Shared Care Guidelines for Methylphenidate, Dexamfetamine, Atomoxetine, Lisdexamfetamine and Guanfacine for Attention Deficit Hyperactivity Disorder (ADHD) in Children, Adolescents and Adults

Sharing of care assumes communication between the specialist, General Practitioner (GP), patient and other members of the care team including pharmacists. The intention of shared care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

ADHD is a neurodevelopmental condition which manifests as cognitive and behavioural deficits. It is characterised by core symptoms of hyperactivity, impulsivity and inattention. ADHD is thought to be a persistent condition and so a diagnosis of ADHD should only be made by a specialist professional with training and expertise in the diagnosis of ADHD. Drug treatments for ADHD only form **ONE** part of a comprehensive treatment programme that focuses on psychological, behavioural, educational and / or occupational needs.

SHARED CARE CRITERIA

- Prescribing responsibility will only be transferred when it is agreed by the specialist and the GP that the patient's condition is reasonably predictable and the treatment regimen has been specified.
- The specialist will continue to provide prescriptions until there has been a successful transfer of the responsibilities as outlined below.
- The patient will be commenced and stabilised on treatment prior to referral to the GP for shared care.
- Referral of the patient to the GP will be subject to the GP's agreement. If the GP is not confident to undertake this role, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient remains with the specialist.
- The patient, on discharge, will be supplied sufficient quantity of the medicine(s) for up to 4 weeks which is to be continued by the GP.

AREAS OF RESPONSIBILITY

GP responsibilities	Specialist service responsibilities
1. Initial referral to specialist raising possibility of ADHD. 2. Provide medical history and perform physical examination if requested. 3. Prescribe by brand name as advised by specialist for modified-release (M/R) preparations. 4. Adjust the dose, (if needed), as advised by specialist and provide repeat prescriptions. 5. Confirm adherence to treatment and monitor for signs of diversion or misuse (e.g. by checking intervals between prescriptions). 6. Report to and seek advice from the specialist any aspect of patient care that is of concern or may affect treatment. 7. Refer patient to specialist if their condition deteriorates. 8. Stop treatment on advice of specialist, (possibly immediately), if an urgent need arises. 9. Report any adverse events to specialist and also on the MHRA Yellow Card scheme. 10. Routine monitoring will be carried out by the specialist service. However, any opportunistic finding the GP considers to be relevant should be referred to specialist service.	1. Inform parents and patients or carers, if using medication outside licensed indications. 2. Discuss benefits and side effects of treatment with patient or carer. In particular stomach pain, nausea, dark urine & jaundice (possibly indicating hepatic disorder) and also suicidal thoughts or self-harming behaviour. 3. Risk assess for diversion and misuse. 4. Assess medical history particularly cardiovascular or convulsive episodes, thyroid disorders, mental health issues and current medications. 5. Initiate treatment taking all of the above into account as well as cost. 6. Initiate prescriptions, titrating the dose against symptoms and side effects until dose optimisation is achieved. Speed of titration depends on pre-existing conditions. 7. Communicate the brand name required for prescribing for MR preparations. 8. Send a letter to GP stating diagnosis and asking if they are prepared to participate in shared care once dose is stable. 9. If GP accepts, do not continue to prescribe. This is to minimise risk of miscommunication and script duplication. 10. Communicate promptly with GP if treatment changes or patient defaults attending clinic. 11. Review patient regularly, with an annual review of medications and communicate this to GP in accordance with NICE. 12. Have a mechanism in place to receive a rapid referral from a GP in the event of rapidly deteriorating clinical condition. 13. Ensure that clear backup arrangements exist for GPs to obtain advice and support. 14. Measure baseline height, (under 18 only), pulse & blood pressure (BP). 15. Examination of cardiovascular system; refer to cardiologist if there any significant concerns.

	16. Arrange an ECG if intended medication may affect the QTc interval. 17. Monitor for onset or exacerbation of motor and verbal tics, worsening behavior or sleep pattern. 18. Monitor for the development or worsening of psychiatric disorders. 19. Review and possibly stop any ADHD treatment that could be contributing to a patient developing new or worsening seizures. Consider cautious re-introduction if later found to be an unlikely cause. 20. In children & young adults where BP is consistently above 95th centile for height & age, refer to paediatric cardiologist. 21. Monitor for sexual dysfunction with atomoxetine. 22. Monitor for orthostatic hypotension or fainting episodes in patients on guanfacine. If they occur reduce the dose or switch to another medication.

Patient and / or carer responsibilities

1. Report any adverse effects.
2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Share any concerns in relation to treatment with any of the drugs listed in this protocol.
4. Inform specialist or GP of any other medication being taken, including over-the-counter products.
5. Co-operate with any monitoring requested by specialist or GP.
6. Order repeat medication in a timely manner and store supplies safely, (liaising with school where necessary).
7. Attend all appointments requested by specialist or GP.

MEDICATION COVERED BY THE AGREEMENT

For full details please see NICE NG 87, SPCs for individual drugs & BNFC/BNF	
Stimulants : methylphenidate, dexamfetamine & lisdexamfetamine All are Schedule 2 Controlled Drugs and prescription requirements should be followed Licensed for use in ADHD in children	
Methylphenidate *NB This is not a complete list of all methylphenidate products*	**Tablets** 5mg, 10mg, 20mg **Tablets M/R** – 18mg, 27mg, 36mg & 54mg (Concerta XL®, Xaggitin XL®) Licensed max. dose is 54mg once daily, higher doses only under direction of specialist to maximum 108mg per day. Duration of action: 12 hours. Prescribe Xaggitin XL® in new patients. Concerta XL® may be continued in existing patients but consider switching at the next review appointment. **Capsules M/R** 10mg, 20mg, 30mg (Equasym XL®) Licensed max. dose is 60mg daily, increased to higher dose only under direction of specialist to maximum 90mg per day. Duration of action: 8 hours. **Capsules M/R** 5mg, 10mg, 20mg, 30mg, 40mg, 50 & 60mg (Medikinet XL®) Licensed max. dose is 60mg daily, increased to higher dose only under direction of specialist to maximum 90mg per day. Duration of action: 8 hours. ***Information on Modified Release:*** The ratio of immediate to extended release methylphenidate varies between products affecting bioavailability. However**,** Concerta XL® & Xaggitin XL® are bioequivalent and can be interchanged. **Worcestershire APC approved Xaggitin XL® in May 2017 and it was agreed that patients on Concerta XL® will be switched to Xaggitin XL®.**
Dose and administration *NB Treatment may be started using a modified-release preparation at any age.*	**Child 4-5 years:** Initially 2.5 mg twice daily, increased in steps of 2.5 mg daily if required, at weekly intervals, increased if necessary up to 1.4 mg/kg daily in 2 to 3 divided doses, discontinue if no response after one month. **Child 6–18 years:** Standard release formulation: Initially 5 mg 1–2 times daily, increased if necessary at weekly intervals by 5–10 mg daily; licensed max. 60 mg daily in 2–3 divided doses but may be increased to 2.1 mg/kg daily in 2–3 divided doses (max. 90 mg daily) under the direction of a specialist. Discontinue if no response after 1 month. Evening dose: If effect wears off in evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose). **Dosing schedules for the individual preparations should be consulted.** **Refer to SPCs or BNFC for dosing schedules.** Administration

	Contents of Equasym XL® capsules and **Medikinet XL®** capsules can be sprinkled on a tablespoon of apple sauce and then swallowed immediately without chewing. Then patients should take a drink. **Concerta XL® -** tablet membrane can pass through Gastrointestinal (GI) tract unchanged. Dose form not appropriate for dysphagia or if GI lumen is restricted. **Concerta XL® and Xaggitin XL®** must be swallowed whole with the aid of liquids and must not be chewed, divided or crushed. **Adult:** Initially 5 mg 2 to 3 times a day increased if necessary at weekly intervals according to response to a maximum of 100 mg daily in two or three divided doses. If effect wears off in the evening with rebound hyperactivity dose at bedtime may be appropriate.
Dexamfetamine	**Tablets -** (generic manufacturers) 5mg, 10mg and 20mg Tablets. Tablets may be halved. **Liquid -** Dexamfetamine sulfate 5mg/5ml oral solution S/F is available from Martindale (unlicensed for treatment of ADHD)
Dose and administration	**Child 6–17 years** initially 2.5mg, 2 – 3 times a day, increasing if necessary by weekly increments of 5mg in the daily dose, according to tolerability and degree of efficacy observed – usually this should at least weekly intervals; usual max. 1 mg/kg daily, up to 20 mg (40 mg daily has been required in some children). Maintenance dose given in 2–4 divided doses. **Adult** Initially 10 mg daily in divided doses, increased in steps of 10 mg every week, maintenance dose to be given in 2 to 4 divided doses; maximum 60 mg per day.
Lisdexamfetamine	**Capsules** 20mg, 30mg, 40mg, 50mg, 60mg and 70mg
Dose and administration	**Age 6 upwards** 30mg taken once daily in the morning. If clinically appropriate begin treatment with 20 mg once daily in the morning. The dose may be increased by 10 or 20 mg increments, at approximately weekly intervals. Administered at the lowest effective dosage. Discontinue if response insufficient after 1 month; maximum 70 mg per day. Lisdexamfetamine may be taken with or without food. It may be swallowed whole, or the capsule opened and the entire contents emptied and mixed with a soft food such as yogurt or in a glass of water or orange juice. If the contents include any compacted powder, a spoon may be used to break apart the powder in the soft food or liquid. The contents should be stirred until completely dispersed. The patient should consume the entire mixture of soft food or liquid immediately; it should not be stored. The active ingredient dissolves completely once dispersed; however, a film containing the inactive ingredients may remain in the glass or container once the mixture is consumed. Afternoon doses should generally be avoided because of the potential for insomnia although If effect wears off in evening (with rebound hyperactivity) a dose of dexamfetamine at bedtime may be appropriate (establish need with trial bedtime dose).
Non-Stimulants : Atomoxetine & Guanfacine These are not Controlled Drugs and are licensed for use in ADHD as described below.	
Atomoxetine	**Capsules** 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg **Liquid** 4mg/ml NB. Liquid approved for patients with more complex needs; e.g. younger patients and those with swallowing difficulties
Dose and administration *NB: Atomoxetine oral solution should only be prescribed when patients are unable to take tablets/capsules whole*	**Child over 6 years body-weight under 70 kg**: Initially 500 micrograms/kg daily for 7 days, increased according to response. Usual maintenance 1.2 mg/kg daily but may be increased to 1.8 mg/kg daily (max. 120 mg daily) under the direction of a specialist. **Child/Adolescent body-weight over 70 kg**: Initially 40 mg daily for 7 days, increased according to response. Usual maintenance 80 mg daily but may be increased to a maximum recommended total daily dose 120mg under the direction of a specialist. Dose generally needs to increase as children grow - indicated when there is loss of control of symptoms. **Doses above 100mg daily are not licensed but are stated in the BNF for Children.** Total daily dose may be given either as a single dose in the morning or in 2 divided doses with last dose no later than early evening. Halve dose in moderate hepatic impairment, quarter dose in severe hepatic impairment. **Adults:** Dose by weight as for children above

<table>
<tr><td>Guanfacine</td><td>Tablets 1mg, 2 mg, 3mg, 4 mg prolonged-release tablets</td></tr>
<tr><td>Dose and administration

NB: Children only; NOT for adults</td><td>
<table>
<tr><td></td><td>6–12 years</td><td colspan="4">13–17 years</td></tr>
<tr><td></td><td>(>25 kg)</td><td>(34–41.4 kg)</td><td>(41.5–49.4 kg)</td><td>(49.5–58.4 kg)</td><td>>58.5kg</td></tr>
<tr><td>Initiation</td><td colspan="5">1 mg once daily; adjusted in steps of 1 mg every week if necessary and if tolerated</td></tr>
<tr><td>Maintenance</td><td colspan="5">0.05–0.12 mg/kg once daily</td></tr>
<tr><td>Maximum dose</td><td>4 mg</td><td>4 mg</td><td>5 mg</td><td>6 mg</td><td>7mg</td></tr>
<tr><td colspan="6">For optimal weight-adjusted dose titrations, consult product literature.http://www.medicines.org.uk/emc/medicine/31294</td></tr>
</table>
</td></tr>
<tr><td colspan="2">Common adverse effects - See SPC and BNFC/BNF for full details</td></tr>
<tr><td>Methylphenidate
Dexamfetamine
Lisdexamfetamine</td><td>Decreased appetite, weight loss, growth retardation, insomnia, mood changes, headache, dizziness, drowsiness, tachycardia, increased BP, cough, gastrointestinal side effects, rashes, delusions, hallucinations, anxiety, panic, stimulant related tics, sexual dysfunction.</td></tr>
<tr><td>Atomoxetine</td><td>Emergence of suicidal behaviour, self-harm or hostility; serious liver damage; weight loss, drowsiness, increased heart rate and BP, dysmenorrhoea, sexual dysfunction</td></tr>
<tr><td>Guanfacine</td><td>Bradycardia, hypotension, somnolence, sedation, weight increase, depression, anxiety, mood lability, nightmares, enuresis, dry mouth; less commonly dyspepsia, tachycardia, sinus arrhythmia, first-degree AV block, syncope, chest pain, convulsion, agitation, hallucination, pollakiuria, pallor, pruritus; rarely hypertension, hypersomnia; also reported suicidal ideation.</td></tr>
<tr><td colspan="2">Potentially serious drug interactions</td></tr>
<tr><td>Stimulants</td><td>▪ Enhance anticoagulant effect of warfarin
▪ Can increase the plasma levels of some anticonvulsants (phenytoin, primidone, phenobarbitone) and tricyclic antidepressants
▪ Can exacerbate CNS adverse effects of alcohol (abstention advised)
▪ Concurrent use of methylphenidate with atomoxetine or guanfacine does not appear to increase adverse effects of either drug
▪ Use of clonidine may result in an increased duration of action of dexamfetamine
▪ Monoamine oxidase inhibitors (MAOIs) - amfetamines should not be administered during or within 14 days following the administration of MAOIs as they may precipitate hypertensive crisis
▪ Antihypertensives – stimulants may reduce effectiveness
▪ Amfetamines potentiate the analgesic effect of narcotic analgesics
▪ Effect of stimulants can be decreased by: beta-blockers (e.g. propranolol), lithium and phenothiazines
▪ Concurrent use of beta-blockers may result in severe hypertension
▪ Concurrent use of tricyclic antidepressants may increase risk of cardiovascular side effects</td></tr>
<tr><td><u>Atomoxetine</u></td><td>▪ Atomoxetine should not be used with MAOIs
▪ SSRIs (e.g., fluoxetine, paroxetine) can increase atomoxetine levels
▪ High dose nebulised or systemically administered salbutamol (or other beta$_2$ agonists) may potentiate cardiovascular effects
▪ Potential increased risk of QT interval prolongation when atomoxetine is administered with other QT prolonging drugs (e.g. neuroleptics, class IA and III anti-arrhythmics, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium)
Increased risk of seizures with drugs known to lower the seizure threshold (e.g. tricyclic antidepressants or SSRIs, neuroleptics, phenothiazines or butyrophenone, mefloquine, chloroquine, bupropion or tramadol) or when stopping concomitant treatment with benzodiazepines
▪ Atomoxetine may decrease the effectiveness of anti-hypertensive drugs
▪ Possible additive effects when used with drugs that affect noradrenaline; e.g. antidepressants (imipramine, venlafaxine, and mirtazapine) or decongestants (pseudoephedrine or phenylephrine)</td></tr>
</table>

Guanfacine	▪ As guanfacine may reduce heart rate use with drugs that may prolong the QT interval should be avoided ▪ Co-administration of guanfacine with moderate and strong CYP3A4/5 inhibitors elevates plasma guanfacine concentrations and increases the risk of adverse reactions such as hypotension, bradycardia, and sedation; (e.g. ciprofloxacin, clarithromycin, erythromycin, fluconazole, grapefruit juice) ▪ CYP3A4 inducers may reduce guanfacine levels (e.g. carbamazepine, phenobarbital, phenytoin, primidone, rifampicin) ▪ Guanfacine can increase levels of valproic acid (valproate) ▪ Potential for additive pharmacodynamic effects such as hypotension and syncope if given with antihypertensives ▪ Potential for additive pharmacodynamic effects such as sedation and somnolence with CNS depressants (e.g., alcohol, sedatives, hypnotics, benzodiazepines, barbiturates, and antipsychotics)
Contraindications/Cautions For all preparations - Hypersensitivity to the active substance or to any of the excipients (see SPC for full details)	

Stimulants	• Known intolerance of sympathomimetic amines or product excipients
	• Marked anxiety, agitation, tension or psychosis, poorly controlled Bipolar Affective Disorder or psychopathic/borderline personality disorder
	• Severe depression, anorexia/anorexic disorders
	• Suicidal ideation
	• History of drug or alcohol abuse
	• Glaucoma
	• Hyperthyroidism or thyrotoxicosis
	• Structural cardiac abnormalities
	• Current or recent (within 14 days) treatment with MAOI's
	• *Some cardiovascular disease – including hypertension
	• Motor tics, or family history of Tourette's syndrome
	• Phaeocromocytoma
	• *Although listed as contraindications, in some circumstances, methylphenidate can be used with caution and careful monitoring by the specialist
	• Use with caution in:-
	  • If a person with ADHD develops new seizures or a worsening of existing seizures, review their ADHD medications and stop any medication that might be contributing to the seizures. After investigation, cautiously reintroduce ADHD medications if it is unlikely to be the cause of the seizures.
	  • Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Atomoxetine	• Patients on MAOIs (or within 2 weeks after discontinuing therapy with a MAOI) • Severe cardiovascular disease, severe cerebrovascular disease • QT-interval prolongation, aggressive behaviour, cardiovascular disease, cerebrovascular disease, emotional lability, history of seizures, hostility, hypertension, mania, psychosis, structural cardiac abnormalities, susceptibility to angle-closure glaucoma, tachycardia.
Guanfacine	• Hypotension, heart block, bradycardia, or cardiovascular disease, syncope or a predisposition to syncope (such as hypotension, orthostatic hypotension, bradycardia, or dehydration). • Concomitant antihypertensive or medicines that can reduce BP or heart rate or increase the risk of syncope. • Patients should be advised to drink plenty of fluid. • QTC interval caution patients with a known history of QT prolongation, risk factors for torsade de pointes (e.g., heart block, bradycardia, hypokalaemia) or patients who are taking medicinal products known to prolong the QT interval. These patients should receive further cardiac evaluation based on clinical judgement. • Sedation and somnolence - Concomitant use with centrally active depressants (such as alcohol, sedatives, phenothiazines, barbiturates, or benzodiazepines) consider the potential for additive sedative effects. • Alcohol - Patients should not drink alcohol whilst taking guanfacine. • Suicidal ideation – monitor for suicidal ideation or behaviour • Effects on height, weight and Body Mass index (BMI) as increases in the later may occur.

Therapy Choices

Drug treatments for ADHD only form **ONE** part of a comprehensive treatment programme that focuses on psychological, behavioural, educational and / or occupational needs.

Medication choice – Children aged 5 years to 18 years. See Figure 1

1. Offer methylphenidate (either short or long acting) as the first line pharmacological treatment for children aged 5 years and over and young people with ADHD.
2. Consider switching to lisdexamfetamine for children aged 6 years and over and young people who have had a 6-week trial of methylphenidate at an adequate dose without sufficient benefit.
3. Lisdexamfetamine may be appropriate first choice if patient cannot swallow tablets/tolerate opened capsules.
4. Consider dexamfetamine for children aged 6 years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile.
5. Offer atomoxetine or guanfacine to children aged 6 years and over and young people if a) they cannot tolerate methylphenidate or lisdexamfetamine **or** b) their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.

Medication choice – Adults. See Figure 2

1. Offer lisdexamfetamine or methylphenidate as first-line pharmacological treatment for adults with ADHD.
2. Consider switching to lisdexamfetamine for adults who have had a 6-week trial of methylphenidate at an adequate dose but have not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.
3. Consider switching to methylphenidate for adults who have had a 6-week trial of lisdexamfetamine at an adequate dose but have not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.
4. Consider dexamfetamine for adults whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile.
5. Offer atomoxetine to adults if a) they cannot tolerate lisdexamfetamine or methylphenidate **or** b) their symptoms have not responded to separate 6-week trials of lisdexamfetamine or methylphenidate, having considered alternative formulations and doses

Considerations when prescribing ADHD medication

- When prescribing medication for ADHD, think about modified-release once-daily preparations for convenience, improving adherence, reducing stigma (because there is no need to take medication at school or in the workplace), reducing problems of storing and administering controlled drugs at school, and the risk of stimulant misuse and diversion with immediate-release preparations
- Consider pharmacokinetic profiles especially long acting methylphenidate preparations
- Immediate-release preparations may be suitable if more flexible dosing regimens are needed, or during initial titration to determine correct dosing levels

Contact Details

Worcestershire Community Paediatric Service. Covercroft, Coleman Rd., Droitwich, Worcestershire WR9 8QU
TEL: 01905 681071.
NB These details apply for all of the Worcestershire localities. If you wish to speak to a particular specialist you will be advised how they can be reached.

REFERENCES

1. NICE Guideline 87; Attention Deficit Hyperactivity Disorder: diagnosis and management; March 2018.
2. North of Tyne & Gateshead APC Shared Care Guidelines for children and young people with ADHD June 2018
3. Derbyshire JAPC Shared Care Agreement for Children & Adults with ADHD Sept 2018
4. Leicestershire MSG SCA for Children & Adolescents March 2018 (also covers transition to adult care).
5. BNF – September 2018. https://www.medicinescomplete.com/mc/bnf/current/
6. eMC medicines compendium of SpCs

Figure 1
Medication Choice: Children aged 5 to 18 years

STEP 1: FIRST LINE pharmacological treatment is **methylphenidate** (short or long acting). Note: Risk of appetite suppression. Best results from ensuring regimen is bespoke

If good response, titrate and transfer to GP for shared care and continued prescribing.

If ADHD symptoms are NOT reduced after a six week trial at an adequate dose then proceed to Step 2.

STEP 2: SECOND LINE pharmacological treatment is **lisdexamfetamine** for those with inadequate control on methylphenidate

If good response, transfer to GP for shared care and continued prescribing.

For those whose ADHD symptoms are NOT responding to lisdexamfetamine OR they cannot tolerate it (or methylphenidate) then proceed to Step 4: atomoxetine or guanfacine

For those whose ADHD symptoms ARE responding to lisdexamfetamine but cannot tolerate the longer effect profile then proceed to Step 3: Dexamfetamine

STEP 3: THIRD LINE **Dexamfetamine**

If good response, titrate and transfer to GP for shared care and continued prescribing.

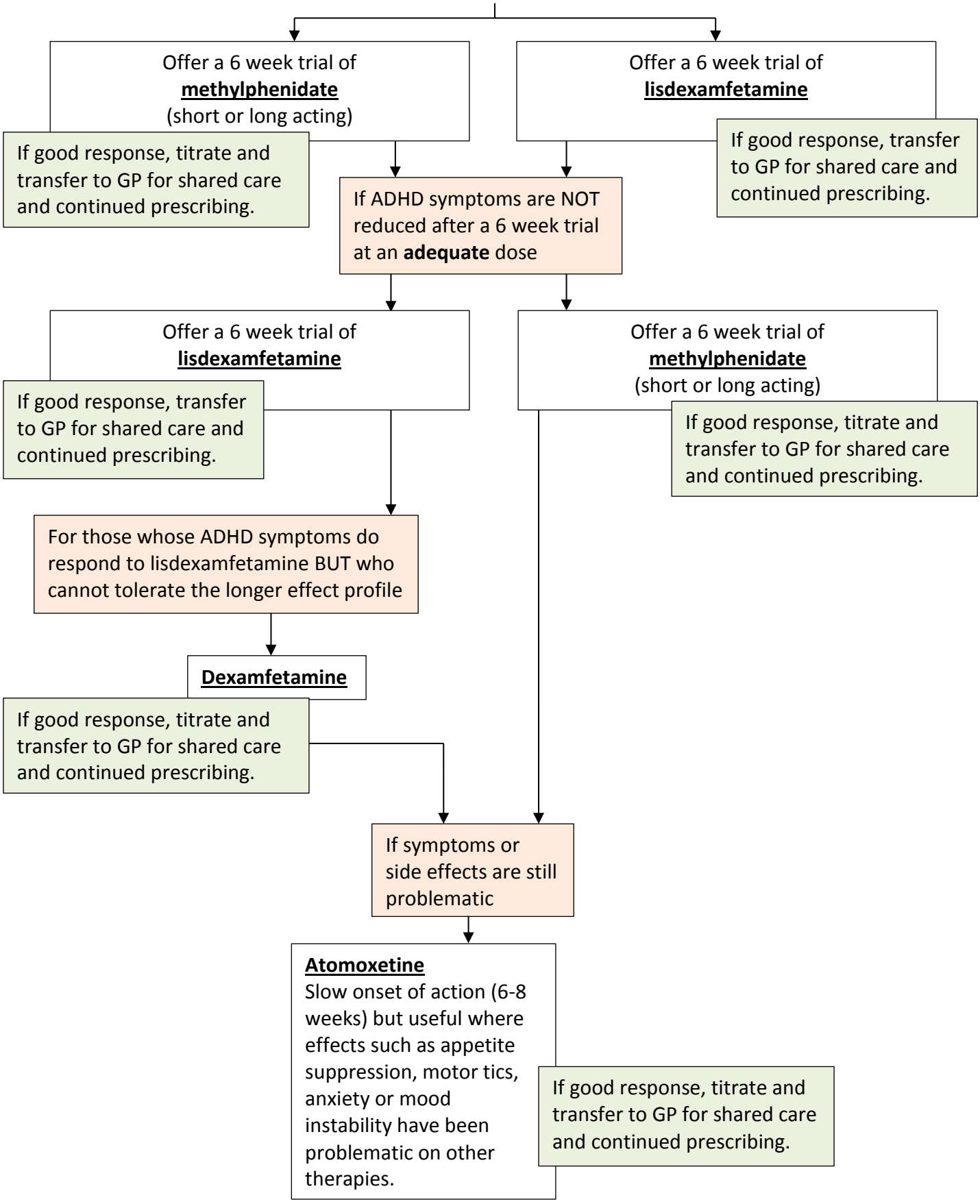
If symptoms or side effects are still a problem, then proceed to Step 4: atomoxetine or guanfacine

STEP 4: Atomoxetine
Alternative non-stimulant therapy.

STEP 4: Guanfacine
Alternative non-stimulant therapy.

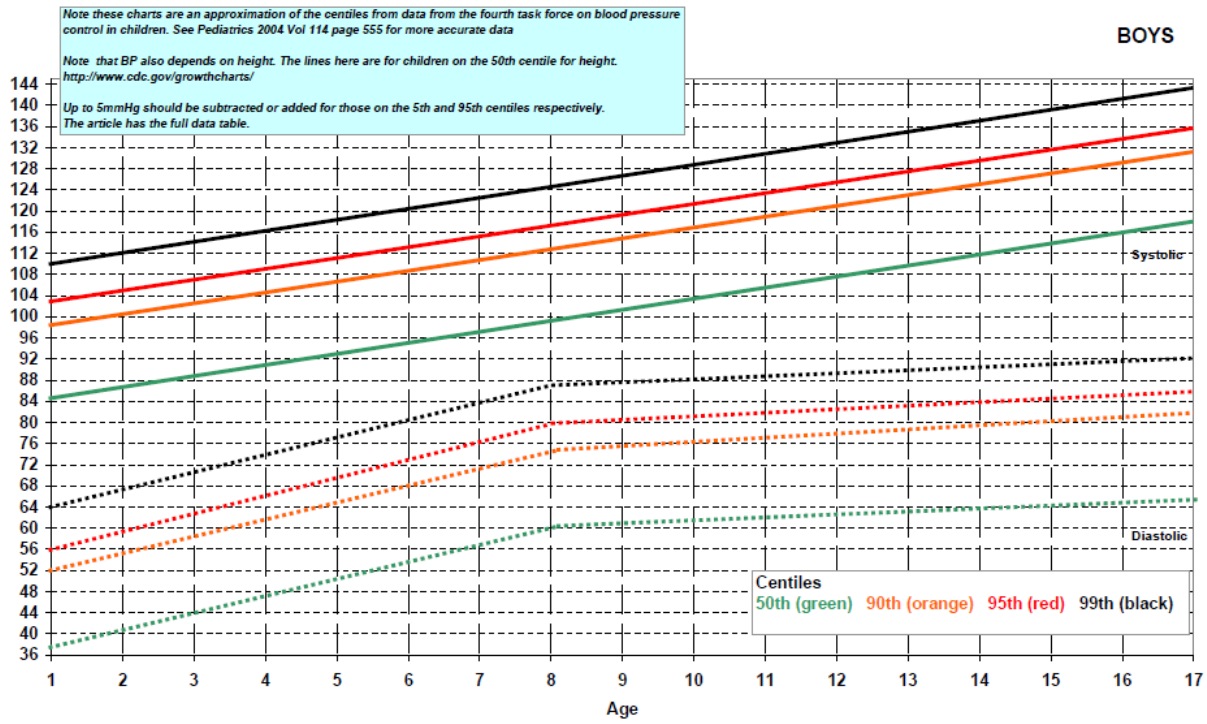
If good response, titrate and transfer to GP for shared care and continued prescribing.

Figure 2
Medication Choice: Adults

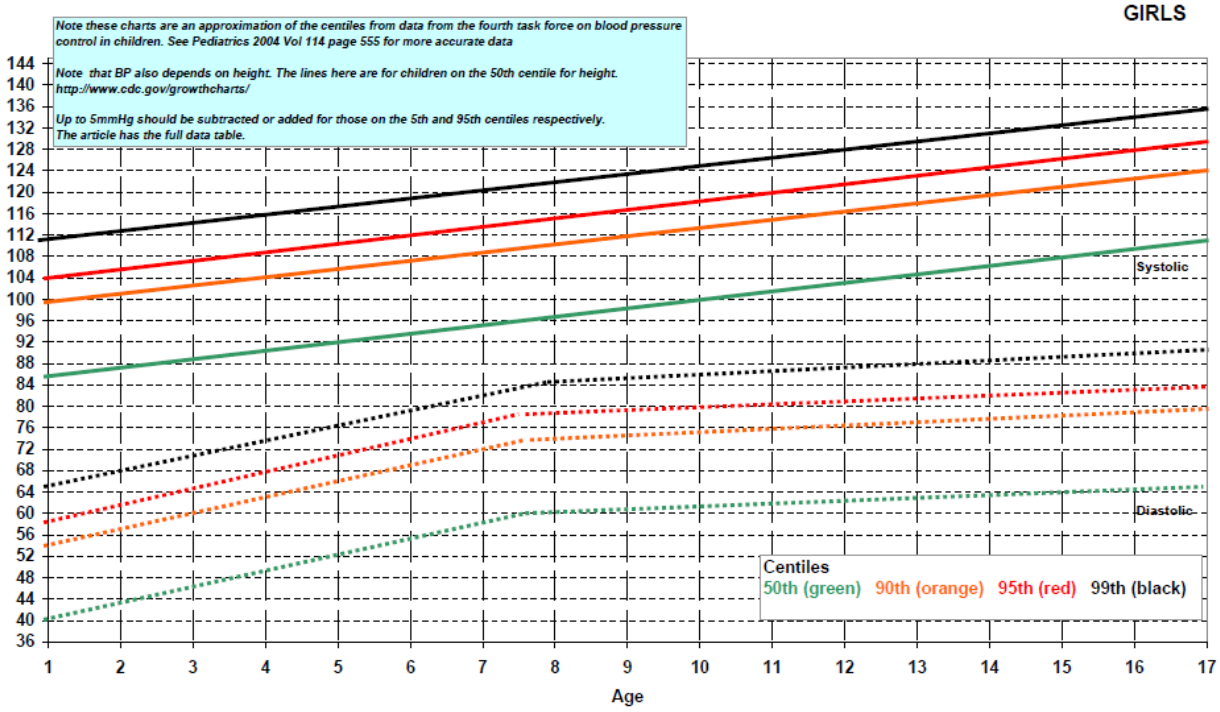


Appendix 1. Blood Pressure Centile Charts

A. Blood Pressure Centile Chart – Paediatric; Boys



B. Blood Pressure Centile Chart – Paediatric; Girls



Data from: Jackson LV, Thalange NKS, Cole TJ (2007) **Blood pressure centiles for Great Britain**. *Arch Dis Child*, 92; 298-303.

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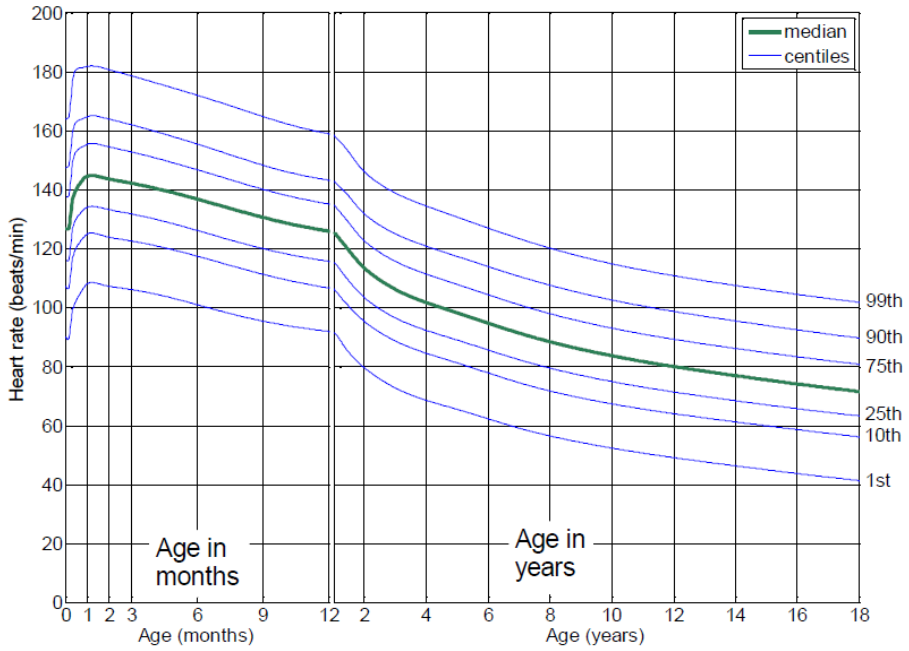
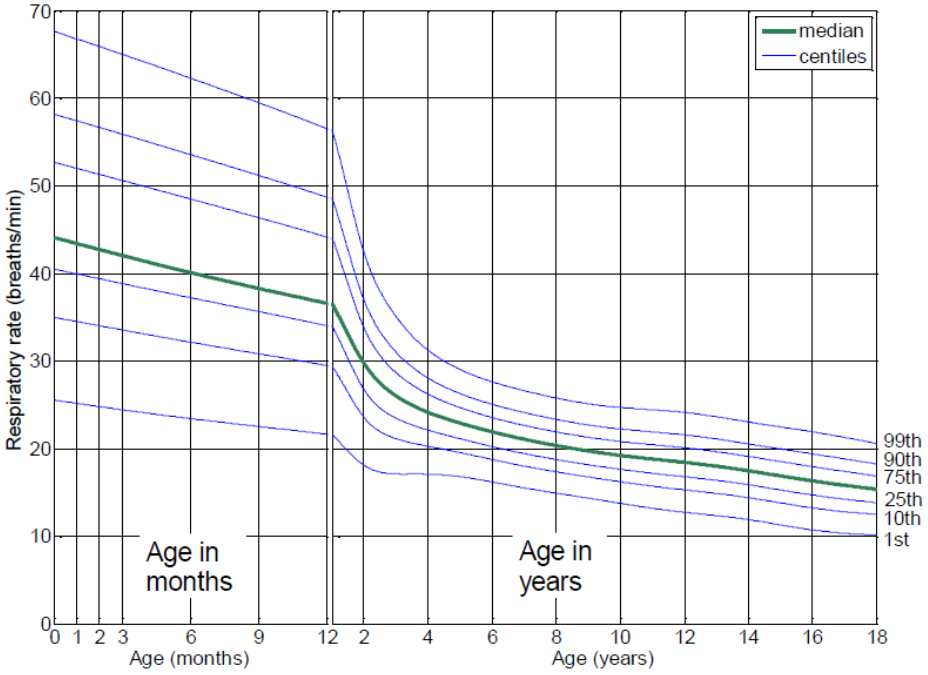
Expiry date: December 2021

Appendix 2. Pulse Rate Centile Chart – Paediatric



Data from: Fleming S, et al (2011) **Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies**. *Lancet*, 377(9770); 1011–8. Available at: http://www.thelancet.com/article/S014067361062226X/fulltext [Accessed March 10, 2015]

Appendix 3. Respiratory Rate Centile Chart – Paediatric



Data from: Fleming S, et al (2011) **Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies**. *Lancet*, 377(9770); 1011–8. Available at: http://www.thelancet.com/article/S014067361062226X/fulltext [Accessed March 10, 2015]