Dexamfetamine

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

Licensed Indications

Narcolepsy

Therapeutic Summary

Dexamfetamine 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 third line if modafinil and methylphenidate are ineffective or unsuitable.

Medicines Initiation

Dexamfetamine 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

Dexamfetamine sulphate is available generically as 5mg immediate release tablets. Cost x 28 x 5mg tablets between £21.63 and £37.09 depending on supplier.
Dexamfetamine (Amfexa® ▼).Cost x 30 x 5mg, 10mg, 20mg immediate release tablets =£19.89, £39.78, £79.56 respectively.
Oral solution is non formulary.

Dexamfetamine 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.
Dexamfetamine has the potential for misuse and diversion.
Patients should be advised to avoid alcohol which may exacerbate the central nervous system (CNS) side-effects of dexamfetamine. Dexamfetamine is subject to additional monitoring by the Medicines and Healthcare products Regulatory Agency (MHRA) and healthcare professionals are encouraged to report any suspected adverse reactions. Amfetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amfetamines may interfere with urinary steroid determinations.

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

- Known hypersensitivity to the active substance, any of the excipients, or sympathomimetic amines
- Glaucoma
- Phaeochromocytoma
- Certain pre-existing cardiovascular disorders constitute contraindications unless specialist cardiac advice is obtained and documented. These include; structural cardiac abnormalities and/or moderate or severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels)
- Advanced arteriosclerosis
- Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days of MAOI treatment
- Hyperthyroidism or thyrotoxicosis.
- Severe depression, anorexia nervosa/anorexic disorders, suicidal ideation, hyperexcitability, psychotic symptoms, severe and episodic (Type I) Bipolar (affective) Disorder (that is not well-controlled), schizophrenia, psychopathic/borderline personality disorder
- Gilles de la Tourette syndrome or similar dystonias
- Cerebrovascular disorders (cerebral aneurysm, vascular abnormalities including vasculitis or stroke)
- Porphyria
- History of drug abuse or alcohol abuse
- Pregnancy (see pregnancy and breast-feeding section)

Cautions:

- History of epilepsy (discontinue if seizures occur)
- Mild hypertension, history of cardiovascular disease, or concomitant medications that elevate blood pressure
- Susceptibility to angle-closure glaucoma
- Psychiatric and neuropsychiatric symptoms or disorders, including manic or psychotic symptoms, aggressive or hostile behaviour, tics, anxiety/agitation, or bipolar disorder
- Depressive symptoms; patients should be screened for risk of bipolar disorder, including psychiatric and family histories.
- Renal and hepatic insufficiency (due to lack of data).
- Family history of sudden cardiac or unexplained death or malignant arrhythmia
- Breast-feeding (see pregnancy and breast-feeding section)
- Potential for abuse, misuse, or diversion.

Dosages and route of administration

Dexamfetamine will be given initially in a dose of 5 mg od, increasing by 5mg weekly up to a usual maintenance dose of 10-20mg per day taken in 2-4 divided doses. Occasionally, doses of up to 60mg a day may be required (in 2-4 divided doses), but only on advice of the joint Neurology-Respiratory Narcolepsy clinic.

Tablets can be halved. Dexamfetamine should not be taken too late after lunch time to avoid disturbances of sleep. 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)

Medical history and cardiovascular assessment, taking into account conditions that may be contraindications), risk of pregnancy (where applicable and assessment for mental health illness.

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- A risk assessment for substance misuse and drug diversion
- Blood pressure (BP) and heart rate (for cardiovascular status)
- Height, weight and body mass index (BMI)
- 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

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

Ongoing monitoring requirements

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 recommended by specialist team** 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
Mental health Assessment for new or worsening 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.
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
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 context of recent dose increase, revert to previous dose and discuss with specialist for ongoing management
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.
Insomnia , sleep disturbance/nightmares, sedation, sexual dysfunction	May respond to dose reduction or timing adjustment. Give advice on sleep hygiene Discuss with 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.
Nausea, diarrhoea, abdominal cramps, constipation, dry mouth, headache, dizziness, enuresis, increased daytime urination, tics	Continue treatment unless severe. Some symptoms may be alleviated by concomitant food intake. Discuss with specialist if required
Development or worsening of psychiatric disorders (anxiety, depression, psychotic symptoms, mania, behavioural changes) NB: psychosis may occur following consumption of very high doses.	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
Seizures with no previous history	Withhold and discuss with specialist team immediately. Discontinuation may be indicated.
Clear, sustained increase in seizure activity in patients with previous history of seizures	Withhold and discuss with specialist team immediately. Discontinuation may be indicated.
Symptoms of serotonin syndrome, e.g. agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, rigidity, nausea, vomiting, diarrhoea	Discontinue dexamfetamine as soon as possible. Management depends on severity; use clinical judgement and seek advice if necessary. Discuss with specialist team to determine whether dexamfetamine can be re-started
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:

Dexamfetamine is contraindicated during pregnancy, because there is insufficient evidence to know if it is safe to use. The limited data available shows a risk of premature birth and reduced birth weight. Infants may also develop withdrawal symptoms such as dysphoria, hyperexcitability and pronounced exhaustion If appropriate, female patients should be advised to use effective contraception during treatment with dexamfetamine. In the event of a female patient becoming pregnant whilst taking dexamfetamine or wishing to start a family she should be advised to contact the specialist as soon as possible.

Breastfeeding:

Dexamfetamine is excreted in human milk, therefore a risk to infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from dexamfetamine, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. High doses may interfere with lactation, although this is not confirmed in practice. If breastfeeding does take place, 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.

Paternal exposure:

No evidence regarding adverse outcomes following paternal exposure was identified.

Clinically relevant medicine interactions and their management

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

The following medicines must not be prescribed without consultation with the specialist:

Monoamine oxidase inhibitor (MAOIs) and other sympathomimetics (e.g. rasagiline, selegiline, safinamide)	Additive hypertensive effect . Amfetamines should not be administered during or within 14 days following the administration of monoamine oxidase inhibitors (MAOI) because it can increase the release of norepiniephrine and other monoamines, causing severe headaches and other signs of hypertensive crisis.
Clonidine	Increased duration of action of dexamfetamine, reduced antihypertensive action of clonidine

Other clinically significant interactions:

Agents that acidify urine (ammonium chloride, sodium acid phosphate, etc)	Increase urine excretion. Both decrease the half-life of amphetamine.
Alcohol	May exacerbate the CNS adverse reactions of psychoactive medicines, including dexamfetamine. It is therefore advisable for patients to abstain from alcohol during treatment
Antacids:(sodium bicarbonate, etc) and urinary alkalinizing agents (e.g. acetazolamide, some thiazides)	May increase exposure to dexamfetamine
Anticonvulsants	Amfetamines may delay the absorption of ethosuximide, phenobarbital, primidone, and phenytoin. Dose adjustment may be required when stopping or starting dexamfetamine.
Antihistamines	Sedative effect may be counteracted
Antihypertensives including guanethidine	Effects may be reduced by dexamfetamine
Antipsychotics (chlorpromazine, haloperidol and lithium carbonate)	May reduce the effects of dexamfetamine:

Apraclonidine	Effects decreased by dexamfetamine
Beta-blockers (e.g. propranolol)	Risk of severe hypertonia. May reduce effects of dexamfetamine
Coumarin anticoagulants, anticonvulsants, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)	Metabolism may be inhibited by dexamfetamine. Dose adjustment may be required when starting or stopping dexamfetamine
Cytochrome P450 (CYP450) substrates, inducers or inhibitors:	Use with caution; role of CYP450 in dexamfetamine metabolism is not known
Gastrointestinal acidifying agents (eg ascorbic acid, fruit juices) and urinary acidifying agents (e.g. ammonium chloride, sodium acid phosphate)	May reduce exposure to dexamfetamine
Halogenated anaesthetics	Risk of sudden blood pressure increase during surgery. Avoid dexamfetamine on the day of planned surgery.
Haloperidol, lithium, phenothiazines	May reduce the effects of dexamfetamine
Serotonergic drugs eg bupropion, linezolid, SSRIs, tapentadol, triptans, tramadol	Risk of serotonin syndrome
TCAs and nabilone	May increase risk of cardiovascular adverse events.
Opioids	Analgesic effects may be increased and the depressant effects (e.g. respiratory depression) may be decreased by dexamfetamine
Ritonavir, tipranavir	May increase exposure to dexamfetamine
Urinary alkalizing agents (acetazolamide, some thiazides)	Decrease urinary excretion. Both groups of agents increase blood levels and efficacy of amfetamines.

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

Information Given to Patient

- The specialist will provide, where relevant, written information to people with narcolepsy and their families and carers about diagnosis, assessment, support groups, self-help, psychological treatment, medicine treatment and possible side-effects.
- The patient must be warned to report any suspected adverse reactions to the GP for assessment and to report to their GP or specialist without delay:
    - Any mood changes, such as depression, paranoia, anxiety or agitation, psychosis, mania, and suicidal ideation
    - Palpitations, chest pain or syncope
    - Cerebrovascular symptoms, such as 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
- Onset or increase in seizures.
- Female patients of childbearing potential must be warned to inform the GP or specialist of any pregnancy or planned pregnancy.
- Female patients of childbearing potential must be advised to use effective and reliable contraception or to discuss this with their GP or specialist.

The patient/carer should be advised:

- The patient should be advised to not stop medication suddenly, but discuss withdrawal with their specialist first.
- The patient should be advised about storing this medication securely at home and, if applicable, at work.
- 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.

- Dexamfetamine can affect impair cognitive function and is subject to drug driving laws, therefore patients must ensure their ability to drive is not impaired before driving. For information on 2015 legislation regarding driving whilst taking certain controlled drugs, including amfetamines, see drugs and driving: the law. People who drive must inform the DVLA if their ,narcolepsy or medicines affect their ability to drive safely. See https://www.gov.uk/adhd-and-driving or https://www.gov.uk/narcolepsy-and-driving.

- Avoid alcohol while taking dexamfetamine, as it may make some side effects worse. Avoid recreational drugs. Due to the risks of severe depression, over-activity, extreme fatigue as well

as changes in the EEG during sleep, abrupt withdrawal after a prolonged period of intake of high doses of dexamfetamine should be avoided. Patients wishing to reduce their dose or stop dexamfetamine treatment should discuss with their specialist before doing so.

- Dexamfetamine is a schedule 2 controlled drug. Patients may be required to prove their identity when collecting prescriptions and should store dexamfetamine 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 dexamfetamine 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 – dexamfetamine. https://www.narcolepsy.org.uk/resources/dexamfetamine
- NHS – Narcolepsy - https://www.nhs.uk/conditions/narcolepsy/

References

1. Dexamfetamine 5mg tablets – Brown & Burk UK Ltd. Summary of product characteristics [02/2022] available at https://www.medicines.org.uk/emc/product/11004/smpc [accessed 13/02/2023].
2. The Electronic Drug Tariff. Accessed via dm+d browser (nhsbsa.nhs.uk) on 03/07/2023
3. BNF,DexamfetamineAccessed via https://bnf.nice.org.uk/ on 03/07/2023
4. Hypertension in adults: diagnosis and management. NICE Clinical Guideline 136 (March 2022 2019). Available: https://www.nice.org.uk/guidance/ng136
5. DVLA. Narcolepsy and driving [accessed 03/07/2023]. Available from: https://www.gov.uk/narcolepsy-and-driving
6. Dexamfetamine sulfate Prescribing Support (risk minimisation materials). Accessed via http://www.dexamfetamine-guide.co.uk/ on 03/07/23
7. 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
8. NICE. NG46: Controlled drugs: safe use and management. April 2016. Accessed via https://www.nice.org.uk/guidance/ng46/ on 03/07/2023

Other relevant national guidance

- 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/
- NHSE guidance Dexamfetamine for patients within adult services . Available at NHS England » Shared Care Protocols (SCPs)
- 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- Dexamfetamine in Narcolepsy Amber 2 Information Sheet			
Version	Author(s)	Date	Changes
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 • Added link to NICE guidance on CDs • Added additional information regarding potential misuse, alcohol use and effects on blood tests results • Updated formulations available and prices • Added administration advice • Added advice on omitted doses • Updated monitoring requirements (baseline ongoing monitoring) as per RMOC SCP • Updated adverse effects management requirements as per RMOC SCP • Updated contraindications and cautions as per RMOC SCP and moved this a couple pages up • Updated pregnancy and breastfeeding advice as per RMOC SCP • Added advice on paternal exposure • Updated interactions as per RMOC SCP and formatted in a table • Updated advice to patients and carers as per RMOC SCP and added link to patient information • Updated contact details • Updated references • 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	