

Shared Care Guideline for		Reference Number
METHYLPHENIDATE and ATOMOXETINE FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN ADULTS		
Author(s)/Originator(s): (please state author name and department)		To be read in conjunction with the following documents: Current Summary of Product characteristics http://www.medicines.org.uk BNF
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1. Unlicensed Indications

Methylphenidate and atomoxetine do not have UK marketing authorisation for use in adults with ADHD. Atomoxetine is licensed for adults with ADHD when the drug has been started in childhood.

2. Therapeutic use & background

NICE Guideline CG72 recommends that drug treatment should be the first-line approach in adult ADHD. Methylphenidate, atomoxetine and dexamfetamine are the drug treatments available to treat Adult ADHD but only atomoxetine is licensed in this indication. However NICE supports the first line use of methylphenidate in adults (despite the lack of licence). This SCG therefore only includes the use of atomoxetine and methylphenidate.

ADHD is a neuropsychological /developmental condition which is defined by core symptoms of inattention, hyperactivity and impulsiveness. For a diagnosis of ADHD to be made, the symptoms should be pervasive, not accounted for by any other psychiatric or developmental disorder, and normally present before the age of 7.

Of those diagnosed in childhood, approximately 65% carry the disorder into adulthood. This represents 15% who retain the full symptoms of ADHD by the age of 25, and a further 50% may be considered to be in partial remission, displaying reduced levels of impairment due to symptoms. In addition, adults may present to adult mental health services showing the symptoms of ADHD, which have persisted since childhood, but have never been diagnosed. Adults with ADHD may be significantly functionally and occupationally impaired, and experience other concomitant mental health problems (for example self harm, substance misuse, anxiety).

	<p>Methylphenidate should be the first drug to be tried.</p> <p>Methylphenidate is classed as a Schedule 2 Controlled Drug under the Misuse of Drugs Act 1971. Prescriptions must therefore conform to the Misuse of Drugs Regulations 2001 and include</p> <ul style="list-style-type: none"> • The name and address of the patient • The name, form (including immediate- or modified-release) and strength of the preparation. • Total quantity to be supplied, in words and figures • The dose to be taken, and the frequency. • Prescriber's signature, address and the date. (Prescriptions for Sch 2 Controlled Drugs are valid for 28 days from the date stated thereon.) <p>Caution should be exercised when prescribing methylphenidate to those likely to be at risk from stimulant misuse or diversion.</p> <p>Atomoxetine may be considered where adequate trials of methylphenidate (or dexamfetamine) have proved unsatisfactory, or where there is likely to be risk from stimulant misuse or diversion.</p>
<p>3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).</p>	<p>Methylphenidate:</p> <ul style="list-style-type: none"> • Known sensitivity to methylphenidate or any of the excipients; • Glaucoma; • Pheochromocytoma • During treatment with non-selective, irreversible monoamine oxidase (MAO) inhibitors , or within a minimum of 14 days of discontinuing those drugs due to risk of hypertensive crisis • Hyperthyroidism or Thyrotoxicosis; • Diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder. • Diagnosis or history of severe and episodic (Type I) Bipolar (affective) Disorder (that is not well-controlled) • Pre- existing cardiovascular disorders including 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). • Pre-existing cerebrovascular disorders cerebral aneurysm, vascular abnormalities including vasculitis or stroke. <p>Atomoxetine:</p> <ul style="list-style-type: none"> • Atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders whose condition would be expected to deteriorate if they experienced increases in blood pressure or heart rate that could be clinically important (for example, 15 to 20 mm Hg in blood pressure or 20 beats per minute in heart rate). 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. • Hypersensitivity to atomoxetine or to any of the excipients. • Atomoxetine should not be used in combination with monoamine oxidase inhibitors (MAOIs).

	<p>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.</p> <ul style="list-style-type: none"> 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 pheochromocytoma or a history of pheochromocytoma. 	
<p>4. Prescribing in pregnancy and lactation</p>	<p>The following is for information. Prescribing in these groups should be done in consultation with an obstetrician.</p> <p>Methylphenidate</p> <p>There is a limited amount of data from the use of methylphenidate in pregnant women. Cases of neonatal cardiorespiratory toxicity, specifically foetal tachycardia and respiratory distress have been reported in spontaneous case reports.</p> <p>Studies in animals have only shown evidence of reproductive toxicity at maternally toxic doses. Methylphenidate is not recommended for use during pregnancy unless a clinical decision is made that postponing treatment may pose a greater risk to the pregnancy.</p> <p>Methylphenidate has been found in the breast-milk of a woman treated with methylphenidate. There is one case report of an infant who experienced an unspecified decrease in weight during the period of exposure but recovered and gained weight after the mother discontinued treatment with methylphenidate. A risk to the suckling child cannot be excluded.</p> <p>A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from methylphenidate therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.</p> <p>Atomoxetine</p> <p>For atomoxetine, no clinical data on exposed pregnancies are available. Animal studies in general do not indicate direct harmful effects with respect to pregnancy, embryonal/foetal development, parturition, or postnatal development.</p> <p>Atomoxetine should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.</p> <p>Atomoxetine and/or its metabolites were excreted in the milk of rats. It is not known if atomoxetine is excreted in human milk. Because of the lack of data, atomoxetine should be avoided during breast-feeding.</p>	
<p>5. Dosage regimen for continuing care</p>	<p>Route of administration</p>	<p>Methylphenidate and atomoxetine are both given orally</p>

Preparations available

Methylphenidate is available as 5mg, 10mg, 20mg, 30mg and 40mg modified release capsules, 18mg, 27mg and 36mg modified release tablets and 5mg, 10mg and 20mg tablets.

Dose equivalents of methylphenidate preparations (all strengths are in mg):

Immediate release methylphenidate	Concerta-XL	Equasym-XL	Medikinet-XL
10	-	10	10
15	18	-	-
20	-	20	20
30	36	30	30
-	-	-	40
45	54	-	-
60	72	60	-

Care should be taken when prescribing different preparations of methylphenidate (immediate and slow release). Different preparations are not interchangeable.

Atomoxetine is available as 10mg, 18mg, 25mg, 40mg, 60mg and 80mg capsules.

Dosage

Methylphenidate 5mg three times a day (or modified release equivalent dose) increased if necessary at weekly intervals according to response, max. 100mg daily in 2-3 divided doses (may be given up to four times a day).

Modified release preparations may increase adherence and be preferred if there is concern about misuse or diversion. Normally offer these once daily, but no more than twice daily.

Atomoxetine (body weight >70kg) initially 40mg daily for 7 days, increased according to response; usual maintenance 80-100mg daily (can be offered in divided doses). NICE recommend trialing at this dose for 6 weeks to determine effectiveness. May be increased to max. 120mg daily under direction of a specialist. Note doses above 100mg are unlicensed.

Is titration required	Yes ✓ Dose should be titrated by specialist	No
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Adjunctive treatment regime
Not needed

Conditions requiring dose reduction
Seek advice of specialist

See section 7 for details of side effects to methylphenidate which may respond to dose reduction.

	<p>Usual response time Dependant on treatment. Atomoxetine response time longer. (weeks to months). To be reviewed by specialist initiating and requesting shared care</p> <p>Duration of treatment As per agreement with the specialist team</p> <p>Treatment to be terminated in agreement with Consultant / Specialist team</p>
<p>6. Drug Interactions</p>	<p><i>For a comprehensive list consult the BNF appendix 1 or Summary of Product Characteristics (www.medicines.org.uk)</i></p>
<p>7. Adverse drug reactions</p> <p><i>For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF</i></p>	<p>Listed are some of the common ($\geq 1/100$ to $< 1/10$) and uncommon ($\geq 1/1000$ to $< 1/100$) side effects seen with methylphenidate and atomoxetine:</p> <p>Methylphenidate</p> <p>People treated with methylphenidate should be monitored for weight loss, sustained tachycardia, arrhythmia, increased systolic blood pressure, tics, psychotic symptoms, anxiety, panic. These may respond to dose reduction, or require a switch to atomoxetine.</p> <p>In the case of dose reduction or proposed switch to atomoxetine patient should be referred back to specialist mental health services.</p> <p>Cardiovascular changes may require referral to specialist services.</p> <p>Atomoxetine</p> <p>In both paediatric and adult placebo-controlled trials, patients taking atomoxetine experienced increases in heart rate, systolic and diastolic blood pressure.</p> <p>People treated with atomoxetine, particularly younger adults, aged 30 or younger, should be monitored for agitation, irritability, suicidal thinking and self-harming behaviour, particularly in the first months of treatment, or after a change of dose.</p> <p>Very rarely atomoxetine may cause liver damage, causing abdominal pain, nausea, malaise, darkening of urine or jaundice. This is rare. Routine liver function tests are not recommended.</p> <p>Sexual dysfunction may occur.</p>

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

Atomoxetine – Following rare reports of hepatic disorders, patients and carers should be advised of the risk and be told how to recognize symptoms; prompt medical attention should be sought in the case of abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice. Routine liver tests are not recommended.

Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the “Yellow Card” scheme

Other important co morbidities:

	<p>Substance misuse: Potential misuse or diversion of stimulants must be minimised by careful selection of patients, prescribing of small amounts of medication and prompt discussion between consultant and the GP in the event of non-attendance at appointments or suspected drug misuse.</p>				
<p>8. Baseline investigations</p>	<p>List of investigations / monitoring :</p> <p>Consider using standard symptom and side effect rating scales during treatment as an adjunct to clinical assessment.</p> <p>Routine blood tests and ECGs are not recommended unless there is clinical indication.</p> <p>Weight, heart rate and blood pressure should be measured on initiation by specialist.</p>				
<p>9. Ongoing monitoring requirements to be undertaken by GP</p>	<p>Is monitoring required?</p>	<p>Yes</p> <p>All patients who may respond to dose reduction or change of treatment to atomoxetine should be referred back to their specialist mental health team.</p>			
	<p>Monitoring</p>	<p>Frequency</p>	<p>Results</p>	<p>Action</p>	<p>By whom</p>
	<p>Efficacy and side effects</p>	<p>As appropriate, see below.</p>		<p>As indicated by assessment findings</p>	<p>GP / Specialist team</p>
	<p>Monitoring of significant side effects. Monitor side effects at each clinical review (6 monthly). Consider using standard symptom and side effect rating scales during treatment.</p> <p>Reproductive system and sexual function</p> <ul style="list-style-type: none"> • Monitor for dysmenorrhoea, erectile dysfunction and ejaculatory dysfunction <p>Seizures</p> <ul style="list-style-type: none"> • If exacerbated in an adult with epilepsy or de novo seizures emerge, discontinue methylphenidate or atomoxetine immediately. • Consider dexamfetamine instead after discussion with a regional tertiary specialist treatment centre. <p>Tics</p> <ul style="list-style-type: none"> • Consider whether tics are stimulant-related, and whether tic-related impairment young people outweighs the benefits of ADHD treatment • If stimulant-related, reduce the dose or stop drug treatment or consider using atomoxetine instead. <p>Psychotic symptoms (delusions, hallucinations)</p> <ul style="list-style-type: none"> • Withdraw drug treatment and carry out full psychiatric assessment. • Consider atomoxetine instead. <p>Anxiety symptoms including panic</p> <ul style="list-style-type: none"> • Where symptoms are precipitated by stimulants, particularly in adults with a history of coexisting anxiety, use lower doses of the stimulant and/or combined treatment with an antidepressant used to treat anxiety. • Switching to atomoxetine may be effective. <p>Agitation, irritability, suicidal thinking and self-harm</p> <ul style="list-style-type: none"> • Closely observe especially during the initial months of treatment or after a change in dose. Warn parents/carers about the potential for suicidal thinking and self-harm with atomoxetine, and ask them to report these effects. • Warn adults (aged 30 years or younger) of possible increased agitation, anxiety, suicidal thinking and self-harming behaviour, especially in the first weeks of treatment. <p>Drug misuse and diversion</p> <ul style="list-style-type: none"> • Monitor changes in potential for misuse and diversion, which may come with changes in circumstances and age. Modified-release methylphenidate or atomoxetine may be preferred. 				

	Weight	Measure at 3 and 6 months after the start of treatment and every 6 months thereafter		As indicated by physical findings	GP
	Heart rate and blood pressure	Measure before and after each dose change and every 3 months	Action to be taken if resting heart rate >80bpm or blood pressure >140/90mmHg (particularly raised systolic blood pressure) or sustained arrhythmia on two occasions.	Refer immediately to specialist team for dose reduction. If patients develop symptoms suggestive of cardiac disease during treatment they should be referred for prompt specialist cardiac evaluation. Life threatening changes should be referred to accident and emergency.	GP
10. Pharmaceutical aspects	As described in section 5 care is required when prescribing different methylphenidate preparations (immediate and modified release). Different preparations are not interchangeable..				
11. Secondary care contact information	If stopping medication or needing advice please contact:				
	Dr _____				
	Contact number: _____				
	Hospital: _____				
12. Criteria for shared care	Prescribing responsibility will only be transferred when <ul style="list-style-type: none"> ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements 				

13. Responsibilities of initiating specialist

- a) Assessment of the patient and diagnosis of ADHD
- b) Documentation of full medical and psychiatric history.
- c) physical health monitoring.
- d) Prescribing for first 3 months or until stable.
- e) Completion of medication assessment pro-forma
- f) Measurement of baseline parameters
- g) Informing patients and carers of the diagnosis, and discussing with them the care plan, treatment options and side effects of medications.
- h) Promoting access to any appropriate supporting therapies or education.
- i) Contacting GP to ascertain willingness to participate in shared care.
- j) Provision of 6-monthly review appointments and assessment of mental state.
- k) Reporting of any adverse drug reactions to the Medicines and Healthcare Products Regulatory Agency (MHRA) via the Yellow Card Scheme.
- l) Advising GP of discontinuation of treatment if considered clinically appropriate.
- m) Advising GP of options if the patient fails recurrently to attend follow-up appointments.

14. Responsibilities of the GP

- a) Responding to the request for shared care as soon as possible.
- b) Prescribing of medication as agreed with consultant/ specialist
- c) team.
- d) Referring to consultant any queries regarding treatment, side effects, concerns about drug misuse or diversion that cannot be answered
- e) Stopping treatment on the advice of the consultant/ specialist team
- f) Reporting of any adverse drug reactions to the Medicines and
- g) Healthcare Products Regulatory Agency (MHRA) via the Yellow Card Scheme.

15. Responsibilities of the patient

- a) Report and side effects to their GP / specialist team
- b) Report cessation of medication to their GP / specialist team

16. Additional Responsibilities	List any special considerations	Action required	By whom	Date
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet.			
19. Shared care agreement form	Attached below			

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]*

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 monitoring and 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. The patient will not be discharged from out-patient follow-up while taking *[insert text here]*.

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

Thank you.

Yours

[insert Specialist name]

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