SHARED CARE GUIDELINE FOR THE USE OF ATOMOXETINE IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

INDICATION

Atomoxetine is a non-stimulant non-amphetamine inhibitor of noradrenaline reuptake. It is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children of 6 years and older and in adolescents as part of a comprehensive treatment programme. In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment with Atomoxetine into adulthood. However, **starting treatment with atomoxetine in adults is an off-label indication**.

The NICE clinical guideline no.72, Attention Deficit Hyperactivity Disorder makes recommendations for the diagnosis and management of attention deficit hyperactivity disorder (ADHD) in children, young people and adults. The guideline states that "drug treatment is the first-line treatment for adults with ADHD with either moderate or severe levels of impairment. Methylphenidate is the first-line drug. If methylphenidate is ineffective or unacceptable, atomoxetine or dexamfetamine can be tried. Where there may be concern about the potential for drug misuse and diversion (for example, in prison services), atomoxetine may be considered as the first-line drug treatment for ADHD in adults. The drug treatment for adults with ADHD should always form part of a comprehensive treatment programme that addresses psychological, behavioural and educational or occupational needs."

The NICE guideline states that a pre-drug treatment assessment should be completed, including:

- A full mental health and social assessment,
- A full history and physical examination, including:
    - Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms,
    - Heart rate and blood pressure (plot on a centile chart)
    - Weight
    - Family history of cardiac disease and examination of the cardiovascular system
- An electrocardiogram (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.

Drug treatment for adults with ADHD should be started only under the guidance of a psychiatrist, nurse prescriber specialising in ADHD, or other clinical prescriber with training in the diagnosis and management of ADHD. As a general principle the NICE guideline states that following titration and dose stabilisation, prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care

Drug treatment for adults with ADHD who also misuse substances should only be prescribed by an appropriately qualified healthcare professional with expertise in managing both ADHD and substance misuse. For adults with ADHD and drug or alcohol addiction disorders there should be close liaison between the professional treating the person's ADHD and an addiction specialist. These patients will not be considered for shared care.

NICE recommends that **"prescribers should advise people with ADHD and their parents or carers of the implications of prescribing unlicensed or 'off-label' drugs. Informed consent should be obtained and documented."**

Note: For the purposes of treatment an adolescent is defined as a person aged 16 to 18 years undergoing a period of psychological, social, and physical transition between childhood and adulthood. However, a pragmatic approach should be applied to this cut-off point depending on the patient's physiological and psychological development and condition. (Children's BNF 2007).

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines ways in which the responsibilities for managing prescribing can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug, ensuring that the patient has had a thorough assessment and access to a programme of care and support through the multidisciplinary team.

REFERRAL AND INITIATION

Shared Care is only appropriate if it provides the optimum solution for the patient.

- Patients will only be referred to the GP once the GP has agreed in each individual case
- Arrangements to transfer treatment from secondary to primary care may be made between 8 weeks and 6 months from initiation of treatment, once the condition has been stabilised

Specialist Responsibilities	
1	To make a diagnosis based on timely, comprehensive assessment using appropriate validated questionnaires and including an assessment of the patient's cultural/social circumstances. To determine a comprehensive management strategy and discuss with the patient/carer the risks, benefits and alternatives of/for treatment.
2	Initiate treatment and adjust according to patient response. Doses should be gradually increased until there is no further improvement and as long as side effects are tolerable.
3	Inform patient of side effects, including potential damage to liver (usually manifesting as abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice). Patients (aged 30 years or younger) of possible increased agitation, anxiety, suicidal thinking and self-harming behaviour, especially in the first few weeks.
4	Inform patient of long term monitoring required before initiating treatment.
5	The specialist will discuss with the patient that the initiation of atomoxetine in adults is "off label" and obtain informed consent .
6	Supply medication until treatment is stable. Initiation takes a minimum of 6 weeks and therefore patients should remain under the care of a specialist for a minimum of 8 weeks.
7	Review the patient in clinic
8	Adjust the dose and formulation of the drug as required. Communicate this information to the GP.
9	Develop a treatment regime including possible dose and timing of dose alterations for the GP to follow. Communicate this to the GP.
10	Stop medication when indicated.
11	**Monitoring:** - to undertake initial monitoring of heart rate and blood pressure and record on a centile chart before and after each dose change, and every 3 months (where measurements are required between outpatient appointments the consultant may request the GP to undertake the measurement and contact the specialist with the result.) - Weight (measure 3 and 6 months after the start of treatment, and every 6 months thereafter) - Routine blood tests and ECG if past medical or family history of serious cardiac disease or an abnormal cardiac examination.

12	**Disease monitoring** **- See the patient at least twice per year to monitor and review the drug treatment, concordance of effect, diurnal variations, changes in mood, adverse effects, tolerance and compliance.** - Consider the need for a trial reduction of medication on an annual basis. (NB an actual reduction of medication may not be necessary where there is ample evidence that when doses have been missed symptoms of ADHD have re emerged).
13	Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
14	Ensure that clear backup arrangements exist for GPs to obtain advice and support.
15	To ensure the patient has sufficient supply of medication until such time as is appropriate for the GP to assume prescribing responsibility. This may include times to cover initial transfer of responsibility and/or after 6 month reviews
16	To provide the patient/carers with comprehensive advice and information.
17	A supplementary prescriber may be involved in prescribing atomoxetine as part of a clinical management plan.
18	To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).

General Practitioner Responsibilities	
1	Initially to refer the patient and family for specialist advice.
2	Reply to the request for shared care as soon as practicable.
3	Prescribe atomoxetine at the dose recommended by the specialist.
4	Monitor weight, heart rate and blood pressure when requested by the consultant if it is required between outpatient appointments and communicate the results back to the consultant. Monitor for dysmenorrhoea, erectile dysfunction and ejaculatory dysfunction.
5	Make adjustments to the timing of medication within the agreed dosage regime if these are indicated and communicate these to the specialist in writing. Note the dose should be tapered when stopping.
6	To deal with general health issues of the patient.
7	Consider any side effects reported by the patient and to discuss with the specialist
8	Refer patient to the specialist if the patient's condition deteriorates.
9	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
10	Report adverse events to the specialist and CSM

Patient's role (or that of carer)	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Attend appropriate consultant and GP appointments
3	Report any adverse effects to the specialist or GP whilst taking atomoxetine.
4	Share any concerns in relation to treatment with atomoxetine.
5	Use written and other information on the medication.
6	Seek help urgently if it is suspected that atomoxetine is causing side effects, or if the patient is otherwise unwell.

SUPPORTING INFORMATION

Refer to Summary of Product Characteristics for full prescribing information.

Dosage and administration
In children and adolescents up to 70kg in body weight atomoxetine is initiated at a daily dose of 0.5mg /kg and increased after a minimum of 7 days to 1.2mg /kg with the total daily dose not exceeding 100mg. In adults the same dosage applies with a suggested maintenance dose of 1.2 mg /kg day e.g. 80mg daily with a total daily dose not exceeding 100mg.

Atomoxetine can be administered as either a single daily dose in the morning or as evenly divided doses in the morning and late afternoon/early evening.

In patients with moderate and severe hepatic insufficiency doses should be reduced to 50% and 25% of the standard dose, respectively. No adjustments are required for those with renal insufficiency.

Contraindications
Atomoxetine is contra-indicated in patients known to be hypersensitive to atomoxetine or to any of the excipients.
Atomoxetine should not be used in combination with monoamine oxidase inhibitors (MAOIs), or within 2 weeks after discontinuing therapy with a MAOI. Treatment with a MAOI should not be initiated within 2 weeks after discontinuing atomoxetine.
In clinical trials, the use of atomoxetine was associated with an increased risk of mydriasis and, therefore, its use is not recommended in patients with narrow angle glaucoma.

Side Effects
The most commonly reported adverse events are influenza-like symptoms, decreased appetite, anorexia/decreased weight, early morning awakening, irritability, mood swings, dizziness, somnolence, mydriasis, abdominal pain, vomiting, constipation, dyspepsia, nausea, dermatitis, pruritus, rash, fatigue.
See the SPC for further details on adverse effects.
In September 2005 the CSM issued a warning about possible risk of suicidal thoughts/behaviour with Atomoxetine. An analysis of clinical trial data showed suicide related behaviours occurred at a frequency of approximately 4 in 1000 Strattera treated patients. In the UK up to 15,000 patients have been treated with Atomoxetine and there have been 11 Yellow card reports of suicidal thoughts and behaviour (Sept 2005).
Atomoxetine was launched in 2004 and has black triangle status. ***All*** *suspected reactions (including those considered not to be serious and where the causal link is uncertain) should be reported to the CSM.*

Drug Interactions
The SPC recommends that the following drugs be used with caution if co-administered with atomoxetine because of potential or theoretical drug interactions: CYP2D6 inhibitors, salbutamol, pressor agents, and drugs that affect noradrenaline. Atomoxetine should not be used with MAOIs. See the SPC for further details.

Drug costs

Cost for 28 days at 80mg daily = £120.12 (Drug Tariff, August 2009)

References

1. British Association of Psychopharmacology. Evidence based guidelines for management of attention-deficit/hyperactivity disorder in adolescents in transition to adult services and in adults: recommendations from the British Association of Psychopharmacology. Journal of Psychopharmacology 2006.
2. Banaschewski T et al. Long-acting medications for the hyperkinetic disorders: A systematic review and European treatment guideline. Eur Child Adolesc Psychiatry 2006; 15: 476-495.
3. BMA, RPSGB. British National Formulary No 54: Sept 2007
4. www.medicines.org.uk
5. Attention Deficit Hyperactivity Disorder (NICE Guideline 72)

The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

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