

**796FM.5 METHYLPHENIDATE, ATOMOXETINE, LISDEXAMFETAMINE AND DEXAMFETAMINE
FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN ADULTS
Shared Care Protocol**

This protocol is under review.

- For continued prescribing in patients transferred to adult services.
- For newly diagnosed adults.
- For guidance in <18 year olds refer to [Guideline 809FM Methylphenidate, Lisdexamfetamine, Dexamfetamine, Guanfacine and Atomoxetine for the Treatment of Attention Deficit Hyperactivity Disorder – Shared Care Protocol for ≥6 - <18-year olds.](#)

It should be read in conjunction with the [shared care responsibilities](#), Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc, and the [BNF](#).

Contents

1.	SUMMARY	1
2.	BACKGROUND	2
3.	RESPONSIBILITIES AND ROLES.....	3
4.	ONGOING PHYSICAL MONITORING SCHEDULE.....	4
5.	SUPPORTING INFORMATION	5
	Methylphenidate	5
	Atomoxetine.....	8
	Lisdexamfetamine.....	11
	Dexamfetamine.....	12
6.	CONTACT DETAILS	14
7.	REFERENCES	14
	Appendix 1: Algorithm for initial prescribing pathway for ADHD treatment at BHT	16

1. SUMMARY

1. ADHD is a heterogeneous behavioural syndrome characterised by the core symptoms of hyperactivity, impulsivity and inattention. While these symptoms tend to cluster together, some people are predominantly hyperactive and impulsive, while others are inattentive.
2. Methylphenidate, atomoxetine, lisdexamfetamine and dexamfetamine are licensed as part of a comprehensive treatment programme for ADHD in children (over 6 years of age) and adolescents when remedial measures alone prove insufficient.
3. NICE ADHD guideline¹ states that treatment should only be initiated by an appropriately qualified healthcare professional with expertise in ADHD. Young people with ADHD should normally be transferred to adult psychiatric services if they continue to have significant symptoms of ADHD or other co-existing conditions, with adult services carrying out a comprehensive assessment of the person with ADHD.
4. ADHD continues into adulthood in approximately one third of patients. Studies have shown that stimulants work on core symptoms in adults with ADHD. Although unlicensed for use in adults, NICE recommends methylphenidate as first line treatment of adults diagnosed with ADHD, with atomoxetine (licensed for continuation from adolescence into adulthood) and dexamfetamine (unlicensed) as alternatives if methylphenidate is ineffective. Dexamfetamine should be considered a third-line option. NICE guidance was issued in 2008, before lisdexamfetamine became available in the UK. Lisdexamfetamine is the only licensed stimulant in adult patients and has a product licence as a first line treatment option in this age group. It has similar average effect sizes to methylphenidate and dexamfetamine and shares a similar side effect profile. It has the advantage of being administered once daily. It can be considered as an alternative first line treatment to methylphenidate in adults.
5. NICE recommends that continued prescribing and monitoring of drug therapy may be performed by general practitioners, under shared care arrangements, ensuring clear lines of communication between primary and secondary care are maintained.

6. When a consultant psychiatrist adults feels that the patient may benefit from continued care by the primary care team then he/she may seek the agreement of the GP concerned to share care, providing the following conditions are met:
 - a. The patient's condition is stable.
 - b. The dose of ADHD treatment is stable (this includes ensuring that a patient is stable following a switch from an immediate to a prolonged release preparation).
 - c. The GP is provided with sufficient information to ensure they are confident to adequately monitor the patient.
 - d. Support and advice regarding all aspects of therapy will be provided by the specialist team.
 If a GP is not confident to undertake these roles then he or she is under no obligation to do so.
7. If patients from abroad come to stay temporarily or permanently in Buckinghamshire and formulations previously prescribed are not covered by these guidelines they will need to obtain their medication from their country of origin. Any patient coming from abroad for more than 3 months who are requesting repeat medication for ADHD, will need referring into the appropriate clinic for confirmation of diagnosis according to ICD-10 diagnostic criteria. Patients requesting other formulations will be prescribed the closest alternative within these guidelines. As there are different thresholds for diagnosis of ADHD in other countries, any patients prescribed medication within this guidance must fit into ICD-10 diagnostic criteria for ADHD to receive treatment.

2. BACKGROUND

For a diagnosis of ADHD, based on a complete history and evaluation of the patient, symptoms of hyperactivity/impulsivity and/or inattention should:

- Meet the diagnostic criteria in DSM-IV or ICD-10 (hyperkinetic disorder)¹, **and**
- Be associated with at least moderate psychological, social and/or educational or occupational impairment based on interview and/or direct observation in multiple settings, **and**
- Be pervasive, occurring in two or more important settings including social, familial, educational and/or occupational settings.

Current treatments for ADHD include a range of social, psychological, and behavioural interventions, which may be focused on the child/patient, parents and/or caregivers, or teachers.

NICE recommends when deciding to treat children or young people with drugs, professionals should consider:

- Methylphenidate for ADHD without significant comorbidity.
- Methylphenidate for ADHD with comorbid conduct disorder.
- Methylphenidate or atomoxetine when tics, Tourette syndrome, anxiety disorder, stimulant misuse or risk of stimulant diversion are present.
- Atomoxetine if methylphenidate 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.
- In consultation with a regional tertiary specialist treatment centre, dexamfetamine may be considered in children and young people whose ADHD is unresponsive to a maximum tolerated dose of methylphenidate or atomoxetine.
- NICE guidelines have not yet been updated to include lisdexamfetamine, however in Buckinghamshire young people and adults can be prescribed lisdexamfetamine according to its product licence (children aged 6 years and over: when response to previous methylphenidate treatment is considered clinically inadequate; adults: as a first line treatment option).

General treatment principles

- In order to optimise drug treatment, the initial dose should be titrated against symptoms and side effects over 4 - 6 weeks, during which symptoms and side effects should be recorded at each dose change by the prescriber after discussion with the person with ADHD by phone or direct contact.
- Dose titration should be slower if tics or seizures are present in people with ADHD.
- If side effects are troublesome a reduction in dose should be considered.
- Treatment response for all drugs should be reviewed at least annually, including: Comprehensive assessment of clinical need, benefits and side effects - taking into account views of patient and carers; the effect of missed doses, planned dose reductions and brief periods of no treatment. Treatment with methylphenidate should be interrupted at least yearly to determine whether continuation is needed.²

3. RESPONSIBILITIES AND ROLES³

Specialist responsibilities

1. Oxford Health adult psychiatrist a) for patients transferring from CAMHS at age 18 and for 18 year olds discharged by community paediatrics who have been referred to adult psychiatry services: To carry out a full assessment of the person with ADHD (see point 12 below); and b) for new patients (without a current diagnosis of ADHD): To provide a comprehensive diagnostic assessment of people presenting for the first time
2. To decide on the most appropriate drug treatment and discuss benefits and side effects with the patient and/or parents/carer and provide written information where appropriate. In the case of atomoxetine, this should also include an explanation of the very rare risk of adverse hepatic reactions, what symptoms to look out for and what action to take should they occur.
3. To carry out and record all necessary baseline physical measurements as follows:
 - a. Height and weight
 - b. Baseline cardiovascular status, including blood pressure and pulse, a history of exercise syncope, undue breathlessness and other cardiovascular symptoms, family history of cardiac/unexplained death. An ECG should be carried out if indicated.
4. The initial dose should be titrated against symptoms and side effects over 4 - 6 weeks. Symptoms and side effects should be recorded at each dose change. The patient's progress should be reviewed regularly (this may be by telephone, if appropriate).
5. To prescribe for a patient who is being switched from an immediate to a prolonged release preparation – usually for a period of 1 month – until they are re-stabilised.
6. In adults (Oxford Health): To measure blood pressure and pulse following every dose increase, then at 3 and 6 months and every 6 months until care is shared by the GP. The patient should be referred to a cardiologist if symptoms suggestive of cardiac disease develop. See [ongoing monitoring schedule](#) below.
7. In adults (Oxford Health) to measure weight every 6 months until care is shared by the GP – if there is evidence of weight loss, measure the BMI and review treatment if weight loss persists. See [ongoing monitoring schedule](#) below.
8. To review the patient annually (adults). Adult patients do not need to remain open to secondary care between their annual reviews. However, if the GP has any concerns between the annual reviews they can contact the consultant by phone for advice. The review should include a comprehensive assessment of clinical need, benefits and side effects, and monitoring of blood pressure, pulse and weight/height/BMI where appropriate. Maintaining close clinical contact by means of a telephone review may be beneficial for some patients. Communicate diagnosis, behavioural problems, cognitive and functional scores, any dose changes of the same formulation needed and results of any physical monitoring to the GP.
9. After transition to adult services, adult services healthcare professionals should carry out a comprehensive assessment of the person with ADHD that includes personal, educational, occupational and social functioning, and assessment of any co-existing conditions, especially drug misuse, personality disorders, emotional problems and learning difficulties.
10. To give support and advice to the prescribing GP as needed.
11. To communicate to the GP non-attendance of patients at outpatient appointments. The patient should be sent a letter asking them to make another appointment as soon as possible.
12. To report serious adverse events to the MHRA and inform the GP.
13. To take responsibility for stopping treatment if appropriate, including any treatment breaks. Patients prescribed methylphenidate should have a yearly treatment break to assess the need to continue drug treatment.² The effect of missed doses, planned dose reductions and brief periods of no treatment should be taken into account for all treatments.

General Practitioner responsibilities

1. To reply to the request for shared care as soon as practicable.
2. To ensure a full understanding of the responsibilities for managing a patient on methylphenidate atomoxetine, lisdexamfetamine, or dexamfetamine including identification of side-effects in line with the relevant [SPC](#).
3. To provide repeat prescriptions after stabilisation.
4. Methylphenidate, lisdexamfetamine and dexamfetamine are controlled drugs, subject to safe custody and specific regulations for prescribing. Prescriptions for these medicines are only valid for dispensing within 28 days from the date of signature and, unless there are exceptional circumstances, each prescription should be for no more than 30 days supply.
6. To monitor for any signs of diversion, misuse or abuse of methylphenidate, lisdexamfetamine and dexamfetamine.
7. To report any evidence of change in symptom control to the specialist.
8. To ask the patient whether they are experiencing adverse effects and liaise with the specialist if necessary.
9. To report to, and seek advice from, the specialist on any aspect of patient care which is of concern to the GP and which may affect treatment. Refer anyone who develops signs of heart disease to a cardiologist.
10. Report adverse events to the specialist and the MHRA.
11. Follow specialist advice (backed up by supporting information) on any changes in treatment.
12. To notify the specialist of the patient's failure to attend appointments.

Patient's/Carer's role

1. To attend all appointments with the patient's GP and specialist.
2. To report any adverse effects to their specialist or GP whilst under treatment.
3. To share any concerns they have in relation to treatment.
4. Ask the specialist or GP if they do not have a clear understanding of their treatment.

4. ONGOING PHYSICAL MONITORING SCHEDULE (carried out by specialist)

(Ref: NICE Guideline 72: ADHD, September 2008, Lilly communication – Important safety information on Strattera® and risks of increased BP & HR, 5.12.11, SPCs, and Oxford Health DTC decision, Aug 2012 ratified by CEC Nov 2012.)

Adult monitoring

	Frequency		Intervention
Weight	6 monthly	If there is evidence of weight loss, measure the BMI. Record weight on a chart.	Strategies to reduce weight loss, or manage decreased weight gain include: <ul style="list-style-type: none"> • Taking medication with or after food rather than before meals • Eating additional meals or snacks early morning or late evening when stimulant effects have worn off • Obtaining dietary advice and eating high calorie foods of good nutritional value Review treatment if weight loss persists.
Pulse	6 monthly (and before and after each dose change)	Record on a chart	If there is sustained resting tachycardia (or a significant increase in pulse, e.g. 20 bpm) or arrhythmia, consider reducing the dose and refer to the GP for treatment of symptoms
Blood pressure	6 monthly (and before and after each dose change)	Record on a chart	If blood pressure is raised above normal or there is a clinically significant increase (e.g. 15 – 20 mmHg) measured on two occasions consider reducing the dose and refer to the GP for treatment of raised BP.

5. SUPPORTING INFORMATION

Methylphenidate – 1st line treatment for all ages

Licensed indications www.medicines.org.uk/emc

Methylphenidate is indicated as part of a comprehensive treatment programme for ADHD in children (over 6 years of age) and adolescents when remedial measures alone prove insufficient. N.B. The product licence does not include adults.

Methylphenidate products on the Bucks formulary

Immediate release tablets

Methylphenidate 5 mg, 10 mg, 20 mg tablets

Prolonged release formulations:

Xaggitin XL[®] modified release 18 mg, 27 mg, 36 mg, 54 mg tablets.

Designed to replace three times daily dosing with the immediate release preparations (22:78 release profile). It is bioequivalent to Concerta XL[®]. It has a 12 hour duration.

Xaggitin XL[®] is on the Bucks formulary as a first line agent for ADHD patients who have not yet started methylphenidate M/R and for whom a preparation with a 12 hour duration of action is appropriate.

Delmosart[®] modified release 18 mg, 27 mg, 36 mg, 54 mg tablets.

Designed to replace three times daily dosing with the immediate release preparations (22:78 release profile). It is bioequivalent to Concerta XL[®]. It has a 12 hour duration.

Delmosart[®] is on the Bucks formulary as a first line agent for ADHD patients who have not yet started methylphenidate M/R and for whom a preparation with a 12 hour duration of action is appropriate.

Concerta XL[®] 18 mg, 27 mg, 36 mg, 54 mg tablets.

Designed to replace three times daily dosing with the immediate release preparations (22:78 release profile). It has a 12 hour duration.

Medikinet XL[®] 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg capsules.

Designed to be similar to twice daily dosing with immediate release formulations (50:50 release profile). It has an 8 hour duration.

Equasym XL[®] 10 mg, 20 mg, 30 mg capsules.

Designed to be similar to twice daily dosing with immediate release formulations (30:70 release profile). It has an 8 hour duration.

Concerta XL[®], Xaggitin XL[®], Delmosart MR[®], Equasym XL[®] and Medikinet XL[®] are more expensive than methylphenidate immediate release preparations, but may be useful in certain situations e.g. to avoid the need to take medicines to school.

Product	Maximum Licensed Dose*
Methylphenidate – ordinary release	60 mg daily in divided doses
Xaggitin XL [®] , Delmosart MR [®] or Concerta XL	54 mg once daily with or after breakfast
Equasym XL [®]	60 mg once daily before breakfast
Medikinet XL [®]	60 mg once daily with or after breakfast

* NICE³ recommends that doses of immediate release methylphenidate, should be titrated according to response, up to a total maximum of 90 mg/day in children and young adults (after consultation with a tertiary or regional centre) and 100 mg/day in adults may be indicated.

Stimulant dose equivalents³

Immediate release methylphenidate: Xaggitin XL[®], Delmosart MR[®], Concerta XL[®], Equasym XL[®] and Medikinet XL[®]:

IR-MPH	Xaggitin XL [®]	Delmosart MR [®]	Concerta XL	Equasym XL	Medikinet XL
5		-	-	-	5
10		-	-	10	10
15	18	18	18	-	15 (10 + 5)
20		-	-	20	20
30	36	36	36	30	30
40		-	-	40 (2 x 20)	40
45	54	54	54	-	45 (40 + 5)
50		-	-	50 (20 + 30)	50
60	72* (2 x 36)	72* (2 x 36)	72* (2 x 36)	60 (2 x 30)	60
90	108 (2 x 54)	108 (2 x 54)	108 (2 x 54)	90 (3 x 30)	90 (60 +30)

Dosage and administration of methylphenidate

Shared care is only recommended for children aged 6+ (within licence) and for adults.

Careful dose titration is necessary at the start of treatment with methylphenidate. This may be achieved using an immediate release formulation taken in divided doses or using an XL preparation. The recommended starting daily dose is 5 mg once daily or twice daily (e.g. at breakfast and lunch), increasing if necessary by increments of 5 - 10 mg in the daily dose according to tolerability and degree of efficacy observed. If twice daily dosing is impracticable, an XL preparation may be used.

Evidence shows that adults with ADHD do better on higher doses (in terms of mg/kg) than children/adolescents.

Methylphenidate is a schedule 2 controlled drug and is therefore subject to the regulations for controlled drugs (see [BNF](#) for more details). Supplies should be limited to no more than 30 days.

Contraindications with methylphenidate

Psychiatric	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 1) Bipolar (affective) disorder (that is not well controlled).
Endocrine	Hyperthyroidism or thyrotoxicosis, phaeochromocytoma
Cardiac	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 dysfunction of cardiac ion channels
	Pre-existing cerebrovascular disorders cerebral aneurysm, vascular abnormalities including vasculitis or stroke or known risk factors for cerebrovascular disorders
Pregnancy	Pregnancy, breastfeeding.
Ophthalmic	Glaucoma
Monoamine oxidase inhibitors (MAOI)	Patients currently taking, or who have taken within the preceding two weeks, a non-selective, irreversible monoamine oxidase inhibitor.

Cautions with methylphenidate

- Medical conditions that might be compromised by increases in blood pressure or heart rate
- Epilepsy - seizure frequency may be increased therefore use with caution in epilepsy.
- Tourette's syndrome and tics.
- Behavioural disturbance and thought disorder may be exacerbated in psychotic children.
- Anyone on methylphenidate who develops signs of heart disease should be referred to a cardiologist.⁴
- During long term therapy, check full blood count only if leucopenia/thrombocytopenia/anaemia is suspected.

Interactions with methylphenidate

Drug	Action	Management
Alcohol	May increase methylphenidate levels and exacerbate some of its CNS effects.	Advise avoidance of alcohol or use with caution in patients with a history of alcohol use.
Anticoagulants	Anticoagulant effect of coumarins may be increased.	Monitor INR if methylphenidate is started or stopped.
Phenytoin, phenobarbitone, primidone	Concentrations of antiepileptics may be increased.	This is not an established interaction and is based on a handful of case reports only. However, be alert for an increase in antiepileptic side effects and take levels or reduce the dose if appropriate.
Antidepressants	Metabolism of some SSRIs and TCAs may be inhibited and levels increased.	Concomitant use may be therapeutically beneficial, however be alert for an increase in side effects and reduce doses if necessary.
Monoamine oxidase inhibitors	Possible hypertensive crisis may result from the combination.	Methylphenidate is contraindicated in patients being treated (currently or within the preceding two weeks) with non-selective, irreversible MAO-inhibitors.
Clonidine	Adverse effects on blood pressure and pulse may occur.	The combination has not been systematically evaluated so the combination should only be used very cautiously.
Antihypertensive drugs	Methylphenidate may decrease the effectiveness of antihypertensives	Monitor blood pressure

Adverse effects with methylphenidate (for full list see [SPC](#))

Incidence	Adverse Effect	Management
Very common (>10%)	Nervousness and insomnia.	Mainly at beginning of treatment and can be controlled by dose adjustment.
Common (1 - <10%)	Abdominal pain, nausea and vomiting. Headache, drowsiness, dizziness, dyskinesia, rash and dry mouth, headache, drowsiness, decreased appetite. Changes in BP and heart rate. Dizziness, dyskinesia. Decreased appetite, moderately reduced weight gain and slight growth retardation.	Mainly at the beginning of treatment and may be helped by taking with food. These effects are usually transient. Usually an increase (monitor BP and pulse). For children and young people, plot height and weight on growth charts and review regularly. For adults, consider monitoring BMI if weight loss occurs.
Less common (>0.1% to <1%)	Blurred vision, apathy, confusion, tics, worsening of pre-existing tics, psychotic disorders, mood changes.	If tics occur, consider whether they are stimulant related and whether tic related impairment outweighs the benefits of ADHD treatment. Development of new or worsening of pre-existing psychiatric symptoms should be monitored at every dose change and at least 6 monthly.
Rarely (>0.01%)	Difficulties in visual accommodation, angina pectoris	
Very rarely (<0.01%)	Abnormal liver function, leucopenia, thrombocytopenia and anaemia.	If there are signs and symptoms of liver dysfunction or of haematological abnormalities, discontinue methylphenidate and perform appropriate blood tests. There is no evidence for regular blood testing during methylphenidate treatment.

Time to response:

Within a few hours or days. May take a few weeks for the full effect.

Onset and duration of action differ depending on the preparation used:

	Dose	% of IR in tablet	% of MR in tablet	Duration of action
IR methylphenidate	5 – 60 mg in divided doses daily (max. 90 mg)	100%	0%	2 – 4 hours
Xaggitin XL [®]	18 – 54 mg daily (max. 108 mg)	22%	78%	12 hours
Delmosart MR [®]	18 – 54 mg daily (max. 108 mg)	22%	78%	12 hours
Concerta XL [®]	18 – 54 mg daily (max. 108 mg)	22%	78%	12 hours
Equasym XL [®]	10 – 60 mg daily (max. 90 mg)	30%	70%	8 hours
Medikinet XL [®]	10 – 60 mg daily (max. 90 mg)	50%	50%	8 hours

Atomoxetine – 2nd line treatment

Atomoxetine 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg capsules and 4 mg/ml oral solution.

Licensed indications www.medicines.org.uk/emc:

Treatment of ADHD in children (over 6 years of age), adolescents and in adults (according to ICD-10 diagnosis). If symptoms persist into adulthood, atomoxetine is also licensed to continue from adolescence into adulthood as long as a clear benefit from the treatment has been shown.

Dosage and administration of atomoxetine

- Administer once daily in the morning with or without food. When atomoxetine is administered as a single daily dose, therapeutic benefit has been seen to persist for 24 hours throughout the morning and evening.
- Patients who experience unwanted effects when taking atomoxetine as a single daily dose may benefit from taking two evenly divided doses – the first dose in the morning and second dose in the late afternoon/early evening.

	Starting dose	Recommended maintenance dose
<70 kg	0.5 mg/kg/day	1.2 mg/kg/day
>70 kg	40 mg/day	80 mg/day

- The maximum recommended total daily dose is 120 mg. The safety of single doses >120 mg and total daily doses >150 mg have not been systematically evaluated but NICE³ guidelines indicate that doses up to 120 mg/day may be necessary where there is a poor response to treatment (in consultation with a tertiary or regional centre in the case of children or young people). Side effects should be monitored carefully.
- As no distinct withdrawal effects have been identified, atomoxetine can be discontinued without the need for tapering of the dose in cases of severe adverse effects. Otherwise the recommendation is to taper the dose when stopping treatment.

Contraindications with atomoxetine

Atomoxetine is contraindicated in patients with:

- Known hypersensitivity to atomoxetine or other capsule ingredients.
- A concomitant MAOI or those who have discontinued an MAOI within the last two weeks.
- Narrow angle glaucoma, phaeochromocytoma or a history of phaeochromocytoma.
- Severe cardiovascular or cerebrovascular disorders which would be expected to deteriorate following a clinically significant increase in blood pressure (e.g. 15 – 20 mmHg) or heart rate (e.g. 20 beats per minute). 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. Severe cerebrovascular disorders include cerebral aneurysm or stroke.

Cautions with atomoxetine

Caution	Advice
Patients with hypertension, tachycardia, cardiovascular or cerebrovascular disease	<p>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 mmHg) that may not be clinically important.</p> <p>However, combined data from controlled and uncontrolled ADHD clinical trials show that some patients (approximately 6 - 12% of children and adults) experience clinically relevant changes in heart rate (20 beats per minute or greater) and blood pressure (15 - 20 mmHg or greater). Analysis of this clinical trial data showed that approximately 15 - 32% of patients experiencing clinically relevant changes in blood pressure and heart rate during atomoxetine treatment had sustained or progressive increases.</p> <p>As a result of these findings, patients who are being considered for treatment with atomoxetine should have a careful history and physical examination to assess the presence of cardiac disease and should receive further specialist cardiac evaluation if initial findings suggest such history or disease.</p> <p>Atomoxetine should be used with caution in patients whose underlying medical conditions could be worsened by increases in blood pressure and heart rate, such as patients with hypertension, tachycardia, or cardiovascular or cerebrovascular disease.</p> <p>Patients who develop symptoms suggestive of cardiac disease during atomoxetine treatment should undergo a prompt specialist cardiac evaluation.</p>
Patients with congenital or acquired long QT or a family history of QT prolongation ⁵	There have been case reports of QT interval prolongation. Therefore atomoxetine should be used with caution in this group of patients.
Cerebrovascular effects	Patients with additional risk factors for cerebrovascular conditions (such as a history of cardiovascular disease, concomitant medications that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with atomoxetine.
Jaundice/laboratory evidence of liver injury	<p>There is a risk of rare, but sometimes severe, hepatic disorders. Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury and should not be restarted.</p> <p>Patients and carers should be advised of the risk and told how to recognise symptoms. Prompt medical attention should be sought in case of abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice. All suspected hepatic reactions should be investigated and LFTs taken.</p> <p>Routine monitoring of liver function is not recommended. The reactions are seemingly idiosyncratic in nature and therefore routine monitoring is unlikely to be helpful in minimising the risk.</p>
Growth and development retardation	<p>For children and young people, plot height and weight on growth charts and review regularly.</p> <p>For adults, consider monitoring BMI if weight loss occurs.</p> <p>Consideration should be given to dose reduction or interrupting therapy in patients who are not growing or gaining weight satisfactorily.</p>
Suicidal ideation and psychotic/manic symptoms	Patients treated for ADHD should be carefully monitored for appearance or worsening of suicide related behaviour, hostility, emotional lability and symptoms suggestive of psychosis or mania developing ⁵ as these have been reported as uncommon adverse events.
Seizures	Seizures are a potential risk with atomoxetine. It should be introduced with caution in patients with a history of seizure. Discontinuation should be considered in any patient developing a seizure or if there is an increase in seizure frequency where no other cause is identified. ⁵
Pregnancy and lactation	Clinical data lacking – avoid.

Interactions with atomoxetine

	Adverse effect	Management
CYP2D6 inhibitors, e.g. fluoxetine, paroxetine.	May markedly increase atomoxetine levels.	Dose adjustment and slower titration of atomoxetine may be necessary in those patients who are also taking CYP2D6 inhibitor drugs. Monitor for any increase in atomoxetine adverse effects.
Drugs that affect noradrenaline, e.g. venlafaxine, imipramine, mirtazapine, pseudoephedrine, phenylephrine.	Potential for additive or synergistic pharmacological effects.	Monitor for adverse effects.
Drugs which can increase blood pressure.	Possible additive effects on blood pressure.	Monitor blood pressure when drug is started.
Antihypertensive drugs	Atomoxetine may potentially increase blood pressure and therefore decrease the effectiveness of antihypertensive medication.	Monitor blood pressure.
Salbutamol (or other beta ₂ agonists) – high dose nebulised or oral or intravenous administration.	May cause increase in heart rate and blood pressure due to additive side effects.	Monitor BP and pulse.
QT interval prolonging drugs (such as neuroleptics, class IA and III anti-arrhythmics, moxifloxacin erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium or cisapride).	Potential for an increased risk of QT interval prolongation when administered with other QT prolonging drugs.	No extra monitoring indicated unless ongoing QTc problem.
Drugs that lower seizure threshold, e.g. antidepressants, neuroleptics, mefloquine, bupropion, tramadol.	Seizures are a potential risk with atomoxetine.	Consider using alternative treatments that do not lower the seizure threshold where possible, otherwise use with caution at the lowest effective doses.

Adverse effects with atomoxetine include (for full list see [SPC](#)):

Very common (>10%)	Headache, abdominal pain, somnolence, nausea, vomiting, appetite decreased, blood pressure increased, heart rate increased.
Common (1% to <10%)	Dizziness, insomnia, constipation, fatigue, mood changes.
Uncommon (0.01% to 1%)	Suicide related events, aggression, hostility, and emotional lability, tremor, syncope, tachycardia, migraines, QT prolongation, blurred vision.
Rarely (>0.01%)	Abnormal liver function*, seizures, urinary hesitation and retention.

Sexual dysfunction (erectile and ejaculatory dysfunction) and dysmenorrhoea should be monitored.³

*See additional information in [Cautions](#) section above.

Time to response with atomoxetine

Onset of action is three to four weeks, sometimes longer.

Lisdexamfetamine (2nd or 3rd line in children and adolescents; 1st or 2nd line in adults)

Lisdexamfetamine 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg capsules are on the Bucks formulary.

Licensed indications:

6 – 17 year olds: Lisdexamfetamine is indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate. For this age group, licensed strengths available are 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg capsules.

Adults: Lisdexamfetamine is indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in adults as a first line treatment option. For this age group, licensed strengths available are 30 mg, 50 mg and 70 mg.

Dose and titration:

For 6 – 17 year olds: the starting dose is 30 mg taken once daily in the morning. When in the judgment of the clinician a lower initial dose is appropriate, patients may begin treatment with 20 mg once daily in the morning.

The dose may be increased by 10 or 20 mg increments, at approximately weekly intervals. Lisdexamfetamine should be administered orally at the lowest effective dosage. The maximum recommended dose is 70 mg/day; higher doses have not been studied.

For adults: the starting dose is 30 mg taken once daily in the morning. The dose may be increased by 20 mg increments at approximately weekly intervals. The maximum recommended dose is 70 mg/day; higher doses have not been studied.

Caution should be exercised when prescribing lisdexamfetamine to those at risk of stimulant misuse or diversion.

Lisdexamfetamine is a schedule 2 controlled drug and is therefore subject to the regulations for controlled drugs (see [BNF](#) for more details). Supplies should be limited to no more than 30 days.

Known contraindications:

- Symptomatic cardiovascular disease including moderate to severe hypertension and advanced arteriosclerosis structural cardiac abnormalities
- Hyper excitability or agitated states
- Hyperthyroidism, thyrotoxicosis
- Glaucoma
- During or for 14 days after treatment with an MAO inhibitor

Lisdexamfetamine should be used with caution in the following situations:

Caution	Advice
History of cardiovascular disease or abnormalities	Avoid or take specialist cardiology advice.
Psychosis or bipolar disorder	Monitor for aggressive behaviour or hostility during initial treatment
History of drug or alcohol abuse	
May lower seizure threshold	Discontinue if seizures occur
Anorexia	
Tics and Tourette's syndrome (use with caution)	Discontinue if tics occur
Susceptibility to angle-closure glaucoma	
Avoid abrupt withdrawal.	
Acute porphyria	

Drug interactions:

MAOIs	Contraindicated – do not co-prescribe. May cause severe headaches or other signs of a hypertensive crisis.
SSRIs and SNRIs	May cause serotonin syndrome
Antihypertensives	Amfetamines may decrease the effectiveness of guanethidine or other antihypertensive medications
Opioid analgesics	Amfetamines potentiate the analgesic effect of narcotic analgesics
Antipsychotics such as chlorpromazine and haloperidol	Block dopamine receptors and may inhibit the central stimulant effects of amfetamines

Adverse effects of lisdexamfetamine include (for full list see SPC):

Very common: decreased appetite, weight decreased, insomnia, headache

Common: dry mouth, diarrhoea, nausea, vomiting, tachycardia, irritability, fatigue

Uncommon: agitation, dysphoria, buxism, mania, hallucination, dyskinesia, mydriasis, blood pressure increased

Refer to [SPC](#) for full list of adverse effects.

Dexamfetamine – 3rd line treatment

Dexamfetamine 5 mg, 10 mg, and 20 mg tablets and 1 mg/ml oral solution are on the Bucks formulary.

Adderall® (Shire US). A sustained release preparation which contains a mixture of amfetamine/dexamfetamine - is not available in UK. American patients who come to live in Buckinghamshire as temporary residents will be asked to obtain their own supply from the US. If required, the dose equivalent from Adderall® to dexamfetamine would be 1:1 but the latter needs to be taken in divided doses. Any patients treated for ADHD in Buckinghamshire need to fit ICD-10 diagnostic criteria.

Licensed indications

For ADHD in children and adolescents aged 6 – 17 years old when response to previous methylphenidate is considered inadequate.

Dosage and administration of dexamfetamine

Age	Usual starting dose	Maximum dose
3 – 5 years Hospital responsibility to prescribe	2.5 mg daily increased if necessary by 2.5 mg at weekly intervals. ¹³	
>6 years	5 mg once or twice a day (breakfast and lunch) increased if necessary at weekly intervals by 5 mg. Maintenance dose is given in two to four divided doses.	Usual upper limit is 1 mg/kg daily up to 20 mg daily (though some children have needed 40 mg or more for optimal response).
Adults	5 mg twice a day increased by 5 – 10 mg weekly as necessary.	NICE ³ indicates that treatment of adults may require up to 60 mg daily in 2 - 4 divided doses.

Caution should be exercised when prescribing dexamfetamine to those at risk of stimulant misuse or diversion.

Dexamfetamine is a schedule 2 controlled drug and is therefore subject to the regulations for controlled drugs (see [BNF](#) for more details). Supplies should be limited to no more than 30 days.

Contraindications with dexamfetamine

Patients with symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertensive disease; patients with advanced arteriosclerosis; during or for 14 days after treatment with an MAO inhibitor; patients with a history of drug abuse or alcohol abuse; patients with hyperthyroidism, glaucoma, porphyria or hyperexcitability; patients with Tourette's syndrome or similar dystonias; patients with hypersensitivity to dexamfetamine or any of the excipients.

Cautions with dexamfetamine

- Concomitant guanethidine use.
- Mild hypertension.
- Family history of dystonias.
- Tics - discontinue if tics develop.
- Epilepsy (dexamfetamine may reduce the seizure threshold).
- Growth and development - monitor during treatment with dexamfetamine and interrupt treatment if weight gain is lower than expected.
- Impaired kidney function.
- Unstable personality.
- Drug dependence and tolerance to doses.
- Stopping treatment - abrupt cessation may produce fatigue and mental depression so treatment should be stopped gradually.
- Co-morbid bipolar disorder.

Interactions with dexamfetamine

Drug	Action	Management
MAOI	Can result in potentially fatal hypertensive crisis.	Do not co-prescribe
SSRI	May lead to serotonin syndrome. Fluoxetine and paroxetine may reduce dexamfetamine levels.	Consider if patient reports any unusual side effects. Prescribe alternative SSRI.
Tricyclic antidepressants	May increase risk of CV side effects.	No extra monitoring indicated.
Beta blockers	May result in severe hypotension.	Caution when co-prescribing.
Acidifying agents, e.g. ascorbic acid, ammonium chloride	Reduced absorption, increased excretion resulting in reduced levels.	No action is generally necessary. However, consider the possibility of an interaction if therapeutic efficacy is reduced.
Alkalisating agents, e.g. sodium bicarbonate, acetazolamide	Increased absorption, decreased excretion resulting in increased dexamfetamine levels.	No action is generally required. However, if side effects increase, consider stopping the alkalisating agent or reduce the dose of dexamfetamine.
Alcohol	CNS adverse effects may be exacerbated.	Advise avoidance of alcohol or use with caution in patients with a history of alcohol use.
Phenothiazines	Will inhibit central stimulant effects of dexamfetamine.	Do not co-prescribe.

Adverse effects include:

Very common: Decreased appetite, reduced weight gain and weight loss during prolonged use in children, insomnia, nervousness.

Common: Arrhythmia, palpitations, tachycardia, abdominal pain, nausea and vomiting, dry mouth, changes in blood pressure and heart rate, arthralgia, vertigo, headache, abnormal behaviour, anxiety, depression.

Refer to [SPC](#) for full list of adverse effects.

Time to response:

Within a few hours or days. May take a few weeks for the full effect.

Onset: 20 - 60 minutes, duration 3 - 6 hours.

6. CONTACT DETAILS

Whiteleaf Centre Switchboard	01865 902000	
Oxford Health Medicines Advice Service	Tel: 01865 904365 medicines.advice@oxfordhealth.nhs.uk	

7. SHARED CARE AGREEMENT FORM

Available on DocGen. When not available, use the Word version linked [here](#).

8. REFERENCES

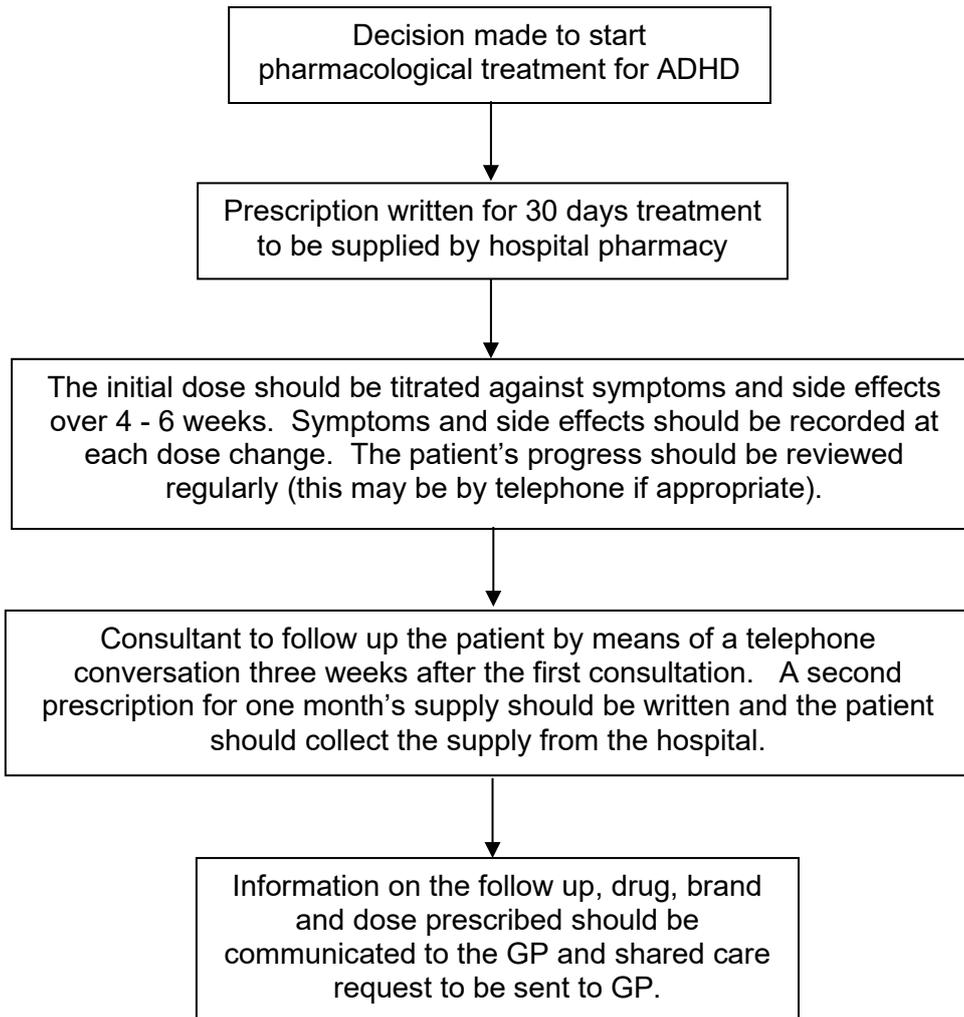
1. National Institute for Health and Clinical Excellence. TA 98. [Attention deficit hyperactivity disorder \(ADHD\) - methylphenidate, atomoxetine and dexamfetamine \(review\)](#). March 2006.
2. MHRA Drug Safety Update Vol 3 (issue 6), January 2010. [Methylphenidate: new patient information](#).
3. National Institute for Health and Clinical Excellence. CG 72. [Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. September 2008](#).
4. MHRA Drug Safety Update, Vol 2 March 2009. [Methylphenidate: safe and effective use to treat ADHD](#).
5. MHRA Safety Warning. Strattera® (atomoxetine) - Conclusions of a risk:benefit review. February 2006. Janssen-Cilag Ltd. Concerta XL® Summary of Product Characteristics. Last Updated on eMC 20-Mar-2017 (accessed via www.medicines.org.uk/emc)
6. Novartis Pharmaceuticals UK Ltd. Ritalin® Summary of Product Characteristics. Last Updated on eMC 28-Mar-2017 (accessed via www.medicines.org.uk/emc)
7. Eli Lilly and Company Ltd. Strattera® Summary of Product Characteristics. Last Updated on eMC 08-Jun-2015 (accessed via www.medicines.org.uk/emc)
8. Shire Pharmaceuticals Ltd. Elvanse Summary of Product Characteristics. Last Updated on eMC 03-Nov-2016 (accessed via www.medicines.org.uk/emc)
9. Flynn Pharma Ltd. Amfexa tablets Summary of Product Characteristics. Last Updated on eMC 03-Oct-2016 (accessed via www.medicines.org.uk/emc)
10. Stockley's Drug Interactions. Pharmaceutical Press 2017 (accessed via www.medicinescomplete.com)
11. BMJ Group, Pharmaceutical Press and RCPCH Publications Ltd. BNF for Children 2016 - 2017.
12. MHRA Drug Safety Update Vol 5 (issue 6), January 2012. [Atomoxetine: increases in blood pressure and heart rate](#).
13. National Heart, Lung and Blood Institute Blood Pressure Tables for Children and Adolescents, available at: https://www.nhlbi.nih.gov/files/docs/guidelines/child_tbl.pdf
14. Ethypharm UK Ltd. Xaggitin Summary of Product Characteristics. Last updated on eMC 28-Jun-2017 (accessed via www.medicines.org.uk/emc)
15. Actavis UK Ltd. Delmosart prolonged release tablet. Summary of Product Characteristics. Last updated on eMC 25-Jul-2017

See also:

[Guideline 809FM Methylphenidate, Lisdexamfetamine, Dexamfetamine, Guanfacine and Atomoxetine for the Treatment of Attention Deficit Hyperactivity Disorder – Shared Care Protocol for ≥6 - <18-year olds](#)

Title of Guideline	Methylphenidate, Atomoxetine and Dexamfetamine for the Treatment of Attention Deficit Hyperactivity Disorder – Shared Care Protocol
Guideline Number	796FM
Version	3
Effective Date	June 2021
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Original Version Produced	November 2008
<i>Approvals:</i>	
Medicines Value Group	15 th April 2021
Medicines Check (Pharmacy OH)	12 th May 2021
Clinical Guidelines Group	18 th May 2021
Author/s	Rachel Hogan, Clinical Lead Pharmacist, Oxford Health NHS Foundation Trust Dr Mark Addison, Dr Joe Clacey – Consultant CAMHS Psychiatrists, Bucks CAMHS, Oxford Health NHS FT
SDU(s)/Department(s) responsible for updating the guideline	Oxford Health NHS Foundation Trust
Uploaded to Intranet	21 st June 2021
Buckinghamshire Healthcare NHS Trust/Buckinghamshire Clinical Commissioning Group/Oxford Health Foundation NHS Trust	

Appendix 1: Algorithm for initial prescribing pathway for ADHD treatment at BHT



It is the hospital consultant's responsibility to prescribe for a patient who is being switched from an immediate to a prolonged release preparation – usually for a period of 1 month – until they are re-stabilised.