South West Yorkshire Area Prescribing Committee

Methylphenidate Shared Care Guideline for Attention Deficit Hyperactivity Disorder (ADHD) in school-aged children, adolescents and adults.

Introduction	
General Statements	• This guideline relates to children, adolescents and adults with ADHD with moderate to severe levels of impairment. • This guideline sets out details for the shared care of patients taking methylphenidate, and follows the recommendations of NICE clinical guideline and NICE Technology Appraisal. • This guideline covers methylphenidate immediate-release and modified-release products for the treatment of ADHD. The available immediate-release products are Ritalin® and Medikinet®. The available modified-release products are Concerta XL®, Equasym XL®, Matoride XL®, Medikinet XL® and Xenidate XL®. • Methylphenidate is a Schedule 2 Controlled Drug (CD) and is therefore subject to CD prescription requirements. The quantity prescribed needs to be written in words and figures. • Patients will receive prescriptions for supplies of medication from secondary care until shared care is agreed with the primary care doctor. • Prior to seeking shared care with the patient's GP: 1. The patient's clinical condition will be stable or predictable. 2. The patient will have been stabilised on the drug with time allowed for common adverse events and side-effects to have occurred. • Patients will receive prescriptions for supplies of medication from secondary care until shared care is agreed with the primary care doctor. • If a patient changes GP, then the new GP and the Secondary Care Prescriber will need to discuss setting up shared care for the patient. • The full summary of product characteristics (SPC – formerly datasheet) for the appropriate product should be read before prescribing – for Xenidate XL®, the SPC can be found at www.mhra.gov.uk/spc-pil; for Ritalin®, Medikinet®, Concerta XL®, Equasym XL®, Matoride XL® and Medikinet XL®, the SPCs can be found at www.medicines.org.uk.
Indication	• Methylphenidate is indicated for the treatment of ADHD in children of 6 years and older, in adolescents and in adults as part of a comprehensive treatment programme. Treatment must be initiated by a Specialist in the treatment of ADHD, such as a paediatrician or psychiatrist. Diagnosis should be made according to current DSM criteria or the guidelines in ICD. • Although unlicensed in adults, NICE recommends pharmacological intervention as the first-line treatment for adults with ADHD with moderate to severe levels of impairment.
Background	NICE clinical guideline states Diagnosis of ADHD • Diagnosis should only be made by a specialist psychiatrist, paediatrician or other healthcare professional with training and expertise in the diagnosis of ADHD. • Diagnosis should be based on: – a full clinical and psychosocial assessment. Discuss behaviour and symptoms in the different domains and settings of the person's everyday life – a full developmental and psychiatric history, and

	– observer reports and an assessment of mental state. • Diagnosis should be made when symptoms of hyperactivity/impulsivity and/or inattention: – meet the criteria in DSM-5 or ICD-10 (hyperkinetic disorder), and – are associated with at least moderate psychological, social and/or educational or occupational impairment based on interview and/or observation in multiple settings, and – are pervasive, occurring in at least two settings. • As part of the diagnostic process, include an assessment of needs, coexisting conditions, social, familial and educational or occupational circumstances and physical health. For children and adolescents also include an assessment of the parents' or carers' mental health. Drug treatment in children and adolescents • Drug treatment should: – only be started by a healthcare professional with expertise in ADHD – be based on comprehensive assessment – always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions. • Drug treatment is not indicated as the first-line treatment for all school-age children and adolescents with ADHD. It should be reserved for those with severe symptoms and impairment, or for those with moderate levels of impairment who have refused non-drug interventions or whose symptoms have not responded sufficiently to parent-training/education programmes or group psychological treatment. • GPs may continue prescribing and monitoring drug treatment under shared care arrangements. • If improvement of symptoms is not seen after appropriate dose adjustment, methylphenidate will be discontinued. Drug treatment in adults • NICE recommends pharmacological intervention as the first-line treatment for adults with ADHD with moderate to severe levels of impairment. • GPs may continue prescribing and monitoring drug treatment under shared care arrangements. • If improvement of symptoms is not seen after appropriate dose adjustment, methylphenidate will be discontinued.
Pharmacological Summary	• Methylphenidate is a dopamine and noradrenaline reuptake inhibitor. It acts on both the prefrontal cortex and the subcortical striatum, modulating catecholaminergic tone. Its main action is the inhibition of the dopamine transporter, resulting in increased extracellular dopamine, as well as noradrenaline. It may also enhance the direct release of dopamine. • Methylphenidate is readily absorbed orally, particularly if taken with food. Peak plasma concentrations are reached 1 to 2 hours after oral administration, although this may vary according to the formulation.

Individuals' Responsibilities	
Specialist's Responsibilities	1. Confirm the diagnosis of ADHD following full assessment, drawing upon information from all sources and first-hand observation of the patient. 2. Before starting drug treatment, children, adolescents and adults with ADHD should have a full pre-treatment assessment, which should include: – a full mental health and social assessment – a full history and physical examination, including: o assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms o heart rate and blood pressure (plotted on a centile chart for children and adolescents) o height and weight (plotted on a growth chart for children and adolescents)

	o family history of cardiac disease and examination of the cardiovascular system – an electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination – risk assessment for substance misuse and drug diversion. 3. Initiation of methylphenidate therapy and supply of the medicine for one further month after the dose has been stabilised before considering shared care. 4. Consider the formulation and frequency of dosing which best suits the patient and their lifestyle. 5. Ensure that the patient has an adequate supply of medication until GP prescribing can be agreed and arranged. 6. Review the patient at regular intervals 4-weekly initially and then as necessary, but all patients should be seen once a year by the Specialist. 7. Review the patient promptly if requested to do so by the GP. 8. Review the need for treatment at school leaving age and if necessary arrange transition to adult services. 9. Monitor heart rate and blood pressure before and after any dose change, and monitor height and weight before treatment and then 3 months and 6 months into treatment (see below). It is recommended that these measurements are recorded on a centile chart or other appropriate monitoring chart to detect clinically-informed increases. 10. Adjusting treatment as appropriate e.g. varying dosage or timing, and informing the GP of any changes in writing. 11. Continuing supply of methylphenidate for children under 6 years old. 12. Inform and decide with GP any action if patient misses an appointment. 13. If requested to provide a prescription once shared care has been agreed, undertake steps to ensure the medicine is not being diverted or misused, by contacting the primary care surgery for example. 14. Stopping treatment when appropriate. Baseline tests: Height, weight, blood pressure and heart rate (height does not need to be measured in adults). Patient Information to be received by the GP from the Specialist: • Details of patient follow-up, including Care Plan. • The Specialist's review letter - sent after initial assessment and following each further appointment and including any changes to the patient's medication regimen. • The specialist should specify the brand of methylphenidate to be prescribed. • When dose titration has been completed and the treatment is stable, the GP should be asked by the Specialist to continue prescribing and monitoring under a shared care arrangement. A copy of this Shared Care Guideline should then be sent to the GP.
General Practitioner's Responsibilities	1. The GP must reply in writing to the request for shared care within two weeks if unwilling to participate in shared care. 2. Arrange to see the patient on a regular basis to monitor their health and well-being. This includes undertaking any necessary physical health monitoring to ensure that monitoring requirements are maintained beyond Specialist review appointments (see below). 3. Report and discuss with Specialist any adverse effects of medication, possible drug interactions or deteriorating behaviour. 4. Upon acceptance of shared care, provide the patient with monthly prescriptions of methylphenidate. 5. To be mindful of the possibility of drug diversion or misuse if asked to provide a prescription at less than monthly intervals. 6. To only continue prescriptions if monitoring, compliance and results are satisfactory.

	7. To ensure no drug interactions with concomitant medicines. Maintenance physical health monitoring: Height and weight measured every 6 months (height does not need to be measured in adults). Heart rate and blood pressure measured every 3 months. Methylphenidate can cause tachycardia and elevated blood pressure. If there is a **persistent** increase above baseline there should be a discussion with secondary care on whether medication should be reduced or referral made to paediatrics for an opinion to ensure that there are no other medical reasons for **the persistent** elevation. Further information on monitoring blood pressure in children can be found at http://www.gosh.nhs.uk/health-professionals/clinical-guidelines/blood-pressure-monitoring Patient Information to be received by the Specialist from the GP: • Details of any adverse effects experienced by the patient. • Any relevant medical information, including any test results. • Any changes to the patient's medication regimen. • Notification of patient's failure to attend regularly for monitoring.
Joint Responsibilities of GP and Specialist	It is the joint responsibility of the GP and Specialist to ensure the patient/parent/carer are aware of their responsibilities: • To attend appointments. • To have the recommended tests. • To inform the GP if health problems arise. • To be aware of side effects listed in the patient information leaflet supplied with the medication and report any relevant symptoms.
When and How to Discontinue Treatment (Only on the advice of the Specialist, except in the case of significant adverse effects)	• The medication may be stopped abruptly, but more gradual withdrawal is recommended as abrupt withdrawal can unmask depression as well as renewed overactivity. • When a patient shows improvement and their condition appears stable, the Specialist may suspend treatment periodically in order to assess the need for continuation of therapy.
Information given to the patient	A pharmaceutical company patient information leaflet (PIL) will be provided with each supply. NICE website address for further information is www.nice.org.uk. www.choiceandmedication.org/swyp
Contact Details	To be included in Specialist's letter

Product Information	
The information in this Shared Care Guideline should be used in conjunction with the latest edition of the BNF and Summary of Product Characteristics	
Dosage and Administration	Methylphenidate immediate-release: • Child 6-18 years – initially 5mg 1–2 times daily, increased if necessary at weekly intervals by 5–10mg daily; usual max. 60mg daily in 2–3 divided doses but may be increased to 2.1mg/kg daily in 2–3 divided doses (max. 90mg daily [unlicensed]) under the direction of a Specialist. • Adult over 18 years [unlicensed use] – initially 5mg 2–3 times daily, increased if necessary at weekly intervals according to response and tolerability; max. 100mg daily in 2–3 divided doses. Methylphenidate modified-release: • Different versions of modified-release preparations may not have the same clinical effect. Prescribers should therefore specify the brand to be dispensed. • Modified-release preparations are usually given as a single dose in the morning. • Modified-release preparations may increase adherence and be preferred if there are concerns about misuse or drug diversion. • Equasym XL® should be taken before breakfast. All other products may be taken with or without food.

	• For Equasym XL® and Medikinet XL®, the contents of the capsule can be sprinkled onto a tablespoon of apple sauce then swallowed immediately without chewing. • Please see BNF and SPC for recommended dosing of individual preparations.
Adverse Effects and their Suggested Management	<u>Very common (≥ 1 in 10):</u> Appetite decreased – This is most common at the start of treatment. It usually settles after a couple of weeks. Headache – Patients should be advised to try a mild analgesic such as paracetamol. <u>Common (≥ 1 in 100 to < 1 in 10):</u> Abdominal pain – This is most common at the start of treatment. It usually settles after a couple of weeks. The dose can be taken with or after food. Alopecia – Treatment may need to be discontinued for alopecia attributable to methylphenidate treatment. Arthralgia – Lifestyle modifications such as weight reduction and regular exercise, with increasing joint mobility, may help patients to regain muscle strength and may improve fatigue, posture, and flexibility. An analgesic such as paracetamol may be beneficial. If arthralgia remains unresolved, discontinuation of methylphenidate may be required. Diarrhoea – This is most common at the start of treatment. It should be managed conservatively (e.g., via oral replenishment of fluid losses and over-the-counter remedies such as loperamide). Dizziness – Patients should be advised to avoid standing up quickly. If they feel dizzy, they should try to lie down. Patients should be advised not to drive (if applicable). Dyspepsia – Patients should be advised to try sleeping propped up on pillows. Dry mouth and cough – Patients should be advised that frequent sips of water, sugar-free boiled sweets, chewing gum or citrus fruits will often help. Fatigue – Patients should be advised not to drive (if applicable). Hypertension – The effect is mild in most cases, but some patients with borderline baseline blood pressure may develop frank hypertension which may require methylphenidate to be discontinued. Insomnia and nervousness – This is most common at the start of treatment. It usually settles after a couple of weeks. It is continues, it may be appropriate to reduce the dose or change the dosage regimen. Irritability and emotional lability – This is most common at the start of treatment. It usually settles after a couple of weeks. It is continues, it may be appropriate to reduce the dose or change the dosage regimen. Movement disorders – This should be assessed. It may be appropriate to change the medication. Nausea and vomiting – This is most common at the start of treatment. Patients should be advised to try taking the dose with or after food. Palpitations and tachycardia – These should be investigated, and the treatment may need to be discontinued. Sexual dysfunction – This should be assessed. It may be appropriate to reduce the dose or change the medication. Weight loss with loss of appetite – Weight gain and growth should be monitored. If there is notable weight loss or lack of weight gain consider stopping treatment. <u>Uncommon (≥ 1 in 1000 to < 1 in 100):</u> Allergic reactions, blurred vision, constipation, drowsiness, dyspnoea, growth restriction, haematuria, nasopharyngitis, rashes, suicidal ideation, sweating. <u>Rare (≥ 1 in 10,000 to < 1 in 1000):</u> Accommodation disturbance, angina, confusion, psychosis. <u>Very rare (< 1 in 10,000):</u> Blood disorders including leucopoenia and thrombocytopenia, cerebral arteritis, hepatic dysfunction, myocardial infarction, neuroleptic malignant syndrome, seizures.

Precautions and Contra-indications	Precautions: • Anxiety or agitation. • Driving – may affect performance of skilled tasks such as driving. • Drug or alcohol dependence. • Epilepsy – discontinue if seizure frequency increases or new-onset seizures occur. • Monitor for aggressive behaviour or hostility during initial treatment. • Monitor for emergence of new or worsening of pre-existing psychiatric disorders. • Susceptibility to angle-closure glaucoma. • Tics or a family history of Tourette's disorder. Pregnancy – 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. Breast-feeding – Methylphenidate excretion in human breast milk has been noted in case reports. The decision whether to discontinue breast-feeding or to discontinue/abstain from methylphenidate treatment is a clinical one and must consider the benefit of breast-feeding for the child and the benefit of treatment for the mother. Contra-indications: • Diagnosis or history of severe depression, anorexia nervosa, suicidal tendencies, psychotic symptoms, schizophrenia, psychopathic/borderline personality disorder, severe and episodic Bipolar I Disorder (that is not well-controlled). • During or within 14 days following the administration of a MAOI. • Hypersensitivity to methylphenidate or any of the excipients. • Hyperthyroidism or thyrotoxicosis. • Glaucoma. • Phaeochromocytoma. • 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). • Pre-existing cerebrovascular disorders – cerebral aneurysm, vascular abnormalities including vasculitis or stroke. • Specific to Medikinet XL - a history of pronounced gastric anacidity with pH > 5.5, treatment with H_2-antagonists, or treatment with antacids.
Clinically-relevant Drug Interactions and their Suggested Management	• Alcohol may increase the plasma concentration of methylphenidate and enhance its adverse effects. Patients should be advised to avoid alcohol consumption during methylphenidate treatment. • Antihypertensives: Methylphenidate may diminish the antihypertensive effect of antihypertensives. Monitor response to antihypertensive medications when starting, stopping, or changing the dose of concomitant methylphenidate. • Antipsychotics: Concomitant use of antipsychotics and methylphenidate may enhance the adverse effects of each other. Due to the varying degree with which individual antipsychotics effect dopamine neurotransmission, there is likely considerable variability among the antipsychotics in the manner in which they interact with methylphenidate. Caution is therefore advised and patients should be monitored closely for signs of altered clinical response to either methylphenidate or antipsychotic when using these drugs in combination. • Carbamazepine may decrease the plasma concentration of methylphenidate. Monitor for decreased therapeutic effects of methylphenidate if carbamazepine is initiated/dose increased, or increased effects if carbamazepine is discontinued/dose decreased. • Coumarin anticoagulants: Methylphenidate may increase the plasma

	concentration of coumarin anticoagulants. Increase monitoring of clinical response to these drugs when starting/stopping or altering the dose of concurrent methylphenidate. Monitor for increased anticoagulant response with increased methylphenidate doses or initiation of therapy, and monitor for decreased anticoagulant response with reduced methylphenidate doses or discontinuation. • Dopamine agonists: Methylphenidate may enhance the adverse effects of dopaminergic drugs used in Parkinson's disease. Patients should be monitored closely for dopamine agonist-related toxicities (e.g., dyskinesias). • Halogenated anaesthetics: Methylphenidate may enhance the hypertensive effect of halogenated anaesthetics, and their combined use should be avoided. For planned surgery, methylphenidate should not be taken on the day of surgery. • MAOIs may enhance the hypertensive effect of methylphenidate and precipitate hypertensive crisis. Methylphenidate use is contra-indicated during or within 14 days following the administration of a MAOI. • Phenytoin/Phenobarbital/Primidone: Methylphenidate may increase the plasma concentration of phenytoin, phenobarbital and primidone. Monitor for increased plasma concentrations/toxicity of these drugs if methylphenidate is initiated/dose increased, or decreased concentrations/effects if methylphenidate is discontinued/dose decreased. • Sympathomimetics may enhance the adverse effects of methylphenidate. Monitor for tachycardia and hypertensive effects during concomitant use. • Tricyclic antidepressants: Methylphenidate may increase the plasma concentration of tricyclic antidepressants and enhance their adverse effects. Monitor for increased adverse effects of tricyclic antidepressants if methylphenidate is initiated / dose increased."

References	
References	• SPC/PIL for Ritalin®, Medikinet®, Concerta XL®, Equasym XL®, Matoride XL®, Medikinet XL®, Xenidate XL®. • NICE Technology Appraisal No 98. – Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. • NICE clinical guideline No 72. – Attention deficit hyperactivity disorder - Diagnosis and management of ADHD in children, young people and adults