GREATER MANCHESTER INTERFACE PRESCRIBING GROUP

On behalf of the
GREATER MANCHESTER MEDICINES MANAGEMENT GROUP

SHARED CARE GUIDELINE: Atomoxetine for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents		**Reference Number** Version 6
Scope: Pennine Care NHS Foundation Trust Commissioning CCG		**Classification** SHARED CARE GUIDELINE
Issue date	28 May 2014	
Author(s)/Originator(s)	Pennine Care NHS Foundation Trust	
To be read in conjunction with the following documents	British National Formulary (BNF) and BNF for Children. Latest Editions. Summary of Product Characteristics (SPC) for atomoxetine. NICE Clinical Guideline 72 (2008) ADHD	
Approved by:	Drugs and Therapeutics Committee. Pennine Care NHS Foundation Trust	16 May 2014
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1 Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a neuropsychological / developmental condition with secondary behavioural, social and educational difficulties. ADHD is defined by the 'core' symptoms of inattention, hyperactivity and impulsiveness. To make a diagnosis, the core symptoms should be pervasive, present before age 7 years, and not better accounted for by other psychiatric or developmental disorders [1].

Diagnosis should be based on comprehensive assessment conducted by child / adolescent psychiatrist (or nominated specialist nurse/ advanced practitioner in supervision with psychiatrist), or by a Paediatrician with expertise in ADHD. Two main diagnostic criteria are currently used to diagnose ADHD; International Classification of Mental and Behavioural Disorders 10th revision (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V).
Atomoxetine is recommended within its licensed indications, as an option for first or second line treatment for ADHD in children and adolescents. The

choice between atomoxetine or methylphenidate/ dexamfetamine (see separate protocol for stimulants) will be based on: presence of co-morbid conditions, different adverse effects of the drugs, compliance, potential for drug diversion with stimulants, and preference of child and carer [1].

The Summary of Product Characteristics (SPC) for atomoxetine recommends that if adolescents treated with atomoxetine have shown clear benefit, then it may be appropriate to continue treatment with atomoxetine into adulthood [5]. The NICE guideline also recognises that ADHD is a persisting disorder and may continue into adulthood [1].

2 Scope

Pennine Care NHS Foundation Trust and associated Commissioning CCGs, Acute Trust SLA partners.

3 Treatment of Clinical condition

Atomoxetine is indicated for the treatment of ADHD in children of 6 years and older and in adolescents as part of a comprehensive treatment programme. Diagnosis should be made according to DSM-IV criteria or the guidelines in ICD-10.

Dosing of children/adolescents up to 70kg body weight: Atomoxetine should be initiated at a total daily dose of approximately 0.5mg/kg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is approx 1.2mg/kg/day (depending on the patient's weight and available dosage strengths of atomoxetine) and while no additional benefit in ADHD symptom management has been demonstrated for doses higher than 1.2mg/kg/day, some patients have shown improvements in social/emotional functioning at higher doses. The safety of single doses over 1.8mg/kg/day and total daily doses above 1.8mg/kg have not been systematically evaluated.

Dosing of children/adolescents over 70kg body weight: Atomoxetine should be initiated at a total daily dose of 40mg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is 80mg. No additional benefit has been demonstrated for doses higher than 80mg. The maximum recommended total daily dose is 100mg. The safety of single doses over 120mg and total daily doses above 150mg have not been systematically evaluated.

Treatment with atomoxetine need not be indefinite. Re-evaluation of the need for continued therapy beyond 1 year should be performed, particularly when the patient has reached a stable and satisfactory response [5].

Monitoring required:

- Patients being treated for ADHD should be carefully monitored for the appearance or worsening of depression, suicide related behaviour, hostility and emotional lability.
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.

- Pulse and blood pressure should be recorded appropriately after every dose adjustment and at least every 6 months during treatment.
Atomoxetine causes clinically important changes in blood pressure and heart rate, or both, in a small proportion of patients. Regular monitoring of cardiovascular status is recommended and specialist cardiac advice should be sought if symptoms suggesting cardiac disease are found during treatment.

- Growth and development should be monitored during treatment.

- Patients with additional risk factors for cerebrovascular conditions (eg, history of certain cardiovascular diseases or concomitant use of medicines that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with atomoxetine.

4 Product information

Atomoxetine is a selective noradrenaline (norepinephrine) reuptake inhibitor, developed for treatment of ADHD. Atomoxetine is classified as a centrally acting sympathomimetic by the British National Formulary (BNF). It has a different mode of action to methylphenidate and is not classed as a Controlled Drug.

Atomoxetine is usually given as a single dose but can be given twice daily if tolerability e.g. nausea or somnolence becomes an issue.
The capsules can be given with or without food, but must be taken whole and cannot be opened [5].

Name	**Dosage** **6 – 18 years**
Atomoxetine (Straterra®) 10mg, 18mg, 25mg, 40mg. 60mg, 80mg, 100mg capsules	0.5mg/kg/day in one or two divided doses. Dose titrated up to maintenance dose of 1.2mg/kg daily. Maximum dose 1.5mg/kg daily

5 Regimen Management

Aspects of care for which the Consultant/ Specialist Team is responsible. Child and Adolescent Psychiatrist, Paediatrician.

- Direct assessment or supervision of specialist team assessment, diagnosis of ADHD, evaluation of prior treatment, and rationalisation of treatment with medication.

- Completion of ADHD Pre-medication Assessment Pro-forma (Appendix 1) Pre-treatment screening: baseline blood pressure and pulse, height and weight, measured and plotted on appropriate charts.

- Documentation of concomitant medicines; past and present medical and psychiatric disorders/symptoms; family history of sudden cardiac death, unexplained death, or malignant arrhythmia

- Screening/Identification of any patients with previous history of depression, suicidal behaviour or seizures for more frequent review appointments by the specialist as clinically indicated. Informing GP and family of such arrangements.

- A cardiovascular examination is required if a patient presents with cardiovascular symptoms (through GP or paediatrics if necessary). An ECG is also recommended for those with a significant family history of cardiac illness or abnormal findings on cardiovascular examination. In this circumstance, specialist advice or assessment should be sought prior to commencing medication (see ADHD Pre-medication Assessment Pro-forma).

- Informing patient/ carer of diagnosis, care plan, treatment including side effects use of Patient Information Leaflets (PILs), user-friendly information for children/ adolescents.

- Informing the patient/ parents of the latest regulatory advice.

- Patients and their carers should be informed of risk of emotional lability and suicidal ideation/ behaviour, and advised to alert the Specialist Team to any changes in mood or behaviour whilst on treatment.

- Patients and their carers should be informed of the potential risk of seizures with atomoxetine, and advised to alert the Specialist Team to any patients developing seizure or if there is an increase in seizure frequency.

- Treatment decisions being shared between the patient, parents and the Consultant and GP.

- Asking the General Practitioner (GP) if they would be willing to participate in shared care.

- Initiation and titration of medication to a suitable dose or provide instructions/directions to the GP for titration of medication to a suitable dose where agreed.

- Written correspondence to GP summarising progress and recommendations for continued treatment.

- Ensure clear arrangements for GP back up, advice and support.

- Promoting access to any appropriate supporting therapies, carer education, and appropriate school liaison.

- Minimum 6 monthly Specialist Team review appointments and as clinically indicated. Follow up all aspects of progress, plus height, weight, appetite, blood pressure and pulse.

- Development of new or worsening of pre-existing, psychiatric symptoms should be monitored at every dose adjustment and then at least every 6 months, and at every visit.

- Reporting suspected adverse events to the GP and the MHRA via the Yellow Card scheme to www.mhra.gov.uk/yellowcard

- Consideration (and evaluation) of annual 'drug holiday' to determine continued benefit.

- Discontinuation of treatment or transfer if appropriate.
- If a patient is to be discharged from specialist follow-up due to recurrent failure to attend appointments, the specialist team should write to the GP informing them of this plan and clarifying whether continued GP prescribing is recommended.

Conditions of assuming responsibility by the GP

- Communication of satisfactory baseline physical checks.

- Satisfactory directions/instructions for titration to optimum dosage, and response to treatment.

	Consultant	**Usual GP**
Then 6 monthly follow up of height, weight,	Yes	N/A

BP and pulse If changes noted	Amend dose accordingly	Refer to Consultant

Aspects of care for which the GP is responsible

- Replying to requests for shared care as soon as possible, ideally within 14 days.
- Continued prescribing of medication in the community under guidance of Consultant/ Specialist Team.
- To undertake tests appropriate to primary care, during treatment, if requested to do so by the Consultant.
- Refer to the Consultant/Specialist Team for queries regarding treatment/side effects, and concerns about compliance.
- Refer to the Consultant/Specialist Team any concerns about mood changes or suicidal behaviour, development of seizures or increase in seizure frequency.
- Refer to the Consultant/Specialist Team any patients who develop symptoms that suggest heart disease to allow prompt specialist cardiac evaluation.
- Ensure compatibility of atomoxetine with concomitant prescribed medication.
- Stopping treatment on the advice of the Consultant/Specialist team.
- Continuation without specialist review is not recommended.
- Reporting noted adverse events to the Consultant/Specialist Team and the MHRA via the Yellow Card scheme to www.mhra.gov.uk/yellowcard

6 Summary of cautions, contra indications, side-effects

Please refer to the current edition of the BNF and BNF for Children and Summary of Product Characteristics (SPC) for atomoxetine for the latest list of contraindications, cautions, side effects and interactions.

Contra indications:

- Children under 6 years of age
- Hypersensitivity to atomoxetine or any of the excipients

- 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

- Atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders in which clinical deterioration would be expected with increases in blood pressure or heart rate that could be clinically important (eg, 15–20 mm Hg in blood pressure or 20 beats per minute in heart rate).

- Atomoxetine should not be used in patients with narrow angle glaucoma

- Atomoxetine should not be used in patients with pheochromocytoma or a history of pheochromocytoma

Cautions:

- Atomoxetine should be used in caution in patients whose underlying medical conditions could be worsened by increases in blood pressure or heart rate, such as with hypertension, tachycardia, or cardiovascular or cerebrovascular disease.

- Caution in any condition that may predispose patients to hypotension.

- Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury and should not be restarted.

- Seizures are a potential risk with atomoxetine and therefore it should be introduced 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 subtype.

- Susceptibility to open-angle glaucoma.

Side effects:

- Abdominal pain
- Decreased appetite
- Nausea
- Dry mouth
- Insomnia (usually transient at initiation of treatment)
- Mild increase in pulse and blood pressure
- Signs and symptoms of liver disease (pruritus, jaundice, dark urine, right sided abdominal tenderness, unexplained “flu-like” symptoms)
- Increased risk of emotional lability and suicidal thoughts or behaviour
- Development of seizures or increased frequency
- QT interval prolongation

7 Special considerations

Handover for shared care largely by written agreement, individual consideration of patients to occur when issues of tolerance, inconsistent response to treatment, pre-existing medical conditions or issues of patient compliance.

8 Back-up care available to GP from Hospital, including emergency contact procedures and help line numbers

Written correspondence following Consultant/ Specialist Team appointments, specifically detailing the next review date and any dose adjustments.

Telephone advice/ information from the Consultant / Specialist Team during office hours, and plans for earlier review by team if necessary.

Out of hours on call/ emergency mental health service contactable through hospital switchboards.

9 Statement of agreement

Shared care is an agreement between the GP and the Consultant. This form is a request by the consultant to share the suggested care pathway of your patient. If you are unable to agree to the sharing of care and initiating the suggested medication, please make this known to the consultant within 14 days, ideally stating the nature of your concern.

10 Written information provided to the patient

a) Handbook/leaflets for families on ADHD.

b) Product Patient Information Leaflet (PIL)

11 Supporting References

1. NICE Clinical Guideline 72. Diagnosis and Management of ADHD in children, young people and adults. September 2008. Last modified March 2013.

2. NICE Technology Appraisal 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents March 2006. Reviewed March 2009.

3. BNF Number 66, September 2013

4. BNF for Children, 2013-2014.

5. Summary of Product Characteristics. www.medicines.org.uk

6. MHRA Drug Safety Update. Atomoxetine (Strattera): increase in blood pressure and heart rate – new contraindications, warnings and advice for monitoring. Volume 5 Issue 6. January 2012

Shared Care Agreement Form

Specialist request

***IMPORTANT: ACTION NEEDED**

Dear Dr *[insert Doctors name here]*

Patient name: *[insert Patients name here]*
Date of birth: *[insert date of birth]*
Diagnosis: *[insert diagnosis here]*

This patient is suitable for treatment with *[insert drug name]* for the treatment of
[insert indication]
The parents/responsible carer(s) have consented to its use.

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / LHB / AWMSG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on [insert date started] [insert dose].

If you are in agreement, please undertake treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

Baseline tests: *[insert information]*

Next review with this department: *[insert date]*
You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice.

Please use the reply slip overleaf and return it as soon as possible.
Thank you.

Yours

[insert Specialist name]

Contact number: *[insert text here]*_____

Shared Care Agreement Form

GP Response

Dear Dr *[insert Doctors name]*

Patient *[insert Patients name]*

Identifier *[insert patient date of birth/address]*

I have received your request for shared care of this patient who has been advised to start *[insert text here]*

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

GP signature Date

GP address/practice stamp

Appendix 1

ADHD PRE-MEDICATION ASSESSMENT PRO FORMA

Name of Child: **Date:**
DOB: **RT NO:**

Consultant/Psychiatrist: **Case Worker:**
Please clarify if previous or current history

	Child	**Family**
Significant anxiety		
Expresses suicidal ideas		
Low mood or depression		
Angina/MI under 55 or history of sudden death		
High or low BP/P		
Arrhythmia		
History of exercise syncopy or cardiovascular Symptoms		
Epilepsy		
Drug/alcohol misuse or dependency		
Tics/Tourettes		
Thyroid Disorder		
Glaucoma		
Kidney Disease		
Liver Disease		

Drug allergies:

Other medication prescribed:

Clinical examination:

Height:_____ **Centile** _____

Weight:_____ **Centile** _____

Plot on centile charts

B/P: _____ **Pulse** _____

Cardiovascular examination
If family history of sudden death, MI under 55 or young person with history of cardiovascular symptoms e.g. exercise syncope or breathlessness.

Options:
1. CAMHS, including documentation of findings.
2. PAEDS. Referral
3. GP. Referral

Request ECG if abnormal physical examination or significant family history of cardiovascular illness. Seek paediatric advice or assessment prior to commencing treatment.