Methylphenidate Adult ADHD

Part of the shared care protocol for Adult ADHD
Traffic light classification - AMBER 1
Information sheet for Primary Care Prescribers

Indications

Attention Deficit Hyperactivity Disorder (ADHD) in adults who are under the care of a specialist (Consultant Psychiatrist or Non-Medical Prescriber specializing in ADHD) as part of a comprehensive treatment program. Although the initiation of some methylphenidate products is unlicensed in adults for ADHD, it is recommended by NICE as a first line treatment[1].

Any patient groups to be excluded from shared care

- Treatment of ADHD in children and young people is covered by a separate shared care protocol.
- Adult patients who are not under the care of a specialist.

Therapeutic Summary

Methylphenidate is a first-line treatment option recommended by NICE for the management of ADHD in adults[1]. It is usually used for ADHD where there is no significant co-morbidity. It is a CNS stimulant, although the precise mechanism of action by which it works in ADHD is unknown.
Following titration and dose stabilisation, it is recommended by NICE that prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care[1].

Medicines Initiation

NICE guidance (2018), suggests prescribing methylphenidate as first line pharmacological treatment for adults with ADHD. Treatment with methylphenidate should only be initiated by a specialist with expertise in ADHD following a comprehensive assessment and diagnosis[1].

Products available[2,3]

Please refer to the Nottinghamshire Joint Formulary for guidance on preferred brand prescribing.

Immediate release

- Generic methylphenidate immediate-release tablets – 5mg, 10mg and 20mg. Cost x 30 tablets = £3.03, £3.99 and £10.92 respectively.
- Ritalin® 10mg immediate-release tablets. Cost x 30 tablets = £6.68.
- Medikinet® immediate-release tablets – 5mg, 10mg and 20mg. Cost x 30 tablets = £3.03, £5.49 and £10.92 respectively.

Modified release

- *Delmosart*® - 18mg, 27mg, 36mg and 54mg modified-release tablets. Cost x 30 tablets = £15.57, £18.39, £21.21 and £36.79 respectively.
- *Xaggitin XL*® - 18mg, 27mg, 36mg and 54mg modified-release tablets. Cost x 30 tablets = £15.58, £18.40, £21.22 and £36.80 respectively.
- *Xenidate XL*® - 18mg, 27mg, 36mg and 54mg modified-release tablets. Cost x 30 tablets = £15.57, £18.39, £21.21 and £36.79 respectively.

- *Concerta XL*® - 18mg, 27mg, 36mg and 54mg modified-release tablets. Cost x 30 tablets = £31.19, £36.81, £42.45 and £73.62. Branded generics are now available e.g. Delmosart®, Xenidate XL®, Xaggitin XL®.
- *Equasym XL*® - 10mg, 20mg and 30mg modified-release capsules. Cost x 30 capsules = £25.00, £30.00 and £35.00 respectively.
- *Medikinet XL*® - 5mg, 10mg, 20mg, 30mg, 40mg, 50mg and 60mg modified-release capsules. Cost x 30 capsules = £24.04, £24.04, £28.86, £33.66, £57.72, £62.52 and £67.32 respectively.
- *Ritalin XL*® – 10mg, 20mg, 30mg, 40mg and 60mg modified-release capsules = £23.92, £28.72, £33.49, £57.43 and £66.98 respectively

To avoid confusion modified-release preparations should be prescribed by brand name.

Because different branded modified-release methylphenidate formulations have different pharmacokinetic profiles e.g. immediate vs. modified/sustained release it is important that the formulation/brand is always specified on the prescription.

N.B. The contents of *Equasym XL*® capsules, and *Medikinet XL*® capsules can be sprinkled on a tablespoon of soft food (e.g. apple sauce or yoghurt), then swallowed immediately without chewing.[2]

Methylphenidate is a Schedule 2 Controlled Drug (CD). As such, prescriptions must conform to specific prescription writing criteria and each prescription should be for no longer than 30 days treatment.

Dosages and route of administration

- Initiation, titration and stabilisation of dose will be performed by the specialist.
- Begin with low doses of immediate-release or modified-release preparations consistent with starting doses in the BNF[2]
- Titrate the dose against symptoms and side effects over 4–6 weeks until dose optimisation is achieved (reduced symptoms, positive behavior change, improvement in employment/relationships)[1]
- Doses should be gradually increased until there is no further improvement in symptoms and side effects are tolerable[1]
- Initiation of methylphenidate in adult patients is outside of the product license for most formulations. However, most of the products available specify in their Summary of Product Characteristics (SPCs) that in patients whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood.

***Immediate-release methylphenidate**:*
The usual starting regimen for immediate-release methylphenidate formulations is 5mg 2-3 times per day which can be increased at weekly intervals if necessary up to 100mg daily in 2-3 divided doses. If the effect wears off in the evening (with rebound hyperactivity) a dose in the afternoon may be appropriate (establish need with trial dose).[2]

Modified-release methylphenidate:
Delmosart® tablets, Xaggitin XL® tablets and Xenidate XL® tablets have all been granted marketing authorisation on the bioequivalence to Concerta XL® tablets as the licensed reference product as opposed to clinical studies[4]. As per BNF advice, prescribers should specify the brand when prescribing Delmosart®, Xaggitin XL®, Xenidate XL® or Concerta XL® to ensure the correct product is dispensed. They are prolonged-release forms of methylphenidate (22% IR / 78% PR) administered once daily in the morning. They have the longest duration of the modified-release preparations lasting between 8 to 12 hours. The dose may be adjusted in 18 mg increments, from an initial dose of 18mg once daily, adjusted at minimum weekly intervals according to response.

The maximum dose is 54mg once daily (Delmosart®, Xaggitin XL® and Xenidate XL®) or 108mg once daily (Concerta XL®).[4]

Equasym XL® is a prolonged-release form of methylphenidate (30% IR / 70% PR) administered once daily in the morning. A single dose of Equasym XL typically lasts between 6 to 10 hours. The dose may be adjusted in 10mg increments at weekly intervals up to a maximum of 100mg/day under the direction of a specialist.[4]

Medikinet XL® is a prolonged-release form of methylphenidate (50% IR / 50% PR) administered once daily in the morning. Medikinet XL® has the largest immediate-release fraction and shortest duration of the modified-release formulations, lasting between 6 to 8 hours. The dose may be adjusted in 10mg increments at weekly intervals up to a maximum of 100mg/day under the direction of a specialist.[4]

For more information on pharmacokinetic profiles of extended-release methylphenidate products please see the Specialist Pharmacy Service review.

When switching from immediate-release preparations to modified-release preparations, consult product literature for dose equivalences.

Duration of treatment
Following an adequate treatment response, treatment with medication for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least every 12 months by the specialist.[1]

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, treatment should be continued into adulthood[1].

Monitoring Requirements and Responsibilities
Pre-treatment/baseline assessments to be performed by the specialist and will include: Behavioural rating scales (e.g. SDQ, CAARS self and observer report), descriptive reports from partners/carers, medical history, assessment of mental health and social circumstances and review of physical health (including height, weight, baseline pulse and blood pressure)[1].

Ongoing monitoring[1,2,6,7,8,9,10,11]
During dose titration and stabilisation, the appropriate monitoring will be performed by the specialist. When methylphenidate is being prescribed under a shared care agreement, the ongoing monitoring specified below will be performed by primary care and the results sent to the specialist for recording in the patient's notes.

Ongoing psychological response and assessment of continued need for methylphenidate will be performed by the specialist at least every 12 months.

Ongoing monitoring	Frequency
Heart Rate and Blood Pressure	Baseline and six monthly. Also before and after each dose change. Refer to NICE guidelines for hypertension in adults[5]
Weight	Baseline then every 6 months. Consider BMI monitoring of adults with ADHD if there has been weight change as a result of their treatment.
Development or worsening of psychiatric disorders	Baseline and six monthly. Also before and after each dose change.

Development or worsening of tics	Baseline – collect family history and clinically evaluate for tics or Tourette's syndrome. Six monthly. Also before and after each dose change.
Medication related side-effects	At each visit
Risk of diversion, misuse/abuse	At each visit
ECG	Not recommended unless there is a clinical indication (e.g. family history of cardiomyopathy, cardiac illness, hypertension or concomitant treatment with a medication that may pose an increased cardiac risk)[1].
Routine blood tests	Not recommend unless there is a clinical indication

Explicit criteria for review and discontinuation of the medicine[2,6,7,8,9,10,11]

These recommendations do not replace the need for medical assessments that would be undertaken in response to these signs/symptoms. In any case of withholding/reducing doses, please discuss with the specialist and assess the need for a risk management plan and follow up appointments.

Sustained resting tachycardia (>120bpm)	Withhold/reduce dose and discuss with the specialist. Arrange an ECG and prompt cardiology input if indicated
Arrhythmia (suspected or confirmed)	Withhold/reduce dose if significant and discuss with the specialist. Prompt cardiology input if indicated
A clinically significant increase in blood pressure (measured on 2 occasions)	Withhold/reduce dose if significant and discuss with the specialist. Prompt cardiology input if indicated
Patient fails to attend for physical monitoring	Arrange a further appointment in a timely manner. If follow up appointments are not attended, do not provide further prescriptions and inform the specialist.
Tics	Methylphenidate is associated with the onset or exacerbation of motor and verbal tics. Discuss with the specialist if tics are new or significantly impairing function. Observation over a period of 3 months may be required before a clinical decision can be made. Dose reduction or switch to atomoxetine may be considered.
Insomnia	Monitor changes in sleep pattern (consider a sleep diary) and discuss with the specialist. May respond to dose reduction or timing adjustment.
Reduced appetite and / or clinically significant weight change	Discuss with the specialist. May respond to dose reduction or altered timing.
Development or worsening of psychiatric disorders (anxiety, agitation, depression, psychotic symptoms, mania, behavior changes, suicidal tendencies)	Discuss with the specialist
Anaemia related symptoms (e.g. paleness, lethargy)	Seek medical attention, rarely related to methylphenidate.

Abnormal bruising / bleeding / severe sore throat / skin lesions or severe infection	Seek immediate medical attention, rarely related to methylphenidate.
Seizures in patients with no previous history	Consider urgent medical assessment. Withhold and discuss with the specialist
Increase in seizure activity in patients with previous history of seizures	Withhold and discuss with the specialist
Suspected drug misuse and diversion	Discuss with the specialist

For a full list of Side Effects refer to the BNF or Summary of Product Characteristics (SPC).

Contraindications[2,6,7,8,9,10,11]

- Severe depression, suicidal tendencies, anorexia nervosa, psychosis, uncontrolled bipolar disorder and mania
- Hyperthyroidism or thyrotoxicosis
- Pre-existing cardiovascular disease (including heart failure, structural cardiac abnormalities, cardiomyopathy, severe hypertension, angina, myocardial infarction and arrhythmias)
- Phaeochromocytoma
- Glaucoma
- Pre-existing cerebrovascular disorders (stroke, vasculitis, cerebral aneurysm)
- Concomitant use of MAOIs or within 14 days of MAOI treatment

Precautions[2,6,7,8,9,10,11]

- Tics
- Tourettes syndrome
- Epilepsy
- Susceptibility to angle-closure glaucoma
- Known drug or alcohol dependency (potential for abuse, misuse or diversion). For some high-risk substance abuse patients, methylphenidate or other stimulants may not be suitable and non-stimulant treatment should be considered
- Particular caution is needed in the treatment of patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate.

Concerta XL®, Delmosart® and Xaggitin XL® and Ritalin® are non-deformable formulations and should not ordinarily be administered to patients with pre-existing severe GI narrowing (pathologic or iatrogenic) or in patients with dysphagia or significant difficulty in swallowing tablets.[2,6,9,11]

Pregnancy and Breast-Feeding

There is limited experience of methylphenidate in 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.[2,6,7,8,9,10,11]

If appropriate, female patients should be advised to use effective contraception during treatment with methylphenidate. In the event of a female patient becoming pregnant whilst taking methylphenidate, or wishing to start a family she should be advised to contact the specialist as soon as possible.

Methylphenidate should be avoided in breast-feeding (limited information available).[2,6,7,8,9,10,11]

Driving

Patients must tell the DVLA if their ADHD or ADHD medication affects their ability to drive safely. Please refer to government advice on driving and psychiatric disorders[12.]

Patients should be warned about the potential of methylphenidate to affect their ability to drive as it is an offence to drive if impaired whilst taking it. When driving, patients should be advised to carry suitable evidence that the medicine was prescribed to treat a medical problem, and that it was taken according to the instructions given by the prescriber, or information provided with the medicine (e.g. a repeat prescription form or the medicine's patient information leaflet)[2].

Clinically Relevant Medicine Interactions and their Management[2,6,7,8,9,10,11]
Methylphenidate is not metabolised by cytochrome P450 to a clinically relevant extent. Inducers or inhibitors of cytochrome P450 are not expected to have any relevant impact on methylphenidate pharmacokinetics. Conversely, methylphenidate does not relevantly inhibit cytochrome P450 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 or 3A.

- Monoamine Oxidase Inhibitors (MAOIs) including isocarboxazid, moclobemide, phenelzine and tranylcypromine - methylphenidate should not be used in combination with MAOIs or within 2 weeks of stopping a MAOI due to risk of hypertensive crisis.
- Linezolid – avoid concomitant use due to risk of hypertensive crisis.
- Selegiline/Rasigiline – avoid concomitant use due to risk of hypertensive crisis.
- Paliperidone/risperidone – caution with concomitant use, increased risk of dyskinesias.
- Methylphenidate may decrease the effectiveness of antihypertensives.
- Methylphenidate may inhibit the metabolism of coumarin anticoagulants such as warfarin (i.e. enhance the anticoagulant effect). Increased frequency of INR monitoring may be required.
- Methylphenidate may inhibit the metabolism of some anticonvulsants (phenytoin, phenobarbital, primidone).
- Methylphenidate may inhibit the metabolism of some antidepressants (SSRIs and TCAs).
- A small number of serious adverse events have been reported in patients receiving a combination of clonidine and methylphenidate although causality is not established.
- There is a risk of sudden blood pressure increase during surgery. If surgery is planned, methylphenidate treatment should not be used on the day of surgery.
- Medikinet XL must not be taken together with H_2 receptor blockers, proton pump inhibitors or antacids, as this could lead to a faster release of the total amount of active substance[8].

For a full list of contraindications, precautions and drug interactions refer to the BNF/product SPC.

Information Given to Patient
Written information sheets on the medicines used in ADHD can be found at the following sites:

- http://www.choiceandmedication.org/nottinghamshirehealthcare/
- http://www.rcpsych.ac.uk/mentalhealthinformation

References

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1.0	Based on draft document developed by Dr B Houghton, Professor Chris Hollis and John Lawton. Reviewed and updated by: -**Dr Kiran Jeenkeri**, Consultant Psychiatrist and Clinical Director IDD Services, Nottinghamshire Healthcare NHS Foundation Trust -**Jackie Dziewanowska**, Neurodevelopmental Disorder Nurse Consultant and Neurodevelopmental Service	March 2021	

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