This policy statement is approved by Southport and Formby, South Sefton, CCGs

Southport and Formby | South Sefton

NHS

South Sefton Clinical Commissioning Group
Southport and Formby Clinical Commissioning Group

Shared Care Framework for

Atomoxetine for the treatment of ADHD in adults

Date approved by Joint Medicines Operational Group 5/10/2018

1. Background	Attention deficit hyperactivity disorder (ADHD) is a chronic, neurodevelopmental disorder associated with inattention, hyperactivity and impulsiveness. In about two thirds of all patient's symptoms of ADHD can persist into adulthood. NICE recommend that treatment for ADHD should 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 can be performed by the primary care clinicians, under shared care arrangements.
2. 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.
3. Locally agreed off-label indications	N/A
4. Specialist Initiation and dose titration	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. • The dose should be titrated against symptoms and side effects over 4-6 weeks. • A trial of 6 weeks on a maintenance dose should be allowed to evaluate the full effectiveness of atomoxetine. • All dose adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician • 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.**
5. **Baseline investigations, initial monitoring and dose titration to be**	**Baseline Investigations**: • A comprehensive history of concomitant medications • Full mental health and social assessment

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<td>undertaken by the specialist.</td>
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Full medical 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.
Family history of cardiac disease
Examination of the cardiovascular system
Pregnancy or breastfeeding status

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.
Risk assessment for substance misuse and drug diversion.

Ongoing monitoring by specialist:

To optimise drug treatment, the initial dose should be titrated against symptoms and side effects over 4–6 weeks. Doses are gradually increased until there is no further clinical improvement in ADHD symptoms (behaviour change, improvements in education and or relationships) and side effects are tolerable
Blood pressure and pulse every 6 months or at each visit and after every dose adjustment.
Clinical need, benefit and side effects should be reviewed annually. Atomoxetine should be continued for as longs as it remains effective.
Weight 3 months after starting treatment then every 6 months and at each visit or at each dose adjustment.
Treatment should be discontinued if there is no response after 1 month of maximum tolerated dose.

Duration of treatment to be determined by the specialist based on clinical response and tolerability.

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

Termination of treatment will be carried out by the specialist
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<td>6. Ongoing monitoring requirements to be undertaken by Primary Care.</td>
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Following initiation and stabilisation continue prescribing and monitoring as advised by the specialist in accordance with the shared care agreement.
<table>
<tr><th>Monitoring</th><th>Frequency</th></tr>
<tr><td>Blood pressure and pulse</td><td>Every 6 months</td></tr>
<tr><td>Weight</td><td rowspan="3">Every 6 months</td></tr>
<tr><td>Compliance check including checking for any signs of diversion</td></tr>
<tr><td>Side effects</td></tr>
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<tr><td rowspan="4">7. 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.
• This should be in line with the commissioner’s recommendation</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></td><td>Legal Category</td><td>Atomoxetine is a prescription only medicine (POM). It is not a controlled drug.</td></tr>
<tr><td>8. Contraindications
(Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.)</td><td colspan="2">• Hypersensitivity to active substance or any of the excipients (including sorbitol in the liquid formulation) as listed in 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>9. Significant Drug Interactions

(For a comprehensive list consult the BNF or Summary of Product Characteristics)</td><td colspan="2">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.</td></tr>
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- **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 antiarrhythmics, 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.

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<tr><td>10. Adverse effects and management
(For a comprehensive list consult the BNF or Summary of Product Characteristics)</td><td>

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.

<table>
<tr><th>Adverse Effect</th><th>Action</th></tr>
<tr><td>Sustained resting tachycardia, cardiomyopathy, unexplained chest pains, dyspnoea and unexplained syncope</td><td>Notify the initiating specialist.
Seek prompt cardiac specialist advice.</td></tr>
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	Clinically significant increases in blood pressure, arrhythmia	Exclude other causes and seek advice from the initiating specialist.
	Reduced weight	Continue treatment. Provide advice on healthy diet. The patient should be advised to consider taking additional meals or snacks early in the morning or late in the evening when the effects of the drug have worn off. If weight loss becomes a concern, seek ADHD specialist advice.
	Increase in seizure frequency or new-onset seizures	Refer to the initiating specialist team.
	Development or worsening of psychiatric disorders including psychotic or manic symptoms, aggressive or hostile behavior, anxiety, agitation, motor or vocal tics and suicidal ideation	Refer to the initiating specialist team. Continue treatment
	Moderate to severe liver disorders (incidental finding on blood tests)	Exclude other causes. Repeat blood tests for confirmation. Seek ADHD specialist advice if it is suspected the adverse effect is secondary to the drug.
	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.
	Insomnia	Continue treatment, usually transient. Provide sleep hygiene advice. Contact specialist for advice as dose and timing of dose may need to be adjusted by the specialist.
	Sexual dysfunction (i.e. erectile and ejaculatory dysfunction) and dysmenorrhoea	Refer to the ADHD specialist Team.
	Headache, dizziness, fatigue, lethargy	Continue treatment. Exclude other causes. If severe seek ADHD specialist advice.
	Any serious reaction to atomoxetine should be reported to the MHRA via the "Yellow Card" scheme on http://yellowcard.mhra.gov.uk/	
11. Advice to patient and carers	**WARNINGS**: Atomoxetine has been associated with increased rates of fatigue, somnolence, and dizziness in pediatric 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. 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
12. Pregnant or Breast feeding	Refer to initiating specialist
13. Specialist Contact Information	Mersey Care NHS Foundation Trust South Sefton Neighbourhood Centre Park Road Waterloo Liverpool L22 3XR Tel: 0151 330 8500
14. Additional information	Where patient care is transferred from one provider to another, a new shared care agreement must be completed.
15. References	1. Various summaries of product characteristics atomoxetine. 2. NICE guidelines (CG72) 2008: Attention deficit hyperactivity disorder: diagnosis and management **Updated August 2018** with Nice Guidelines (NG87) 2018: Attention deficit hyperactivity disorder: diagnosis and management https://www.nice.org.uk/guidance/ng87 3. NICE CKS for ADHD 4. British National Formulary

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 patient's 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, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
    - Is counselled with regard to the risks and benefits of the medicine.
    - Provide any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
    - Obtain and document informed consent from the patient when any medicines is prescribed for an off-label indication for any condition
- To be familiar with the shared care framework.
- To provide all information to the patient's 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.
- 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 initiate, prescribe and monitor the new drug in accordance with the relevant shared care agreement including subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated for the new drug.

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 provide prescribe 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 report any adverse effects of treatment to the specialist team.
- 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 patient’s 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 / Associate Specialist / Specialist registrar or Specialist Nurse (who must be a prescriber)

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 / Associate Specialist / Specialist Registrar / Specialist Nurse ****circle or underline as appropriate***

Signature _____

In all cases, please also provide the name and contact details of the Consultant.
When the request for shared care is made by a Specialist Nurse, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details*:*

Telephone number: _____Ext:_____

Address for return of documentation _____

_____

_____

Part 2

To be completed by Primary Care Clinician

I agree to prescribe_____for the above patient in accordance with the enclosed shared care framework.

GP signature_____Date _____

GP name _____Please print

GP: *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

Part 3 Other Relevant Information

Part 4 Monitoring Requirements

Monitoring requirements are detailed in section 6 of the attached shared care framework.

Date	Weight	Pulse	Blood Pressure
Refer if:	[Please specify threshold]	[Please specify threshold]	[Please specify threshold]

Details of any recent relevant monitoring results:

Previous investigations completed	**Date**	**Result**	**Next date due**