SHARED CARE GUIDELINE

Drug: Methylphenidate, Dexamfetamine, Atomoxetine and Guanfacine for Attention Deficit Hyperactivity Disorder in children and adolescents aged 6 to 16 years

Introduction

Indication:

Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents aged from 6 years up to but not including 16 years of age. This shared care guideline relates to patients with ADHD whose condition is stable at hand over from secondary to primary care.

This shared care guideline is in accordance with NICE clinical guideline 72 and NICE Quality Standard 39.

Guanfacine is licensed for the treatment of ADHD in children and adolescents 6-17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.

This shared care guideline excludes:

Treatment of children under 6 years
Treatment of children and adolescents (aged 6 to 16 years) with doses of ADHD medication outside the licensed recommendations
Treatment of adults aged 16 years and over (see separate guideline)
Treatment using more than one ADHD medication (use of different formulations of the same medication is not excluded e.g. immediate and prolonged release methylphenidate)
Treatment of patients with ADHD and substance misuse problems
Treatment of patients with ADHD also on complex psychotropic medication regimens
Treatment with lisdexamfetamine.
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
- Guanfacine is a selective alpha2A-adrenergic receptor agonist and a non-stimulant. Its mode of action in ADHD has not been fully established.
- The choice of medication should take into consideration the patient's co-morbid conditions, the medication's adverse effect profile, potential for drug misuse, and preferences of the patient and carers
- Symptoms of ADHD become evident during childhood and patients have been comprehensively assessed and diagnosed by specialists in the treatment of ADHD in children. For some young people with a sustained diagnosis, symptoms may persist into adulthood requiring treatment. This is addressed in NICE Clinical Guideline 72 and a separate shared care document for the treatment of ADHD in adults aged 16 years and over, can be found here

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- **Methylphenidate and dexamfetamine are both Schedule 2 Controlled Drugs. Controlled drug prescription requirements should be followed.**

Form

Methylphenidate	**Atomoxetine**	**Dexamfetamine**	**Guanfacine**
Tablets 5mg, 10mg, 20mg Tablets M/R 18mg, 27mg, 36mg (Concerta® XL) Capsules M/R 10mg, 20mg, 30mg (Equasym XL®) Capsules M/R 5mg, 10mg, 20mg, 30mg, 40mg (Medikinet XL®) Tablets M/R 18mg, 36mg, 54mg (Matoride XL®) **Modified Release preparations are not interchangeable. Prescribe by brand.**	(Strattera®) Capsules 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg	Tablets 5mg	(Intuniv®) 1 mg, 2 mg, 3 mg, 4 mg prolonged-release tablets

Dose & Administration (For full details see NICE CG72, the individual SPCs and the BNFC)	**Methylphenidate** Child 6–18 years: For 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. Drinking some fluids, e.g. water, should follow the intake of the sprinkles with applesauce. *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 Matoride XL must be swallowed whole with the aid of liquids, and must not be chewed, divided, or crushed.	**Atomoxetine** (Strattera®) 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 **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	**Dexamfetamine** **Child aged 6–18 years** Initially 2.5 mg 2–3 times daily, increased if necessary at weekly intervals by 5 mg daily Usual max. 1 mg/kg (up to 20 mg) daily (40 mg daily has been required in some children). Maintenance dose given in 2–4 divided doses. There is no proprietary product **Administration** Tablets can be halved	**Guanfacine** (Intuniv®) **Child 6–13 years:** ***body-weight over 25 kg*** initially 1 mg once daily, increased by 1 mg at weekly intervals if necessary and tolerated; usual maintenance dose 0.05-0.12 mg/kg daily; max. 4 mg daily **Child 13-18 years:** ***Body-weight 34–41.5 kg*** initially 1 mg once daily, increased by 1 mg at weekly intervals if necessary and tolerated; usual maintenance dose 0.05-0.12 mg/kg daily; max. 4 mg daily ***Body-weight 41.5–49.5 kg*** initially 1 mg once daily, increased by 1 mg at weekly intervals if necessary and tolerated; usual maintenance dose 0.05-0.12 mg/kg; max. 5 mg daily ***Body-weight 49.5–58.5 kg*** initially 1 mg once daily, increased by 1 mg at weekly intervals if necessary and tolerated; usual maintenance dose 0.05-0.12 mg/kg; max. 6 mg daily ***Body-weight over 58.5 kg*** initially 1 mg once daily, increased by 1 mg at weekly intervals if necessary and tolerated; usual maintenance dose 0.05-0.12 mg/kg; max. 7 mg daily
Secondary Care Responsibilities	**Secondary Care Responsibilities are:** 1. To conduct pre-treatment assessments in line with NICE Clinical Guideline 72 namely: • A full mental health and social assessment • A full history and physical examination, including: ○ assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms ○ heart rate and blood pressure (plotted on a centile chart) ○ weight and height (plotted on a growth chart) ○ family history of cardiac disease and examination of the cardiovascular system ○ an electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination ○ Risk assessment for substance misuse and drug diversion. 2. To initiate treatment in line with NICE clinical guideline 72. 3. To provide information about the medication to patients and carers, including common side effects, necessary monitoring, and where that monitoring will take place. 4. To advise patients and carers of the rare reports of hepatic disorders providing guidance on suggestive symptoms, and rare reports of suicidal ideation with atomoxetine and instruct patients as			

	to whom they should report these, should they occur. 5. To titrate doses according to the NICE CG 72 recommendations for the medication prescribed. 6. To continue all necessary physical health monitoring during the titration period and monitor for side effects. 7. To prescribe the medication until the patient is on a stable dose. 8. To write to the General Practitioner once this state is achieved and request that they consider prescribing under shared care arrangements, providing full details of the medication, brand and formulation prescribed, dose, response, side effects experienced, baseline monitoring assessments and on-going monitoring required. A further supply of medication at this point will enable consideration of the request by the GP and give time for the Practice to make any necessary changes to their prescribing systems. 9. To keep the patient and carers informed of the process at all stages to ensure continuity of treatment. 10. To explain to the patient / carer their role in the provision of appropriate and safe treatment, ensuring the patient's understanding of their condition, drug treatment and need for concordance; their need to share any concerns and to participate in the monitoring of therapy and assessment of outcomes of treatment. 11. To conduct reviews every six months to monitor physical health in line with NICE guidance for those in the service. 12. To conduct an annual face to face medication review for all patients in the service, and consider discontinuation if the patient is: o Well-controlled and has been free of ADHD symptoms for at least one year whilst taking medication o There has been no need to increase the dose of medication despite growth and weight gain over the preceding one to two years o ADHD symptoms are not evident on days when medication is forgotten or missed o There is evidence of misuse or diversion of ADHD medication. Inform GP of any decisions made and monitoring performed with results. 13. To resume prescribing and monitoring of the patient when a decision for managed withdrawal of treatment has been taken. 14. To provide prompt on-going advice to General Practitioners as required. 15. To provide advice promptly about on-going monitoring requirements to the GPs on discharge from the service. 16. To continue to provide urgent review appointments where patients are receiving prescriptions from their GP and they feel that a prompt assessment or review of their ADHD treatment is required. 17. Provide advice to the GP as to the changes in parameters that should trigger urgent referral back to the specialist. 18. Liaise with the school, providing education about drug therapy and storage. 19. Refer for additional behavioural therapy (social skills, anger management or parents group/parenting skills) if appropriate and where available. 20. Facilitate the transition of specialist-led care to adult services, as necessary, when the young person approaches 16 years of age.
Primary Care Responsibilities	**Primary Care Responsibilities are:** ***Ensure that shared care arrangements are all in place before taking over prescribing/monitoring*** 1. To consider requests to prescribe under shared care arrangements and reply in a timely manner following titration and stabilisation by specialist. 2. To provide continuation prescriptions, or identify any concerns about the request to the prescriber in the specialist team. (It is expected that primary care prescribers will not make changes to the dose/formulation, unless it is in consultation with the specialist team). 3. To inform specialists of any relevant pre-existing or new medical history (e.g. cardiovascular, neurological, endocrine) and of any adverse effects of ADHD treatment. 4. To monitor the patient in accordance with Appendix A and the section below and contact specialist team if results give rise to concern. (Refer to paediatric secondary care services as appropriate if a serious physical side effect occurs). 5. To contact specialists within the team where concerns arise about a patient's presentation or advice is needed. E.g. new or worsening seizures, development of psychotic symptoms, suicidal thinking with atomoxetine and guanfacine and self-harm of an urgent nature with atomoxetine; or if diversion of medication is suspected with methylphenidate or dexamfetamine. 6. To inform secondary care if the patient is: • Well controlled and has been free of ADHD symptoms for at least one year whilst taking medication • There has been no need to increase the dose of medication despite growth and weight gain over the preceding one to two years • ADHD symptoms are not evident on days when medication is forgotten or missed • There is evidence of misuse or diversion of ADHD medication 7. To confirm the patient / carer understands role in the provision of appropriate and safe treatment, ensuring the patient's understanding of their condition, drug treatment; and their need to share any concerns and to participate in the monitoring of therapy and assessment of outcomes of treatment. ***Discontinuation of treatment in Primary Care arrangements*** • As a joint decision with specialist team providing specific advice • In case of serious adverse effects pending assessment (see appendix A for details of adverse effects monitoring).

	• Following non-attendance at annual specialist team review pending that review taking place • If there is a failure to engage with the review process e.g. if the patient regularly DNAs for appointments **Note: the Manufacturer of guanfacine advises to avoid abrupt withdrawal—consider dose tapering to minimise potential withdrawal effects if discontinuation of guanfacine is required.**

Monitoring Required in Primary Care	**See Appendix A for full details** Ongoing monitoring requirements for patients discharged from the service will be identified by the specialist service as part of the discharge information to the GP. Primary care should contact specialists within the team where concerns arise about a patient's presentation or when advice is needed. E.g. new or worsening seizures, development of psychotic symptoms, suicidal thinking with atomoxetine and guanfacine and self-harm of an urgent nature with atomoxetine or if diversion of medication is suspected with methylphenidate or dexamfetamine.
Common Adverse Effects	**Please refer to the SPC or BNFC for full list.** **Methylphenidate and Dexamfetamine:** 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. **Atomoxetine:** Emergence of suicidal behaviour, self-harm or hostility; serious liver damage; decreased appetite, weight loss, insomnia, irritability, headache, drowsiness, dizziness, gastrointestinal side effects, lethargy, increased heart rate and blood pressure, dysmenorrhoea, sexual dysfunction, rashes. **Guanfacine:** abdominal pain, vomiting, diarrhoea, nausea, constipation, bradycardia, hypotension, somnolence, headache, sedation, decreased appetite, weight increase, depression, anxiety, mood lability, irritability, malaise, dizziness, insomnia, nightmares, enuresis, dry mouth, rash; *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.
Potentially Serious Drug Interactions	**Methylphenidate:** Adrenergic neurone blockers: antagonism of hypotensive effect Coumarins: possible increased anticoagulant effect MAOIs and Moclobemide: risk of hypertensive crisis SSRIs and tricyclic antidepressants: Methylphenidate may inhibit metabolism of the antidepressants **Dexamfetamine:** Guanethidine: antagonism of hypotensive effect MAOIs and Moclobemide: risk of hypertensive crisis **Atomoxetine:** Methadone, amiodarone, disopyramide, moxifloxacin, parenteral erythromycin, mefloquine, antipsychotics which prolong QTc interval, sotalol, hypokalaemia secondary to diuretics: Increased risk of ventricular arrhythmias. Antidepressants: increased risk of seizures. Additionally: SSRIs: Potential for increased atomoxetine levels with paroxetine and fluoxetine. MAOIs: Two week washout period required between and MAOI and atomoxetine prescriptions. Tricyclics: Increased risk of ventricular arrhythmias. **Guanfacine:** **Plasma concentration of guanfacine possibly reduced by (increase dose of guanfacine):** bosentan, carbamazepine, efavirenz, etravirine, modafinil, nevirapine, oxcarbazepine, phenobarbital, phenytoin, primidone, rifabutin, rifampicin, St John's Wort. **Plasma concentration of guanfacine increased by (halve dose of guanfacine):** ketoconazole, boceprevir, clarithromycin, indinavir, itraconazole, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin **Please refer to the SPC or BNFC for full list.**
Contraindications	**Methylphenidate:** Severe depression, suicidal ideation, anorexia nervosa, psychosis, uncontrolled bipolar disorder, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorders, hyperthyroidism or thyrotoxicosis, cardiovascular disease, structural cardiac abnormalities, phaeochromocytoma, vasculitis, cerebrovascular disorders, glaucoma **Dexamfetamine:** cardiovascular disease including moderate to severe hypertension, structural cardiac abnormalities, advanced arteriosclerosis, hyperexcitability or agitated states, hyperthyroidism, glaucoma, porphyria, history of drug or alcohol abuse, patients with Gilles de la Tourette syndrome or similar dystonias **Atomoxetine:** Phaeochromocytoma, narrow-angle glaucoma, severe cardiovascular or

	cerebrovascular disorders – **Please refer to the SPC or BNFC for full list.**

This guidance does not replace the SPCs, which should be read in conjunction with this guidance.

References	NICE Clinical Guideline 72 Attention deficit hyperactivity disorder: Diagnosis and Management of ADHD in children, young people and adults NICE Quality Standard 39 Attention deficit hyperactivity disorder. July 2013 Royal Pharmaceutical Society. British National Formulary, Vol. 71, London: Pharmaceutical Press, 2016. Accessed via www.evidence.nhs.uk [access online: 28th November 2016]. **Dexamfetamine SPC** http://www.mhra.gov.uk/spc-pil/?prodName=DEXAMFETAMINE%20SULPHATE%205MG%20TABLETS&subsName=DEXAMPHETAMINE%20SULPHATE&pageID=SecondLevel **Methylphenidate SPCs** Concerta modified release http://www.medicines.org.uk/emc/medicine/8382/ Equasym modified release http://www.medicines.org.uk/emc/medicine/15804/ Medikinet immediate release tablets http://www.medicines.org.uk/emc/medicine/19664/ Medikinet modified release http://www.medicines.org.uk/emc/medicine/19510/ Ritalin immediate release tablets http://www.medicines.org.uk/emc/medicine/1316/ **Atomoxetine SPC** Strattera http://www.medicines.org.uk/emc/medicine/14482 **Guanfacine SPC** Intuniv 1 mg, 2 mg, 3 mg, 4 mg prolonged-release tablets https://www.medicines.org.uk/emc/medicine/31294

APPENDIX A: Monitoring Requirements and Information

To be read in conjunction with the SPC.

Physical health monitoring during the titration and stabilisation phase will be the responsibility of the specialist ADHD prescriber who will continue to provide six monthly physical health checks and annual medication reviews under the shared care agreement.

PRIMARY CARE MONITORING REQUIREMENTS
Monitoring to be completed on timelines as indicated below
Adverse effects to be informed back to specialist team.
Refer to paediatric secondary care services as appropriate if a serious physical side effect occurs, and suspend shared care until review.

Monitoring for ongoing appropriateness of treatment

Signs that would indicate an early referral back to specialist team for medication withdrawal:

- The patient has been well controlled and has been free of ADHD symptoms for at least one year whilst taking medication
- There has been no need to increase the dose of medication despite growth and weight gain over the preceding one to two years
- ADHD symptoms are not evident on days when medication is forgotten or missed
- There is evidence of misuse or diversion of ADHD medication

Physical Health Monitoring	Methylphenidate	Atomoxetine	Dexamfetamine	Guanfacine
Cardiac function and blood pressure • Monitor heart rate and blood pressure every 6 months (weekly during dose titration for those receiving guanfacine); this should take place in between the six monthly monitoring by the specialist team as the requirement is to monitor every 3 months. • Signs of bradycardia and hypotension should prompt referral to the specialist service for those receiving guanfacine	✓	✓	✓	✓

A number of charts are available on which results can be recorded, but local CAMHS service practice is to plot both heart rate and blood pressure on the blood pressure charts available at: http://www.healthforallchildren.com/shop-base/growth-charts/blood-pressure-charts/ ➢ Sustained resting tachycardia, arrhythmia or systolic blood pressure greater than the 95th percentile measured on two occasions (or a clinically significant increase) should prompt referral to specialist ADHD prescriber (and pediatric secondary care services for immediate care as appropriate). ➢ Stop ADHD medication and suspend shared care until review by specialist team.				
Somnolence and sedation Monitor every 3 months for the first year for those receiving guanfacine and 6 monthly thereafter	NA	NA	NA	✓
On-going monitoring for adverse effects. (See Shared Care Protocol/SPC for more Information)				
Reproductive system and sexual function for young people • Monitor for dysmenorrhea, erectile dysfunction and ejaculatory dysfunction	N/A	✓	N/A	NA
New or worsening seizures • GP to contact specialist immediately for review of treatment. • Stop ADHD medication; suspend shared care until reviewed by specialist team.	✓	✓	N/A	NA
New or worsening psychotic symptoms (delusions, hallucinations, anxiety, panic) • GP to refer to specialist ADHD team for full assessment and review of treatment. • Stop ADHD medication; suspend shared care until reviewed by specialist team.	✓	N/A	✓	✓
Agitation, tics, irritability, suicidal thinking and self-harm • Closely observe especially during initial months of treatment or after a change in dose • Contact specialist ADHD team for urgent advice and an urgent assessment	N/A	✓	N/A	NA
Drug misuse and diversion • Monitor changes in potential for misuse and diversion, which may come with changes in circumstances and age. Modified-release methylphenidate or atomoxetine may be preferred • Refer to specialist ADHD team for review of treatment	✓	N/A	✓	NA

Monitoring in response to symptoms only				
Full blood count To be carried out in response to symptoms of recurrent infections or development of purpuric rash • GP to arrange test and copy to specialist	✓	✓	✓	NA
Blood tests for liver function To be carried out in response to symptoms and abdominal pain, unexplained nausea, jaundice, darkened urine or malaise • If an adverse effect is suspected, specialist prescriber and paediatrics should be contacted for advice and an urgent assessment • GP to copy in specialist to any blood tests undertaken	N/A	✓	N/A	NA

SECONDARY CARE MONITORING **Physical health monitoring**				
Height This will be checked every six months	✓	✓	✓	✓
Weight This will be checked every six months Strategies to reduce weight loss or manage decreased weight gain in children, include: • Taking medication either with or after food, rather than before meals • Eating additional meals or snacks early morning or late evening when stimulant effects have worn off • Obtaining dietary advice and eating high-calorie foods of good nutritional value.	✓	✓	✓	✓
Cardiac function and blood pressure • Monitor heart rate and blood pressure every 6 months (weekly during dose titration for those receiving guanfacine); this should take place in between the six monthly monitoring by the GP as the requirement is to monitor every 3 months.	✓	✓	✓	✓