National shared care protocol: Adapted for use as WY ICS amber guidance

Dexamfetamine for patients within adult services

Please ensure that summaries of product characteristics (SPCs), British National Formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis. Ensure the diagnosis is communicated to patient's GP.
- Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 10), to enable the patient to reach an informed decision. Obtain informed consent in line with current local processes. Provide an appropriate patient information leaflet.
- Discuss with the patient their responsibilities outlined below, confirm understanding, and confirm that the patient is happy to adhere to them.
- Ensure the patient and/or their carer understands that treatment may be stopped if they do not attend for monitoring and treatment review
- Assess for contraindications and cautions (see section 3) and interactions (see section 6).
- Conduct required baseline investigations and initial monitoring (see section 7).
- Initiate and optimise treatment as outlined in section 4. Prescribe the maintenance treatment for at least 4 weeks and until stabilised.
- Prescribe in line with controlled drug prescription requirements (section 5).
- Write to the patient's General Practitioner (GP) to ask if they are willing to take over the prescribing and monitoring responsibilities under this amber drug guidance.

- Send information to the patient's GP practice detailing the current and ongoing dose including brand and formulation, any relevant test results and when the next monitoring is required. Provide a link or a copy of the most up to date amber guidance to the patient's GP practice.
- Conduct the required monitoring in section 8 and communicate the results to primary care. This monitoring, and other responsibilities below, may be carried out by a healthcare professional in primary or secondary care with expertise and training in ADHD, depending on local arrangements.
- Determine the duration of treatment and frequency of review. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate. Trial discontinuations should be managed by the specialist.
- Inform patient's GP if review date has exceeded 18 months, to stop treatment.
- Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects when requested. This should be ongoing until the patient ceases to be on dexamfetamine.

Primary care responsibilities

- Ensure the specialist is notified within 2 weeks if unwilling to undertake prescribing and monitoring when requested
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 8 taking into account any potential drug interactions in section 6.
- Prescribe in line with controlled drug prescription requirements (see section 5).
- Adjust the dose of dexamfetamine prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 8. Communicate any abnormal results to the specialist.
- Assess for possible interactions with dexamfetamine when starting new medicines (see section 6)
- Manage adverse effects as detailed in section 9 and discuss with specialist team when required.
- Stop dexamfetamine and make an urgent referral for appropriate care if cerebral ischaemia, new or worsening seizures, or serotonin syndrome are suspected.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.

- Stop treatment as advised by the specialist. Trial discontinuations should be managed by the specialist.
- To stop treatment if annual review date has exceeded 18months.

Patient and/or carer responsibilities

- To agree and accept responsibility for taking dexamfetamine as prescribed.
- To understand how to take dexamfetamine safely.
- Be aware that dexamfetamine can affect cognitive function and is subject to drug driving laws, therefore patients must ensure their ability to drive is not impaired before driving
- To understand the duration of treatment prescribed initially by the hospital specialist.
- To understand the most common adverse events/side effects and inform the Specialist/GP as soon as reasonably possible should they occur and significantly affect the use of the medicines.
- Report suspected adverse effects to the Medicines and Healthcare products Regulatory Agency. https://yellowcard.mhra.gov.uk/
- To understand the circumstances under which the medicines should be immediately stopped and what action to take.
- To understand contents of written information provided by the Specialist and in the patient information leaflet supplied with the medicines and to seek clarification if required.
- To attend for blood tests/disease monitoring on time.
- To check with the community pharmacist that there are no interactions with dexamfetamine, and other medications taken including other prescribed medications, medicines bought over the counter and herbal/homoeopathic products.
- To check with dentists or other specialists who may prescribe medicines that there are no interactions with dexamfetamine.
- Avoid alcohol while during treatment, as it may make some side effects worse. Avoid recreational drugs.
- 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.
- To read the information supplied by the GP, specialist, pharmacist or other healthcare professional, and contact the relevant practitioner if they do not understand any of the information given.
- More information on asking about medication can be found in the Me & My Medicines Charter https://meandmymedicines.org.uk/the-charter/
- Use an appropriate form of contraception, as agreed with their doctor/nurse/sexual health service.

- Inform the specialist or primary care prescriber immediately if they become pregnant or wish to become pregnant.

The NHS Website – NHS information on health link and medicines link

Patient information leaflets for mental health conditions and treatments:

- Leeds and York Partnership NHS Foundation Trust https://www.choiceandmedication.org/leedsandyorkpft
- South West Yorkshire Partnership NHS Foundation Trust https://www.choiceandmedication.org/swyp/
- Bradford District Care NHS Foundation Trust https://www.choiceandmedication.org/bradford

1. Background

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Dexamfetamine sulfate is a sympathomimetic amine with central stimulant and anorectic activity indicated for the treatment of attention deficit hyperactivity disorder (ADHD). It may be offered as an alternative treatment in patients who have been appropriately diagnosed and whose symptoms are responding to lisdexamfetamine but are unable to tolerate the drug's longer effect profile (see NICE Guidance NG87 Attention deficit hyperactivity disorder: diagnosis and management). NICE recommends that people with ADHD have a comprehensive, holistic shared treatment plan that addresses psychological, behavioural and occupational or educational needs.

Dexamfetamine is not licensed for all the indications listed in section 2. However, its use for the indications below are established and supported by various sources and bodies including the BNF and NICE.

Dexamfetamine is a schedule 2 controlled substance; all legal requirements for prescribing controlled drugs should be followed. See NICE Guidance NG46 Controlled drugs: safe use and management.

Where a person with ADHD is treated by a Child and Adolescent Mental Health Service (CAMHS) but is approaching their 18th birthday, it is expected that CAMHS will refer to the appropriate adult service if need for ongoing treatment is anticipated.

Long-term usefulness of dexamfetamine for extended periods (over 12 months) should be periodically re-evaluated by a healthcare professional with expertise in ADHD for the individual

patient with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended a trial discontinuation at least once yearly to assess the patient's condition. Improvement may be sustained when the medicinal product is either temporarily or permanently discontinued.

This guidance is for use between NHS providers.

2. Indications

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- Attention deficit hyperactivity disorder (ADHD) in adults ǂ

ǂ Off-label indications. (Please note licensed indications vary by manufacturer. See SPCs for full details).

3. Contraindications and cautions

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Please see BNF & SPC for comprehensive information.

4. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been stabilised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

ADHD: Initially 5 mg twice daily, dose should be increased according to response at intervals no shorter than 1 week.

Dexamfetamine must be prescribed by the initiating specialist during initiation and dose stabilisation.

Maintenance dose (following initial stabilisation):

ADHD: maximum 60 mg per day to be given in 2–4 divided doses.

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

Consider trial periods of stopping medication or reducing the dose when assessment of the overall balance of benefits and harms suggests this may be appropriate. This should be undertaken and supervised by the specialist who will advise the patient and primary care prescriber of the outcome.

5. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	Dexamfetamine sulfate 5mg, 10mg and 20mg immediate release tablets (Amfexa®▼) Dexamfetamine sulfate 5mg immediate release tablets Dexamfetamine sulfate 5mg/5mL sugar-free oral solution▼ Please note licensed indications vary by manufacturer. See SPCs for full details
Administration details:	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 should not be taken to make up for a missed dose.
Other important information:	Dexamfetamine is a schedule 2 controlled drug and is subject to legal prescription requirements. It 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

6. Significant medicine interactions

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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 or other healthcare professional with expertise in ADHD:

- **Mono-amine oxidase inhibitors (MAOIs) and other sympathomimetics** (e.g., rasagiline, selegiline, safinamide) – additive hypertensive effect

Other clinically significant interactions

- **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.
- **SSRIs (e.g., fluoxetine, paroxetine)**: may increase exposure to dexamfetamine. Risk of serotonin syndrome.
- **Serotonergic drugs, bupropion, tapentadol, tramadol:** Risk of serotonin syndrome
- **TCAs and nabilone**: may increase risk of cardiovascular adverse events.
- **Anticonvulsants (e.g., phenobarbital, phenytoin, primidone)**: Metabolism may be inhibited, and absorption may be delayed by dexamfetamine. Dose adjustment may be required when stopping or starting dexamfetamine.
- **Antacids** (e.g., sodium bicarbonate) **and urinary alkalinizing agents** (e.g., acetazolamide, some thiazides): may increase exposure to dexamfetamine
- **Gastrointestinal acidifying agents** (e.g., ascorbic acid, fruit juices) and **urinary acidifying agents** (e.g., ammonium chloride, sodium acid phosphate): may reduce exposure to dexamfetamine
- **Antihistamines:** sedative effect may be counteracted
- **Antihypertensives, including guanethidine**: effects may be reduced by dexamfetamine

- **Beta-blockers (e.g., propranolol)**: risk of severe hypertonia. May reduce effects of dexamfetamine
- **Lithium, phenothiazines, haloperidol**: may reduce the effects of dexamfetamine
- **Disulfiram**: may inhibit metabolism and excretion of dexamfetamine
- **Opioids**: analgesic effects may be increased and the depressant effects (e.g., respiratory depression) may be decreased by dexamfetamine
- **Halogenated anaesthetics:** risk of sudden blood pressure increase during surgery. Avoid dexamfetamine on the day of planned surgery.
- **Cytochrome P450 (CYP450) substrates, inducers or inhibitors**: use with caution; role of CYP450 in dexamfetamine metabolism is not known
- **Alcohol:** may exacerbate adverse CNS effects of dexamfetamine
- **Apraclonidine:** effects decreased by dexamfetamine
- **Ritonavir, tipranavir:** may increase exposure to dexamfetamine

7. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is stabilised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations:

- A medical history and cardiovascular assessment, taking into account conditions that may be contraindications, risk of pregnancy (where applicable), and to ensure the patient meets the criteria for ADHD and that pharmacological treatment is required
- A risk assessment for substance misuse and drug diversion
- Blood pressure (BP) and heart rate
- 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

Initial monitoring:

- Before every change of dose: assess heart rate, blood pressure, and weight.
- After every change of dose: assess heart rate and blood pressure, and any new or worsening psychiatric symptoms
- Assessment of symptom improvement. Discontinue if no improvement is observed after one month.

Follow up

Ensure the patient receives a review at least annually with a healthcare professional with training and expertise in managing ADHD. This may be in primary or secondary care, depending on local arrangements, and should include a review of ADHD medication, including patient preferences, benefits, adverse effects, and ongoing clinical need. Consider trial periods of stopping medication or reducing the dose when assessment of the overall balance of benefits and harms suggests this may be appropriate. If continuing medication, document the reasons why.

Review outcomes should be communicated to the primary care prescriber in writing, with any urgent changes also communicated by telephone.

8. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
• Blood pressure and heart rate, and assessment for cardiovascular signs or symptoms • Weight and appetite • Assessment for new or worsening psychiatric and neurological signs or symptoms (e.g., tics, anxiety, symptoms of bipolar disorder)	Every 6 months, and 1-2 weeks after any change of dose recommended by specialist team.

• Explore whether patient is experiencing any difficulties with sleep	
• Assessment of adherence, and for any indication of dexamfetamine abuse, misuse, or diversion	As required, based on the patient's needs and individual circumstances
• Review to ensure patient has been offered and attended an annual review with a healthcare professional with expertise in ADHD	Annually
(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.	

9. Adverse effects and other management

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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

Result	Action for primary care
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.	
Resting HR greater than 120bpm, arrhythmia/palpitations, clinically significant increase in systolic BP	• 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.
New or worsening seizures	Stop dexamfetamine and discuss with specialist. Permanent discontinuation may be indicated.
Anorexia or weight loss, weight or BMI outside healthy range	Exclude other reasons for weight loss. Exclude other reasons for weight loss. Give advice as per NICE NG87:

	• take medication with or after food, not before • additional meals or snacks early in the morning or late in the evening when stimulant effects have worn off • obtaining dietary advice • consuming high-calorie foods of good nutritional value Discuss with specialist if difficulty persists; dose reduction, treatment break, or change of medication may be required.
Insomnia, sleep disturbance/nightmares, sedation, sexual dysfunction	Review timing of doses and continue treatment unless severe, Give advice on sleep hygiene. Discuss with specialist if required
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
New or worsening psychiatric or neuropsychiatric symptoms, e.g., mania, depression, paranoia, anxiety and agitation. NB: psychosis may occur following consumption of very high doses.	Discuss with specialist. Stop treatment and consider referral to acute mental health team if suicidal thoughts, mania, or psychosis are present
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.
Suspicion of abuse, misuse, or diversion	Discuss with specialist team

10. Advice to patients and carers

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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/carer should be advised to report any of the following signs or symptoms to their primary care prescriber 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
- 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/carer 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.
- 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 ADHD, 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.

Patient information:

- Royal College of Psychiatrists – ADHD in adults. https://www.rcpsych.ac.uk/mental-health/problems-disorders/adhd-in-adults
- NHS – Attention deficit hyperactivity disorder. https://www.nhs.uk/conditions/attention-deficit-hyperactivity-disorder-adhd/
- South West Yorkshire Partnership NHS Foundation Trust Home (choiceandmedication.org)
- Patient information leaflets: www.choiceandmedication.org/leedsandyorkpft

11. Pregnancy, paternal exposure and breast feeding

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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 not recommended for use during pregnancy 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 a patient becomes pregnant or is planning a pregnancy during treatment, they should discuss treatment options with their specialist. The specialist will reassume prescribing responsibility, ending the shared care agreement.

Healthcare professional information available from: https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-AMFETAMINES-IN-PREGNANCY/

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.

Healthcare professional information available from: https://www.sps.nhs.uk/articles/safety-in-lactation-drugs-for-adhd/

Paternal exposure:

No evidence regarding adverse outcomes following paternal exposure was identified.

12. Specialist contact information

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See clinic letter for details

Bradford District Care NHS Foundation Trust
Bradford phone number and e-mail: **(01274) 363230**
pharmacy@bdct.nhs.uk

For BDCT: Clinic letters to specialist. No dedicated phoneline.
BANDS team
Horton Park centre
CITY CMHT
99 Horton Park Avenue
Bradford

Leeds and York Partnership Foundation Trust
Leeds phone number and e-mail: **(0113) 855 5534**
Pharmacyleedspft.lypft@nhs.net

South West Yorkshire Partnership Foundation Trust

Team	Email Address	Contact number
Wakefield	FieldheadPharmacy@swyt.nhs.uk	01924 316820
Barnsley	KendrayPharmacyTeam@swyt.nhs.uk	01226 644338 or 644145
Calderdale	PharmacyTeamCK@swyt.nhs.uk	01422 222933
Huddersfield		01484 343108
Dewsbury		01924 316374

website address for SWYPFT ADHD team

Adult attention deficit hyperactivity disorder (ADHD) service - South West Yorkshire Partnership NHS Foundation Trust
And here is the email
ADHDandAutismService@swyt.nhs.uk