PAN MERSEY AREA PRESCRIBING COMMITTEE
SHARED CARE FRAMEWORK
RED: SC11 FINAL
APC BOARD DATE: 30 NOV 2016

NHS
Pan Mersey
Area Prescribing Committee

ATOMOXETINE

1. Background	Attention deficit hyperactivity disorder (ADHD) is a chronic, neurodevelopmental disorder associated with inattention, hyperactivity and impulsiveness. The National Institute for Health and Clinical Excellence (NICE) issued a clinical guideline, Attention Deficit Hyperactivity Disorder: diagnosis and management (NG87) in 2018. This document advises that treatment for ADHD should only be initiated by a healthcare professional with expertise in ADHD and should be based on a comprehensive assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by the primary care clinicians, under shared care arrangements. Methylphenidate, atomoxetine, dexamfetamine, lisdexamfetamine and guanfacine are recommended within their licensed indications, as options for the management of ADHD. Some prescribing of ADHD medication is 'off-label' but clearly supported by the NICE guideline, British National Formulary (BNF) and BNF for Children. Symptoms of ADHD can persist into adulthood in about two thirds of all patients. For patients transitioning into adulthood, specialists should ensure appropriate arrangements are made for referral into adult services. In such circumstances a new shared care agreement will need to be made between the primary care clinician and the new secondary care provider.
2. Mode of Action	Atomoxetine is a highly selective and potent inhibitor of the pre-synaptic noradrenaline transporter, its presumed mechanism of action, without directly affecting the serotonin or dopamine transporters. Atomoxetine is not a psychostimulant and is not an amphetamine derivative.
3. Licensed Indications	Atomoxetine is indicated for the treatment ADHD in children of 6 years and older, in adolescents and in adults as part of a comprehensive treatment programme. Treatment must be initiated by a specialist in the treatment of ADHD, such as a paediatrician, child/adolescent psychiatrist, or psychiatrist.
4. Locally agreed off label indications	Not applicable

Version: 1.7
Review date: November 2019
(or earlier if there is significant new evidence relating to this recommendation)

<table>
<tr><td>5. Contraindications</td><td colspan="2">(Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Refer to the manufacturers SPC for complete up-to-date list.)
Hypersensitivity to active substance or any of the excipients (including sorbital in the liquid formulation) as listed on the SPC.
Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days after MAOI treatment
Severe cardiovascular disorders (including severe hypertension, heart failure, arterial occlusive disease, angina, congenital heart disease, cardiomyopathies, life-threatening arrhythmias)
Severe cerebrovascular disorders (including cerebral aneurysm or stroke)
Phaeochromocytoma or a history of phaeochromocytoma
Narrow-angle glaucoma.</td></tr>
<tr><td rowspan="5">6. Pharmaceutical aspects
(including route of administration, formulation, method of administration, legal category)</td><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Formulation</td><td>Hard capsules in 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg or 100 mg
Oral solution 4 mg/mL
It is more cost effective to prescribe the exact strength of atomoxetine instead of combining different strengths for an increased dose.</td></tr>
<tr><td>Method of administration</td><td>Capsules or liquid should be taken with or without food.
It is not recommended to mix oral solution in food or water as it can prevent the patient receiving a full dose or could negatively affect the taste.</td></tr>
<tr><td>Other important information</td><td>No distinct withdrawal symptoms have been reported.
In cases of significant adverse effects, atomoxetine may be stopped abruptly; otherwise the drug may be tapered off over a suitable time period.
Atomoxetine may exacerbate hypertension in patients with end-stage renal disease</td></tr>
<tr><td>Legal category</td><td>Atomoxetine is a prescription only medicine (POM). It is not a controlled drug</td></tr>
<tr><td>7. Specialist initiation And titration</td><td colspan="2">Dosage should be individualised according to the therapeutic needs and response of the patient.

Children and adolescents weighing up to 70 kg body weight:
The initial total daily dose of approximately 0.5 mg/kg should be initiated. The dose should be titrated after 7 days, if necessary up to a maximum of 1.8mg/kg/day, either as a single dose or in two divided doses, according to clinical response and tolerability.

Children and adolescents weighing over 70 kg body weight:
The initial total daily dose of 40 mg should be initiated. The dose should be titrated after 7 days according to response and tolerability to a usual maintenance dose of 80 mg/day. The maximum recommended total daily dose is 100mg.

A single daily dose can be given; however, two divided doses may be</td></tr>
</table>

<table>
<tr><td>Specialist initiation and titration -
continued</td><td colspan="2">prescribed to minimise side effects.

Adults:
The initial total daily dose of 40 mg should be initiated. The dose should be titrated after 7 days according to response and tolerability to a usual maintenance daily dose of 80 mg to 100mg. The maximum recommended total daily dose is 100mg.

In order to optimise drug treatment, the initial dose should be titrated against symptoms and side effects over 4–6 weeks [NICE CG72]. Doses should be gradually increased until there is no further clinical improvement in ADHD (that is, symptom reduction, behaviour change, improvements in education and/or relationships) and side effects are tolerable.

For adults, a trial of 6 weeks on a maintenance dose should be allowed to evaluate the full effectiveness of atomoxetine.

Dose reduction may be required in patients with different degrees of hepatic impairment – refer to SPC

Shared Care may only be commenced following initiation, stabilisation and review of treatment. In addition, formal agreement must have been received from the primary care prescriber.</td></tr>
<tr><td rowspan="4">8. Dosage regimen for continued prescribing in Primary Care</td><td colspan="2">Following initiation and stabilisation continue prescribing and monitoring as advised by the specialist in accordance with the shared care agreement.</td></tr>
<tr><td>Duration of treatment
To be determined by the specialist based on clinical response and tolerability.</td><td>Following an adequate treatment response, atomoxetine should be continued for as long as it remains clinically effective. This should be reviewed at least annually.

Trial periods off medication (drug holiday) to assess the patient’s condition without treatment may be deemed appropriate by the ADHD specialist. This will be undertaken and supervised by the specialist who will advise the patient and GP of the outcome.</td></tr>
<tr><td>Termination of treatment</td><td>This will be carried out by the specialist</td></tr>
<tr><td colspan="2">NB. All dose adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.</td></tr>
</table>

9. Significant Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics

Seek advice from the initiating Specialist if any of the following drugs are co-prescribed.

MAOIs: contra-indicated, risk of hypertensive crisis

CYP2D6 inhibitors (**SSRIs (e.g., fluoxetine, paroxetine), quinidine, terbinafine):** atomoxetine exposure may be 6-to 8-fold increased and max steady state serum levels 3 to 4 times higher.

Salbutamol (or other beta2 agonists): high dose nebulised or systemically administered salbutamol (or other beta2 agonists) may potentiate cardiovascular effects.

Increased risk of QT interval prolongation when atomoxetine is administered with other **QT prolonging drugs** (such as antipsychotics, class IA and III anti-arrhythmics, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium, or cisapride), drugs that cause electrolyte imbalance (such as thiazide diuretics), and drugs that inhibit CYP2D6.

Concomitant use of **medicinal drugs which are known to lower the seizure threshold** (such as tricyclic antidepressants or SSRIs, antipsychotics, mefloquine, chloroquine, bupropion or tramadol). Increased risk of seizures. In addition, caution is advised when stopping concomitant treatment with benzodiazepines due to potential withdrawal seizures.

Anti-hypertensives: atomoxetine may increase in blood pressure.

Pressor agents: atomoxetine may increase in blood pressure.

Drugs that affect noradrenaline because of the potential for additive or synergistic pharmacological effects. Examples include antidepressants, such as imipramine, venlafaxine, and mirtazapine, or the decongestants pseudoephedrine or phenylephrine.

10. Adverse drug reactions

For a comprehensive list consult the BNF or Summary of Product Characteristics

The most common adverse effects include:

- Gastrointestinal effects such as anorexia, dry mouth, nausea, vomiting, abdominal pain, constipation, dyspepsia, and flatulence.
- Cardiovascular effects such as palpitation, tachycardia, increased blood pressure, postural hypotension, and hot flushes.
- Central nervous system effects such as sleep disturbance, dizziness, headache, fatigue, lethargy, drowsiness, irritability, tremor, and rigors.
- Dermatological effects such as dermatitis, pruritus, and rash.
- Other effects including sweating, weight changes, urinary retention, enuresis, prostatitis, sexual dysfunction, menstrual disturbances, and conjunctivitis.

In children, parents/patients will have been advised by the ADHD specialist to report any suspected side effects directly to them. GPs should refer any patients with suspected side effects to the ADHD specialist irrespective of the advice in the following table.

Adverse event System – symptom/sign	**Action to be taken and by whom**
Sustained resting tachycardia, cardiomyopathy, unexplained chest pains, dyspnoea and unexplained syncope	Seek prompt cardiac specialist advice and notify the ADHD specialist Team

Adverse event System – symptom/sign	Action to be taken and by whom
Clinically significant increases in blood pressure, arrhythmia	Exclude other causes and seek ADHD specialist advice.
Development or worsening of psychiatric disorders including psychotic or manic symptoms, aggressive or hostile behaviour, anxiety, agitation, motor or vocal tics and suicidal ideation.	Continue treatment. Seek ADHD specialist advice. Discontinuation of treatment may be considered by the specialist
Reduced weight and growth retardation	Continue treatment. Provide advice on healthy diet and consider taking additional meals or snacks early in the morning or late in the evening when the effects of the drug have worn off. Refer to a dietician if appropriate. If weight loss becomes a concern, seek ADHD specialist advice.
Increase in seizure frequency or new-onset seizures	Refer to the ADHD specialist Team. Discontinuation of treatment may be appropriate.
Moderate to severe liver disorders	Exclude other causes. Repeat blood tests for confirmation. Seek ADHD specialist advice if the adverse effect is secondary to the drug. Discontinuation of treatment may be considered
Constipation, abdominal pain, decreased appetite, nausea, vomiting, dyspepsia	Continue treatment, usually transient. Initial symptoms may be alleviated by concomitant food intake. Exclude other causes. Seek ADHD specialist advice if symptoms become severe. Dose reduction or discontinuation of treatment may be considered
Insomnia	Continue treatment, usually transient. Provide sleep hygiene advice. Timing of doses may need to be adjusted with ADHD specialist advice.
Headache, dizziness, fatigue, lethargy	Continue treatment. Exclude other causes. If severe seek ADHD specialist advice. Dose reduction or discontinuation of treatment may be considered.
Sexual dysfunction (i.e. erectile and ejaculatory dysfunction) and dysmenorrhoea	Refer to the ADHD specialist Team. Discontinuation of treatment may be appropriate.
WARNINGS: Atomoxetine has been associated with increased rates of fatigue, somnolence, and dizziness in paediatric and adult patients. Patients should be advised caution when driving a car, cycling or operating hazardous machinery until they are reasonably certain that their performance is not affected by atomoxetine.	
Any serious reaction to atomoxetine should be reported to the MHRA via the "Yellow Card" scheme on http://yellowcard.mhra.gov.uk/	

<table>
<tr><td>11. Advice to patient/carers</td><td colspan="2">The patient should be advised to report any of the following signs or symptoms to their GP without delay:
Symptoms suggestive of cardiac or psychiatric (e.g. suicidal ideation, self-harming behavior) disorders, seizures.
Symptoms suggestive of liver damage e.g. abdominal pain, unexplained nausea, malaise, darkening of urine or jaundice
In children, parents/patients will have been advised by the ADHD specialist to report the above signs or symptoms directly to them.</td></tr>
<tr><td>12. Pregnancy and breast feeding</td><td colspan="2">Seek specialist advice for prescribing decision.</td></tr>
<tr><td>13. Baseline investigations to be undertaken by the specialist centre</td><td colspan="2">A comprehensive history of concomitant medications
Full mental health and social assessment
Full medical history and physical examination including
Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms
Heart rate and blood pressure
Weight (in adults); height and weight plotted on a growth chart (in children and adolescents) repeat following each dose adjustment and at 3 months and 6 months after treatment has started
Family history of cardiac disease and examination of the cardiovascular system.
Pregnancy or breastfeeding
An 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.</td></tr>
<tr><td rowspan="6">14. Ongoing monitoring requirements to be undertaken in Primary Care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>Blood pressure and pulse

(appropriate for age, using information supplied in attached request letter – children & adolescents only)</td><td>At every adjustment of dose or visit and then every 6 months

Primary care – every 6 months</td></tr>
<tr><td>Weight (in adults); Height and weight (in children and adolescents)</td><td>At every adjustment of dose or visit or at least every 6 months

Primary care – every 6 months

Weight every 3 months in children 10 years and under</td></tr>
<tr><td>Side effects</td><td>Every 6 months</td></tr>
<tr><td>Compliance</td><td>Every 6 months</td></tr>
<tr><td>Clinical need, benefits, side effects</td><td><u>Annual review by Specialist</u></td></tr>
<tr><td colspan="2">Refer to ‘Adverse Drug Reactions’ section for advice and actions to be taken.</td></tr>
<tr><td rowspan="2">15. Specialist contact information</td><td colspan="2">If stopping medication or needing advice please contact:</td></tr>
<tr><td colspan="2">Refer to the shared care agreement (Appendix 2)</td></tr>
<tr><td>16. Additional information</td><td colspan="2">Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.</td></tr>
</table>

17. References	1. Summary of product characteristics for atomoxetine Strattera® 2. NICE guidelines NG87 March 2018: Attention deficit hyperactivity disorder: diagnosis and management 3. NICE CKS for ADHD 4. British National Formulary 5. British National Formulary for Children
18. To be read in conjunction with the following documents	Shared Care Policy (appendix 1) Shared Care Agreement (appendix 2)

Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey **Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary** document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.
- All information required by the shared care framework for the individual medicine has been provided to the patients GP.
- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- To initiate the medicine, prescribing and monitoring toxicity and efficacy as required until the patient is stabilised and reviewed as described by the shared care framework.
- To ensure the patient or their carer is counselled with regard to the medicine.
- To provide any necessary written information to the patient with regard to the individual medicine.
- To be familiar with the shared care framework.

- To provide all information to the patients GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- To assess the patient regularly as necessary for the duration of therapy as specified in the individual medicine shared care framework.
- To review the patient promptly if required by the GP concerned.
- To meet any additional requirements as required by the individual medicine shared care framework.
- To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.
- Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must recall the patient for re-titration, stabilisation and subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated.

Primary Care Responsibilities in Shared Care

- To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked to:

- To prescribe and/or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
- To review the patient as required by the Shared Care Framework
- To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient`s clinical record. A READ code of “6652 Shared Care- Specialist/GP” can be used.
- To be familiar with the individual Shared Care Framework.
- To monitor patient’s general wellbeing.
- To report any adverse effects of treatment to the consultant
- To inform the Specialist of any relevant change in the patient’s circumstances.
- To seek Specialist advice as appropriate.
- To meet any additional requirements as required by the individual Shared Care Framework.

- To respond to Specialist communication relating to any change or addition to the patients treatment covered by the Shared Care Agreement.

Appendix 2: Shared Care Agreement

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1
To be signed by Consultant / Prescribing member of specialist team

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

If using addressograph label please attach one to each copy

Dear Dr_____

I request that you prescribe

(1) _____

(2) _____

for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: ….. / ….. / ….. Next Supply Due: ….. / ….. / …..

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy. ☐

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received. ☐

Details of Specialist Clinicians

Name _____Date_____

Consultant / Prescribing member of Specialist Team ****circle or delete as appropriate***

Signature _____

In <u>all</u> cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the consultant, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details*:*

Telephone number: _____Ext:_____

Address for return of documentation _____

_____

_____

<u>Part 2; To be completed by Primary Care Clinician</u>

I agree to prescribe _____for the above

patient in accordance with the enclosed shared care framework.

GP signature _____Date _____

GP name _____Please print

<u>GP:</u> *Please sign and return a copy* ***within 21 calendar days*** *to the address above*

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: