Sunderland and South Tyneside Area Prescribing Committee

Methylphenidate, Dexamfetamine, Lisdexamfetamine, Atomoxetine and Guanfacine for treatment of Attention Deficit Hyperactivity Disorder (ADHD) in Children and Young People

Shared Care Guidance

Introduction

Indication

Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents aged from 6 to 17 years.

This shared care guideline is in accordance with NICE clinical guideline NICE Clinical Guideline 87 and NICE Quality Standard 39

This shared care guideline excludes:

- Treatment of children under 6 years
- Treatment of adults aged 18 years and over (separate guideline is available)

It is expected that excluded patients will be retained within specialist services unless otherwise specified

Background

- ADHD is a heterogeneous behavioural syndrome characterised by the core symptoms of hyperactivity, impulsivity and inattention. While these symptoms tend to cluster together, some people are predominantly hyperactive and impulsive, while others are principally inattentive
- Symptoms of ADHD are distributed throughout the population and vary in severity; only those with significant impairment meet criteria for a diagnosis of ADHD. Symptoms of ADHD can overlap with symptoms of other related disorders therefore care in differential diagnosis is needed
- Diagnosis and initiation of treatment must be made by a specialist in the treatment of ADHD
- Stimulants used to treat ADHD work by increasing dopamine levels in the brain to improve focus and functioning
- Atomoxetine is a selective noradrenaline reuptake inhibitor and a non-stimulant
- Guanfacine is a selective alpha2A-adrenergic receptor agonist and a non-stimulant

Symptoms of ADHD become evident during childhood and patients have been comprehensively assessed and diagnosed by specialists in the treatment of ADHD in children. Symptoms may persist into adulthood requiring treatment. This is addressed in NICE Clinical Guideline 87 and a separate shared care document for the treatment of ADHD in adults aged 18 years and over is available.

Medication

For full details see NICE CG 87, SPCs for individual drugs, preparations and BNFC

Stimulants

Methylphenidate, dexamfetamine + lisdexamfetamine - Schedule 2 Controlled Drugs - Controlled drug prescription requirements should be followed

Formulary status – Amber

Licensed Indication

Methylphenidate	**Tablets** 5mg, 10mg, 20mg **Tablets M/R** – 18mg, 27mg, 36mg + 54mg (Concerta XL®, Xaggitin XL®) licensed max. dose is 54 mg once daily, higher doses only under direction of specialist to maximum 108 mg per day (Concerta XL®). Duration of action 12h **Capsules M/R** 10mg, 20mg, 30mg (Equasym XL®) licensed max. dose is 60 mg daily, increased to higher doses only under direction of specialist maximum 90 mg per day, duration of action 8h **Capsules M/R** 5mg, 10mg, 20mg, 30mg, 40mg, 50+60mg (Medikinet XL®) licensed max. dose is 60 mg daily, increased to higher dose only under direction of specialist to maximum 90 mg per day, duration of action 8h **Ratio of immediate: extended release methylphenidate varies between products –see individual SPC**

Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)	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) Note - Treatment may be started using a modified-release preparation. **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 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.
Dexamfetamine	**Tablets -** 5mg (generic manufacturers), or as Amfexa® 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 (for full details see NICE CG 87, individual SPCs and BNFC)	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
Lisdexamfetamine	**Capsules** 20mg, 30mg, 40mg, 50mg, 60mg and 70mg (Elvanse®)
Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)	All ages 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 *Formulary status – Amber*	

<table>
<tr><td colspan="2">Licensed Indication</td></tr>
<tr><td>Atomoxetine</td><td>Capsules 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg (Strattera®)
Liquid 4mg/ml (Strattera®)
Nb. Liquid approved for patients with more complex needs e.g. younger patients and those with swallowing difficulties</td></tr>
<tr><td>Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)</td><td>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
Atomoxetine oral solution should only be prescribed when patients are unable to take tablets/capsules whole</td></tr>
<tr><td>Guanfacine</td><td>Tablets
1mg, 2 mg, 3mg, 4 mg prolonged-release tablets (Intuniv®)</td></tr>
<tr><td>Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)</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

Can also be prescribed in primary care by GPs in adults who started treatment in childhood and wish to continue, for whom stimulants are not suitable, not tolerated or have been shown to be ineffective under specialist supervision.</td></tr>
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</td></tr>
<tr><td colspan="2">Common adverse effects - See SPC and BNFC 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 blood pressure, 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 blood pressure, 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</td></tr>
</table>

	hypertension, hypersomnia; *also reported* suicidal ideation.
Potentially Serious drug interactions	
Stimulants	▪ 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

Atomoxetine	▪ 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)
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 manufacturers SPC for 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) • Children and adolescents may show an increase in their BMI.

Medication choice – children aged 6 years and over and young people

- Offer methylphenidate (either short or long acting) as the first line pharmacological treatment for children aged 6 years and over and young people with ADHD.
- 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
- Lisdexamfetamine may be appropriate first choice if patient cannot swallow tablets/tolerate opened capsules
- 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.
- Offer atomoxetine or guanfacine to children aged 6 years and over and young people if:
  - they cannot tolerate methylphenidate or lisdexamfetamine **or**
  - Their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate 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

Shared care for medication

After titration and dose stabilisation, prescribing of ADHD medication may be undertaken by primary care.

Specialist responsibilities	
Contact Details ADHD Specialists Mon – Fri 09:00 – 17:00 ▪ Gateshead QE Paediatricians via switchboard: 0191 482 0000 ▪ Newcastle Upon Tyne Hospitals Paediatricians via 0191 233 6161 ▪ Northumbria North Tyneside CAMHS:- 0191 2196725 (Albion Road Clinic) ▪ NTW Newcastle and Gateshead CYPS:- 0191 246 6913 (Benton House) ▪ NTW Northumberland CYPS:- 01670 798265 (Villa 9, Northgate)	
Baseline assessment	Before initiating patients on medication for ADHD, the specialist should undertake a full assessment in line with NICE guidance.
Prescribing	• Initiation, titration and dose stabilisation of ADHD medication
Maintenance and monitoring	• Monitor effectiveness of medication for ADHD and adverse effects, and document in the person's notes. • Encourage people taking medication for ADHD to monitor and record their adverse effects • Consider using standard symptom and adverse effect rating scales • Monitor young people for sexual dysfunction (erectile and ejaculatory dysfunction) as potential adverse effects of atomoxetine. • Monitor changes in sleep pattern • Ensure necessary physical health monitoring is done - document reasons why if monitoring cannot be completed e.g. uncooperative disabled/autistic child • Review the results of the physical health monitoring, highlight any concerns and action necessary • If a person taking guanfacine has sustained orthostatic hypotension or fainting episodes, reduce their dose or switch to another ADHD medication • Monitor the behavioural response to medication, and if behaviour worsens adjust medication and review the diagnosis • A healthcare professional with training and expertise in managing ADHD should review ADHD medication at least once a year and discuss with the person with ADHD (and their families and carers as appropriate) whether medication should be continued. • Consider trial periods of stopping medication or reducing the dose when appropriate. • Monitor changes in the potential for stimulant misuse and diversion, which may come with changes in circumstances and age.

Physical health monitoring – stimulants + atomoxetine

	Height	Weight	Heart rate	Blood pressure
6-17 years	Every 6 months	See below	Compare with the normal range for age before and after each dose change and every 6 months. If a person taking ADHD medication has sustained resting tachycardia (more than 120 beats per minute), arrhythmia or systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on 2 occasions, reduce their dose, review medication and if required refer them to a paediatric hypertension specialist.	
6-10 years	See above	Every 3 months		
10 years and over	See above	measure weight at 3+6 months after starting treatment + every 6 months thereafter*		
All ages	Plot height and weight on a growth chart and ensure review by the healthcare professional responsible for treatment.			

*or more often if concerns arise

Physical health monitoring – guanfacine

Monitoring Frequency	Assess	Monitor	
	somnolence + sedation	*hypotension + bradycardia (BP standing + sitting+ heart rate)	weight + height (growth chart)
Weekly - during Titration	✓	✓	X
3 monthly during first year of treatment	✓	✓	✓
6 monthly - Ongoing treatment	✓	✓	✓
	More frequent monitoring following any dose adjustments *If a person taking ADHD medication has sustained resting tachycardia (more than 120 beats per minute), arrhythmia or systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on 2 occasions, reduce their dose, review medication and if required refer them to a paediatric hypertension specialist.		

Primary Care Responsibilities
▪ Prescribe medication following recommendations of the specialist ▪ Provide the specialist with relevant medical history and background information ▪ To contact the specialist if concerned about any aspects of the patient's treatment ▪ Report significant deviations from the prescribing pattern to the specialist ▪ Monitor and record the therapy in accordance with written directions of specialist ▪ Report any adverse events to the specialist, and the usual bodies. (E.g. MHRA)

Private and Confidential

ADHD - Shared Care Request/Confirmation

- Specialist Prescriber to complete first section of form and send to patient's GP.
- GP to complete second section of form and return to specialist prescriber within 28 days
- A copy of the full shared care guideline can be viewed at www.northoftyneapc.nhs.uk

Specialist Prescriber				
Department				
Hospital				
Telephone				
Patient details (use hospital label if preferred)				
Name				
Address				
Postcode				
NHS or Hosp reg no		**Male / Female**	**DoB**	

Treatment Requested for Prescribing in Accordance with an Approved Shared Care Arrangement					
Drug Information					
Name/Formulation		**Dose**		**Frequency**	
Name/Formulation		**Dose**		**Frequency**	
Name/Formulation		**Dose**		**Frequency**	
Indication – ADHD					
Other information (if appropriate)					
Signed (Specialist Prescriber)		**Name (Print)**		**Date**	

To be completed by GP	**Please tick one box**
I ACCEPT the proposed shared care arrangement for this patient	❑
I ACCEPT the proposed shared care arrangement with the caveats below	❑
I DO NOT ACCEPT the proposed shared care arrangement for this patient	❑
My caveats/reason(s) for not accepting include:	

Signed		**Name (print)**		**Date**	