**Methylphenidate, atomoxetine and lisdexamfetamine▼**

**Shared Care Guidelines: For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents**

**AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE**

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of methylphenidate, atomoxetine and lisdexamfetamine for ADHD in children and adolescents can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with ADHD are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for methylphenidate, atomoxetine and lisdexamfetamine and the consequences of its use.

**RESPONSIBILITIES and ROLES**

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<thead>
<tr>
<th>Specialist responsibilities</th>
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</table>
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8 To review the patient and monitor the following on a six monthly basis and communicate these results to the GP
   • Height, weight and appetite, recorded on a growth chart.
   • Blood pressure and pulse, recorded on a centile chart (also following dose adjustments)
   • To refer patients who develop symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of heart disease for prompt cardiac evaluation.
   • The development of new or worsening of pre-existing, psychiatric symptoms (also following dose adjustments and at every visit)

9 To notify GP of patient’s failure to attend appointments and give advice on stopping the medication.

10 To liaise with the child’s school as appropriate.

11 All test results should be notified to the patient’s GP

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**General Practitioner responsibilities**

1 Initial referral to Secondary care with a full history of any diagnosis or history where caution is needed or methylphenidate, atomoxetine or lisdexamfetamine are contraindicated.

2 To inform specialist if unwilling to enter into shared care arrangements.

3 Complete relevant physical and cardiovascular assessments, if requested by the specialist.

4 To provide repeat prescriptions after stabilisation of dose. Prescriptions for methylphenidate and lisdexamfetamine should be restricted to 30 days supply and are only valid for 28 days from the date of signature. This is because methylphenidate and lisdexamfetamine are controlled drugs subject to safe custody and specific regulations for prescribing.

5 To contact the specialist if deterioration in behaviour.

6 To refer patients who develop symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of heart disease for prompt specialist cardiac evaluation.

7 To look out for signs of diversion (transfer of the medicine from the individual for whom it was prescribed to one for whom it is not prescribed), misuse and abuse of methylphenidate or lisdexamfetamine.

8 To act upon results communicated by the specialist

9 To take responsibility for either stopping the drug, referring to adult services or agreeing aftercare when the patient reaches 18 years of age

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**Patient’s and guardians role**

1 Report to the specialist or GP if he or she does not have a clear understanding of the treatment.

2 Share any concerns in relation to treatment with medicine.

3 Report any adverse effects to the specialist or GP whilst taking the medicine.

4 Return any unused or no longer needed medication promptly to the supplying pharmacy for destruction.
**Shared care guidelines for ADHD**

**BACK-UP ADVICE AND SUPPORT**

<table>
<thead>
<tr>
<th>Contact details</th>
<th>Telephone number</th>
<th>Email address</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFT ADHD specialists</td>
<td>01722 425270</td>
<td><a href="mailto:Patricia.May@salisbury.nhs.uk">Patricia.May@salisbury.nhs.uk</a></td>
</tr>
<tr>
<td>Dr Trisha May (Consultant Paediatrician)</td>
<td></td>
<td><a href="mailto:Tamsin.Griffiths@salisbury.nhs.uk">Tamsin.Griffiths@salisbury.nhs.uk</a></td>
</tr>
<tr>
<td>Dr Tamsin Griffiths (Consultant Paediatrician)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicines Information</td>
<td>023 8120 6908 /9</td>
<td><a href="mailto:medicinesadvice@uhs.nhs.uk">medicinesadvice@uhs.nhs.uk</a></td>
</tr>
<tr>
<td>(University Hospitals Southampton)</td>
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**Summary of medication used and licensed indications** for the full summary of product characteristics visit [www.medicines.org.uk](http://www.medicines.org.uk)

**First Choice**

*Methylphenidate (available as immediate or extended release forms) – Treatment of Attention-Deficit Hyperactivity Disorder (under specialist supervision)*

A Central Nervous Stimulant thought to regulate dopamine and noradrenaline neurotransmission. Methylphenidate is a Schedule 2 controlled drug and is not currently licensed for use in children less than 6 years old. It is available in immediate-release tablets (e.g. Ritalin®, Equasym®, Medikinet®) that are usually given in two or three daily doses. Methylphenidate is also available in modified-release formulations that enable once-daily dosing (e.g. Concerta XL®, Equasym XL®, Medikinet XL®, other brands are available). Modified-release brands provide different release profiles of methylphenidate and switching between brands should be avoided.

**Second choice options**

*Lisdexamfetamine (Elvanse)▼ is a long acting prodrug of dexamfetamine, a CNS stimulant occasionally used where methylphenidate has not been effective. Lisdexamfetamine allows for once daily dosing and has a lower abuse potential than dexamfetamine. It is a schedule 2 controlled drug and not licenced in children under 6 years old. Lisdexamfetamine has a black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.*

**Atomoxetine – Treatment of attention deficit hyperactivity disorder (under specialist supervision)**

Atomoxetine is a non-stimulant, non-amphetamine inhibitor of noradrenaline reuptake, although the precise mechanism by which it works on ADHD is unknown. It is not currently licensed for use in children less than 6 years old, and is not a controlled drug. It is occasionally used when CNS stimulants have not been effective or poorly tolerated or concerns are raised over the abuse potential of the CNS stimulants. Atomoxetine usually takes between 4-12 weeks to be fully effective.

**Treatment Aims (Therapeutic plan)**

Attention deficit hyperactivity disorder is usually diagnosed according to criteria specified in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-V).

ADHD is a chronic condition, which may require long-term treatment. All children with ADHD will benefit from behavioural, educational and psychological input. For some this is all that is required, but for others pharmacological measures will also be needed. These are initiated by a hospital specialist and shared care can be used to minimise the disruption caused by multiple and ongoing outpatient appointment.

In September 2008, NICE issued clinical guidance titled “Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults.” In 2016 this guidance was briefly updated to include dietary recommendations¹.

Please consult the NICE quick reference guide for more information:


**Treatment Schedule (including dosage and administration)**
Methylphenidate
The usual initial dose of the immediate release preparation is 5mg once or twice daily increased in weekly increments. Occasionally slower starting regimens may be used depending upon the individual patient. The dose should then be titrated to response and is usually divided two or three times a day. The maximum recommended dose for methylphenidate is 60mg daily and this is rarely exceeded in clinical practice. Modified release preparations usually start at the lowest available dose (18mg for Concerta or 10mg for Equasym XL and Medikinet XL) and are then increased gradually in weekly increments. The maximum licensed daily dose for Concerta XL is 54mg daily while for Equasyma and Medikinet is 60mg per day.

Lisdexamfetamine (Elvanse)
Lisdexamfetamine is usually initiated at 30mg daily and increased by 10-20mg weekly depending on response and tolerability. Occasionally a lower starting dose of 20mg per day is used if clinically indicated. The maximum daily dose is 70mg / day.

Atomoxetine
For children over 6 years/adolescents weighing less than 70kg, start with 0.5mg/kg/day. The initial dose should be maintained for a minimum of seven days prior to upward titration according to response and tolerability. The recommended maintenance dose is 1.2mg/kg/day (depending upon weight and available dosage strengths). No additional benefit has been demonstrated for doses above this but doses up to 1.8mg/kg/day may be used if thought to be appropriate under specialist advice.

For children/adolescents weighing more than 70kg the initial dose should be 40mg, maintained for a minimum of seven days before increasing according to response and tolerability. The recommended maintenance dose is 80mg per day. No additional benefit has been demonstrated for doses above this but the maximum recommended daily dose is 100mg. Doses can be taken with or after food.

Contra-indications, precautions for use

Methylphenidate
- Anxiety or agitation; severe depression, suicidal ideation; tics or a family history of Tourette’s syndrome; drug or alcohol dependence; psychosis; hyperthyroidism; cardiovascular disease; breast feeding.
- Diagnosis or history of severe depression, anorexia nervosa or anorexic disorders, suicidal tendencies, psychotic symptoms, mania, schizophrenia, severe mood disorders, or psychopathic or borderline personality disorder.
- Diagnosis or history of severe and episodic (type 1) bipolar (affective) disorder that is not well-controlled.
- Pre-existing cerebrovascular disorders – e.g cerebral aneurysm and vascular abnormalities, including vasculitis or stroke. Unless specialist cardiac advice has been obtained: in pre-existing cardiovascular disorders, including severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant.
- Congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias, and dysfunction of cardiac ion channels.
- Misuse and cardiovascular events: Misuse of stimulants of the central nervous system may be associated with sudden death and other serious cardiovascular adverse events.
- Growth: Moderately reduced weight gain and growth retardation have been reported with long-term use of methylphenidate.
- Seizures: Methylphenidate may lower the convulsive threshold and should be used with caution in patients with epilepsy.

Lisdexamfetamine
As for methylphenidate above
Shared care guidelines for ADHD

**Atomoxetine**
- Cardiovascular disease including hypertension and tachycardia; monitor growth in children; QT interval prolongation (avoid concomitant administration of drugs that prolong QT interval); history of seizures; susceptibility to angle-closure glaucoma; hepatic impairment or hepatic disorders; pregnancy; breast-feeding. Seizures are a potential risk with atomoxetine and therefore it should be used with caution in patients with a history of seizure. Discontinuation of atomoxetine should be considered in any patient developing seizure or if there is an increase in seizure frequency.
- Reports of QT interval prolongation have been received in association with atomoxetine. Therefore, it should be used with caution in those with congenital or acquired long QT or a family history of QT prolongation. This risk may be increased if atomoxetine is used concomitantly with other drugs that produce QT prolongation, drugs that can cause electrolyte disturbances and those that inhibit cytochrome P450 2D6 (may increase atomoxetine plasma levels).
- Due to concerns about an increased risk of suicidal thoughts and behaviour, patients should be monitored for signs of depression, suicidal thoughts or suicidal behaviour and referred for appropriate treatment if necessary. Patients and their carers should be informed about the risk and told to report clinical worsening, suicidal thoughts or behaviour, irritability, agitation, or depression.
- There is a risk of rare, but sometimes severe, hepatic disorders. Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted. Patients and carers should be advised of the risk and be told how to recognise symptoms; prompt medical attention should be sought in case of abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice.
- In addition to these warnings, the MHRA issued a further safety update in March 2009 concerning atomoxetine and provides the following advice to healthcare professionals
  - At normal doses, atomoxetine can be associated with treatment emergent psychotic or manic symptoms (e.g. hallucinations, delusional thinking, mania, or agitation) in children and adolescents without a history of psychotic illness or mania
  - If such symptoms occur, consideration should be given to a possible causal role of atomoxetine and discontinuation of treatment
  - It remains possible that atomoxetine might exacerbate pre-existing psychotic or manic symptoms.

**Side-effects**
Undesirable effects. Only very common (greater or equal than 10% incidence), and common (between 1% and 10% incidence) are listed, for all others consult the latest SmPC

**Methylphenidate**
- Very common (≥1/10): Headache, insomnia, nervousness
- Common (≥1/100 to ≥1/10): Nasopharyngitis, tic, aggression, anxiety, affect lability, mood swings, depressed mood, dizziness, cough, pharyngolaryngeal pain, abdominal pain, vomiting, nausea, diarrhoea, stomach discomfort, irritability, pyrexia, decreased weight and appetite. growth retardation during prolonged use and changes in blood pressure and heart rate (usually an increase).

**Lisdexamfetamine**
- Very common (≥ 1/10): Decreased appetite, insomnia, headache, weight decreased,
- Common (≥1/100 to ≥1/10): Anxiety, Tics, aggression, dizziness, somnolence, tachycardia, dry mouth, diarrhoea, constipation, nausea, vomiting, irritability

**Atomoxetine**
- Very common (≥ 1/10): decreased appetite, headache, somnolence, abdominal pain, vomiting, nausea, blood pressure and heart rate increased
- Common (≥1/100 to ≥1/10): Anorexia, irritability, mood swings, insomnia, agitation, anxiety and depression, tics, dizziness, mydriasis, constipation, dyspepsia, rash, fatigue, lethargy, weight decreased
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Pregnancy and Lactation
Females of child-bearing potential (females post-menarche) should use effective contraception. Please take expert advice if dealing with patient groups likely to be affected by pregnancy and lactation.

Interactions
Please consult the relevant SPC or the BNF for relevant information concerning drug interactions.
Issues to note are:-

Atomoxetine
Undergoes biotransformation primarily through the cytochrome P450 2D6. Caution in CYP2D6 inhibitors such as fluoxetine, paroxetine, quinidine and terbinafine.

Methylphenidate and lisdexamfetamine
Contraindicated in patients treated with an MAOI, caution when administering with dopaminergic drugs (such as antipsychotics).

Monitoring for Methylphenidate and lisdexamfetamine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency of monitoring</th>
<th>Action</th>
<th>By whom</th>
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</thead>
<tbody>
<tr>
<td>Full blood count</td>
<td>As clinically indicated</td>
<td>Low threshold for investigation rather than schedule for routine testing e.g. if recurrent infections or purpuric rash occur</td>
<td>Specialist/GP as agreed</td>
</tr>
<tr>
<td>Blood pressure and pulse (appendix 1)</td>
<td>At initiation, every 6 months or following a dose change</td>
<td>Monitor whilst taking medication to ensure within published range for age of child</td>
<td>Specialist/GP as agreed</td>
</tr>
<tr>
<td>Growth development (height and weight)</td>
<td>At initiation, every 6 months or following a dose change</td>
<td>Failure to gain weight appropriately may require withdrawal If adversely affected consideration should be given to dose reduction or interrupting therapy in those on long-term treatment.</td>
<td>Specialist/GP as agreed</td>
</tr>
<tr>
<td>Monitor for insomnia, mood and appetite changes and the development of tics</td>
<td>Ongoing basis and at follow up</td>
<td>If adversely affected consideration should be given to dose reduction or interrupting therapy in those on long-term treatment.</td>
<td>Specialist/GP as agreed</td>
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Monitoring for atomoxetine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency of monitoring</th>
<th>Action</th>
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<tr>
<td>Appearance of suicidal behaviour, self-harm or hostility</td>
<td>Ongoing basis and at follow up</td>
<td>Patients/parents should be advised of this risk and made aware of possible signs/symptoms to report back to the specialist immediately if noticed</td>
<td>Specialist</td>
</tr>
<tr>
<td>Blood pressure and pulse (appendix 1)</td>
<td>At initiation, 6 monthly or following a dose change</td>
<td>Monitor whilst taking medication to ensure within published range for age of child</td>
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### Shared care guidelines for ADHD

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<th>Growth development (height and weight)</th>
<th>At imitation, 6 monthly or following a dose change</th>
<th>If adversely affected consideration should be given to dose reduction or interrupting therapy in those on long-term treatment</th>
<th>Specialist/GP as agreed</th>
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<tr>
<td>LFTs</td>
<td>As clinically indicated - If physical examination reveals jaundice or other signs of liver abnormalities</td>
<td>Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted</td>
<td>Specialist/GP as agreed</td>
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### Costs
At March 2017 electronic drug tariff prices, the cost of one month’s treatment is as follows

#### Methylphenidate (30 days)
- Non-proprietary methylphenidate: £5.49 - £32.76 (10-60mg daily)
- Medikinet XL: £25-£67.32 (10-60mg daily)
- Equasym XL: £25 - £70 (10-60mg daily)
- Concerta XL: £31.19 - £73.64 (18-54mg daily)

#### Atomoxetine (28 days)
- Capsules: £53.09 (10mg, 18mg, 25mg, 40mg)
- Oral solution 4mg/1ml: £85 (300mls)

#### Lisdexamfetamine (Elvanse) (28 days)
- 30mg caps: £58.24
- 50mg caps: £68.60
- 70mg caps: £83.16

### Document review

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<tr>
<th>First edition</th>
<th>March 2010</th>
<th>Dr M Lwin Consultant Paediatrician</th>
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<td></td>
<td>March 2010</td>
<td>Approved by the Salisbury NHS Foundation Trust: Drugs and Therapeutics Committee</td>
</tr>
<tr>
<td>Second edition</td>
<td>January 2017</td>
<td>Dr Tamsin Griffiths Consultant Paediatrician (SFT) Dr Patricia May Consultant Paediatrician (SFT) Steve Bleakley Chief Pharmacist (SFT)</td>
</tr>
<tr>
<td></td>
<td>February 2017</td>
<td>Approved by the Salisbury NHS Foundation Trust: Drugs and Therapeutics Committee tbc</td>
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### References

### Appendix 1:
Shared care guidelines for ADHD