity; may cause allergic-type reaction (tablets)                                                                                                                                                                                                                        |  | √ ADHD age ≥ 6 yr; adjunctive therapy for narcolepsy<br><b>Duration: Tab:~4-6hr (short);</b><br><b>Spansule</b> both IR & ER pellets: <b>6-8hr (intermediate)</b><br><b>More potent than MPH</b> (10mg MPH ≈ 5mg Dextroamp.)<br><b>Short-acting</b> often used as <b>initial</b> Tx in small kids, but bid-tid dosing; <b>longer acting</b> greater convenience, confidentiality but may ↓evening appetite & ↓sleep<br><b>Spansules</b> may be opened & sprinkled on soft foods<br><b>DI:</b> as in Adderall XR<br><b>M:</b> as in Adderall XR<br>Fruit juice or ascorbic acid(vitamin C) may ↓ absorption                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  | <b>Peds:</b> Tab: 2.5mg qam & qnoon / <b>10mg bid</b> (20 <sup>CADDRA</sup> -40mg/d) Titrate 5mg q7d by adding 4pm dose<br>Spansule: 10mg qam / <b>15mg qam</b> <sup>AAP 11: 5mg am</sup> (30 <sup>CADDRA</sup> -40mg/d) Titrate 10mg q7d by adding 4pm dose<br><b>Adolescents:</b><br>Tab: 2.5mg qam & qnoon / <b>10mg bid</b> (30 <sup>CADDRA</sup> -40mg/d) Titrate 5mg q7d by adding 4pm dose<br>Spansule: 10mg qam / <b>15mg qam</b> (30 <sup>CADDRA</sup> -40mg/d) Titrate 10mg q7d by adding 4pm dose<br><b>Adult:</b> Tab: 5mg qam & qnoon / <b>15mg bid</b> (40 <sup>CADDRA</sup> -50 mg/d) Titrate 5mg q7d by adding 4pm dose<br>Spansule: 10mg qam / <b>30mg qam</b> (40 <sup>CADDRA</sup> -50 mg/d) Titrate 10mg q7d by adding 4pm dose                                                                                                                                                                                                                                                                              |  | 27 / 83 (121)<br><br>36 / 42 (78)<br><br>27 / 83 (121)<br><br>36 / 42 (78)<br><br>47 / 121 (197)<br><br>36 / 78 (113)           |  |
| <b>Lisdexamfetamine VYVANSE</b>   <b>NEW</b> <sup>CDN</sup> : 20,30,40,50 & 60mg cap daily <sup>S90-140</sup> in morning; √ADHD age ≥6yr & adults; caps taken whole or dissolved in water; a prodrug & slower rate controlled absorption thus hope to ↓ abuse.<br>Dosing: Peds: 20-30mg qam / 30mg qam (60mg/d) <sup>AAP 11 70mg/d</sup> ; Titrate 10mg q7day. <b>Adolescents</b> & Adult: 20-30mg qam / <b>30mg qam</b> (60-70 <sup>CADDRA</sup> mg/d), titrate 10mg q7day. (no additional benefit but ↑SE at >30mg/d). <sup>10</sup> Duration ≥12hr.                                                                                                   |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                 |  |
| <b>Methylphenidate (MPH)</b><br><b>RITALIN</b> <sup>®</sup> , g <sup>▼</sup> 5, 10 <sup>c</sup> , 20 <sup>c</sup> mg tab<br><b>RITALIN SR</b> <sup>®</sup> , g <sup>▼</sup> 20mg tab<br>-do not chew or crush tablet<br>[MOA: blocks DA reuptake] wax matrix <br>{SK Formulary: max \$20/Rx for age ≤14yrs.}                                                                                                                                                                                                                                                                                                                                                                                                                            |  | <b>Common:</b> Insomnia 13%, ↓appetite 26%, nausea 12%, vomiting 10%, weight loss 9%, tic 7%, emotional instability 6%, anorexia 5%, nasal congestion 6%, nasopharyngitis 5%, headaches<br><b>Serious:</b> blood dyscrasia (very rare), angioedema, hallucinations, sudden death (see Cardiac Risk note below)<br><b>CI:</b> Anxiety, tension, agitation, thyrotoxicosis, advanced arteriosclerosis, symptomatic CV disease, ↑BP, glaucoma & pheochromocytoma, patients with motor tics or with a family hx or diagnosis of Tourette's syndrome <sup>‡</sup> , MAOI use within 14 days.                                               |  | √ ADHD age ≥ 6yr <sup>(narcolepsy in the USA). AAP 11: consider tx if ≥ 4yr.</sup><br><b>Duration: Tabs: ~3-5hr (short-acting);</b><br><b>SR: ~3-8hr (intermediate-acting)</b><br><b>Short-acting</b> often used as <b>initial</b> Tx in small kids, but bid-tid dosing; <b>Intermediate acting</b> ↑convenience & confidentiality but may ↓evening appetite & ↓sleep<br><b>DI:</b> clonidine <sup>ECG changes/ ? CV risk</sup> ; linezolid & MAOI <sup>↑BP</sup> ; phenobarbital & phenytoin <sup>↑ level</sup> ; sympathomimetic <sup>↑HR &amp; BP</sup> , TCAs <sup>↑ TCA levels</sup> , warfarin <sup>↑ INR</sup> ↓ <b>MPH level</b> : carbamazepine<br><b>M:</b> as in Adderall XR. Also CBC, differential & platelets: periodically long-term Tx<br><b>Consider abuse &amp; diversion risk</b> especially with any short acting stimulant (e.g. children may be targeted for the drug). Take reasonable precautions to ↓ risk (e.g. use of treatment agreement; refrain from informing others, etc.; consider long-acting stimulant or non-stimulant). |  | <b>Peds:</b> IR tab: 5mg qam & qnoon <sup>0.3 mg/kg/day</sup> / <b>10mg tid</b> (60mg/d) Titrate 5-10mg <sup>0.2 mg/kg/day</sup> q7d by adding 4pm dose<br>SR tab: 20mg qam / <b>40mg qam</b> (60mg/d) Titrate 20mg q7d by adding 2pm dose<br><b>Adolescents:</b><br>IR tab: 5mg qam & qnoon / <b>20mg tid</b> (60 mg/d) Titrate 5mg q7d by adding 4pm dose<br>SR tab: 20mg qam / <b>60mg qam</b> (60-80 <sup>CADDRA</sup> mg/d) Titrate 20mg q7d by adding 2pm dose<br><b>Adult:</b><br>IR tab: 10mg qam & qnoon / <b>20mg tid</b> (60-100 <sup>CADDRA</sup> mg/d) Titrate 5-10mg q7d by adding 4pm dose<br>SR tab: 20mg qam / <b>60mg qam</b> (60-100 <sup>CADDRA</sup> mg/d) Titrate 20mg q7d by adding 2pm dose<br>(Combo strategies: e.g. kick start & avoid noon dosing → Ritalin SR qam + small Ritalin IR dose qam; "rebound" → Ritalin SR qam + small Ritalin IR dose late afternoon)<br>(Ritalin no sub is typically \$15-30 more than generics/month; may crumble less when tabs split, but has ↑ street abuse value) |  | 14 / 22 (33)<br><br>17 / 26 (35)<br><br>14 / 33 (33)<br><br>17 / 35 (44)<br><br>17 / 33 (46)<br><br>17 / 35 (54)<br><br>(21-37) |  |
| <b>Precautions:</b> CV disease (HF, MI, ↑BP, QT syndrome) → ↑BP/↑HR, sudden death reported;<br><b>Hx of drug/alcohol dependence</b> → ↑ abuse;<br><b>Psychosis</b> → may worsen Sx; hyperthyroidism<br><b>Seizures/EEG changes</b> → may ↓ seizure threshold;<br><b>Severe depression or normal fatigue</b> → cautious/avoid use.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                 |  |
| <b>Methylphenidate</b><br><b>BIPHENTIN</b> <br>10, 15, 20, 30, 40, 50, 60, 80mg cap<br>Multilayer-release delivery system: 40% immediate, 60% gradual                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  | √ ADHD age ≥ 6yr (somewhat lower cost for once daily)<br><b>Duration: 10-12hr (long-acting).</b> <sup>AAP 11: consider tx if ≥ 4yr.</sup><br>Capsules should be swallowed whole & must never be crushed or chewed. Contents may be sprinkled on these soft foods: apple sauce, ice cream or yogurt.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  | <b>Peds:</b> 10mg qam / <b>30mg qam</b> (60mg/d) Titrate 10mg q7d<br><b>Adolescents:</b><br>10mg qam / <b>40mg qam</b> (60-80 <sup>CADDRA</sup> mg/d) Titrate 10mg q7d<br><b>Adults:</b><br>10mg qam / <b>60mg qam</b> (80 mg/d) Titrate 10mg q7d                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  | 31 / 66 (114)<br><br>31 / 82 (151)<br><br>31 / 114 (151)                                                                        |  |
| <b>Methylphenidate</b><br><b>CONCERTA</b> <br>18, 27, 36, 54mg tab<br>(g: Novo-Methylphenidate ER non-OROS <br>Osmotic release oral system OROS:<br>22% immediate, 78% gradual<br>{SK Formulary: max \$20/Rx for age ≤14yrs.}                                                                                                                                                                                                                                                                                                                                                                                                                        |  | See Methylphenidate above; tablet does not change in shape in GI tract → should not be administered to pts with pre-existing GI narrowing Dx (e.g. small bowel inflammatory dx, "short gut" syndrome, hx of peritonitis, cystic fibrosis, intestinal pseudo-obstruction, or Meckel's diverticulum). <sup>7</sup><br><b>Dose conversion:</b><br>Methylphenidate 5mg bid/tid or 20mg SR od → 18mg qam<br>Methylphenidate 10mg bid/tid or 40mg SR od→ 36mg qam<br>Methylphenidate 15mg bid/tid or 60mg SR od→ 54mg qam<br>(A 27 mg is avail for Drs to prescribe between 18 mg & 36 mg dosages)                                          |  | √ ADHD age ≥ 6yr. <sup>AAP 11: consider tx if ≥ 4yr.</sup><br><b>Duration: 8-12hr (long-acting)</b><br>Swallow whole with liquids; tablet shell may be in stool.<br><b>Non-deformable shell</b> makes it very difficult to break, cut or crush, which may dramatically ↓ its abuse risk<br>(If inadequate immediate effects and/or effects too prolonged esp. at high doses → consider Biphentin)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |  | <b>Peds:</b> 18mg qam / <b>36mg qam</b> (54-72 <sup>CADDRA</sup> mg/d) Titrate 18mg q7d<br><b>Adolescents:</b> 18mg qam / <b>54mg qam</b> (54-90 <sup>CADDRA</sup> mg/d) Titrate 18mg q7d<br><b>Adults:</b> 18mg qam / <b>54mg qam</b> (72-108 <sup>CADDRA</sup> mg/d)Titrate 18mg q7d<br><b>**Full formulary SK since July/08 in effort to ↓ stimulant abuse &amp; diversion**</b><br>To get one responder after 6weeks: Concerta NNT=3 vs Strattera NNT=5 <sup>Newcom 08 n=516</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  | 76 / 98 (119)<br><br>76 / 119 (119)<br><br>76 / 119 (231)<br><br>Generic= ~25% less costly, but unproven clinically.            |  |



NON-STIMULANT (non-controlled)/ SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR: Effect size ~0.6 Atomoxetine ↓core ADHD Sx by at least ~25% in ~65% of pts after 6-12wks of Tx.

CONSIDER IF: non-responsive/CI's to stimulants, potential co-morbid substance abuse, anxiety, tics, <sup>2enuresis 11</sup>; **kids** with low weight/status or stimulant SE (mood lability,tics).

Atomoxetine  Approved 2005

**STRATTERA g**   

10, 18, 25, 40, 60mg cap

(New CDN 80, 100 mg)   USA initially

♦cap **cannot** be opened/sprinkled

[MOA: NE reuptake inhibitor]

{SK: if EDS<sup>2</sup> approved, max \$20/Rx for age ≤14yrs.}

**Common:** Headache ~20%, insomnia 16%, xerostomia>10%, abdominal pain 20%, vomiting ~10%, ↓appetite ~40%, nausea 12%, cough 11%; mild ↑BP ~5% & HR 3%; fatigue 8%, ↓weight 2%, urinary hesitation

{↑risk of vomiting & somnolence 7% vs MPH-IR; but ↓appetite concern. Poor 2D6 metabolizers have higher rates of ↓appetite}

**Serious:** liver toxicity rare, suicidal thinking 0.4%, blackbox warning, sudden death (see below), dyskinesia, seizures peds 0.2%; adults 0.1%, priapism rare

**CI:** MAOI within 14days; narrow angle glaucoma; symptomatic CV Dx; ↑BP; advanced atherosclerosis; uncontrolled hyperthyroidism

✓ADHD age ≥ 6 yrs **Duration: 24hrs (long-acting)**

Swallow capsules whole; do not open (GI irritation)

**DI:** hepatic CYP450 2D6 **metabolism:** 5-10% are poor metabolizers

↑atomoxetine effect: fluoxetine, linezolid, MAOIs, paroxetine, quinidine; salbutamol <sup>↑HR & BP</sup>

**M:** weight, height, BMI; attention, hyperactivity, anxiety, worsening of aggressive behaviour or hostility; BP & HR (baseline & following ↑dose & during Tx), emergence of irritability, agitation, changes in behaviour, & suicidal ideation, esp. during initial months of Tx or if ↑ dosage.

**Peds:** 10mg 0.5mg/kg/d / **25mg qam** 1.2mg/kg/d (Lower of 1.4 mg/kg/d or 60mg/d)

Titrate 0.8mg/kg/d at week 2 & 1.2mg/kg/d at week 4 -slower titration to ↓SE

**Adolescents:** (if patient >70kg, use adult dosing & titration)

18mg 0.5mg/kg/d / **40mg qam** 1.2mg/kg/d (Lower of 1.4mg/kg/d or 100mg/d)

**Titrate 0.8mg/kg/d at week 2 & 1.2mg/kg/d at week 4** -slower titration to ↓SE

**Adults:**

25mg 0.5mg/kg/d / **60-80mg qam** 1.2mg/kg/d (Lower of 100mg/d or 1.4 mg/kg/d)

Titrate 40mg, 60mg, 80mg & max 100mg q14days

(slower titration will ↓SE or divide dose bid; give at **bedtime** may ↓nausea & fatigue)

93 / 116 (144)





105/130(168-264)

(168 <sup>1 cap/264 2 cap</sup>)

116/ 144-250

(144 <sup>1 cap/250 2 cap</sup>)

**Precautions:** **suicidal ideation/clinical worsening** → **↑risk in kids** during first few months of Tx or after ↑dose; behavioral changes eg. aggression & hostility → may be precursor to suicidality; orthostatic hypotension → use cautiously; CV disease (CAD, MI, BP, cardiomyopathy, arrhythmias, QT syndrome)→ risk ↑BP/↑HR & sudden death; jaundice or liver injury → risk of liver failure/transplant; psychotic or bipolar/manic Sx → hallucinations, delusional thinking or mania may emerge.

| Agents <b>WITHOUT</b> Official Indication for ADHD:                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                          |                 |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|--------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Generic / <b>TRADE</b> / form                                                                                                                                                                                                                                                                                 | Role in ADHD                                                                                                                                                                                                                                                                                                                                                                                                             | Adv: Advantages | Dis: Disadvantages | Side effects <b>SE</b> / Drug Interactions <b>DI</b> / Comments                                                                                                                                                                                                                                                                                                                                                                                              | Dose                                                                                                                                                                                                                                                                                                                                                   |
| <b>Bupropion SR</b><br><b>WELLBUTRIN g</b><br>(100,150mg <b>SR</b> tab):<br>(150,300mg <b>XL</b> tab) <br><b>Antidepressant</b> [MOA:↑DA,NE]                                                                                 | Moderately effective for improving the core Sx of ADHD<br><b>Adv:</b> no abuse or diversion risk, not assoc. with rebound hyperactivity, ↓cost, useful in ADHD pts with comorbid depression &/or nicotine use.<br><b>DI's:</b> 2-4 weeks before effects seen; safety in combo with other ADHD meds not proven. Swallow tablets whole with fluids, & <b>not</b> to chew, divide, or crush                                 |                 |                    | <b>SE:</b> insomnia, headache, constipation, N/V, nervousness, dizziness, sweating, ↑BP, ↑HR, tics, <b>suicidal ideation, seizures</b> <sup>0.5-1%</sup> ↑Seizure with IR doses > 400 mg/day.<br><b>DI:</b> CYP2D6/3A4 Inducers e.g., carbamazepine, phenytoin, rifampin may ↓bupropion level & ↑level of hydroxybupropion active metabolite. ↑venlafaxine/TCAs <sup>eg imipramine, desipramine, nortriptyline</sup> levels by bupropion. MAOI ↑serotonin Sx | <b>SR</b> tab: <b>Peds:</b> 3-6 mg/kg/day; single dose not > 150 mg 100-150mg bid 2-3 mg/kg/day, single dose not > 150 mg; max 450mg/d <b>XL</b> tab: <sup>12</sup> Initial: 150mg XL once daily Usual: 150-300mg XL once daily                                                                                                                        |
| <b>Clonidine CATAPRES g</b><br>0.1, 0.2mg tab <br><b>DIXARIL g</b> 0.025 mg tab<br><b>Kapavy XR</b> (0.1,0.2 mg/tab)USA/ADHD                                                                                                 | ↓aggression, impulsivity, ↑arousal & ↑activity, but not benefit: inattention or ↓concentration<br><b>As an adjunct:</b> Used concurrently with stimulants, to target <b>sleep</b> disruptions, <b>conduct</b> issues, aggression, impulsivity, comorbid oppositional defiant disorder & <b>tics</b> . <sup>Kollins 11</sup><br><b>Guanfacine</b> → available through Health Canada's Special Access Program              |                 |                    | <b>SE:</b> ↓BP/HR, sedation & dizziness initially; dry mouth; may ↑depression.<br><b>DI:</b> Avoid use with TCAs. Additive effects with other CNS depressants.<br><b>Caution:</b> CV disease/depression; 2 deaths on MPH & clonidine reported but recent RCT showed clonidine ± MPH to be safe in childhood ADHD <sup>13</sup>                                                                                                                               | <b>Peds:</b> Usual dose in children: 5-8µg/kg/day; may divide dose Initial 0.05-0.1 mg/day often at bedtime Usual dose in adults: 0.05 - 0.4 mg /day                                                                                                                                                                                                   |
| <b>Desipramine</b> [MOA: ↑NE]<br>10,25,50,75,100mg tab<br><b>Imipramine</b><br>10, 25, 50; 75 <sup>X</sup> mg tab<br><b>Nortriptyline</b> 10, 25mg cap<br><b>Tricyclic antidepressants</b>                                                                                                                    | Beneficial in some pts who cannot take stimulants, atomoxetine or bupropion, or if a concurrent tic Dx, enuresis, sleep problems, anxiety or depression.<br><b>Adv:</b> no abuse potential, not associated with rebound hyperactivity <sup>6</sup><br><b>Dis:</b> 3-4 weeks before effects seen, risk of overdose, CV side effects<br>Combos with other ADHD meds can be made but referral to ADHD specialist is advised |                 |                    | <b>SE:</b> sedation, dizziness, constipation, heart block (check ECG), ↑weight, overdose toxicity, ↑HR; sudden death in kids Tx with TCAs reported<br><b>DI</b> see RxFiles Antidepressants DI chart.<br><b>Caution:</b> avoid in pts with hx of cardiac conduction disorder baseline ECG to rule out, urinary retention, seizure disorders or hyperthyroidism.<br><b>Monitor:</b> HR, BP, cardiac exam, weight:baseline→q3-6month while on TCA              | <b>Desipramine</b> 6-12 y: 10-20 mg/day; <b>adolescent:</b> 30-50 mg/day; (Peds: 2-5 mg/kg/day; Adult dose: 100-300 mg/day).<br><b>Imipramine</b> 6-12 y: 10-20mg/day; <b>adolescent:</b> 30-50 mg/day; max 150 mg/day) (may divide dose)<br><b>Nortriptyline</b> 6-12 y: 10-20mg/day; <b>adolescent:</b> 30-50mg/day; max 150mg/day (may divide dose) |
| <b>Risperidone RISPEDAL g</b><br>(0.25,0.5 <sup>1</sup> , 1.2 <sup>3</sup> ,3 <sup>4</sup> ,4 <sup>5</sup> mg tab; (Depot not used for ADHD)<br><b>M-TAB</b> melts 0.5,1,2,3,4 mg tab:<br>1mg/ml soln;  <b>Antipsychotic</b> | Systematic review: lack of quality evidence. <sup>15</sup> Little effect on inattention.<br>As an adjunct: <sup>1</sup> to target <b>aggressive</b> , ↑impulsive or if hyperactive when stimulants alone are ineffective/not tolerated; to ↓behaviours in kids with comorbid conduct Dx, <b>oppositional</b> defiant Dx, autistic Dx, impulse control Dx & Tourette's Sx. May ↑ compliance                               |                 |                    | <b>SE:</b> Weight gain, drowsiness, headache, orthostatic hypotension, dyspepsia, dose-related extrapyramidal effects; hyperprolactinemia, may negatively affect cognition in pts with ADHD                                                                                                                                                                                                                                                                  | Initial: 0.25-0.5mg hs; ↑weekly by 0.5 mg/day Usual maintenance dose 0.75-1.5 mg/day                                                                                                                                                                                                                                                                   |
| <b>Modafinil ALERTEC g</b> <sup>4</sup><br>100mg tab  (Provigil in US)<br>CNS stimulant; also ↑glutamate                                                                                                                     | For narcolepsy, but some evidence modafinil is superior to placebo in ↓core ADHD Sx <sup>kids adults</sup><br><b>Adv:</b> mild abuse potential; samples avail. & anecdotally a weaker stimulant effect & ↓SE's<br><b>Dis:</b> <b>serious skin rx</b> ; not ADHD approved; <b>SE</b> when combined with stimulants e.g. ↑BP                                                                                               |                 |                    | <b>SE:</b> headache, nausea, rhinitis & anxiety & rare psychiatric Sx<br><b>Caution:</b> Serious skin reaction, including erythema multiforme, hallucinations<br><b>Stevens-Johnson syndrome</b> , & toxic epidermal necrolysis reported <sup>16</sup>                                                                                                                                                                                                       | Adult: 100mg bid \$70/month; max 400mg/day<br><br>non-controlled substance                                                                                                                                                                                                                                                                             |

♦=dose for renal dysfx c=scored tab x=Non-formaldehyde Sack =Exception Drug Status Sack ≠not covered by NIHB ◊=prior approval for NIHB ac=before meals **BMI**=body mass index **BP**=blood pressure cc=with meal CGI=Clinical Global Impression scale  
CV=cardiovascular disease **CI**=contraindication **DA**=dopamine **DI**=drug interaction **DF**=heart failure **HR**=heart rate ht=height **IR**=immediate release **MI** monitor MAOI=monoamine oxidase inhibitor **MI**=myocardial infarction **MOA**=mechanism of action  
MPH=methylphenidate **NE**=norepinephrine **PI**=patient **Rx**=reactions **SNAP-IV**=revised version of Swanson, Nolan & Pelham Questionnaire **SR**=sustained release **Sx**=symptoms **SE**=side effect **Tx**=treatment **wt**=weight \* MAX dose listed in 2007-08 Canadian ADHD Guidelines, which may differ from product monograph <sup>†</sup> Psychostimulants are used with precaution in tic spectrum disorders but the Canadian guidelines committee agrees that use can be indicated if ADHD symptoms warrant treatment. Medications for ADHD may be combined with other drugs for tics.<sup>4</sup>

**PREVALENCE:** worldwide prevalence 5% <sup>17</sup>; 3-7% of children<sup>18</sup>, 4% of adults <sup>4</sup>; boys > girls (9:1 to 2.5:1)<sup>10</sup>

**SYMPTOMS:** Core Sx: inattention, hyperactivity, impulsiveness. **Other:** impaired behavioural, cognitive, academic, emotion &/or social.

**COMORBID/ RESEMBLING CONDITIONS:** age-appropriate behaviour, mental retardation, understimulating environments, learning disabilities; disorders {conduct, oppositional defiant, stereotypic movement, mood (e.g. bipolar), anxiety, personality (e.g. narcissistic, antisocial, borderline, passive-aggressive personality), substance-related, pervasive developmental, psychotic, depression, of impulse control}; chronic fatigue, fetal alcohol syndrome, hyper- or hypothyroidism, drug/substance-induced (see below), OCD, pathological gambling, pheochromocytoma, PTSD, seizure, situational disturbances, Tourette's<sup>19-20</sup>

**DRUG/SUBSTANCE-INDUCED:** anticonvulsants, antihistamines, bronchodilators, caffeineism, decongestants, isoniazid, lead poisoning, mercury, neuroleptics (from akathisia), nicotine, phenobarbital, phenytoin, steroids <sup>21-22</sup>

**DIAGNOSIS:**<sup>23</sup> a) **Inattentive subtype** (10-20%): ≥ 6 (of 9) inattentive Sx: inattention to details/makes careless mistakes, difficulty sustaining attention, seem not to listen, fail to finish tasks, difficulty organizing, avoid tasks requiring sustained attention, lose things, easily distracted, forgetful;

b) **hyperactive-impulsive subtype** (5-10%): ≥ 6 (of 9) hyperactive-impulsive Sx: fidgety, unable to stay seated, inappropriate running/climbing, difficulty engaging in leisure activities quietly, "on the go", talks excessively, blurt out answers before question finished, difficulty waiting turn, interrupt/intrude others;

c) **combined subtype** (70-80%): if criteria met for both inattentive & hyperactive-impulsive subtypes. **ADHD Sx must:** persist for ≥ 6-9 AAP 11 if preschool months, present prior to age 7, & present in ≥ 1 setting. **Significant impairment** in social, academic or occupational fx. Sx not explained by another mental dx.

**Screening** <sup>age 4-18yr</sup> **Tools:** SNAP-IV, T-CAPS, Weiss Symptom Screen, Weiss Functional Impairment Rating Scale; psychoeducational testing. **Tools:** <http://www.caddra.ca/> **Tx GOAL:** ↓core Sx; improve behaviour, academic, social & self-esteem; minimize med SE

**NON-DRUG Interventions:** behavioural therapy may be considered: for milder ADHD; when psychosocial Tx preferred; in preschool-age children; & adult ADHD<sup>24-25</sup> In kids with ADHD & comorbid dx, behavioural therapy alone was less effective than meds alone in ↓ADHD core Sx.<sup>26</sup> Combined medication & behavioural Tx do not offer substantial improvement over meds alone in ↓ADHD Sx, but may add benefit for some non-ADHD Sx areas <sup>27-28-29-30</sup>; (eg. parent training, contingency management, daily school report cards) **environmental interventions**, e.g adherence to regular daily schedules, structured home & school settings, sitting at the front of the classroom, using white noise during homework time; role for academic remediation, social skills training, etc.; **diet modifications** has limited anecdotal evidence supporting benefits but ↓food additives, preservatives (eg. sodium benzoate) & food colourings may be useful if true sensitivities or supplement fatty acids; **complementary & alternative medicine** lack evidence:<sup>31</sup> natural health products (St. John's Wort, chamomile, melatonin, valerian for calming/sedating; others: blue-green algae, B vitamins, pycnogenol, omega-3), homeopathy, neurofeedback, hypnosis.

**CARDIAC Risk:** 45 deaths (31 kids, 14 adults), Jan 1992 to Feb 2005, related to stimulants or atomoxetine.<sup>32</sup> But the rate of sudden death in those taking psychostimulants or atomoxetine did not exceed the background rate.<sup>33</sup> Pts with known CV diseases should not be prescribed these drugs.<sup>34</sup> AHA cardiovascular guidelines suggest: prior to initiation of Tx to 1) chance of identifying CV conditions: i) pt & family history, ii) physical examination, & iii) ECG, read by a Dr with expertise in pediatric ECGs. Consult pediatric cardiology if significant finding.<sup>35</sup> Routine ECG **not** necessary AAP 08<sup>CCS & CPS09</sup>.

**PSYCHIATRIC Risk:** **Suicidal thinking** atomoxetine 0.4%; <sup>35</sup> Canadian cases reported. Although risk is small, it should be discussed with pts & family, & kids should be monitored for this esp. in the first few months of Tx.<sup>5</sup> **Aggression/emotional lability:** Stimulants & atomoxetine trials show not ↑aggression <sup>5 36</sup>. Clinicians should distinguish between aggression/ emotional lability that is present when the stimulant is active & ↑hyperactivity/impulsivity in the evening when the stimulant is no longer effective.<sup>5</sup> Note: oppositional-defiant Sx usually decrease with therapy.

**GROWTH Suppression Risk:** Stimulant Tx may be assoc. with a ↓in height, at least in the first 1-3 yrs of Tx.<sup>37</sup> One study had ↓growth rates after 3yrs of stimulant Tx compared to those with no meds (average growth of 2 cm & 2.7 kg less than non-med subgroup).<sup>38-39</sup> Most kids achieve a satisfactory adult height but some growth may be permanently attenuated. Monitor: ht, wt & BMI at baseline & 1-2 times/yr during Tx. If pt has a change in height, weight or BMI that crosses two percentile lines, a **drug holiday** during summer & breaks or consider switching to an alternative med.<sup>5</sup>

**MISUSE/DIVERSION:** Lifetime diversion rates: 16-29% of students with stimulant scripts asked to give, sell, or trade their meds.<sup>40</sup> Strategies to ↓risk → see ADHD Newsletter/Treatment Agreement. Stimulant Tx does not appear to ↑risk for substance use Dx. Proper Tx may ↓risk.<sup>41,42,43</sup> Other Strategies: 1) Educate patient/family: *handle medication like you would your wallet!!!*; 2) Refrain from informing others about being on the drug; 3) Remove labels when discarding; 4) Use random pill counts; 5) Weekly dispensing; 6) School program & collaboration; 7) Non-Ritalin options. 8) ...

**SE MANAGEMENT:** <sup>4,6,44</sup> headaches → acetaminophen; usually ↓after meds used for 1-3 weeks; divide dose ↓appetite → give med with meals; give high-calorie meals when stimulant effects are low (breakfast, bedtime); supplemental Boost, Ensure; engage child in meal prep & shopping for favourite foods; manage drug-induced dry mouth → ↑fluids intake; rebound appetite in the evening → spread out supper into 2 or 3 session to prevent GI distress; ↓dose &/or titrate dose slowly; insomnia → optimal sleep hygiene; give doses earlier in the day; avoid stimulant dose after 2 pm if possible, change to shorter-acting meds; ↓noon or afternoon stimulant dose; consider clonidine, trazodone, an antihistamine, or melatonin 3-6 mg ½ hr before bedtime; others: benzos, TCAs, atypical antipsychotics; tics → switch stimulant or switch to a non-stimulant; add clonidine or an atypical antipsychotic; irritability → ↓dose; adjust longer-acting meds; assess for Sx of comorbid conditions ; rebound hyperactivity → Overlap stimulant dosing pattern, switch to longer-acting stimulant, combine IR with SR forms, or add other meds; switch to a non-stimulant.

**Pregnancy:** Dextroamphetamine has the most evidence (low birth weight, but no known teratogenicity). Limited data on methylphenidate & atomoxetine. Taper if mother wishes to discontinue medication during pregnancy and/or lactation.<sup>45</sup>

**In USA:** Dexamethylphenidate: **Focalin** (2.5,5,10mg cap, XR 5,10,15,20,25,30,35,40mg cap); Methylphenidate: **Methylin** 5,10,20mg tab, susp; **Methylin ER** 10,20mg tab; **Metadate ER** 10,20mg tab; **Metadate CD** 10,20,30,40,50,60mg cap can open & sprinkle; **Ritalin LA** 10,20,30,40mg cap; **Daytrana Patch** 10,15,20,30mg; **Adderall** 5,7.5,10,12.5,20,30mg tab; Dextroamphetamine: **Dextrostat** 5,10mg tab; **Mekinet**, Modafinil: **Sparlon** (Skin rx (SJS) → Cephalexin **not** pursue ADHD indication), Guanfacine: **Intuniv** <sup>FDA-SNAP-Age 6yrs</sup> 1mg tab, **Tenex** 1,2mg tab <sup>(FDA-ADHD pending)</sup>; Methamphetamine: **Desoxyn** 5mg tab (Biovail: Canadian approval *Altenade*® - not yet marketed); **Quilivant XR** 20%IR & 80% ER sus

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