Methylphenidate For Narcolepsy

Traffic light classification - Amber 2
Information sheet for Primary Care Prescribers

Indications

Narcolepsy (unlicensed but established treatment).

Therapeutic Summary

Methylphenidate is a CNS stimulant. It is an established treatment for narcolepsy and if effective and tolerated, treatment is envisaged to be lifelong. Locally it is used second line if modafinil is ineffective or sometimes first line if modafinil is unsuitable (eg woman planning pregnancy).

Medicines Initiation

Methylphenidate will be initiated by a Sleep Specialist and any decision to use it will be a joint decision made in the Neuro-respiratory Sleep Clinic at NUH.

Products available

Please see the preferred prescribing list for the brands to be prescribed in primary care

Standard release tablets:

- Medikinet®: 5mg, 10mg, 20mg. Cost x 30 tablets (scored) = £3.03 £5.49, £10.92 respectively
- Methylphenidate hydrochloride (generic): 5mg, 10mg, 20mg. Cost x 30 tablets (scored) = £3.03, £3.30, £10.92 respectively
- Ritalin®: 10mg. Cost x 30 tablets (scored) =£6.68
- Tranquilyn®: 5mg, 10mg, 20mg Cost x 30 tablets (scored) =£3.03, £5.49,£10.92 respectively

Prolonged-release tablets:

- Affenid XL®: 18mg, 27mg, 36mg, 54mg. Cost x 30 tablets = £10.90, £12.87, £14.85, £25.75 respectively
- Concerta XL®: 18mg, 27mg, 36mg, 54mg. Cost x 30 tablets = £31.19, £36.81, £42.45, £73.62 respectively
- Delmosart®: 18mg, 27mg, 36mg, 54mg. Cost x 30 tablets = £15.57, £18.39, £21.21, £ 36.79 respectively
- Matoride XL®: 18mg, 36mg, 54mg. Cost x 30 tablets = £15.58, £21.22, £36.80 respectively
- Xaggitin XL®: 18mg, 27mg, 36mg, 54mg. Cost x 30 tablets = £15.58, £18.40, £21.22, £36.80 respectively

- Xenidate XL®: 18mg, 27mg, 36mg, 54mg. Cost x 30 tablets = £15.57, £18.39, £21.21, £36.79 respectively

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.
See NICE Guidance NG46 Controlled drugs: safe use and management.

Methylphenidate has the potential for misuse and diversion. Risk of misuse can be reduced by using modified-release preparations. The choice of formulation will be decided by the treating specialist on an individual basis and depends on the intended duration of effect. Alcohol may exacerbate CNS adverse effects of methylphenidate and should be avoided during use. Methylphenidate may cause false positive laboratory test results for amphetamines.

Contraindications and cautions

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to methylphenidate or to any of the excipients
- Glaucoma
- Phaeochromocytoma
- During treatment with non-selective, irreversible monoamine oxidase inhibitors (MAOI), or within a minimum of 14 days of discontinuing those drugs, due to the risk of hypertensive crisis
- Hyperthyroidism or thyrotoxicosis
- Diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder.
- Diagnosis or history of severe and episodic (Type I) bipolar (affective) disorder (that is not well-controlled).
- Certain pre-existing cardiovascular disorders constitute contraindications unless specialist cardiac advice is obtained and documented. These include severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias, disorders caused by the dysfunction of ion channels, and structural cardiac abnormalities.
- Pre-existing cerebrovascular disorders cerebral aneurysm, vascular abnormalities including vasculitis or stroke.
- Medikinet XL only: history of pronounced anacidity of the stomach with a pH value above 5.5, or during therapy with H2 receptor blockers, proton pump inhibitors or antacids.

Cautions:

- Family history of sudden cardiac or unexplained death, malignant arrhythmia.
- Cardiovascular status should be carefully monitored (see monitoring section & management of adverse effects section)

- Underlying conditions which might be compromised by increases in blood pressure or heart rate.
- Known drug or alcohol dependency or misuse of central nervous system (CNS) stimulants: potential for abuse, misuse or diversion.
- Alcohol consumption (not recommended during treatment)
- Epilepsy: may lower seizure threshold
- Psychiatric and neuropsychiatric symptoms or disorders, including manic or psychotic symptoms, aggressive or hostile behaviour, motor or verbal tics (including Tourette's syndrome), anxiety, agitation or tension, depressive symptoms, bipolar disorder.
- Renal or hepatic insufficiency (due to lack of data)
- Leukopenia, thrombocytopenia, anaemia, or other haematological abnormalities.
- Prolonged-release tablets only: severe narrowing of the gastrointestinal tract or dysphagia; risk of obstruction
- Safety and efficacy has not been established in patients older than 60 years of age.
- Susceptibility to open-angle glaucoma.
- Pregnancy or breast-feeding (see pregnancy and breast-feeding section)
- Potential for abuse, misuse, or diversion.

Dosages and route of administration

Methylphenidate will be given initially in a dose of 5 mg daily, increasing by 5mg weekly up to a usual maintenance dose of 10-20mg per day taken in 2-4 divided doses. To be taken before meals. The dose can be further increased as required and tolerated up to 60mg daily standard release or 108 mg daily slow release.
If a dose is missed, then the next scheduled dose should be taken as usual; a double dose must not be taken to make up for a missed dose.

Duration of treatment

Following an adequate treatment response, treatment with medication for narcolepsy should be continued for as long as it remains clinically effective.

Monitoring Requirements and Responsibilities

Baseline investigations and ongoing monitoring

Baseline / pre-treatment investigations* (usually performed by the specialist):

- A medical history and cardiovascular assessment, taking into account conditions that may be contraindications, risk of pregnancy (where applicable) and assessment for mental health illness
- Risk assessment for substance misuse and drug diversion
- Height, weight, and body mass index (BMI)
- Blood pressure (BP) and heart rate (for cardiovascular status)

*****Baseline investigations are usually performed by specialists, however there are some cases where primary care maybe requested to carry out these

- Arrange for electrocardiogram (ECG), only if the patient has any of the following:
  - History of congenital heart disease or previous cardiac surgery
  - Sudden death in a first-degree relative under 40 years suggesting a cardiac disease
  - Shortness of breath on exertion compared with peers
  - Fainting on exertion or in response to fright or noise
  - Palpitations
  - Chest pain suggestive of cardiac origin
  - Signs of heart failure, heart murmur or hypertension
  - Current treatment with a medicine that may increase cardiac risk

Ongoing monitoring

Ongoing monitoring	Frequency
Heart rate and blood pressure and assessment for cardiovascular signs or symptoms	Baseline* then every 6 months. Also before and after each dose change**. Refer to NICE guidelines for hypertension in adults
Weight and appetite	Baseline* then every 6 months. Also before and after each dose change recommended by specialist team **. Consider BMI monitoring if weight has been affected.
Development or worsening of psychiatric and neurological signs or symptoms (e.g. tics, anxiety, symptoms of bipolar disorder)	Baseline* then every 6 months. Also before and after each dose change recommended by specialist team**.
Explore whether patient is experiencing any difficulties with sleep	Every 6 months, and after any change of dose recommended by specialist team**.
Medication related side-effects	At each visit
Assessment of adherence, risk of diversion, misuse/abuse	At each visit
ECG	Not recommended unless there is a clinical indication (e.g. family history of cardiomyopathy or cardiac illness or hypertension or concomitant treatment with a medication that may pose an increased cardiac risk).
Routine blood tests	Not recommended unless there is a clinical indication

*****Baseline investigations are usually performed by specialists, however there are some cases where primary care maybe requested to carry out these

** After every change of dose: The specialist should determine the appropriate timing for this monitoring.

Adverse effects and other management

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard
For information on incidence of ADRs see relevant summaries of product characteristics

Explicit criteria for review and discontinuation of the medicine

As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.

Situation for review	Action for primary care
Cardiovascular Resting HR greater than 120bpm, arrhythmia/palpitations, clinically significant increase in systolic BP- systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on two occasions	• In context of recent dose increase, revert to previous dose and discuss with specialist for ongoing management • In absence of recent dose changes, reduce dose by half and discuss with specialist or cardiology for further advice.
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 specialist team.
Reduced appetite and / or clinically significant weight change	Exclude other reasons for weight loss. May respond to dose reduction, treatment break, or change of medication. Discuss with specialist team.
Haematological disorders Including leukopenia, thrombocytopenia, anaemia or other alterations NB: no haematological monitoring is recommended. Haematological disorders would be a chance finding/due to patient reporting adverse drug reactions.	Contact specialist team. Discontinuation should be considered. Referral to haematology is recommended; use clinical discretion.
Psychiatric disorders Development or worsening of psychiatric disorders (anxiety, depression, psychotic symptoms, mania, behavioural changes) suicidal ideation or verbal tics	Withhold and discuss with specialist team in a timely manner. Consider referral to acute mental health team if suicidal thoughts, mania, or psychosis are present. Do not continue methylphenidate unless the benefits outweigh the risks.

(including Tourette's syndrome), anxiety, agitation or tension, bipolar disorder, depression	
Nervous system disorders Symptoms of cerebral ischaemia, e.g. severe headache, numbness, weakness, paralysis, and impairment of coordination, vision, speech, language or memory	Discontinue methylphenidate, refer urgently for neurological assessment
Seizures with no previous history	Withhold and discuss with specialist team immediately.
Clear, sustained increase in seizure activity in patients with previous history of seizures	Withhold and discuss with specialist team immediately.
Symptoms of serotonin syndrome, e.g. agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, rigidity, nausea, vomiting, diarrhoea	Discontinue methylphenidate as soon as possible. Management depends on severity; use clinical judgement and seek advice if necessary. Discuss with specialist team to determine whether methylphenidate can be re-started.
Insomnia or other sleep disturbance	May respond to dose reduction or timing adjustment. Discuss with specialist team.
Suspected drug misuse / diversion	Discuss with specialist team in a timely manner.

For a full list of side effects refer to the BNF or SPC.

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

Pregnancy, paternal exposure and breastfeeding

It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

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. Evidence on exposure to methylphenidate during pregnancy is too limited to draw firm conclusions on adverse outcomes. Clinicians should be aware that patients may have other risk factors which independently alter the risks. Patients who become pregnant while taking methylphenidate, or who plan a pregnancy, should be referred to the specialist team for review. The specialist will reassume prescribing responsibility.

Healthcare professional information available from: USE OF METHYLPHENIDATE IN PREGNANCY – UKTIS

Patient information available from: https://www.medicinesinpregnancy.org/Medicine--pregnancy/Methylphenidate/

Breastfeeding:

Methylphenidate has been found in breast milk in small amounts. Evidence for safety in breastfeeding is limited. Decisions to use while breastfeeding should be made on a case-by-case basis, taking into account the risks to the infant and benefits of therapy. Infants should be monitored for symptoms of CNS stimulation (e.g. decreased appetite/weight gain, sleep disturbances, irritability), although these may be difficult to detect. High doses may interfere with lactation, although this is not confirmed in practice.

Paternal exposure:

No evidence regarding adverse outcomes following paternal exposure was identified.
Further information for patients: bumps - best use of medicine in pregnancy (medicinesinpregnancy.org)

Clinically Relevant Medicine Interactions and their Management

The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Alcohol	May exacerbate the adverse CNS effects of psychoactive medicines, including methylphenidate. It is therefore advisable for patients to abstain from alcohol during treatment
Anticonvulsants	Methylphenidate may increase plasma levels of phenytoin and possibly primidone and phenobarbital. Dose adjustment may be required when starting or stopping methylphenidate.
Antidepressants	Methylphenidate may enhance the effect of some antidepressants (SSRIs and tricyclics). Dose adjustment may be required when starting or stopping methylphenidate.
Antihypertensives	Methylphenidate may decrease the effectiveness of antihypertensives.
Apraclonidine	Effects decreased by methylphenidate.
Carbamazepine	May decrease methylphenidate levels
Clonidine	A small number of serious adverse events have been reported in patients receiving a combination of clonidine and methylphenidate although causality is not established.

Coumarins	Methylphenidate may enhance the anticoagulant effect of warfarin. May require an increased frequency of INR monitoring.
Dopaminergic medicines, including antipsychotics	Increased risk of pharmacodynamic interactions including dyskinesias or hypertensive crisis (e.g. risperidone, paliperidone, selegiline, rasagiline)
Halogenated anaesthetics	Risk of sudden blood pressure increase during surgery. Avoid methylphenidate on the day of planned surgery.
Linezolid	Avoid concomitant use with linezolid – risk of elevated blood pressure.
Monoamine Oxidase Inhibitors (MAOIs)	Methylphenidate should not be used in combination with MAOIs or within two weeks of stopping a MAOI due to risk of hypertensive crisis
Ozanimod	May increase risk of hypertensive crisis
Serotonergic medicines, including SSRIs and MAOIs	Increased risk of central nervous system (CNS) adverse effects, risk of serotonin syndrome

ACCESS AND CONTACT POINTS

In working hours:
Telephone: 0115 924 9924 extension 84777 (Dr Singhal's secretary)
Email: sumeet.singhal@nuh.nhs.uk

Pharmacy Medicines Information
Nottingham University Hospitals - Tel: 0115 970 9200 (patient line)
0115 924 9924 Extension 84185/81200 **(Healthcare professionals only)**

Out of Hours
Neurologist on-call contact via QMC Switchboard 0115 924 9924 **(GPs only)**
Email: sumeet.singhal@nuh.nhs.uk

Advice to patients and carers

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Abnormally sustained or frequent and painful erections: seek immediate medical attention.
- Signs or symptoms of serotonin syndrome (e.g. agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, rigidity, nausea, vomiting, diarrhoea)
- Any mood changes, for example. psychosis, mania, aggressive or hostile behaviour, suicidal ideation or behaviour, motor or verbal tics (including Tourette's syndrome), anxiety, agitation or tension, anxiety, depression
- New or worsening neurological symptoms (e.g. severe headache, numbness, weakness, paralysis, and impairment of coordination, vision, speech, language or memory)
- Abdominal pain, malaise, jaundice or darkening of urine
- Skin rashes, or bruising easily
- If they suspect, they may be pregnant or are planning a pregnancy. Patients of childbearing potential should use appropriate contraception and take a pregnancy test if they think there is a possibility, they could be pregnant.

The patient should be advised:

- Attend regularly for monitoring and review appointments with primary care and specialist and keep contact details up to date with both prescribers. It may not be safe to continue prescribing without regular review, and patients should be aware that their medicines could be stopped if they do not attend appointments.
- Not to drive or operate machines if methylphenidate affects their ability to do so safely, e.g. by causing dizziness, drowsiness, or visual disturbances.
- People who drive must inform the DVLA if their narcolepsy or medicines affect their ability to drive safely. See https://www.gov.uk/narcolepsy-and-driving.
- Avoid alcohol or recreational drugs while taking methylphenidate, as it may make side effects worse.
- Not to stop taking methylphenidate without talking to their doctor. Medical supervision of withdrawal is required, since this may unmask depression or chronic over-activity.
- Methylphenidate is a Schedule 2 Controlled Drug (CD). Patients may be required to prove their identity when collecting prescriptions, and should store methylphenidate safely and securely. It must not be shared with anyone else. There are restrictions on travelling with controlled drugs: see https://www.gov.uk/guidance/controlled-drugs-personal-licences.

Driving

Patients must tell the DVLA of their narcolepsy diagnosis. Please refer to government advice on driving and narcolepsy. 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).

Patient information:

- Narcolepsy UK – methylphenidate. https://www.narcolepsy.org.uk/resources/methylphenidate
- NHS – Narcolepsy. https://www.nhs.uk/conditions/narcolepsy/

References

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2. Hypertension in adults: diagnosis and management. NICE Clinical Guideline 136 (Last updated March 2022). Available: https://www.nice.org.uk/guidance/ng136. Accessed on 29/06/2023
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4. eBNF. Methylphenidate. Accessed via BNF (British National Formulary) | NICE on 03/07/2023
5. Methylphenidate hydrochloride 5 mg tablets (Medikinet®). Date of revision of the text October 2022. Accessed via https://www.medicines.org.uk/emc/product/328/smpc
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7. Methylphenidate hydrochloride 5 mg tablets (Tranquilyn®). Date of revision of the text 21/09/20. Accessed via https://products.mhra.gov.uk/
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14. Specialist Pharmacy Service. Medicines Q&A: Which medicines should be considered for brand-name prescribing in primary care? Prescribing by generic or brand name in primary care – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice last updated 13/09/2022. Accessed on 03/07/2023
15. Home Office. Guidance: List of most commonly encountered drugs currently controlled under the misuse of drugs legislation. Updated August 2022. Accessed via https://www.gov.uk/government/publications/controlled-drugs-list--2/list-of-most-commonly-encountered-drugs-currently-controlled-under-the-misuse-of-drugs-legislation on 03/07/2023

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Other relevant national guidance

- Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE guidance Methylphenidate for patients within adult services . Available at NHS England » Shared Care Protocols (SCPs)
- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
  NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

Version Control- Methylphenidate in Narcolepsy Amber 2 Information Sheet			
Version	Author(s)	Date	Changes
2.1	Vimbayi Mushayi, Specialist Interface Medicine Optimisation Pharmacist. Nottingham and Nottinghamshire ICB	April 26	• Extended review date to December 2026 as ICB is clustering
2.0	Vimbayi Mushayi, Specialist Interface Medicine Optimisation Pharmacist. Nottingham and Nottinghamshire ICB in consultation with Dr Sumeet Singhal, Consultant Neurologist, Nottingham University Hospitals,	July 2023	• Header and version control • Header and version control • Updated formulations available and prices • Added link to preferred prescribing brands • Added link to NICE guidance on CDs • Added additional information regarding potential misuse, choice of formulation, alcohol use and effects on blood tests results • Added new methylphenidate XL brand available • Updated contraindications and cautions as per RMOC SCP and also moved from page 5-6 • Added advice on omitted doses • Updated monitoring requirements as per RMOC SCP • Updated adverse effects management requirements as per RMOC SCP • Updated pregnancy and breastfeeding advice as per RMOC SCP • Added advice on paternal exposure • Updated interactions as per RMOC SCP and formatted them in a table • Updated contact details • Updated references • Updated advice to patients and carers as per RMOC SCP and added link to patient information and this was moved to the last page

			• Added links to other relevant national guidance
1.1	Dr Sumeet Singhal, Consultant Neurologist, Nottingham University Hospitals, Professor Jill Baker, Respiratory Consultant, Nottingham University Hospitals, Lynne Kennell, Interface and Formulary Pharmacist, Nottinghamshire APC	January 2021	