North of Tyne, Gateshead and North Cumbria 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	**Standard Release -** 5mg, 10mg & 20mg Tablets **Modified release** - prescribe by brand name **Xaggitin® XL 18mg, 27mg, 36mg and 54mg m/r tablets** Medikinet® XL 5mg, 10mg, 20mg, 30mg, 40mg, 50mg and 60mg m/r capsules Equasym® XL 10mg, 20mg & 30mg m/r capsules *Existing patients who are prescribed Concerta® XL should be reviewed and switched to Xaggitin® XL as appropriate* *Xaggitin® XL is bioequivalent to Concerta® XL* **Ratio of immediate: extended release methylphenidate varies between products affecting bioavailability - prescribe by brand name –see individual SPC**

	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. **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/quartered
Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)	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
Dose and administration (for full details see NICE CG 87, individual SPCs and BNFC)	30mg taken once daily in the morning. The starting dose can be 20mg/day if clinically indicated; this can be increased at weekly intervals of 10mg – 20mg/week if required. The lowest effective dose should be prescribed and the maximum daily dose is 70mg/day Discontinue if response insufficient after 1 month. 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 - Licensed Indication*	
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 (for full details see NICE CG 87, individual SPCs and BNFC)	Child > 6 years with a body-weight under 70 kg: Usual maintenance dose: 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

<table>
<tr><td></td><td>Usual maintenance dose: 80 mg/day but may be increased to a maximum recommended total daily dose of 120mg, under the direction of a specialist
Dose to be reviewed and amended in line with changing weight
Doses above 100mg daily are not licensed but are stated in the BNF
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
.</td></tr>
<tr><td>Guanfacine</td><td>Tablets
1mg, 2 mg, 3mg, 4 mg prolonged-release tablets</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.
https://www.medicines.org.uk/emc/product/5099/smpc</td></tr>
</table>
</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, decreased appetite, depression, anxiety, mood lability, nightmares, enuresis, dry mouth, irritability , fatigue, headache, rash, abdominal pain, headache and dizziness are commonly listed side effects..</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</td></tr>
</table>

	▪ 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. ▪ 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	• Guanfacine causes a decrease in heart rate, due to this co-prescribing of medicines that have the potential to prolong QTc is not recommended. ▪ Guanfacine + Moderate/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) – a dose reduction in Guanfacine is recommended ▪ Guanfacine + CYP3A4 inducers may reduce guanfacine levels (e.g. carbamazepine, phenobarbital, phenytoin, primidone, rifampicin) ▪ Guanfacine can increase levels of valproic acid (valproate)
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 • 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 • Although listed as contraindications, in some circumstances, methylphenidate can be used with caution if there is careful monitoring by the specialist e.g. Cardiovascular disease – including hypertension • Motor tics, or family history of Tourette's syndrome

	• Phaeocromocytoma
	• Use with caution in:-
	  • Epilepsy, stimulants may lower the seizure threshold in patients with a prior history of seizures. If seizure frequency increases, the specialist should discontinue methylphenidate
	  • Or where there is a diagnosis or history of severe and episodic Bipolar Affective disorder that is not well controlled
	• 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

- Offer the same medication choices to people with ADHD and anxiety disorder, tic disorder or autism spectrum disorder as other people with ADHD
- If experiencing an acute psychotic or manic episode:
  - stop any medication for ADHD

- consider restarting or starting new ADHD medication after the episode has resolved, taking into account the individual circumstances, risks and benefits of the 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 in the workplace), reducing problems of storing and administering controlled drugs at home, and the risk of stimulant misuse and diversion with immediate-release preparations
- Be aware that effect size, duration of effect and adverse effects vary from person to person; IR and MR preparations can be used as part of the same treatment plan to optimise effect
- 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 and monitoring of ADHD medication may be carried out under Shared Care Protocol arrangements with primary care (NICE 2018)

Specialist Responsibilities

Contact Details ADHD Specialists Mon – Fri 08:00 – 20:00

- Gateshead QE Paediatricians via switchboard: 0191 482 0000
- Newcastle Upon Tyne Hospitals Paediatricians via 0191 233 6161
- Northumbria North Tyneside CAMHS:- 0191 219 6685 (Albion Road Clinic)
- CNTW Newcastle and Gateshead CYPS:- 0191 246 6913 (Benton House & Bensham Hospital)
- CNTW Northumberland CYPS:- 01670 798265 (Craster Unit, SGP)
- CNTW South Tyneside & Sunderland CYPS:- 0191 566 5500 (Monkwearmouth Hospital)
- North Cumbria ADHD Service Mon – Fri 08:00 to 17:00
  - CNTW East Cumbria CAMHS:- 01228 603 017 (Fairfield Centre, Carlisle)
  - CNTW West Cumbria ADHD Team:- 01900 705 800 (Ann Burrow Thomas Health Centre, Workington)

Baseline assessment	Before initiating patients on medication for ADHD, the specialist should undertake a full assessment in line with NICE guidance.
Prescribing	• Initiate, titrate and stabilise dose of ADHD medication • Transfer prescribing to GP after at least 3 months treatment has been supplied by specialist (this should allow enough time for treatment to be stabilised)

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 • Ensure all physical health monitoring results and actions are communicated to the GP. • 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.
Specialist Responsibilities	

Physical health monitoring – stimulants + atomoxetine

	Height	Weight	Heart rate	Blood pressure
6-10 years	Every 6 months	Every 3 months	Compare with the normal range for age before and after each dose change and every 6 months.	
10 years and over		At 3 months then 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		

Review of medication and discontinuation

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. This should be communicated to the GP.

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, including physical health parameters (e.g. tachycardia). ▪ 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) ▪ Physical health monitoring as described in the 'Specialist Responsibilities' section may be completed by the GP in individual cases where there is explicit agreement between the GP, secondary care and the patient/family.

Private and Confidential

ADHD - Shared Care Request/Confirmation – Children & Young People ▪ Specialist Prescriber to complete first two sections of the form and send to patient's GP. ▪ GP to complete last section of form and return to specialist prescriber **within 28 days** ▪ A copy of the full shared care guideline can be viewed at https://www.sunderlandccg.nhs.uk/about-us/prescribing/shared-care-green-plus/				
Specialist Prescriber				
Clinical Team & Base				
Team Telephone				
Team E-mail				
Patient details (use hospital label if preferred)				
Name				
Address				
Postcode				
NHS 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 – Children & Young People					
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**	