GREATER MANCHESTER INTERFACE PRESCRIBING GROUP

On behalf of the
GREATER MANCHESTER MEDICINES MANAGEMENT GROUP

Methylphenidate and Dexamfetamine in children and adolescents: SHARED CARE GUIDELINE		**Reference Number**
Scope: Methylphenidate, dexamfetamine for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents		**Classification** **SHARED CARE GUIDELINE**
Issue date: 2014	**Replaces:** No previous version available.	
Author(s)/Originator(s)	Leopold Kroll, Hilary Lloyd, Hong Thoong	
To be read in conjunction with the following documents	Pharmaceutical company's Patient Information Leaflet; British National Formulary for Children (BNFC) Dec 2013; and Summary of Product Characteristics (SPC); NICE guidance (CG 72, 2008; TA13, 2006)	
Authorised by	Paediatric Medicines Management Committee	**Date** 11th March 2014
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1. Licensed indications	Methylphenidate is licensed for the treatment of moderate to severe ADHD in children over 6 years old. Dexamfetamine is licensed in children aged 3 years. Dexamfetamine is rarely used under the age of 6. Methylphenidate and dexamfetamine do not have UK marketing authorisation for use in adults with ADHD, although Concerta XL (modified release methylphenidate preparation) is licensed for adults with ADHD when the drug has been started in childhood.
2. Therapeutic use and background	Attention Deficit Hyperactivity Disorder (ADHD) is a neuropsychiatric or developmental condition with secondary behavioural, social and educational difficulties. It is defined by the 'core' symptoms of inattention, hyperactivity and impulsiveness. To make a diagnosis, the core symptoms should be pervasive, present before the age of 7 and not better accounted for by other psychiatric or developmental disorders. Diagnosis of ADHD should be based on comprehensive assessment conducted by a child/adolescent psychiatrist (or a nominated specialist nurse/advanced practitioner, supervised by a psychiatrist), or by a paediatrician with expertise in ADHD. Diagnosis should be made according to DSM-IV criteria or ICD-10 (Hyperkinetic Disorder). Treatment aims in ADHD are to improve the ability to concentrate, reduce hyperactive behaviour, detect and treat any co-existing disorders, promote academic and social learning, improve emotional adjustment and self-esteem, and relieve family distress. **Moderate ADHD:** Drug treatment is not indicated as first-line treatment. Psychological interventions such as parent management programmes or, where developmentally appropriate, cognitive behavioural therapy [CBT] etc. should be considered first – see NICE Guideline CG72, 2008) for

	further information. Drug treatment may be considered for children and adolescents with moderate ADHD where non-drug interventions have been refused or failed. **Severe ADHD:** Drug treatment should be offered as first-line treatment, as part of a comprehensive treatment programme. Methylphenidate is recommended as an option, with dexamfetamine or atomoxetine (see separate protocol) being available as alternatives. The choice of drug will be based on presence of co-morbid conditions, different side effect profiles of the drugs, patient compliance, potential for drug misuse, and the preference of child and carer (NICE guideline CG72, 2008). The guidance in this protocol should be used in conjunction with the SPC and Patient Information Leaflet. In general, only licensed doses and preparations will be prescribed under this shared care guideline. In exceptional cases, where the specialist recommends higher doses or the treatment of younger children, prescribing will normally be retained by the specialist. If there are particular reasons to ask primary care to prescribe, specific individual arrangements will be made with reference to this SCG. Children will not be discharged from specialist follow-up with the expectation that the GP will continue to prescribe.
3. Contraindications (NB: to be read in conjunction with SPC and BNF/BNFC)	**Contraindications** • Known sensitivity to methylphenidate, dexamfetamine or any of the excipients; • Glaucoma; • • Phaeochromocytoma (methylphenidate only) • 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 • Severe depression, anorexia nervosa/anorexic disorders, suicidal ideation, psychosis, uncontrolled bipolar disorder • Cardiovascular disease (including severe hypertension, heart failure, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, arrhythmias and channelopathies) • Cerebrovascular disorders cerebral aneurysm. **Cautions** Anxiety or agitation Tics or family history of Tourette's Syndrome Drug or alcohol dependence Epilepsy (discontinue it increased seizure frequency) Susceptibility to angle-closure glaucoma Avoid abrupt withdrawal Side effects will be monitored by the specialist team at each review, which may include the use of side-effect questionnaires.
4. Prescribing in pregnancy and lactation	Prescribing in these groups should be done in consultation with an obstetrician. 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. Studies in animals have only shown evidence of reproductive toxicity at

	maternally toxic doses. Methylphenidate and dexamfetamine are not recommended for use during pregnancy unless a clinical decision is made that postponing treatment may pose a greater risk to the pregnancy. Methylphenidate and dexamfetamine have 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. 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.
5. Dosage regime for continuing care	Treatment with methylphenidate or dexamfetamine should be initiated and supervised by specialists but continued prescribing and monitoring may be performed by GPs under a shared care agreement. Both methylphenidate and dexamfetamine are classified as CNS stimulants and Schedule 2 Controlled Drugs by the British National Formulary (BNF). Prescriptions must, therefore, comply with full legal requirements (see BNF or BNFC). **Methylphenidate** is available as the following preparations: **Immediate release**: Non-proprietary methylphenidate hydrochloride (tablets) Medikinet (tablets) Ritalin (tablets) **Modified release:** Concerta XL (tablets) Equasym XL (capsules) Medikinet XL[1] (capsules) **Dexamfetamine** is available as: Non-proprietary, immediate release tablets Strength of capsules and tablets for each preparation is detailed in the BNFC and BNF. Administration is oral, supervised by the parent or carer and by key staff at school (for repeat doses of immediate-release preparations). Treatment is usually continuous. However, where ADHD symptoms are well-tolerated and managed at home, families may elect to use medication during term times or on school days only. **<u>DOSAGE</u>** <u>Methylphenidate</u> **Short-Acting Preparations**: Methylphenidate doses start at 5mg once or twice daily, increasing at weekly intervals by increments of 5-10mg daily according to response. At this point, the total daily dose is usually divided in two or three doses, more being given in the morning and at lunchtime with a smaller dose at approximately 4pm. Doses above 60mg daily are not usually recommended, as there is no

[1] Medikinet is not currently on formulary at CMFT, but may be a useful option in primary care

evidence supporting clinical efficacy at higher doses. Failure of ADHD symptoms to respond to doses this high should prompt a review of the diagnostic formulation and revision of the treatment plan by the specialist. However, in certain cases dosage can increase up to a maximum of 2.1mg/kg (maximum 108mg daily for Concerta XL, and maximum 90mg daily for other brands, all unlicensed).

For children aged 4-6 years (unlicensed use), the starting dose is 2.5mg twice daily and may be increased at weekly intervals by 2.5mg daily to a maximum 1.4mg/kg daily in 2-3 divided doses; discontinue if no response after 1 month.

If the effect of the drug wears off too early in the evening, and ADHD symptoms are significantly impairing, a small evening dose may reduce disturbed behaviour and inability to sleep.
If there is no improvement in symptoms after appropriate dose adjustments over a one-month period, the clinical formulation of the case should be reviewed by the specialist.

Modified (Slow)–Release Preparations
For many patients and families multiple daily dosing is inconvenient and problematic (e.g. due to compliance problems, the need to administer medication at school, fluctuating control of symptoms or, rarely, because of 'rebound' phenomenon not responsive to changes in timing of dosage or amount). For these reasons, in addition to individual tolerance and patient/carer preference, a single daily dose of a modified release preparation may be preferred.

The modified-release preparations are taken once daily in the morning. Concerta XL® tablets should not be divided, crushed or chewed.

For children who have difficulty in swallowing tablets, Equasym XL® capsules and Medikinet XL® capsules, may be opened and the contents sprinkled on a spoonful of apple sauce (not crushed) and then swallowed immediately without chewing, followed by a drink of water.

According to the summary of product characteristics Equasym XL® and Medikinet XL® have a duration of action of approximately 8, whereas Concerta XL® is effective for up to 12 hours.
The modified-release preparations are not usually used for children under 6 years of age.

In addition to differences in duration of action, the modified release preparations contain different proportions of immediate and sustained release drug. The choice of proprietary modified release preparation is determined by: child's ability to swallow tablets, desired duration of action, preferred release-profile.

Recommended dose conversion from other methylphenidate regimens to Concerta XL®:

Immediate-release preparation methylphenidate	Concerta XL®
5mg TDS	18mg OD
10mg TDS	36mg OD
15mg TDS	54mg OD

	For other preparations the dose conversion is equivalent i.e. mg=mg, although the length of duration of the various modified release preparations need to be taken into account. For some children modified release and immediate release medication may be necessary to control symptoms in the early evening. Effectiveness and side-effect profiles are similar between immediate- and modified-release formulations of methylphenidate. <u>Dexamfetamine</u> The usual starting dose for children aged 6 and over is 2.5mg 2 to 3 times a day increased if necessary by 2.5mg a day at weekly intervals up to 20mg a day in divided doses (maximum of 40mg a day in divided doses in rare cases). **Is titration required?** Yes, this should be done by the specialist in the first three months after initiation of treatment. **Adjunctive treatment regime** Advice on sleep hygiene and appetite change may be required. Consideration of the use of melatonin (as per CAMHS directorate guideline) for sleep initiation problems that either pre-date stimulant medication use, or occur after its introduction may be appropriate. Each of these should be considered in conjunction with careful assessment of stimulant medication response and side effects (see below) **Conditions requiring dose reduction: seek advice of specialist** See section 7 for details of side effects to methylphenidate which may respond to dose reduction. **Usual response time** Immediate for the core symptoms (inattentiveness, impulsivity, hyperactivity). Improvement in functioning (social, behavioural, academic) relationships may take longer (3 to 6 months) **Duration of treatment** Most children and adolescents who respond continue treatment until the end of school year 11. Breaks in medication (holidays and weekends) can occur for various reasons; e.g. side effects, patient/parent preference; evaluation of effectiveness; and review of continued indications in late teenage years. The need for continuing medication should be reviewed at least annually (not necessarily requiring withdrawal of medication). Some young people, whose symptoms remain impairing, may wish to continue with stimulant medication to age 18 years, especially if they are in continuing education. 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).
6. Drug interactions	***For a comprehensive list consult the BNF and BNFC appendix 1 or Summary of Product Characteristics (www.medicines.org.uk)*** Methylphenidate and dexamfetamine may inhibit the metabolism of coumarin anti-coagulants and some anti-convulsants (e.g. phenobarbitone, phenytoin, primidone), tricyclic and selective serotonin reuptake inhibitor anti-depressants, and phenylbutazone – the dosage of these drugs may need to be reduced. Methylphenidate and dexamfetamine should not be used in patients receiving non-selective irreversible monoamine oxidase inhibitors (MAOI) or moclobemide or within 14 days of discontinuing treatment with a non-selective irreversible MAOI or moclobemide, as there is a risk of hypertensive crisis and hyperthermia. Since alcohol may exacerbate the adverse CNS side effects of psychoactive drugs, including methylphenidate and dexamfetamine, patients should abstain from taking alcohol during treatment with this drug. Patients on methylphenidate and dexamfetamine are at increased risk of hypertension when used concomitantly with volatile liquid general anaesthetics or clonidine.
7. Adverse drug reactions (see SPC or BNF and BNFc for comprehensive list	**Common >1/100** • Methylphenidate and dexamfetamine may exacerbate emotional and behavioural symptoms, such as anxiety, depression, anger or irritability. • Reduced appetite often with some initial weight loss and subsequent poor weight gain. • Sleep disturbance • Abdominal pain (initiation usually) • Headache **Uncommon < 1/100** Lowering the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in absence of history of seizures and no prior EEG evidence of seizures. Growth reduction (linear height): This is an idiosyncratic side effect, unrelated to dose. Linear growth should be monitored at 6 to 12 month intervals, or as clinically indicated. Crossing of linear centile requires attention and consideration of the role of medication in causing this. The effects of methylphenidate on final height and final weight are currently unknown and being studied. Risks (benefit and harm) need to be assessed, and be discussed with the patient and family. Exacerbation of tics Constipation Anxiety, depression **Very rare** Leucopenia, other blood disorders, Dermatitis, erythema multiforme

<table>
<tr><td></td><td colspan="4">SVT, bradycardia, arteritis, liver dysfunction
Myocardial infarction
Tourettes
Psychosis
Tolerance and dependence

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.</td></tr>
<tr><td>8. Baseline investigations</td><td colspan="4">Routine blood tests and ECGs are not recommended unless there is clinical indication. Weight, heart rate and blood pressure should be measured on initiation by specialist.</td></tr>
<tr><td>9. On going monitoring requirements</td><td>Monitoring</td><td>Frequency</td><td>Action</td><td>By whom</td></tr>
<tr><td></td><td>Tics</td><td>Assess at 3 to 6 months, and then yearly</td><td>Consider whether stimulant related, and whether impairment outweighs benefits of medication. Consider using atomoxetine</td><td>GP and specialist</td></tr>
<tr><td></td><td>Psychotic symptoms, seizures</td><td>As indicated</td><td>Stop medication</td><td>GP and specialist</td></tr>
<tr><td></td><td>Anxiety, depression, panic</td><td>As indicated</td><td>Consider medication reduction, or switch to atomoxetine, consider use of SSRI in older (adult) population</td><td>GP and specialist</td></tr>
<tr><td></td><td>Weight</td><td>Pre-treatment baseline, and at 3 and 6 months after the start of treatment and every 6 to 12 months thereafter</td><td>As indicated by physical findings</td><td>Specialist (baseline, 3 & 6 months after start and 6-12 months thereafter
By GP as indicated</td></tr>
<tr><td></td><td>Height</td><td>Pre-treatment baseline and, 6 months after start of treatment and every 6-12 months thereafter</td><td></td><td>Specialist at stated frequency and by GP as indicated</td></tr>
<tr><td></td><td>Heart rate and blood pressure</td><td>Before and after each dose change and every 6 to 12 months</td><td>As indicated: if tachycardic for age (refer to child charts), or hypertensive >140/90mmHg (particularly raised systolic blood pressure) or sustained arrhythmia on two occasions: dose reduction
(GP to refer immediately to specialist team for dose reduction) - Life threatening</td><td>Specialist before and after each dose change & 6-12 monthly thereafter
By GP if consulted re symptoms suggestive of consequences of raised BP or tachycardia</td></tr>
</table>

	changes should be referred to accident and emergency.
10. Pharmaceutical aspects	**As described in section 5**
11. Secondary care contact information	*LOCAL CMFT CAMHS as per individual clinical correspondence.*
12, Criteria for shared care	• 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	• Assessment of the patient and diagnosis of ADHD • Documentation of full medical and psychiatric history. • Informing patients and carers of the diagnosis, and discussing with them the care plan, treatment options and side effects of medications. • Ascertaining patient's/family's commitment to safe storage and handling of stimulant treatment • Measurement of baseline parameters • Physical health monitoring (including CVS examination and ordering of ECG if patient presents with cardiovascular symptoms or history, or family history. • Prescribing for first 3 months or until stable. • Promoting access to any appropriate supporting therapies or education. • Contacting GP to ascertain willingness to participate in shared care. • Provision of 6 to 12-monthly review appointments with monitoring of mental state, symptom control, physical health and side effects • Prompt written communication to GP summarising progress and recommendations for continued treatment • Remaining alert to signs of drug diversion or misuse • Regular review of indications for and benefits of continued treatment • Reporting of adverse drug reactions to the Medicines and Healthcare Products Regulatory Agency (MHRA) via the Yellow Card Scheme. • Advising GP of discontinuation of treatment if considered clinically appropriate. • Advising GP about prescribing if the patient fails recurrently to attend follow-up appointments • Retaining prescribing in children under age 6 years or other unlicensed/off-label circumstances (unless specifically negotiated with GP)
14. Responsibilities of GP	• Responding to the request for shared care as soon as possible. • Continued prescribing of medication as agreed with consultant/ specialist team. • Referring to consultant/specialist team queries regarding treatment, side effects, concerns about drug misuse or diversion • Stopping treatment on the advice of the consultant/ specialist team or if serious adverse side effects • Reporting of adverse drug reactions to the Medicines and Healthcare Products Regulatory Agency (MHRA) via the Yellow Card Scheme .

15. Responsibilities of patient/parent	• Attendance at appointments with consultant/specialist team and communication of need to cancel or rearrange • Commitment to safe storage and handling of medication, and administration only as prescribed • Report side effects to GP or consultant/specialist team • Report cessation of medication or problems with compliance to GP or consultant/ specialist team
16. Additional responsibilities	**None**
17 Supporting documentation	The SCG must be accompanied by a patient information leaflet.
18. Shared care agreement form	Attached below

Shared Care Agreement Form (template only, information to GP should include this detail)

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