BNSSG Shared Care Guidance

Section 1: Heading

Drug	Atomoxetine for ADHD in adults
Amber ***three months***	
Indication	Treatment of ADHD in adults
Speciality / Department	Bristol ADHD Service (Attention Deficit Hyperactivity Disorder)
Trust(s)	Avon and Wiltshire Mental Health Partnership NHS Trust

Section 2: Treatment Schedule

Usual dose and frequency of administration	Atomoxetine should be initiated at a total daily dose of 40 mg. 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 daily dose is 80mg to 100mg. The maximum recommended total daily dose is 100 mg. The safety of single doses over 120mg and total daily doses above 150mg have not been systematically evaluated. Atomoxetine can be administered as a single daily dose in the morning, with or without food. Patients who do not achieve a satisfactory clinical response (tolerability [e.g. nausea or somnolence] or efficacy) when taking Atomoxetine as a single daily dose might benefit from taking it as twice daily evenly divided doses in the morning and late afternoon or early evening. Atomoxetine is a non-stimulant, indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (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. In adults, the presence of symptoms of ADHD that were pre-existing in childhood should be confirmed. Third-party corroboration is desirable and Atomoxetine should not be initiated when the verification of childhood ADHD symptoms is uncertain. Diagnosis cannot be made solely on the presence of one or more symptoms of ADHD. Based on clinical judgment, patients should have ADHD of at least moderate severity as indicated by at least moderate functional impairment in 2 or more settings (for example, social, academic, and/or occupational functioning), affecting several aspects of an individual's life. The NICE Guideline CG72 supports the second or third line use of atomoxetine in adults if methylphenidate is ineffective or unacceptable.

	This Shared Care Guidance only covers adult ADHD patients with no other serious mental health co-morbidities who are stabilised on an atomoxetine prescription. Atomoxetine's mechanism of action makes it less likely to have abuse potential or to cause motor ticks. Peak plasma levels are reached 1 -2 hours after ingestion. The effects of atomoxetine last longer than would be expected from its pharmacokinetics, and once a day administration is effective.
Route and formulation	Oral, capsules, brand Strattera available in 10mg, 18mg, 25mg, 40mg, 60mg, 80 mg or 100 mg hard capsules. In case of swallowing difficulties or aversion to tablets/capsules, an oral solution (Atomoxetine 4mg/ml) is available.
Duration of treatment	Patients can choose to try stopping the medication every 1 to 5 years, with the guidance of the specialist clinic if desired. Patients will generally report definitively either way, if they feel they still need the medication once they are off it for longer than a few days.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
1. The AWP ADHD clinic to check BP, pulse and weight at the first appointment and after starting treatment, at every appointment where dose has been adjusted, and at the annual review. 3. No need to check bloods or other parameters unless specific individual concerns exist.
Subsequent tests - where appropriate
If abnormality is found at baseline, investigate and treat appropriately as appropriate for that abnormality. If hypertension or tachycardia due to medication, then psychiatrist will be responsible for adjusting medication regime and/or liaising with the GP to generate a collaborative plan of action.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	**Increase in pulse and BP**: Patients may experience a modest increase in pulse (mean <10 bpm) and/or increase in blood pressure (mean <5 mmHg). In most cases these are not clinically important. Due to potential for additive pharmacological effects, caution is advised in patients with hypertension, tachycardia, cardiovascular or cerebrovascular disease. **GI Disturbance:** Treatment may be associated with transient gastrointestinal side effects of abdominal pain, vomiting, decreased appetite, constipation, dyspepsia and nausea. There is a rare risk of hepatic disorder. **Other side-effects** include dry mouth, urinary retention or hesitancy, insomnia, early wakening, somnolence, irritability, dizziness, fatigue, headache, decreased libido, erectile or ejaculatory disorder, dysmenorrhoea or menstrual irregularities, palpitations, hot flushes and rash. Suicidal ideation is a rare side-effect which has been reported.
Referral back to specialist	• patient finds the medication intolerable for any given reason, or • if you are concerned about observed mental/psychological or physical side effects (e.g. depression or hypertension), or • if the side effects mentioned below appear to persist beyond the first week of medication.

Section 5: Drug Interactions

Please list clinically significant drug interactions (view lisdexamfetamine spc here)

Significant Drug Interactions	• MAOIs • Due to potential for additive pharmacological effects, caution is advised in patients on concomitant treatment with: ▪ High dose nebulised or systemically administered salbutamol (or other beta2 agonists) ▪ Pressor agents (eg. the decongestants pseudoephedrine or phenylephrine) ▪ Drugs that affect noradrenaline (eg. antidepressants such as imipramine, venlafaxine and mirtazapine) ▪ Drugs which inhibit CYP2D6 isoenzyme (eg. fluoxetine, paroxetine) – slower titration may be necessary. • Concurrent use of atomoxetine and methylphenidate does not cause increased side effects of either drug. There is no interaction between atomoxetine and alcohol.
Reminder to ask patient about specific problems	Ask about emergency of any possible side effects/compliance to treatment issues.

Section 6: Contra-indications, Cautions and Special Recommendations

Contra-indications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- 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 narrow-angle glaucoma, as in clinical trials the use of atomoxetine was associated with an increased incidence of mydriasis.
- Atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders. Severe cardiovascular disorders may include severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels). Severe cerebrovascular disorders may include cerebral aneurysm or stroke.
- Atomoxetine should not be used in patients with phaeochromocytoma or a history of phaeochromocytoma.

Cautions

Suicide-related behaviour: Suicide-related behaviour (suicide attempts and suicidal ideation) has been reported in patients treated with atomoxetine. Patients who are being treated for ADHD should be carefully monitored for the appearance or worsening of suicide related behaviour.

Sudden death and pre-existing cardiac abnormalities: Sudden death has been reported in patients with structural cardiac abnormalities who were taking atomoxetine at usual doses. Although some serious structural cardiac abnormalities alone carry an increased risk of sudden death, atomoxetine should only be used with caution in patients with known serious structural cardiac abnormalities and in consultation with a cardiac specialist.

Cardiovascular effects: Atomoxetine can affect heart rate and blood pressure. Most patients taking atomoxetine experience a modest increase in heart rate (mean <10 bpm) and/or increase in blood pressure (mean <5 mm Hg). Long-term sustained changes in blood pressure may potentially contribute to clinical consequences such as myocardial hypertrophy.
As a result of these findings, patients who are being considered for treatment with atomoxetine should have a careful history and physical exam to assess for the presence of cardiac disease, and should receive further specialist cardiac evaluation if initial findings suggest such history or disease.

It is recommended that heart rate and blood pressure be measured and recorded before treatment is started and, during treatment, after each adjustment of dose and then at least every 6 ~~3~~ months to detect possible clinically important increases. For adults, current reference guidelines for hypertension should be followed. Patients who develop symptoms suggestive of cardiac disease during atomoxetine treatment should undergo a prompt specialist cardiac evaluation.
In addition, atomoxetine should be used with caution in patients with congenital or acquired long QT or a family history of QT prolongation

Hepatic effects: Very rarely, spontaneous reports of liver injury, manifested by elevated hepatic enzymes and bilirubin with jaundice, have been reported. Also very rarely, severe liver injury,including acute liver failure, have been reported. Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted.

Psychotic or manic symptoms: Treatment-emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, mania or agitation in patients 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.

Aggressive behaviour, hostility or emotional lability: Hostility (predominantly aggression, oppositional behaviour and anger) was more frequently observed in clinical trials adults treated with Atomoxetine compared to those treated with placebo. Patients should be closely monitored for the appearance or worsening of aggressive behaviour, hostility or emotional lability.
Possible allergic events: Although uncommon, allergic reactions, including anaphylactic reactions, rash, angioneurotic oedema, and urticaria, have been reported in patients taking atomoxetine.

Seizures: Seizures are a potential risk with atomoxetine. Atomoxetine should be introduced with caution in patients with a history of seizure. Discontinuation of atomoxetine should be considered in any patient developing a seizure or if there is an increase in seizure frequency where no other cause is identified.
Patients who are being treated for ADHD with Atomoxetine should be monitored for the appearance or worsening of anxiety symptoms, depressed mood and depression or tics.

<u>Dose reduction and discontinuation</u>
If the symptoms of ADHD do not improve after appropriate dosage adjustment treatment must be stopped by the clinic. If paradoxical aggravation of symptoms or other serious adverse events occur, the dosage should be reduced or discontinued – advice should be sought from and managed by the clinic.

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

There is no specific psychiatric emergency that relates to ADHD. This is a lifelong condition that generally does not wax and wane.

Blood pressure should be monitored at appropriate intervals (see Responsibilities for Primary care and Secondary Care, below) in all patients taking stimulants, especially those with hypertension. It is recommended to check Blood pressure every six months with Atomoxetine.

Caution is called for in emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase the dosage on their own initiative.

Our clinic runs 9am to 5pm weekdays and we welcome enquiries from patients and professionals alike, on any matter relating to ADHD in adults.

Adult ADHD medications are unlikely to increase in dosage once the medication dose is stabilised.

It is not advisable to drink alcohol or take other recreational drugs whilst on Atomoxetine.

Once stabilised the patient should attend an annual review at the clinic, failure to do this could result in the medication being stopped.

Patients can choose to try stopping the medication every 1 to 5 years, with the guidance of the specialist clinic if desired. Patients will generally report definitively either way, if they feel they still need the medication once they are off it for longer than a few days.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing until medication stability has been achieved or at least for the first three months
2. Undertaking the clinical assessment and monitoring until medication stability has been achieved or at least for the first three months.
3. Communicate details of the medication regime and monitoring (see 1. and 2.) to GP within the first month of treatment. Shared care, with all necessary information available for the GP, should be communicated in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Atomoxetine
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Full psychiatric assessment including a structured objective assessment of symptoms.
2. Initiation and prescription of medication for at least 3 months. Reclaiming responsibility of prescription during subsequent times of dose adjustment (e.g. during an attempt to reduce or pause medication)
3. Monitor Blood pressure, pulse and weight at first appointment after initiating drug, at every dose increase and at annual reviews. Inform GP of abnormal results and any actions taken or required
4. Yearly psychiatric review of all patients once stabilised, including a decision on whether to try challenge off medication, and annual monitoring of BP, pulse and weight.
5. Liaising with all professionals and carers involved in the patient's care, as necessary.
6. Providing direction and advice with respect to psychological treatments.
7. Liaising with pharmacies on matters of supply and admin.
8. Being available by phone to GPs during office hours, with a target of 48 hours in work time for a clinician to return any enquiry calls.

Section 9: Responsibilities for Primary Care

Core responsibilities

1. Responsible for taking over prescribing after medication regime has been stabilised, earliest after the first three months
2. Responsible for the clinical assessment and monitoring after transfer of prescribing, earliest after the first three months
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Following a request for shared care of a patient, if the GP or any GP within the practice is unable to take on the prescribing for these patients, then the clinic should be informed as soon as possible.
2. If the GP decides not to prescribe Atomoxetine, it should still be added to the patients repeat list as a 'non-issued item' for information and safety purposes.
3. Checking BP, pulse and weight of patients prior to referral. Treating appropriately and/or consulting

the clinic of abnormality detected
4. Issuing repeat prescriptions once dose is stabilised, on request from specialist clinic.
5. To manage minor adverse events as appropriate.
6. To encourage and maintain a holistic and shared approach to the adult's care, with the adult being primarily responsible for decisions about his/her health and treatment.

Section 10: Contact Details

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Section 11: Document Details

Date prepared	January 2016
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Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

Circulation amongst Commissioners from NHS Bristol, NHS North Somerset and NHS South Gloucestershire, and local GPs

Section 13: References

1. EMC http://www.medicines.org.uk/emc/medicine/14482 [accessed 20.1.16]
2. NICE Guidelines on ADHD (CG72, 2008)
3. British Association of Psychopharmacology Guidelines on Managing ADHD, 2014 http://www.bap.org.uk/pdfs/ADHD_Guidelines.pdf

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The Bristol Care Pathway for Adults with ADHD