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WORKING IN PARTNERSHIP WITH

SHARED CARE PRESCRIBING GUIDELINE

Atomoxetine (Strattera®) for the Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in Childhood

Surrey PCT's Medicines Management Committee classification: Amber

NOTES to the GP

Amber drugs: Prescribing to be initiated by a specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs**.**

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of page 10 to the requesting specialist. Until the requesting specialist has received a signed copy of page 10 indicating that shared care has been agreed all care (including prescribing) remains with the specialist.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the specialist outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your PCT pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

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Background

Definition: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most commonly diagnosed behavioural disorders of childhood, affecting 1-5% of school age children. Its basic symptoms include developmentally inappropriate levels of attention, concentration, activity, distractibility and impulsivity. It causes problems at home, in school and with peer relationships and may have long term adverse effects on self-confidence, academic performance, vocational success and social development.

- It can be divided into three types, depending on whether inattention or hyperactivity is the predominant presentation
- It must have been present for at least six months and be maladaptive and inconsistent for the age of the child (although in the case of developmental delay the developmental age should be taken into account).
- There must be clear evidence of impairment in social and / or academic functioning
- Some impairment must be present in at least two settings
- The symptoms must be present in at least two settings
- The symptoms must be present before the age of seven
- The symptoms must not be accountable for by any other type of mental disorder or illness although they may occur in conjunction with some development disorders.

Its consequences are low self-esteem, emotional and social problems which may lead to further problems with drug abuse etc in the longer term. These children's academic achievements are often very low consequently often leading to employment problems.

Where drug treatment is considered appropriate, methylphenidate, atomoxetine and dexamfetamine are recommended, within their licensed indications, as options for the management of ADHD in children. The decision regarding which product to use should be based on the following[1]:

- The presence of co-morbid conditions (for example, tics disorders, Tourette's syndrome, epilepsy)
- The different adverse effects of the drugs
- Specific issues regarding compliance identified for the individual child, for example problems created by the need to administer a mid-day treatment dose at school
- The potential for drug diversion (where the medication is forwarded on to others for non-prescription uses) and/or misuse
- The preferences of the child and/or his or her parent or guardian.

If there is a choice of one or more appropriate drugs, the product with the lowest cost (taking into account the cost per dose and number of daily doses) should be prescribed[1].

Prescribing of methylphenidate, atomoxetine and dexamfetamine for ADHD by Specialists alone results in significant pressure being put on acute Trusts and is an inconvenience to families. Shared care prescribing guidelines for ADHD allow parents to collect prescriptions from their local GP practice at their convenience, whilst ensuring continuous specialist care of the child through regular monitoring at clinic appointments. A number of resources and support is available to GPs to ensure that they feel confident to take on the prescribing of ADHD drugs (see list on pg 9).

Diagnosis

Should be made by a child / adolescent psychiatrist or paediatrician with a special interest in ADHD, involving the child, its carers and school. A multidisciplinary assessment including educational and clinical psychologists, social workers etc may be necessary in individual cases. **Almost 50% of children who have ADHD may have other co-morbid conditions which include autistic spectrum/Asperger's syndrome, dyslexia, dyspraxia and oppositional-defiant difficulties. Recognising these conditions is important to ensure comprehensive planning is made.**

Technology

- Atomoxetine is a highly selective and potent inhibitor of the pre-synaptic noradrenaline transporter without directly affecting the serotonin or dopamine transporters.
- Atomoxetine is not a psychostimulant and is not an amphetamine derivative.
- Atomoxetine does not worsen tics in patients with ADHD and co-morbid chronic motor tics or Tourette's disorder.
- Atomoxetine is not a controlled drug.

Criteria for Use

1. The diagnosis of ADHD is made by a Child Psychiatrist or a Specialist Paediatrician after a comprehensive assessment which includes the completion of questionnaires by carers and teachers, such as the Conner's questionnaires. If there is significant co-morbidity such as learning difficulties or other mental health problems, a full multidisciplinary assessment is advised. If medication is indicated as part of the treatment package, an initial prescription for atomoxetine is given by the specialist for a trial period of at least one month (ADHD symptoms can show an improvement by the first week of commencing atomoxetine and the maximum therapeutic effect can be seen from four weeks onwards. However, it can take up to three months in some patients to see the desired effect).
2. Atomoxetine is considered second line treatment for ADHD after methylphenidate. Reasons for switching to atomoxetine are: excessive anxiety (particularly if worsened by stimulants), poor effectiveness of stimulants, worsening tics, sleep disturbance, appetite disturbance and any other unacceptable side effects with methylphenidate.
3. If improvement of symptoms is not observed after appropriate dosage adjustment the drug should be discontinued by the specialist. The medication may be stopped abruptly; there is no tailing off necessary.
4. The drug may be discontinued periodically to assess the child's condition as advised by the specialist.
5. It is the specialist's responsibility for stopping atomoxetine or to agree aftercare when the patient reaches 18 years of age.
6. All children and families with a child taking atomoxetine should receive psychological and / or educational interventions with a view to improving the symptoms of ADHD and allowing children to reduce their need for medication. The extent of these interventions and the level of need will be assessed and agreed with the individual clinician and family.
7. Explanations given to the family about medication are important. For example children should not be told that the medication is the only thing that can control their behaviour. Explanations should always seek to foster healthy development trajectories for children.

Information

This does not replace the SPC which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF for children.

This guideline follows the recommendations of NICE guidance 72 on the use of atomoxetine for Attention Deficit / Hyperactivity disorder (ADHD) in childhood [2].

Dose / Licensing

- Atomoxetine is indicated for use as part of a comprehensive treatment programme, where remedial behavioural methods alone have failed.
- Atomoxetine is considered second line treatment for ADHD after methylphenidate. Reasons for switching to atomoxetine are excessive anxiety (particularly if worsened by stimulants), poor effectiveness of stimulants, worsening tics, sleep disturbance, appetite disturbance and any other unacceptable side effects with methylphenidate.
- Treatment must be initiated by a Child Psychiatrist or a Specialist Paediatrician for children and adolescents. For adults treatment must be initiated by a Psychiatrist with appropriate knowledge and experience of ADHD.
- Atomoxetine is licensed for children 6 years of age and older, adolescents and adults.
- Atomoxetine is usually given as a single dose in the morning, however if patients experience unwanted side effects when taking atomoxetine as a single daily dose they may benefit from taking it twice daily as evenly divided doses in the morning and late afternoon or early evening. Atomoxetine can be taken with or without food; however gastrointestinal side effects can be decreased by administering atomoxetine with food.
- Dose:
    - *Children and adolescents up to 70kg:* Initial total daily dose of 0.5mg/kg. This dose should be maintained for a minimum of 7 days before titrating upwards according to clinical response and tolerability. Maintenance dose is approx 1.2mg/kg/day, no additional benefit has been demonstrated for doses higher than 1.2mg/kg/day (however maximum recommended dose is 1.8mg/kg/day).
    - *Children and adolescents over 70kg and adults:* Initial total daily dose of 40mg. This dose should be maintained for a minimum of 7 days before titrating upwards according to clinical response and tolerability. Maintenance dose is 80mg daily. No additional benefit has been demonstrated for doses higher than 80mg (however maximum recommended dose is 100mg / day).
- ADHD symptoms can show an improvement by the first week of commencing atomoxetine and the maximum therapeutic effect can be seen from four weeks onwards. However, it can take up to three months in some patients to see the desired effect.
- If improvement of symptoms is not observed after appropriate dosage adjustment the drug should be discontinued by the consultant.
- Atomoxetine can be discontinued without titrating down the dose.
- If the patient is changing from methylphenidate to atomoxetine, methylphenidate should be continued until desirable dose of atomoxetine is achieved unless methylphenidate is contra-indicated.

Cost

Drug	Dose	Cost (Mims March 2010)
Atomoxetine (Strattera®)	<70kg: Initially 0.5mg/kg/day gradually titrated to a recommended maintenance dose of 1.2mg/kg/day. >70kg: Initially 40mg daily gradually titrated to a recommended maintenance dose of 80mg daily.	28 x 10mg/18mg/25mg/40mg/60mg £62.46 28 x 80mg: £83.28

Cautions[3]

- Must only be used under the supervision of a specialist in childhood behavioural disorders.
- Possible serious allergic events; although uncommon allergic reactions including rash, angioneurotic oedema and urticaria have been reported in patients taking atomoxetine.
- Hepatic insufficiency. For patients with moderate hepatic insufficiency doses should be reduced to 50% of the usual dose. For patients with severe hepatic insufficiency doses should be reduced to 25% of the usual dose.
- Pregnancy. Atomoxetine should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.
- Lactation. Atomoxetine should be avoided during breast-feeding.
- Many patients taking atomoxetine experience a modest increase in pulse and/or blood pressure. Atomoxetine should be used in caution in patients with hypertension, tachycardia, cardiovascular or cerebrovascular disease. Pulse and BP should be monitored.
- Height and weight should be monitored during treatment with atomoxetine.
- There have been rare reports of hepatic disorder in children receiving atomoxetine. The CSM has advised that patients and their carers should be advised of the risk and be told how to recognise symptoms. Prompt medical attention should be sought in case of abdominal pain, unexplained nausea, malaise, darkening of urine and jaundice.
- Following reports of suicidal thoughts and behaviour, the CSM has advised that patients and their carers should be informed about the risk and told to report clinical worsening, suicidal thoughts or behaviour, irritability, agitation or depression.

Contra-indications[3]

- Known hypersensitivity to atomoxetine or to any excipients of the formulation.
- Patients on MAOIs (monoamine oxidase inhibitors). Atomoxetine should not be used within a minimum of two weeks after discontinuing therapy with MAOI. Treatment with MAOI should not be initiated within two weeks of discontinuing atomoxetine.
- Patients with narrow angle glaucoma, increased risk of mydriasis.

Interactions[3]

- MAOIs: atomoxetine should not be used with MAOIs.
- Pressor agents: because of possible effects on blood pressure.
- CYP2D6 inhibitor drugs eg fluoxetine, paroxetine: Atomoxetine is primarily metabolised by the CYP2D6 pathway. Slower titration of atomoxetine may be necessary in patients who are also taking these drugs.
- Drugs that affect noradrenaline eg imipramine, venlafaxine: should be used cautiously with atomoxetine because of the potential for synergistic pharmacological effects.
- Atomoxetine should be used in caution with high dose nebulised or systemically administered (oral or intravenous) salbutamol (or other $beta_2$ agonists) because the action of salbutamol on the cardiovascular system can be potentiated.

Side effects[3]

Frequency	Side effect
Very Common: ≥1/10	• Abdominal pain, vomiting, nausea, decreased appetite • Headache • Somnolence
Common: ≥ 1/100 to < 1/10	• Anorexia (loss of appetite) • Insomnia • Irritability, mood swings • Dizziness • Mydriasis • Constipation • Dyspepsia • Dermatitis, rash • Fatigue • Lethargy • Decreased weight • Increased blood pressure
Uncommon: ≥1/1000 to <1/100	• Palpitations • Sinus tachycardia • Pruritis • Early morning awakening • Suicide related events • Aggression • Hostility • Emotional lability • Syncope • Tremor • Migraines • Mydriasis • Asthenia • Hyperhidrosis • Allergic reactions

Abdominal pain and decreased appetite are the adverse effects most commonly associated with atomoxetine, these effects are usually transient.

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. To assess the patient and establish a diagnosis of attention-deficit hyperactivity disorder, to determine a management strategy and communicate this to the family and GP. The diagnosis must clearly be demonstrated through a detailed report outlining the current problems, developmental history and presence of "core signs" of ADHD. These must meet the diagnostic criteria of the DSM-IV. Almost 50% of children who have ADHD may have other co-morbid conditions which include autistic spectrum/Asperger's syndrome, dyslexia, dyspraxia and oppositional-defiant difficulties. Recognising these conditions is important to ensure comprehensive planning is made.
2. Consider and discuss atomoxetine treatment with the parents / responsible adult for the children who meet the criteria laid down in NICE guidance. This should include a discussion of the reasons for treatment, the possible side effects and the lack of information in relation to longer term outcomes including effectiveness and adverse effects. **Following reports of suicidal thoughts and behaviour, the CSM has advised that patients and their carers should be informed about the risk and told to report clinical worsening, suicidal thoughts or behaviour, irritability, agitation or depression. In addition, the CSM has advised that patients and their carers should be advised of the risks of hepatic disorder and told how to recognise symptoms.**
3. Ensure baseline monitoring of height, weight, BP, pulse rate have been performed plus any additional relevant investigations such as ECG in case of family history of arrhythmia or sudden death.
4. Initiation and stabilisation of drug treatment. The GP is not expected to enter into a shared care agreement until the patient is stabilised on atomoxetine and the parents at this stage are instructed to communicate directly with the clinic. As atomoxetine is not considered first line treatment a GP might have agreed shared care previously with another drug. If the decision to switch treatment due to side effects/ poor response is made by the specialist then another shared care agreement should be made between the specialist and the GP once the patient has stabilised on atomoxetine.
5. Set the review interval and criteria. The Specialist must ensure contact four weeks after initiation of treatment to assess if being effective. An appointment should be arranged three months after initiation of treatment to undertake necessary monitoring (see point 6 below). Once a child's treatment is stabilised, six monthly review appointments are offered by the Specialist. Specialist ADHD nurses, junior doctors and other staff are closely involved with the monitoring of the patients. When junior / middle grade doctors are helping the Specialists in the clinic, changes should be made after discussion with the Specialist only, and should be clearly stated in a letter to the GP.
6. Undertake any necessary monitoring at clinic appointments (initially three monthly, then six monthly in the long term): blood pressure, pulse rate, weight and height (including centiles). Unless the child has symptoms routine monitoring of full and differential blood counts are not carried out.
7. Supply the medication until the dose is stabilised. Prescribing may be transferred to the GP under shared care once the patient is stabilised on medication. The GP will not be asked to prescribe the drug outside its licensed indications
8. Maintain good communication with the GP. A written letter should be sent to the GP after each clinic visit notifying the GP of changes in the medication regime, adverse effects and results of the patient's routine monitoring. The GP must be notified of non-attendance at clinic.
9. Keep the GP fully informed about the patient's condition and medication. The specialist will be available to answer queries from the GP and carers.
10. Stop or modify the dosage as appropriate.
11. Advise the GP when the treatment is being discontinued. The specialist will provide necessary supervision and support during the drug discontinuation phase.
12. Liaison with other members of the multidisciplinary team responsible for the child's development and education. The parents and class teachers should be given information about atomoxetine in particular the monitoring and side effects.
13. Evaluate adverse drug reactions reported by the GP or carer.
14. The appropriateness of medication into adulthood should be carefully reviewed. If the drug is to be continued beyond the age of 18, the specialist will seek to make appropriate arrangements.
15. Continue supply of medication for children under six years.
16. Explain to the patient / carer their roles

General Practitioner responsibilities
1. Some GPs may feel able to make diagnosis of ADHD. Psychoeducation and parent training can take place in primary care for children who have mild or moderate ADHD. Other GPs will initiate referral to a specialist on suspicion of ADHD. 2. GPs should be aware that almost 50% of children who have ADHD may have other co-morbid conditions which include autistic spectrum/Asperger's syndrome, dyslexia, dyspraxia and oppositional-defiant difficulties. Recognising these conditions is important to ensure comprehensive planning is made. 3. Children who are severely affected by ADHD should be referred to secondary care without delay. These children will require medication early as part of the treatment package. 4. Monitor patient's overall health and well being. 5. Continued prescription of treatment, once patient is stabilised on medication and shared care is agreed, at the appropriate intervals given the nature of the drug and the family involved. As it is not necessary for a doctor to see the child more than every 3-6 months, unless there are specific indications, repeat prescriptions can be issued without necessarily seeing the child on each occasion. 6. To check that the patient is attending their six monthly specialist ADHD clinics and thus continued prescription is required. 7. Although the responsibility for carrying out monitoring lies with the specialist, the GP must ensure results are acceptable before generating further prescriptions. 8. Symptomatic management of minor adverse effects. 9. Report any adverse effects to the consultant and Medicine and Healthcare Products Regulatory Agency (MHRA) where appropriate. 10. Referral back to specialist if any problems arise.

Patient's / Carer's role
1 Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment. 2 Share any concerns in relation to treatment with atomoxetine. 3 Tell the specialist or GP of any other medication being taken, including over-the-counter products. 4 Read the patient information leaflet included with the medication and report any side effects or concerns they have to the specialist or GP.

Audit / Survey (To be carried out by specialist clinic)

- Total number of patients assessed
- Number referred to Specialist
- Number of patients receiving treatment
- Are they being monitored correctly according to shared care protocol?
- Length of time drug used
- Evidence of benefit: increase in quality of life
- Length of treatment, number discontinued and reason for discontinuation

BACK-UP ADVICE AND SUPPORT

Hospital / clinic contacts:

Please see details on the referral letter.

Specialist support / resources available to GP - including patient information

1. Contact with relevant specialist / specialist nurse
2. Information in British National Formulary for children
3. References
4. ADHD support groups www.ADDISS.co.uk
5. Diagnostic and statistical manual of mental disorders, DSM IV, published by the American Psychiatric Association
6. Principles of Treatment for Hyperkinetic Disorder: Practice Approaches for the UK. Overmeyer S and Taylor E.
7. ADDmire (ADD multi-agency information resource) – a group of professionals and parents involved in the care of children with Attention-deficit hyperactivity disorder (also known as ADD or ADHD) www.addmire.org.uk. Site managed by Ashford and St Peter's Hospital's NHS Trust.

References:

1. NICE technology Appraisal 98 March 2006: Methylphenidate, atomoxetine and dexamphetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents.
2. NICE clinical guideline 72 September 2008: Attention deficit hyperactivity disorder, Diagnosis and management of ADHD in children, young people and adults.
3. Product specification, Strattera® –www.medicines.org.uk (accessed 23 March 2010).

Other references used:

- SIGN clinical guideline 112 October 2009: Management of attention deficit and hyperkinetic disorders in children and young people.
- Ashford and St Peter's Hospital NHS Trust Shared Care Protocol for the use of Atomoxetine (Strattera®) in Attention Deficit Hyperactivity Disorder in Childhood, August 2004.
- Blackwater valley and Hart, & North Hampshire Primary Care Trusts Treatment Plan and Shared Care Agreement Methylphenidate (Ritalin®, Equasym®, Concerta XL®), Atomoxetine (Strattera®) and Dexamphetamine (Dexedrine®) for attention deficit hyperactivity disorder (ADHD) in children and adolescents Dec 2005.

Shared Care Prescribing Guideline
Atomoxetine (Strattera® for the Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in Childhood

Agreement for transfer of prescribing to GP

Patient details / addressograph:

Name……..

Address……..
……..
……..

DOB…….

Hospital No…….

Drug name and dose:

The following tests, investigations have been carried out:

Blood pressure: Date:

Pulse: Date:

Weight: (including centiles) Date:

Height: (including centiles) Date:

Diagnosis of ADHD made on (date):

Medication started on (date):

Patient stabilised on (drug/dose):

Patient's last clinic visit on (date):

Patient's next clinic visit on: then every 6 months

Specialist: Address: Contact Number	**Agreement to shared care, to be signed by GP and Specialist before transfer of care to GP.** **Specialist Signature:** **……..** **Date:**
GP Address: Contact Number	
Main Carer / parent / guardian: Contact Number:	**GP Signature:** **……..** **Date:**

The GP has the right to refuse to agree to shared care. In such an event the total clinical responsibility will remain with the specialist. The GP should then discuss alternative arrangements with the responsible specialist.

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