NHS South of Tyne and Wear

serving Gateshead Primary Care Trust, South Tyneside Primary Care Trust and Sunderland Teaching Primary Care Trust

SHARED CARE GUIDELINE

For

Atomoxetine in the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and young people and adults

Implementation Date: April 2012

Review Date: March 2014

This guidance has been prepared and approved for use within Gateshead, South Tyneside and Sunderland in consultation with Primary and Secondary Care Trusts and Local Medical Committees.
The guideline sets out the details of the transfer of prescribing and respective responsibilities of GPs and specialist services within shared care prescribing arrangements. It is intended to provide sufficient information to allow GPs to prescribe these treatments within a shared care setting

Further copies are available from

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Approved by:

Committee	Date
Gateshead Medicines Management Committee	**April 2012**
South Tyneside Prescribing Committee	**March 2012**
Sunderland Primary Care Prescribing Group	**March 2012**
South of Tyne and Wear Medicines Management Committee	

SHARED CARE GUIDELINE			
Non proprietary name	Atomoxetine	Brand name	Strattera®
Dosage form and strength	10mg, 18mg, 25mg, 40mg, 60mg, or 80mg hard capsules	BNF class	4.4 CNS stimulants and drugs used for ADHD
Condition(s) to be treated	As part of a comprehensive treatment programme for Attention Deficit Hyperactivity Disorder (ADHD) in children, young people and adults when remedial measures alone prove insufficient. Atomoxetine is currently licensed for use in adults when it has been started in childhood. Its use is recommended as appropriate for shared care by NICE.		
Excluded patients	**Atomoxetine is <u>not</u> licensed for use in children under six years of age.** Occasionally, prescribing for children under six will be recommended by a consultant and in these instances atomoxetine will be prescribed by specialist services until the child reaches the age of six.		
Eligibility criteria for shared care	Children aged 6 years or over, young people and adults who have been assessed by the specialist where: • The patient is stabilised on treatment and has then been supplied with a further month's treatment by the specialist to give time for shared care to be arranged. • In some circumstances it may be more appropriate for the GP to prescribe atomoxetine on the advice of the specialist during the initiation and titration phase. This must be done on a case by case basis by prior arrangement and all the necessary information for the GP to do this safely must be provided by the specialist. • A package of multi-disciplinary support which includes the psychological, behavioural and educational or occupational needs as appropriate will be considered before transfer of prescribing to the GP. • Both the specialist, and GP agree to the shared care arrangement (in accordance with Responsibilities of General Practitioners below)		
Initiation	For children/adolescents and adults of up to 70 kg body weight, treatment should be initiated at a dose of 500 micrograms/kg daily, increased as necessary after a minimum of 7 days. The recommended maintenance dose is approximately 1.2mg/kg/day, but doses may be increased to 1.8mg/kg/day. However no additional benefit has been demonstrated for doses higher than 1.2mg/kg/day. For children/adolescents and adults over 70 kg body weight, treatment should be initiated at a daily dose of 40 mg for a minimum of 7 days and increased according to response to a usual maintenance dose of 80 mg. The maximum recommended total daily dose is 100mg, but may be increased to a maximum of 120mg per day (unlicensed, but recommended by NICE) under the direction of a specialist.		
Duration of treatment	For as long as benefit is maintained. The specialist team will be responsible for reviewing clinical need, benefits and side effects.		

	The specialist will supervise the discontinuation phase. Treatment should be considered for discontinuation in adolescence but it may need to be continued into adulthood if clinically indicated. Drug holidays are not routinely recommended; however, consideration should be given to the parent or carer and child or young person with ADHD working with their healthcare professional to find the best pattern of use, which may include periods without treatment. Spontaneous or accidental omission of doses (e.g. due to a compliance problem) can also provide useful information on the continued benefit of the treatment. If a trial discontinuation is considered, this is usually done when the patient is experiencing a stable routine i.e. avoid exam times, stressful periods at work etc).
Usual maintenance dose	18 – 100 mg daily – Total daily dose may be given *either* as a single dose in the morning *or* in 2 divided doses with the last dose no later than early evening
Maximum dose	In children/adolescents and adults less than 70kg the maximum dose is usually - 1.2mg/kg/day but can be increased up to 1.8mg/kg/day (maximum 120mg daily, unlicensed but recommended by NICE) under supervision of a specialist In child 6-18 years over 70kg usual maximum is 80mg but can be increased to a maximum of 120mg daily (unlicensed dose but recommended by NICE) under the direction of a specialist. In adults over 70kg - 100mg daily (licensed dose) but can be 120mg daily (unlicensed dose, but recommended by NICE)
Preparations	Atomoxetine 10mg, 18mg, 25mg, 40mg, 60mg, or 80mg hard capsules
Cost 28 days (Oct 2011)	For doses up to 60mg there if a flat pricing structure of £62.46 for 28 days supply. The 80mg caps cost £83.28 for 28 days. (N.B. twice daily dosing schedules double treatment costs for any given total daily dose).
Adverse effects Common Uncommon	Headache, abdominal pain and decreased appetite are the adverse events most commonly reported (19%, 18% and 16% of patients respectively), but seldom lead to drug discontinuation – abdominal pain and decreased appetite are usually transient. Associated with decreased appetite, some patients lost weight during early therapy (0.5 to 1.0kg); these effects were found to be dose related. Nausea, Vomiting and somnolence occurred in 10 to 11% of patients. Orthostatic hypotension (0.2%) and syncope (0.8%). Although uncommon, allergic reactions, including anaphylactic reactions, rash, angioneurotic oedema, and urticaria, have been reported in patients taking Atomoxetine.

Contra-indications	Atomoxetine should not be used in combination with monoamine oxidase inhibitors (MAOIs). Atomoxetine should not be used within a minimum of 2 weeks after discontinuing therapy with a MAOI. Treatment with a MAOI should not be initiated within 2 weeks after discontinuing atomoxetine. Glaucoma. Patients with pheochromocytoma or a family history of pheochromocytoma Patients with severe cardiovascular or cerebrovascular disorders whose condition would be expected to deteriorate if the experienced increase in BP or heart rate could be clinically significant (for example, 15 – 20mmHg in BP and/or 20 beats/min in heart rate). This may include severe hypertension, heart failure, angina and cardiomyopathies. Patients who develop symptoms suggestive of cardiac disease during atomoxetine treatment should undergo a prompt specialist cardiac evaluation
Precautions	Psychotic or manic symptoms*:* Treatment-emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, mania or agitation in children and adolescents without a prior history of psychotic illness or mania can be caused by atomoxetine at usual doses. If such symptoms occur, consideration should be given to a possible causal role of atomoxetine, and discontinuation of treatment should be considered. The possibility that atomoxetine will cause the exacerbation of pre-existing psychotic or manic symptoms cannot be excluded. Introduce with caution in patients with a history of seizure. Consider discontinuation in any patient who develops new seizures or where seizure frequency increases. Use 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 (e.g. tricyclic antidepressants, antipsychotics), drugs that can cause electrolyte disturbances and those that inhibit cytochrome P450 2D6 (e.g. erythromycin and other macrolide antibiotics, fluoxetine). As orthostatic hypotension has been reported, Atomoxetine should be used with caution in conditions that predispose patients to hypotension or conditions associated with abrupt heart rate or blood pressure changes Sudden death and pre-existing structural cardiac abnormalities or other serious heart problems: Sudden death has been reported in children and adolescents with structural cardiac abnormalities who

	were taking Atomoxetine at usual doses – consult with cardiac specialist if there is concern
Renal impairment and liver disease	Renal impairment - No dosage adjustment required Hepatic impairment - Patients with moderate hepatic insufficiency, initial and target doses should be reduced to 50% of the usual dose. For patients with severe hepatic insufficiency, initial dose and target doses should be reduced to 25% of usual dose.
Pregnancy and breast feeding (from BNF)	Pregnancy – No information available; avoid unless potential benefit outweighs risk Breastfeeding – Avoid, present in breast milk in *animal* studies.
Drug interactions	In combination with MonoAmine Oxidase Inhibitors (MAOIs) - Atomoxetine should not be used within a minimum of 2 weeks after discontinuing therapy with a MAOI. Treatment with a MAOI should not be initiated within 2 weeks after discontinuing Atomoxetine. Co prescribing with CYP2D6 Inhibitors (Paroxetine, Fluoxetine, Terbinafine) can cause Atomoxetine exposure to increase 6 to 8 fold, the clinical response and tolerability should be re-evaluated to determine if a dose adjustment is needed. When Beta-2 Agonists are co-prescribed attention should be paid to monitoring of heart rate and blood pressure. Dose adjustments may be justified for either medication in the event of significant increases in heart rate and/or blood pressure. Seizures are a potential risk with Atomoxetine. Caution is advised with concomitant use of medicinal drugs known to reduce seizure threshold (Tricyclic Antidepressants, SSRI's, Tramadol) In addition, caution should be taken when stopping concomitant treatment with benzodiazepines due to potential withdrawal seizures. Drugs that affect Noradrenaline should also be used with caution due the possibility of additive effects. Examples include Pseudoephedrine and Tricyclic antidepressants. See above for effects on QTc interval prolongation.
Monitoring	Weight, height, blood pressure, pulse 6 monthly (also see responsibilities section below)
Responsibilities	**<u>Responsibilities of General Practitioner</u>** If the patient is to be referred to secondary care to consider the diagnosis of ADHD, the GP should work in collaboration with the specialist to provide a full history and physical examination, including: • assessment of history of exercise syncope, undue breathlessness and other cardiovascular disease symptoms • heart rate and blood pressure • height and weight • family history of serious cardiac disease and examination of the

	cardiovascular system. In this context, family history of serious cardiac disease includes congenital heart disease, premature sudden death[b] or ventricular arrhythmias. As a minimum, this should be applied to first degree relatives ([b] premature sudden death is defined as less than 55 years in men, less than 65 years in women) • an electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease (defined as above), a history of sudden death in young family members or abnormal findings on cardiac examination Routine blood tests are not recommended unless there is a clinical indication. All of the relevant results should be copied to the specialist.
	• Monitor and liaise with the specialist regarding any adverse effects that arise during treatment including the reporting of serious adverse drug reactions to the MHRA. • Prescribe atomoxetine following stabilisation of the patient by the specialist. It is strongly recommended that prescriptions are issued for a maximum treatment duration of one month, in line with good practice guidance for controlled drug prescribing. Check/act upon any results communicated by the specialist and act upon requests for additional monitoring as agreed with the specialist. **For Adult patients, the following monitoring will be carried out by the GP:** Monitor and record heart rate and blood pressure before and after each dose change and then every 6 months, unless more frequent monitoring is clinically indicated. Clinically significant sustained resting tachycardia, or systolic blood pressure, measured on three occasions, should be discussed with the specialist and the course of action documented. Any arrhythmias should prompt dose reduction and referral to a cardiologist. This information should be communicated to the specialist within 24 hours. Monitor weight 3 and 6 months after the start of treatment and every 6 months thereafter.
	<u>Responsibilities of the specialist team</u> The specialist team will: • Undertake review of relevant medical history and relevant physical examination, including: assessment of history of exercise syncope, undue breathlessness and other cardiovascular disease symptoms • Exclude family history of serious cardiac disease and perform examination of the cardiovascular system. In this context, family

history of serious cardiac disease includes congenital heart disease, premature sudden death[b] or ventricular arrhythmias. As a minimum, this should be applied to first degree relatives ([b]premature sudden death is defined as less than 55 years in men, less than 65 years in women)

- arrange an electrocardiogram (ECG), if not carried out by the GP, if there is past medical or family history of serious cardiac disease (defined as above), a history of sudden death in young family members or abnormal findings on cardiac examination

Usually this information will be available to the specialist. If not, the specialist will work in collaboration with the GP to obtain this. If sufficient information is not available, the specialist should not prescribe atomoxetine, nor make a recommendation to the GP to prescribe.

- Carry out a pre-drug treatment assessment, including a full mental health and social assessment, risk assessment for substance misuse and drug diversion, baseline heart rate and blood pressure and weight.

<u>Children and Young People</u>

- Clinical need, benefits and side effects
- The views of the person with ADHD, and those of the parents, carers and teachers, or close friend as appropriate The effect of missed doses, planned dose reductions and any period of no treatment
- The preferred pattern of drug use
- Co-existing conditions; treat or refer if necessary
- The need for psychological, social and occupational support for the person and their parents or carers
- Monitor heart rate and blood pressure and record on a centile chart at baseline, before and after each dose change and then every 6 months, unless more frequent monitoring is clinically indicated. Sustained resting tachycardia, arrhythmia or systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on two occasions should prompt dose reduction and referral to a paediatrician or physician. This information should be communicated to the GP within 24 hours.
- Monitor weight at baseline then 3 and 6 months after the start of treatment and every 6 months thereafter and plot weight on a growth chart.
- Monitor Height at baseline then every 6 months and plot on a centile chart

<u>Adult patients</u>

Adult patients will be receive a review every 6 months covering:

- Clinical need, benefits and side effects.

	• The views of the person with ADHD, carers, a spouse or close friend as appropriate. • The effect of missed doses, planned dose reductions and any period of no treatment. • The preferred pattern of drug use. • Co-existing conditions; treat or refer if necessary. • The need for psychological, social and occupational support for the person or their carers. • Assessment of Cardiovascular status, in collaboration with GP. For adult patients, heart rate, blood pressure and weight will be monitored by the GP
Communication	**Specialist:** • Contact the GP at the appropriate time after initiating atomoxetine and seek formal agreement for the sharing of patient care. • Provide the patient's GP with information on the dose and formulation of atomoxetine used, and arrangements for review 6 monthly • Ensure that the parent/carer understands the proposed treatment including information contained within the patient information leaflet, problems that may be encountered and how to avoid/minimise them. • Ensure any 'verbal' communication, e.g. dosage changes discussed directly with the patient / carer, is confirmed in writing to the GP as soon as possible (preferably faxed). • Advise the GP when atomoxetine treatment should be discontinued. The specialist will supervise the discontinuation phase. • Provide written guidance e.g. dosage regimen information for parents/teachers/guardians regarding drug treatment, where it is considered appropriate. • Liaise with the GP if any other additional tests/monitoring is required between appointments. • Monitor and liaise with the GP regarding any adverse effects, which occur during treatment, including reporting of all serious adverse drug reactions to the MHRA. • Notify GPs of patients who fail to attend reviews within 1 month, plus specific information on the planned course of action. **GP:** • Notify the specialist promptly if he/she is unwilling to participate in the shared care arrangement. • Notify the specialist of any family/social circumstances, which may preclude treatment with atomoxetine • To contact the specialist if concerned about any aspects of the patient's treatment.

Contact details			
Agreed date		Expiry/Review date	

For full prescribing information on Atomoxetine please refer to the Summary of Product Characteristics (SPC) available from the electronic medicines compendium @ www.emc.medicines.org.uk

Appendix 1 Shared Care Request Form

- **Consultant to complete FIRST SECTION of form**
- **GP to complete SECOND section and RETURN to SECONDARY CARE TRUST CLINICIAN TEAM if transfer declined.**

Section 1

Consultant	
Hospital address	
Contact Phone Number	

Patient's name	
Address	
This patient is stabilised on	
Dose	
Prescription for 28 days supply given on	

Compliance aid	YES/NO
Monitored by	
Designated community pharmacy	

Their treatment has been explained to them and a review has been arranged for

…… ……..

Appointments to continue every …… months

Section 2

Patient's name	
Address	

I do **NOT ACCEPT** the proposed Shared-Care Agreement for this patient

My reasons for not accepting: Please complete this section

Signed ……date……..

Please return to the Secondary Care Trust Clinician team at :

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