PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
SHARED CARE FRAMEWORK
REF: SC12 FINAL
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NHS
Pan Mersey
Area Prescribing Committee

DEXAMFETAMINE

1. Background	**Attention deficit hyperactivity disorder (ADHD):** ADHD is a chronic, neurodevelopmental disorder associated with inattention, hyperactivity and impulsiveness. The National Institute for Health and Clinical Excellence (NICE) issued a clinical guideline, Attention Deficit Hyperactivity Disorder; diagnosis and management (NG87) in 2018. This document advises that treatment for ADHD should only be initiated by a healthcare professional with expertise in ADHD and should be based on a comprehensive assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by the primary care clinicians, under shared care arrangements. Methylphenidate, atomoxetine, dexamfetamine, lisdexamfetamine and guanfacine are recommended within their licensed indications, as options for the management of ADHD. Some prescribing of ADHD medication is 'off-label' but clearly supported by the NICE guideline, British National Formulary (BNF) and BNF for Children. Symptoms of ADHD can persist into adulthood in about two thirds of all patients. For patients transitioning into adulthood, specialists should ensure appropriate arrangements are made for referral into adult services. In such circumstances a new shared care agreement will need to be made between the primary care clinician and the new secondary care provider. **Narcolepsy:** Narcolepsy is a rare, long-term sleep disorder which affects the brain's ability to regulate the normal sleep-wake cycle. This can lead to symptoms such as excessive daytime sleepiness including the sudden urge to sleep, and disturbed night-time sleep. In addition, some patients may experience sudden episodes of a related condition, cataplexy, potentially causing dangerous falls and increasing the risks of accidents, including car accidents. Modafinil is the first-line pharmacological treatment for excessive daytime sleepiness and irresistible episodes of sleep. When excessive daytime somnolence coexists with cataplexy and poor sleep, sodium oxybate may be prescribed. Dexamfetamine and methylphenidate (unlicensed indication) may be options in case modafinil is insufficiently effective and sodium oxybate is not recommended. Dexamfetamine is indicated in narcolepsy in adults and elderly people. It is indicated as 2nd line therapy if modafinil has not been successful or is contraindicated or is poorly tolerated. It is used to treat the intractable sleepiness and sleep attacks that characterise narcolepsy. The dose is titrated to maximum effect. [EFNS guidelines on management of narcolepsy. European Journal of Neurology 2006,13:1035-1048]
2. Mode of Action	Dexamfetamine sulphate is a symphathomimetic amine with central nervous system stimulant and anorectic activity. The mode of action of amfetamines in ADHD is not fully established. Dexamfetamine is thought to work by blocking the reuptake of dopamine and noradrenaline into the presynaptic neurone and releasing dopamine and noradrenaline into the extra-neuronal space.

3. Licensed Indications	Dexamfetamine is indicated as part of a comprehensive treatment programme for ADHD in children and adolescents aged 6 to 17 when response to previous to methylphenidate treatment is considered clinically inadequate. Dexamfetamine is indicated for children aged 3 and above with refractory hyperkinetic states under the supervision of a child psychiatry specialist. Dexamfetamine is indicated in narcolepsy in adults and elderly. *NICE CG72 states: Dexamfetamine should be considered in children and young people whose ADHD is unresponsive to a maximum tolerated dose of methylphenidate or atomoxetine.*	
4. Locally agreed off label indications	This document supports the following off label uses (denoted by *): Treatment of adults with refractory ADHD	
5. Contraindications	*(Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Refer to the manufacturers SPC for complete up-to-date list.)* • Hypersensitivity to dexamfetamine or other amfetamine derivatives or any of the excipients. • Patients with symptomatic cardiovascular disease, structural cardiac abnormalities and/or moderate or severe hypertensive disease. • Patients with cerebrovascular disorders (cerebral aneurysm, vascular adnormalities including vasculitis or stroke) • Patients with advanced arteriosclerosis. • During or for 14 days after treatment with an MAO inhibitor. • Patients with a history of drug abuse or alcohol abuse. • Patients with hyperthyroidism, phaeochromocytoma, glaucoma, porphyria or hyperexcitability. • Patients with Gilles de la Tourette syndrome or similar dystonias. • Severe psychiatric comorbidities (that are not well-controlled) Link to SPC	
6. Pharmaceutical aspects *(including route of administration, formulation, method of administration, legal category)*	Route of Administration	Oral
	Formulation	Dexamfetamine 5 mg Tablets Dexamfetamine 1 mg/ml Oral Solution
	Method of administration	Dexamfetamine should be taken at the same times on each day, relative to the time of meals, preferably with or immediately after meals. Dexamfetamine tablets are scored and can be split along the score line(s)
	Other important information	Dexamfetamine should be withdrawn slowly to avoid inducing depression or rebound hyperactivity Alcohol may exacerbate the CNS adverse effects of dexamfetamine. It is advisable for patients to abstain from alcohol during treatment Caution should be exercised when prescribing dexamfetamine to those likely to be at risk of stimulant misuse or diversion

	Legal Category	Dexamfetamine is a Schedule 2 Controlled Drug and prescriptions must comply with full legal requirements for the prescribing and supply of controlled drugs. NICE NG46 recommends prescribing enough of a controlled drug to meet the person's clinical needs for no more than 30 days, unless there are exceptional circumstances.
7. Specialist Initiation and Titration	**Refractory hyperkinetic states in children** - *For children aged 3-5 years, the usual starting dose is 2.5mg a day, increased if necessary by 2.5mg a day at weekly intervals* - *For children aged 6 years and over, the usual starting dose is 5 -10mg a day increasing if necessary by 5mg at weekly intervals* *The usual maximum dose is 20mg a day though some older children may need 40mg or more daily to achieve an optimal response.* **Refractory attention deficit hyperactivity disorder** - Children *aged* 6 and above: A starting dose of 5mg once or twice daily is recommended; increase if necessary by 5mg at day at weekly intervals according to tolerability and degree of efficacy observed. *The usual maximum dose is 20mg a day though some older children have needed 40mg or more daily for an optimal response.* - *Adults**:*** Initially 5mg twice daily, dose is increased at weekly intervals according to response, maintenance dose to be given in 2-4 divided doses; maximum 60mg* per day. In order to optimise drug treatment, the initial dose should be titrated against symptoms and side effects over 4–6 weeks. Doses should be gradually increased until there is no further clinical improvement in ADHD (i.e. symptom reduction, behaviour change, improvements in education and/or relationships) and side effects are tolerable. Treatment should be discontinued if there is no response after 1 month of maximum tolerated dose. **Narcolepsy** - Adults: usual starting dose is 10mg a day, in divided doses. Dose may be increased if necessary by 10mg a day at weekly intervals to a suggested maximum of 60mg a day. - Elderly: start with 5mg a day and increase by increments of 5mg at weekly intervals. **Shared Care may only be commenced following specialist initiation, stabilisation and review of treatment. In addition, formal agreement must have been received from the primary care prescriber.**
8. Dosage regimen for continued prescribing in Primary Care	**Following initiation and stabilisation continue prescribing and monitoring as advised by the specialist in accordance with the shared care agreement.** **Duration of treatment** *To be determined by the specialist based on clinical response and tolerability.* ADHD Following an adequate treatment response, dexamfetamine should be continued for as long as it remains clinically effective. This should be reviewed by the specialist at least annually [NICE CG72] Trial periods off medication (drug holiday) to assess the patient's condition without treatment may be deemed appropriate by the ADHD specialist; this will be undertaken and supervised by the specialist who will advise the patient and GP of the outcome. Narcolepsy The duration of treatment will be determined by the specialist team.

	Termination of treatment	This will be carried out by the specialist
	NB. All dose adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the GP.	
9. Significant Drug Interactions ***For a comprehensive list consult the BNF or Summary of Product Characteristics***	**Seek advice from the initiating specialist if any of the following drugs are co-prescribed:** **Antidepressants** Risk of cardiovascular, serotonin syndrome and other side effects **MAOIs:** Contraindicated; risk of hypertensive crisis. **Antihypertensive medication**. Possible decrease in antihypertensive effectiveness. **Lithium** attenuates the effects of dexamfetamine. **Disulfiram** Possible inhibition of metabolism and excretion of dexamfetamine **Antiepileptic drugs:** absorption of ethosuximide, phenobarbital and phenytoin is delayed by amphetamines. **Coumarin anticoagulants** (e.g. warfarin): Possibly reduces metabolism and enhances anticoagulant effect. Dose of warfarin may need to be reduced. **Antipsychotics**. Possible decrease effectiveness of dexamfetamine and increase of side effects of antipsychotics. **Opioids**. The analgesic effect of morphine may be increased and its respiratory depressant effects decreased with concurrent use of morphine and dexamfetamine. **Clonidine** increased duration of the action of dexamfetamine. **HIV-protease inhibitors** concurrent use with amfetamines increases the concentration of amfetamines and is potentially fatal. Avoidance or dose reduction is advised. The urinary excretion of amfetamines is increased by **urinary acidifiers** and reduced by **urinary alkalinisers.** **Gastrointestinal acidifying agents** (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, fruit juices etc.) lower the absorption of dexamfetamine.	
10. Adverse drug reactions ***For a comprehensive list consult the BNF or Summary of Product Characteristics***	The most common adverse effects include: • Metabolic effects such as decreased appetite with moderately reduced weight and growth during prolonged use. • Psychiatric effects such as aggression, agitation, labile affect, mood swings, and depression. • Central nervous system effects such as dizziness, dyskinesia, psychomotor hyperactivity, confusion, irritability, and headache. • Cardiovascular system effects such as hypertension, tachycardia, cardiomyopathy, and myocardial infarction. • Gastrointestinal effects such as diarrhoea, abdominal cramps, nausea, vomiting, and ischaemic colitis. • Urogenital effects such as sexual dysfunction. • Ophthalmological effects such as mydriasis. In children, parents/patients will have been advised by the ADHD specialist to report any suspected side effects directly to them. GPs should refer any patients with suspected side effects to the ADHD specialist irrespective of the advice in the following table.	

	Adverse event	Action to be taken and by whom
	Sustained resting tachycardia, exceptional chest pains, dyspnoea and unexplained syncope or other symptoms suggestive of cardiac disease.	Discontinue treatment. Seek prompt cardiac specialist advice and notify the initiating specialist team
	Clinically significant increases in blood pressure, arrhythmia	Exclude other causes and seek advice from the initiating specialist. Dose reduction may be appropriate.
	Reduced weight and growth retardation	Continue treatment. Provide advice on healthy diet. The patient should be advised to consider taking additional meals or snacks early in the morning or late in the evening when the effects of the drug have worn off. Refer to a dietician if appropriate. If weight loss becomes a concern, seek ADHD specialist advice.
	Increase in seizure frequency or new-onset seizures	Refer to the initiating specialist team. Discontinuation or switching of treatment may be appropriate.
	Development or worsening of psychiatric disorders including psychotic or manic symptoms, aggressive or hostile behaviour, anxiety, agitation, motor or vocal tics and suicidal ideation	Refer to the initiating specialist team. Depending on symptoms, discontinuation of treatment, dose reduction or switching may be considered by the ADHD specialist
	Central nervous system effects such as dizziness, dyskinesia, psychomotor hyperactivity, headache	Usually temporary. If persisting, refer to ADHD specialist. Dose reduction or discontinuation of treatment may be appropriate.
	Severe blood, kidney and liver disorders	Exclude other causes. Repeat blood tests for confirmation. Seek advice from the initiating specialist if the adverse effect is secondary to the drug. Discontinuation of treatment may be considered.
	Glaucoma or other severe visual disturbances	Seek ophthalmological advice and notify the initiating specialist Team. Discontinuation of treatment may be considered by the initiating specialist
	Diarrhoea, abdominal cramps, nausea, vomiting *(usually occur at the beginning of treatment)*	Continue treatment. Initial symptoms may be alleviated by concomitant food intake. Exclude other causes. Seek advice from the initiating specialist if symptoms become severe. Dose reduction or discontinuation of treatment may be considered by the ADHD specialist
	Insomnia	Continue treatment, usually transient. Provide sleep hygiene advice. Timing of doses may need to be adjusted with advice from the initiating specialist.
	WARNING: Dexamfetamine can cause dizziness, drowsiness and visual disturbances. It can impair cognitive function and can affect the patient's ability to drive safely. This class	

	of medicine is in the list of drugs included in regulation under 5a of the Road Traffic Act 1988.

	Any serious adverse reaction to dexamfetamine should be reported to the MHRA via the "Yellow Card" scheme on http://yellowcard.mhra.gov.uk/	
11. Advice to patient/carers	The patient should be advised to report any of the following signs or symptoms to their GP without delay: Symptoms suggestive of cardiac or psychiatric disorders or seizures. It is advisable for patients to abstain from alcohol during treatment. Alcohol can worsen the side effects of dexamfetamine. In children, parents/patients will have been advised by the ADHD specialist to report the above signs or symptoms directly to them.	
12. Pregnancy and breast feeding	Seek ADHD specialist advice for prescribing decision.	
13. Baseline investigations to be undertaken by the specialist centre	• A comprehensive history of concomitant medications • Full mental health and social assessment • Full medical history and physical examination including - Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms - Heart rate and blood pressure - Weight (in adults); height and weight plotted on a growth chart (in children and adolescents); repeat following each dose adjustment and at 3 months and 6 months after treatment has started. - Family history of cardiac disease and examination of the cardiovascular system. - Pregnancy or breastfeeding • An ECG if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination. • Risk assessment for substance misuse and drug diversion (where the drug is passed on to others for non-prescription use).	
14. Ongoing monitoring requirements to be undertaken by the specialist team and Primary Care	**Monitoring**	**Frequency**
	Blood pressure and pulse (appropriate for age, using information supplied in attached request letter – children & adolescents only)	At every adjustment of dose or visit to specialist service and then every 6 months Primary care – every 6 months
	Weight (in adults); Height and weight (in children and adolescents)	At every adjustment of dose or visit to specialist service or at least every 6 months Primary care – every 6 months Weight every 3 months in children 10 years and under
	Compliance Indication of abuse, misuse or diversion of dexamfetamine	Every 6 months
	Side effects	Every 6 months

	Clinical need, benefits, side effects	Annual review by Specialist
	Refer to '*Adverse Drug Reactions*' section for advice and actions to be taken.	
15. Specialist contact information	**If stopping medication or needing advice,** please refer to the shared care agreement (Appendix 2)	
16. Additional information	**Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.**	
17. References	1. Summary of product characteristics for dexamfetamine 2. NICE guidelines NG87 March 2018: Attention deficit hyperactivity disorder: diagnosis and management 3. NICE CKS for ADHD 4. British National Formulary 5. British National Formulary for Children	
18. To be read in conjunction with the following documents	Shared Care Policy (appendix 1) Shared Care Agreement (appendix 2)	

Appendix 1
Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey **Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary** document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.

- All information required by the shared care framework for the individual medicine has been provided to the patients GP.

- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- To initiate the medicine, prescribing and monitoring toxicity and efficacy as required until the patient is stabilised and reviewed as described by the shared care framework.
- To ensure the patient or their carer is counselled with regard to the medicine.
- To provide any necessary written information to the patient with regard to the individual medicine.
- To be familiar with the shared care framework.
- To provide all information to the patients GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- To assess the patient regularly as necessary for the duration of therapy as specified in the individual medicine shared care framework.
- To review the patient promptly if required by the GP concerned.
- To meet any additional requirements as required by the individual medicine shared care framework.
- To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.

- Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must recall the patient for re-titration, stabilisation and subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated.

Primary Care Responsibilities in Shared Care

- To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked to:

- To provide prescribe or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
- To review the patient as required by the Shared Care Framework
- To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient`s clinical record. A READ code of “6652 Shared Care- Specialist/GP” can be used.
- To be familiar with the individual Shared Care Framework.
- To monitor patient’s general wellbeing.
- To report any adverse effects of treatment to the consultant
- To inform the Specialist of any relevant change in the patient’s circumstances.
- To seek Specialist advice as appropriate.
- To meet any additional requirements as required by the individual Shared Care Framework.
- To respond to Specialist communication relating to any change or addition to the patients treatment covered by the Shared Care Agreement.

Appendix 2: Shared Care Agreement

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1
To be signed by Consultant / Prescribing Member of the Specialist Team

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

If using addressograph label please attach one to each copy

Dear Dr_____

I request that you prescribe

(1) _____

(2) _____

for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: ….. / ….. / ….. Next Supply Due: ….. / ….. / …..

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy. ☐

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received. ☐

Details of Specialist Clinicians

Name _____Date_____

Consultant / Prescribing member of the Specialist Team ****circle or delete as appropriate***

Signature _____

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the consultant, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details*:*

Telephone number: _____Ext:_____

Address for return of documentation _____

_____

_____

Part 2
To be completed by Primary Care Clinician

I agree to prescribe _____for the above

patient in accordance with the enclosed shared care framework.

GP signature _____Date _____

GP name _____Please print

GP: *Please sign and return a copy* ***within 21 calendar days*** *to the address above*

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: