# Prescribing Arrangements for the use of methylphenidate, dexamfetamine and atomoxetine in adult ADHD (attention deficit hyperactivity disorder) in Berkshire

**For all referrals of adults with possible or previously diagnosed ADHD requiring further assessment, advice or treatment, the primary contact is Dr Trevor Powell Consultant Psychologist, Neuropsychology Department , 25 Erleigh Road, Reading, Berks RG1 5LR. 0118 929 6474**

**The Specialist Adult ADHD Consultant Psychiatrist, Dr Alex Day is contactable via her secretary as above or by email at alex.day@berkshire.nhs.uk (Thursdays only)**

**For all other general mental health issues and illnesses, please use the usual Berkshire Healthcare NHS Foundation Trust's CPE referral pathway.**

**Useful information for patients' carers and clinicians about ADHD and other mental health conditions can be found at the BHFT "choice and medication" website:**
**www.choiceandmedication.org.uk/berkshirehealthcare**
**Or can be accessed via the Berkshire Healthcare NHS Foundation Trust internet site at**
**www.berkshirehealthcare.nhs.uk**
**(Click on "Medicines")**

**Other Useful Contacts:**
**BHFTs Medicines Information Service,**
**Prospect Park Hospital**
**Tel: 0118 960 5075**
**Email: medicines.information@berkshire.nhs.uk**

**Prepared by:**
Kiran Hewitt, Lead Clinical Pharmacist, BHFT
Katie Sims, Specialist Mental Health Pharmacist, BHFT
Dr Alex Day, Consultant Psychiatrist, BHFT

**Approved by:**
Berkshire Healthcare NHS Foundation Trust, Berkshire East and West CCGs
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## Introduction and purpose

These guidelines have been produced following NICE guidance issued in 2008 on the use of methylphenidate, atomoxetine and dexamfetamine in children, young people and adults[(1)]. Clear guidelines are necessary to clarify the roles of primary and secondary care providers when using more specialist medicines that are categorised as amber drugs in the NHS Berkshire traffic light system. This document sets out these responsibilities from initial referral to the adult ADHD service through to on-going treatment maintenance and support.

## Disorder Background & Guidance Summary

See end, Appendix 1.

## Drugs covered by the agreement and their place in treatment

Stimulants are usually the first-choice pharmacological treatment for ADHD in both children and adults. Although they remain unlicensed for use in adults, there is an increasing amount of evidence for efficacy in adults[(5)].

The first line choice of medication in adults is methylphenidate.
The second line choice is atomoxetine (but first line for those at risk of substance misuse or drug diversion, or if previous intolerance/unresponsiveness to methylphenidate).
The third line choice is dexamfetamine.
NB: Lisdexamfetamine has not yet been approved within Berkshire for prescribing.

**Important:** ***Please refer to the full Summary of Product Characteristics (SPC) for each drug for details of side effects, cautions, contraindications and drug interactions.***

**STEP 1:**

| **Initial General Practitioner Responsibilities** |
|---|
| **Pre-Referral to secondary care specialist service:** |
| 1. Take full history and details of any diagnosis or history where caution is needed for potential medication treatment, including -<br>• Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms<br>• past and present medical and psychiatric symptoms<br><br>Full physical assessment should include cardiovascular system examination, weight, blood pressure and heart rate.<br><br>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 previous cardiac examination, then provide ECG details with interpretation (consult a cardiologist for clarification as needed).<br><br>Risk assessment for substance misuse and drug diversion. |
| 2. Provide details of current medication. |

**STEP 2:**

| Secondary Care Specialist Responsibilities |
|---|
| **Initial Consultation/Assessment:**<br>*Diagnostic assessment is initially carried out by psychology. If a diagnosis of ADHD is made then the Specialist Psychiatrist assessment will follow.* |
| 1. Receipt of GP request to assess patient (including full medical, physical and medication history details<br>2. Carry out a comprehensive assessment, to include:<br>• full mental health and social assessment<br>• full history including past and present medical and psychiatric disorders or symptoms<br>• concomitant medicines<br>• history or risk of substance misuse. |
| 3. Diagnosis of Adult Attention Deficit Hyperactivity Disorder. |
| 4. Gain agreement from patient (and GP if not done at pre-assessment phase) to initiate treatment of choice. Ask GP to provide BP & pulse values at any initial dose increments in the first 4 weeks if this is necessary. |
| 5. Provide the patient/carer with information about the medication to be prescribed. (signpost to the choice &medication website for additional information). |
| 6. Provide the initial FP10 prescription for the medication of choice. |
| 7. **Within 4 weeks of initial prescription (and usually within first 2 weeks)**<br>• review efficiency of the prescribed ADHD drug<br>• monitor for side effects and document any problems discussed<br>• adjust dose if necessary and correspond with GP as necessary for sharing of information.<br>• Take pulse and blood pressure |
| 8. Continue prescribing until patient is stabilised (usually 3-4 months) |
| 9. Once the patient is stable, prepare to handover to GP for continuation of treatment. To include details of continual requirements for monitoring and review. |
| 10. Review progress and communicate findings back to GP. Provide support and advice regarding all aspects of medication prescribed to GP. Offer routine appointment for review at 12 month. |
| 11. Review progress if requested by GP - change in behaviour; treatment resistance, increased sedation, etc. Notify the GP of the results of any patient reviews, including changes in prescribed dose. Ensure the patient has sufficient medication until the GP has received this information, at least 14 days. |
| 12. Receive and respond to feedback from GP as appropriate, e.g. progress/status of the patient and in particular noting any dose changes/alterations/discontinuation etc. of treatment under the agreement. |

**STEP 3:**

| General Practitioner Responsibilities – Maintenance |
|---|
| **Once patient is stabilised:** |
| 1. Issue repeat prescriptions after stabilisation. Methylphenidate and dexamfetamine are CDs, so prescriptions should be limited to 30 days' supply (and are only valid for 28 days from the date of signature). Sustained release methylphenidate preparations need to be prescribed by brand as they are NOT interchangeable (they have different release profiles). |
| 2. Continue any required monitoring as per specialist recommendations (will be dependent on the drug prescribed). |
| 3. If there is adequate response to treatment, continue for as long as clinically effective. Offer review at 6 month stage and annually review continued treatment benefit. This will include evaluation of symptom control, adverse effects experienced, tolerance and patient/carer views. Provide feedback to the specialist if appropriate, as to the progress/status of the patient and in particular notifying of any further dose changes/alterations/discontinuation and emergence of further adverse effects. Contact Specialist at any stage for advice or support. |
| 4. In the event of any of the following:<br>• persistent sleep disturbance where there has been a change in sleep pattern<br>• persistent problems with poor attention/deterioration in behaviour<br>• pronounced change in mental state<br>- **Contact Specialist Consultant for advice on management.** |
| 5. To refer patients for prompt specialist cardiac evaluation if symptoms develop such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of heart disease. |
| 6. To be alert for signs of diversion, misuse or abuse of methylphenidate. |

**Considerations for Treatment Withdrawal**

There should be a discussion with the patient at review to consider whether the medication is still needed, especially where treatment has continued for 12 months. If there has not already been a trial off medication, consider withdrawal of medication (except if review by specialist has led to an increase in dose). This should be offered and discussed with the patient and the outcome recorded. Consideration must be given to patient choice.

Methylphenidate and dexamfetamine can generally be withdrawn by treatment discontinuation, but monitor for signs of withdrawal (uncommon). For atomoxetine, reduce the dose at weekly increments and discontinue over a four week period.

If required, refer back to the specialist for advice/guidance on the treatment withdrawal process.

**Pregnancy & Lactation**

The safety of these drugs in pregnancy and lactation cannot be guaranteed. For atomoxetine, no clinical data on exposed human pregnancies are available, nor is it known if it excreted in human breast milk.

There is limited 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 reports. Methylphenidate has been found in breast-milk of a women treated with methylphenidate.

If a patient taking any of these drugs reports a pregnancy or is planning a pregnancy, refer to the specialist for guidance and advice. Alternatively, call the Medicines Information Service on 0118 960 5075.

**Drug & Dosage Details:**

| Drug | Brand | Action | Dosage |
|---|---|---|---|
| Methylphenidate IR | Ritalin®, Equasym®, Medikinet® or generic. | CNS stimulant. Schedule 2 controlled drug.<br>Onset: 20-60 min<br>Duration: 2-4 hours | 5mg TDS up to a max of 100mg daily in divided doses |
| Methylphenidate SR | Concerta XL® tablets | CNS stimulant. Schedule 2 controlled drug.<br>Onset: 30min – 2h<br>Duration: 12hours<br>IR:22%<br>ER:78% | 18mg – 108mg once daily<br>Start at 18mg daily. Adjust at weekly intervals.<br>18mg Concerta® = 15mg Ritalin® |
| | Equasym XL® capsules | CNS stimulant. Schedule 2 controlled drug.<br>Onset: 20-60 min<br>Duration: 8 hours<br>IR:30%<br>ER:70% | 10mg to 100mg once daily<br>Start at 10mg daily. Adjust at weekly intervals. |
| | Medikinet XL® capsules | CNS stimulant. Schedule 2 controlled drug.<br>Onset: 20-60 min<br>Duration: up to 8 hours<br>IR:50%<br>ER:50% | 10mg – 100mg once daily<br>Start at 10mg daily. Adjust at weekly intervals. |
| Dexamfetamine | generic | CNS stimulant<br>Schedule 2 controlled drug<br>Onset: 20-60 min<br>Duration: 3-6 hours | 5mg BD initially. Adjust at weekly intervals up to a max of 60mg daily in divided doses. |
| Atomoxetine | Strattera® | Selective Noradrenaline reuptake inhibitor (not a controlled drug)<br><br>Onset of action: may take 4-6 weeks<br><br>Can be given as a single dose in the morning OR twice daily – last dose no later than early evening. | **For adults of up to 70 kg** - initiate at 500 micrograms/kg daily, increase after 7 days, according to response. Maintenance dose - 1.2 mg/kg daily<br>**For adults of over 70 kg** - initiate at a daily dose of 40 mg for 7 days. Usual maintenance dose - 80-100 mg daily. N.B. May be increased up to 1.8mg/kg daily (max 120mg daily) |

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|---|---|---|---|
| | | | unlicensed under a specialist. |

IR= Immediate Release ER=Extended Release

***IMPORTANT: Please refer to Summary of Product Characteristics for individual products for side effects, cautions, contraindications and interactions.***

**Costs of Medications**
See Appendix 2.

**Monitoring Parameters**
See Appendix 3

**Appendix 1.**
**Disorder Background & Guidance Summary**

The 2007 Adult Psychiatric Morbidity Survey (APMS) estimates that 8% of adults within England have ADHD [(2)].

ADHD is defined by the "core" symptoms of inattention, hyperactivity and impulsivity. The diagnostic criteria for the condition are set down in both the DSM IV (Diagnostic and Statistical Manual – American Psychiatric Association 2000) and ICD 10 (International Classification of Mental and Behavioural Disorders - World Health Organisation 1992) diagnostic manuals. These criteria require that:

- The symptoms have persisted for at least six months to a degree that is maladaptive and inconsistent with the development level of the person
- There must be clear evidence of clinically significant impairment in social or academic/employment functioning
- Some impairment is present in two or more settings (usually at home, at work and social activities)
- There is previous evidence of ADHD in childhood
- The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia or other psychotic disorder and are not better accounted for by other mental disorders (such as bipolar disorder, depression or anxiety)

**Treatment of ADHD in Adults**

**Guidance**
The first UK clinical guideline on ADHD that covered the disorder in adulthood was published in 2007 by the British Association for Psychopharmacology (BAP) [(3)]. This included a consensus statement on ADHD as a neurodevelopmental condition that continued into adulthood, advice on the assessment and treatment of it, and recommendations on service provision. This was followed in 2008 by the online publication of formal guidance from the National Institute for Health and Clinical Excellence (NICE).

The NICE clinical guideline on treatment of ADHD (2008) recognises drug treatment of ADHD as part of a "comprehensive treatment programme addressing psychological, behavioural and educational or occupational needs". It considers drug treatment as the "first line treatment unless the person prefers psychological treatment". The NICE full guideline [(1)] recognises that the treatment strategies for ADHD in adults are essentially "similar to those used in childhood". It also very importantly states that ***"it remains an anomaly that many drugs that are considered to be safe and effective in children and adolescents are not licensed for use in adults".***

The British Association for Psychopharmacology's (BAP) evidence based guidelines for management of ADHD (2006) addresses the issue of off-license prescribing as follows:-
"*The BNF (Joint Formulae Committee 2005) states****; 'unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience'"****.*
*BAP Guidelines further state* ***"Although controlled evidence for prescribing in adults is not extensive, this consensus statement can be considered to meet the criteria for adequate evidence and experience when prescribing standard medications to adults with ADHD, when done in the context or with support of specialist psychiatric services."***

Prescribing for adult ADHD is necessarily off-label since no agent is licensed in adults for this indication (although for atomoxetine and Concerta XL the manufacturers state that "in adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood". This is because historically ADHD was considered a childhood disorder and patients were expected to grow out of this condition by their late teens. It is now widely recognised that in up to 70% to 80% of patients the condition continues into the adulthood and continues to cause impairment of functioning in a large proportion. Hence these patients need continuation of their treatment. Pharmacological companies are in the process of applying for licenses for these products to be used in adults with ADHD.

**Drugs covered by the agreement and their place in treatment**

Stimulants are usually the first-choice pharmacological treatment for ADHD in both children and adults. In the UK, both methylphenidate and dexamfetamine are available, although as yet remain unlicensed for use in adults. There is evidence regarding the safety and effectiveness of stimulants in children, and an increasing amount of evidence for efficacy in adults [(5)].

The second-line choice of medication for ADHD in adults is usually atomoxetine. Atomoxetine is licensed in the US for the treatment of ADHD in both children and adults, although in the UK it is only licensed for treatment of adults who started atomoxetine in childhood or adolescence. Atomoxetine can also be considered as a first line treatment where there is a history of substance misuse, psychosis, or the patient wishes to avoid stimulant medications or has been previously treated effectively with atomoxetine and wishes to restart it.

**Appendix 2:**
**Cost of Medication**

| Drug | Dose | Cost/28 days (BNF 64) |
|---|---|---|
| Methylphenidate IR (generic)<br>**(first line)** | 5mg tds<br>10mg tds<br>100mg daily (max) | £8.48<br>£18.09<br>£50.96 |
| Concerta XL® | 18mg od<br>36mg od<br>108mg od (max) | £29.11<br>£39.62<br>£118.86 |
| Equasym XL® | 10mg od<br>30mg od<br>100mg od (max) | £23.33<br>£32.66<br>£121.32 |
| Medikinet XL® | 10mg od<br>30mg od<br>100mg od (max) | £22.43<br>£31.42<br>£116.68 |
| Atomoxetine<br>**(second line)** | 40mg od<br>80mg od<br>120mg (max – specialist) | £62.46<br>£83.28<br>£145.74 |
| Dexamfetamine<br>**(third line)** | 5mg bd<br>10mg bd<br>60mg daily (max) | £32.26<br>£64.52<br>£193.56 |

**Appendix 3:**
**Monitoring Parameters**

| Parameter | Frequency | Target Results | Action (for GP) on variance |
|---|---|---|---|
| Blood Pressure<br>Pulse | Annually * | Stability | Sustained resting tachycardia, arrhythmia or clinically significant increase in systolic b.p. should prompt dose reduction and referral to other (e.g. cardiac) where appropriate. Approx. 10% patients on atomoxetine may develop more significant rises in b.p. and heart rate with clinical implications. See MHRA warning [(4)]. |
| Weight<br>Appetite | Annually | | Discuss concerns with specialist. Consider monitoring BMI and changing the drug if weight loss persists. |
| FBC<br>LFTs (atomoxetine) | If there is a specific concern/symptoms of hepatic problem. | Results within normal limits | Discontinue if neutropenia develops and discuss with appropriate specialist. Atomoxetine may require dose reduction/discontinuation if laboratory or clinical evidence of abnormal hepatic function. |
| Behaviour including self-harming | At each appointment | Able to cope with daily living | If unexpected change in behaviour is noted review is indicated. |
| Mental state including emergence of psychotic symptoms, irritability, tics, suicidal thinking or anxiety/panic symptoms | Annually<br><br>(by GP or if specialist has been referred to) | | Discuss with secondary care specialist as necessary |

( * NICE CG72 recommends every 3 monthly)

## References:


1. NICE CG72. Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults
2. Adult psychiatric morbidity in England, Results of a household survey. The NHS Information Centre for health and social care, 2007.
3. British Association for Psychopharmacology 2006; Evidence based guidelines for management of Attention-Deficit/hyperactivity Disorder in Adolescents in transition to Adult Services and in Adults.
4. MHRA UK Public Assessment Report. Atomoxetine: a review of the effects on heart rate and blood pressure. May 2012.
5. Retz W, Retz-Junginger P, Thome J, et al. Pharmacological treatment of adult ADHD in Europe. World J Biol Psychiatry 2011 Sep.:89-94.
6. SPCs (Summary of Product Characteristics) for Equasym XL, MedikiNet XL, Concerta XL, Strattera and Ritalin. Available online www.emc.medicines.org.uk
7. BNF 64 September 2012.