Methylphenidate

Traffic light classification- Amber 1
Information sheet for Primary Care Prescribers

Indications
Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 to 17 who are under the care of a Consultant Psychiatrist as part of a comprehensive treatment program — licensed indication.

Any patient groups to be excluded from shared care
Patients > 18 years old — classified as Red in Nottinghamshire
Children < 6 years old — unlicensed, not recommended by NICE — classified as Red in Nottinghamshire

Therapeutic Summary
Methylphenidate is a treatment option recommended by NICE for the management of ADHD in children and young people. It is usually used for ADHD where there is no significant co-morbidity or for ADHD with co-morbid oppositional defiant disorder (ODD) or conduct disorder.

It is a CNS stimulant, although the precise mechanism of action by which it works on ADHD is unknown. Following titration and dose stabilization, prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care.

Medicines Initiation
Treatment with methylphenidate should only be initiated by a specialist (e.g. psychiatrist or specialist community paediatrician) with expertise in ADHD following a comprehensive assessment and diagnosis. GPs may continue prescribing and monitoring medication treatment under shared care arrangements.

Products available
- Delmosart® - 18mg, 27mg, 36mg & 54mg modified-release tablets. Cost x 30 tablets = £15.59, £18.41, £21.23 & £36.81 respectively.
- Xaggitin XL® - 18mg, 27mg, 36mg & 54mg modified-release tablets. Cost x 30 tablets = £15.58, £18.40, £21.22 & £36.80 respectively.
- Xenidate XL® - 18mg, 27mg, 36mg & 54mg modified-release tablets. Cost x 30 tablets = £15.59, £18.39, £21.21 & £36.79 respectively.
- Concerta XL® - 18mg, 27mg, 36mg & 54mg modified-release tablets. Cost x 30 tablets = £31.19, £36.81, £42.45 and £73.62. Branded generics are now available e.g. Xenidate XL®, Matoride XL®.
- Equasym XL® - 10mg, 20mg & 30mg modified-release capsules. Cost x 30 = £25, £30 & £35 respectively.
- Medikinet XL® - 5mg, 10mg, 20mg, 30mg & 40mg modified-release capsules. Cost x 30 = £24.04, £24.04, £28.86, £33.66 & £57.72 respectively.
- Methylphenidate 10mg immediate-release tablets (Ritalin® brand). Cost x 30 tablets (scored) = £5.49

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

Different branded modified-release methylphenidate formulations have different pharmacokinetic profiles e.g. immediate vs. modified/ sustained release so it is important that the formulation/ brand is always specified in 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.6,7 Ritalin® and Medikinet® tablets are scored and may be halved. For dose equivalencies see NICE guideline.1

Methylphenidate is a Schedule 2 Controlled Drug (CD). As such, prescriptions must conform to specific CD 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 determined and performed by the specialist.
- The immediate-release methylphenidate formulation may be used, but simple medication regimens are often preferred (e.g. once daily morning dose of a modified-release preparation).
- The dose will be increased gradually until there is no further improvement in symptoms, behaviour, education and/or relationships and side effects are tolerable.
- Titration usually takes 4-6 weeks, but may be slower if tics, seizures or other co-morbidities are present.1

Dosage may be altered by specialists to reflect the child’s current physical condition, symptoms or social demands. The patient should require no extra monitoring than already described in this guidance if dosage is adjusted by the specialist in this way.

As a child grows, the dose of methylphenidate will need to be amended to ensure the treatment remains at steady state. A patient’s weight and height should be monitored as described under “Ongoing monitoring”, and dosage may be increased if required as per the section above; “dosage and route of administration”. Increases in medication dose due to growth of the patient should be viewed as a patient’s treatment being “stable”. Where a patient has been switched between medications (i.e. methylphenidate to atomoxetine or vice-versa) further monitoring may be required, as per specialist instruction.

Modified-release methylphenidate:

Delmosart® (or Concerta XL®) is a prolonged-release form of methylphenidate (22% IR / 78% PR) administered once daily in the morning, formulated to replace three times daily dosing with the immediate-release formulation. Concerta XL has the longest duration of the modified-release preparations lasting between 8 to 12 hours. The dose may be adjusted in 9mg or 18mg increments, from an initial dose of 18mg once daily (equivalent to 15mg daily immediate-release), to a maximum of 54 mg/day at approximately weekly intervals. Although 54mg/day is the maximum licensed dose (equivalent to 45mg/day of immediate release methylphenidate), the dose may be increased up to 2.1mg/kg daily (max. 108mg/day) under the direction of a specialist.

Equasym XL® is a prolonged-release form of methylphenidate (30% IR / 70% PR) administered once daily in the morning, formulated to be similar to twice daily dosing with the immediate-release formulation. A single dose of Equasym XL typically lasts between 6 to 10 hours. The dose may be adjusted in 10mg increments at weekly intervals to a maximum of 60mg/day. Although 60mg/day is the maximum licensed dose, the dose may be increased up to 2.1mg/kg daily (max. 90mg/day) under the direction of a specialist.

Medikinet XL® is a prolonged-release form of methylphenidate (50% IR / 50% PR) administered once daily in the morning, formulated to be similar to twice daily dosing with the immediate-release formulation. 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 to a maximum of 60mg/day. Although 60mg/day is the maximum...
licensed dose, the dose may be increased up to 2.1mg/kg daily (max. 90mg/day) under the direction of a specialist.

**Immediate-release methylphenidate:**

The usual starting regimen for immediate-release methylphenidate formulations is 5mg once or twice daily (e.g. morning and noon), which can be increased at weekly intervals by 5-10mg, up to 60mg daily in 2-3 divided doses (morning, noon and afternoon). Increasing the total daily dose of immediate-release methylphenidate to 2.1mg/kg/day (max. 90mg/day (adolescents) may occasionally be undertaken by a specialist in cases of poor response to medication treatment.

Doses of methylphenidate above 60mg/day (Concerta XL 54mg/day) are unlicensed and patients should be closely monitored for side-effects during the titration period.

**Duration of treatment**

Following an adequate treatment response, medication treatment for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least annually by the specialist.

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood. However, this scenario is not covered by the existing shared care protocol (RED classification) and arrangements will need to be made for patients approaching their 18th birthday to be referred back to their specialist in plenty of time to ensure continuity of on-going care by an adult ADHD specialist.

**Monitoring Requirements and Responsibilities**

Pre-treatment assessment to be performed by specialist and will include: diagnostic interview (e.g. DIVA), behavioural rating scales (e.g. SDQ, Conners’, CAARS self and observer report), descriptive reports from parents and teachers, medical history and physical examination including heart rate, blood pressure, height, weight and appetite as a baseline.

For children where there is a first degree relative who has suffered from severe cardiac disease (e.g. myocardial infarction, arrhythmia) or sudden death of unknown cause before the age of 40 years, or in children who have a history of cardiac disease themselves, these patients should have further cardiac screening in the form of an ECG and echocardiogram. Cardiology expertise may be required in deciding if it is safe to start medication.

**Ongoing monitoring** – monitoring will be performed monthly by the specialist for the first 3 months. Further physical monitoring will be performed by primary care (see below) and the results sent to the specialist for recording in the patients notes. Ongoing psychological response and assessment of continued need for methylphenidate will be performed by the specialist at 3 months and at 6 months and then at least annually.

If the child / young person fails to attend for physical monitoring, despite attempts to re-appoint, do not issue any further prescriptions, contact the patient/carer and inform the specialist. The patient should be informed of this policy when treatment begins.

<table>
<thead>
<tr>
<th>Ongoing monitoring</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Heart Rate and Blood Pressure</td>
<td>Six monthly. Also before and after each dose change (note that increases in dose due to growth should be viewed as a patient being “stable” on their medication, and should require no extra monitoring). Compare with previous measurements.</td>
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</tbody>
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Blood pressure centile reference tables\(^{10}\) for children and young people (age/sex) are available within the Nottingham University Hospitals Children’s Hospital Hypertension Guidelines (Jan 2019).

### Weight and Appetite
Following initiation, at three months and six months, then:
- Every 3 months in children 10 years and under.
- Every 6 months in children over 10 years and young people

Plot on a growth chart (link: [http://www.rcpch.ac.uk/growthcharts](http://www.rcpch.ac.uk/growthcharts)).
If weight loss or reduced weight gain this should be discussed with the specialist.

### Height
Six monthly.
Plot on a growth chart.
If growth is affected significantly this should be discussed with the specialist.

### Medication Related Side-effects*
At each visit.

### Risk of Diversion, Misuse/Abuse
At each visit

### ECG, LFTs, FBC
Not recommended unless there is a clinical indication.

*Consider using standard symptom and side effect rating scales during treatment as an adjunct to clinical assessment.

### Explicit Criteria for Review and Discontinuation of the Medicine\(^{1,2,4,5,6,7}\)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>Sustained resting tachycardia</td>
<td>Withhold/reduce dose, discuss with specialist team, with cardiology input if necessary.</td>
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<tr>
<td>Arrhythmia</td>
<td>Withhold/reduce dose, discuss with specialist team, with cardiology input if necessary.</td>
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<tr>
<td>Systolic blood pressure &gt;95(^{\text{th}}) percentile (or clinically significant increase)</td>
<td>Withhold/reduce dose, discuss with specialist team, with cardiology input if necessary.</td>
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<tr>
<td>Take three measurements (with appropriate cuff) within 10 minutes, patient at rest</td>
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<tr>
<td>Failure to attend for physical monitoring</td>
<td>Do not issue further prescriptions, discuss as soon as possible with specialist</td>
</tr>
<tr>
<td>Exertional chest pain, unexplained syncope or dyspnoea</td>
<td>Withhold or reduce dose and discuss with specialist team, with prompt cardiology input if necessary.</td>
</tr>
<tr>
<td>Tics</td>
<td>Tics are commonly co-morbid with ADHD and usually unrelated to methylphenidate. Discuss with 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.</td>
</tr>
<tr>
<td>Insomnia and / or reduced appetite</td>
<td>Discuss with specialist team. May respond to dose reduction or timing adjustment</td>
</tr>
<tr>
<td>Psychotic symptoms (delusions, hallucinations)</td>
<td>Withhold and discuss with specialist team.</td>
</tr>
<tr>
<td>Anxiety symptoms, including panic</td>
<td>Discuss with specialist team.</td>
</tr>
</tbody>
</table>
Emergence of worsening of aggressive behaviour or hostility | Discuss with specialist team.
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Priapism | Patients should be advised to seek immediate medical treatment if this rare side-effect should occur.
Anaemia related symptoms (e.g. paleness, lethargy) | Seek immediate 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 | Withhold and discuss with specialist team.
Increase in seizure activity in patients with previous history of seizures | Discuss with specialist team immediately.
Suspected cerebral vasculitis (severe headache, numbness, weakness, paralysis, impairment of co-ordination, vision, speech, language or memory) | Stop methylphenidate and seek immediate medical attention, rarely related to methylphenidate.
Suspected medication misuse and diversion | Discuss with specialist team.

For a full list of Side Effects refer to the BNF or Summary of Product Characteristics (SPC)\(^4,5,6,7\).

**IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE SPECIALIST TEAM.**

European guidelines on managing adverse effects of medication for ADHD were published in 2011. These provide additional guidance for clinicians.\(^8\)

**Relevant Contraindications**
Methylphenidate is contraindicated in patients with severe depression; anorexia nervosa; psychosis; uncontrolled bipolar disorder; hyperthyroidism; cardiovascular disease (including heart failure, cardiomyopathy, severe hypertension, angina, myocardial infarction and arrhythmias); glaucoma; phaeochromocytoma; vasculitis; cerebrovascular disorders.

**Relevant Precautions**
Particular caution is needed in the treatment of patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate.
Methylphenidate should be used with caution in the presence of tics or Tourette’s syndrome, epilepsy and in patients with known drug or alcohol dependency because of a potential for abuse, misuse or diversion.
Concerta XL, Ritalin and Delmosart 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.\(^4,5,6\)

**Pregnancy and Breast-Feeding**
There is limited experience of methylphenidate in pregnancy. It should be avoided in pregnancy unless potential benefit outweighs risk. 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. Discuss with specialist team.

**Clinically Relevant Medicine Interactions and their Management**
Monoamine Oxidase Inhibitors (MAOIs) - Methylphenidate should not be used in combination with MAOIs or within 2 weeks of stopping a MAOI due to risk of hypertensive crisis.

Anticonvulsants – methylphenidate may increase plasma levels of phenytoin and possibly primidone and phenobarbital.

Coumarins – methylphenidate may enhance the anticoagulant effect of warfarin. May require increased frequency of monitoring.

Methylphenidate may decrease the effectiveness of antihypertensive medications.

A small number of serious adverse events have been reported in patients receiving a combination of clonidine and methylphenidate although causality is not established.

Medikinet XL must not be taken together with H₂ receptor blockers or antacids, as this could lead to a faster release of the total amount of active substance.

For a full list of contraindications, precautions and medication interactions refer to the SPC.

Information Given to Patient

- The specialist will provide relevant, age-appropriate written information to people with ADHD and their families and carers about diagnosis, assessment, support groups, self-help, psychological treatment, medication treatment and possible side-effects.
- Written information sheets on the medicines used in ADHD can be found at:
  - https://www.choiceandmedication.org/nottinghamshirehealthcare/condition/attention-deficit-hyperactivity-disorder/
  - http://www.rcpsych.ac.uk/healthadvice/parentsandyouthinfo/parentscarers/adhdhyperkineticdisorder.aspx
  - https://www.medicinesforchildren.org.uk/methylphenidate-attention-deficit-hyperactivity-disorder-adhd

Patient / Carer Roles and Responsibilities

- The patient / carer will report any suspected adverse reactions to the GP for assessment
- The patient / carer will report to their GP or specialist any heart palpitations, tics, psychotic symptoms or onset or increase in seizures.
- The patient / carer will attend all follow-up appointments with GP and specialist. If they are unable to attend any appointments they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.

Pharmacist Roles and Responsibilities

Pharmacists are well placed to stress the value of a balanced diet, good nutrition and regular exercise for all patients with ADHD. Pharmacists can offer support to help improve treatment adherence in people with ADHD. Pharmacists are also well placed to keep any eye out for signs of possible drug misuse and diversion and inform the GP or specialist team of any concerns. Pharmacists can point out that in the cases of Concerta XL & Delmosart formulations the tablet membrane may pass through the gastrointestinal tract undamaged.

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References
2. BNFc Online, Available from https://www.medicinescomplete.com, accessed [27/11/19]
10. NUH Children’s Hospital Hypertension Guidelines (Jan 2019). (link)