SHARED CARE GUIDELINES FOR PRESCRIBING ATOMOXETINE (STRATTERA®) IN CHILDREN AND ADOLESCENTS

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. Treatment must be initiated by a specialist in the treatment of ADHD. Diagnosis should be made according to DSM-IV criteria or the guidelines in ICD-10.

Where patients are continuing treatment with atomoxetine beyond 1 year, re-evaluation of the need for therapy by a specialist in the treatment of ADHD is recommended.

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. A shared care guideline for the use of atomoxetine in adults is available.

The NICE clinical guideline for attention deficit hyperactivity disorder (CG no. 72) states that drug treatment:

- should only be started by a healthcare professional with expertise in ADHD
- be based on a comprehensive assessment
- always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions.
- may be prescribed and monitored by GPs under shared care arrangements

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)
    - Height and weight (plot on a growth chart)
    - 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.

Atomoxetine should be considered:

- As an option alongside methylphenidate when tics, Tourette's syndrome, anxiety disorder, stimulant misuse or risk of stimulant diversion are present.
- As an alternative to methylphenidate where this has been tried and has been ineffective at the maximum tolerated dose, or the child or young person is intolerant to low or moderate doses of methyphenidate.

If there is a choice of more than one drug, use the drug of lowest overall cost.

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 the way in which the responsibilities for managing the prescribing of atomoxetine for ADHD 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 and the consequences of its use.

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 4 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 child'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	To initiate treatment and stabilise the dose. Initiation takes a minimum of 6 weeks and therefore patients should remain under the care of a specialist for a minimum of 2 months.
3	To ask the GP whether he or she is willing to participate in shared care. Requests to GPs should be made in writing and must include appropriate information to allow an informed decision to be made.
4	On agreement from the GP, to provide the GP with appropriate information, including relevant clinical and physical assessment information to support the transfer of clinical responsibility.
5	To communicate promptly with the GP when treatment is changed, stopped or adjusted and to communicate changes in response to treatment or the condition itself.
6	Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
7	Ensure that clear backup arrangements exist for GPs to obtain advice and support.
8	In accordance with the recommendations from NICE: o 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 consultant with the result); o To undertake initial height and weight measurements; measure height every 6 months, plot on a growth chart and weight three and six months after the start of treatment and every 6 months thereafter. In children and young people, plot weight on a growth chart, this should be reviewed by the healthcare professional responsible for treatment. o closely observe for agitation, irritability, suicidal thinking and self-harm especially

	during the initial months of treatment and after a change in dose. Warn parents/carer about the potential for suicidal thinking and self-harm with Atomoxetine, ask them to report these effects. o monitor general response to medication and progress at school and mood.
9.	Ensure that patients know what to do and who to contact if they experience adverse events or an exacerbation of their condition.
10.	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
11.	To ensure the patient/ carer has given informed consent to their treatment.
12.	To provide the patient, carers/parents and teachers with comprehensive advice and information
13.	To be available for advice if the patient's condition changes, ensuring that procedures are in place for the rapid re-referral of the patient by the GP.
14.	To liaise with the GP on any suggested changes in prescribed therapy and to stop treatment where appropriate.
12	To refer to an adult psychiatrist where appropriate, including discussing the patient's case and transferring care to them.
13	Report adverse events to the CSM.

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 or adjust the dose, as advised by the specialist.
4.	o Monitor 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. Height and weight should be carefully monitored in children as growth retardation may occur. Children who are not gaining weight as expected should be referred back to specialist care for interruption of treatment. o Monitor for dysmenorrhoea, erectile dysfunction and ejaculatory dysfunction. o If seizures are exacerbated in a child with epilepsy or de novo seizures emerge, discontinue Atomoxetine immediately. o Closely observe for agitation, irritability, suicidal thinking and self-harm especially during the initial months of treatment and after a change in dose.
5.	To deal with general health issues of the patient.
6.	Refer patient to the specialist if the patient's condition deteriorates.
7.	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
8.	To provide support to specialists if they are transferring patients to adult psychiatric services.
9.	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
Atomoxetine is available as 10 mg, 18 mg, 25 mg, 40 mg or 60 mg capsules, to be taken orally. It may be taken with or without food and can be discontinued without reducing the dose. It is normally given as a single dose in the morning. Patients who suffer from side effects may benefit from dividing the dose, which should then be taken in the morning and late afternoon or early evening.
In children and adolescents under 70 kg body weight, atomoxetine should be initiated at a total daily dose of 0.5 mg/kg, maintained for at least seven days. The dose should then be titrated upwards according to response and tolerability to the recommended maintenance dose of 1.2 mg/kg/day.
In children and adolescents over 70 kg body weight the initial dose is 40mg, maintained for seven days prior to titration up to 80mg daily where necessary according to response and tolerability.
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.

N.B. NICE CG72 states that if there is a poor response to treatment, following review and consultation with a tertiary or regional centre, consider increasing the dose of atomoxetine to 1.8mg/kg/day (up to a total maximum dose of 120mg/day). These doses are higher than recommended in the BNF. Monitor closely for side effects.

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.

Cost
Costs for 28 days:
40mg daily £60.06 (Drug Tariff Aug 2009)
80 mg daily: £120.12 (Drug Tariff Aug 2009)

References

1. NICE CG 72. Attention deficit Hyperactivity Disorder. Sept 2008
2. NICE TA98 Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents – guidance (Review Date March 2009)
3. Bournemouth, Dorset and Poole Prescribing Forum pharmacological intervention in ADHD, Oct 2007.
4. Summary of Product Characteristics http://emc.medicines.org.uk/emc/assets/c/html/displayDocPrinterFriendly.asp?documentid=14482
5. British National Formulary and/or British National Formulary for Children http://www.bnf.org/bnf/ or http://bnfc.org/bnfc/

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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