South West Yorkshire Area Prescribing Committee

Dexamfetamine and Lisdexamfetamine Shared Care Guideline for Attention Deficit Hyperactivity Disorder (ADHD) in school-aged children, adolescents and adults.

Introduction	
General Statements	• This guideline relates to children, adolescents and adults with ADHD with moderate to severe levels of impairment. • This guideline sets out details for the shared care of patients taking dexamfetamine and lisdexamfetamine, and follows the recommendations of NICE clinical guideline and NICE Technology Appraisal. • Dexamfetamine and lisdexamfetamine are Schedule 2 Controlled Drugs (CD) and are therefore subject to CD prescription requirements. The quantity prescribed needs to be written in words and figures. • Patients will receive prescriptions for supplies of medication from secondary care until shared care is agreed with the primary care doctor. • Prior to seeking shared care with the patient's GP: 1. The patient's clinical condition will be stable or predictable. 2. The patient will have been stabilised on the drug with time allowed for common adverse events and side-effects to have occurred. • Patients will receive prescriptions for supplies of medication from secondary care until shared care is agreed with the primary care doctor. • If a patient changes GP, then the new GP and the Secondary Care Prescriber will need to discuss setting up shared care for the patient. • The full summary of product characteristics (SPC – formerly datasheet) for the appropriate product should be read before prescribing – for dexamfetamine, the SPC can be found at www.mhra.gov.uk/spc-pil; for Elvanse® and Elvanse Adult® (lisdexamfetamine), the SPCs can be found at www.medicines.org.uk.
Indication	• Dexamfetamine and lisdexamfetamine are indicated for the treatment of refractory ADHD in children of 6 years and older, in adolescents and in adults as part of a comprehensive treatment programme. Treatment must be initiated by a Specialist in the treatment of ADHD, such as a paediatrician or psychiatrist. Diagnosis should be made according to current DSM criteria or the guidelines in ICD. • Elvanse Adult® (lisdexamfetamine) is licensed for use in adults with ADHD. Dexamfetamine is unlicensed for use in adults with ADHD.
Background	NICE clinical guideline states Diagnosis of ADHD • Diagnosis should only be made by a specialist psychiatrist, paediatrician or other healthcare professional with training and expertise in the diagnosis of ADHD. • Diagnosis should be based on: – a full clinical and psychosocial assessment. Discuss behaviour and symptoms in the different domains and settings of the person's everyday life – a full developmental and psychiatric history, and – observer reports and an assessment of mental state. • Diagnosis should be made when symptoms of hyperactivity/impulsivity and/or inattention: – meet the criteria in DSM-5 or ICD-10 (hyperkinetic disorder), and

	– are associated with at least moderate psychological, social and/or educational or occupational impairment based on interview and/or observation in multiple settings, and – are pervasive, occurring in at least two settings. • As part of the diagnostic process, include an assessment of needs, coexisting conditions, social, familial and educational or occupational circumstances and physical health. For children and adolescents also include an assessment of the parents' or carers' mental health. Drug treatment in children and adolescents • Drug treatment should: – only be started by a healthcare professional with expertise in ADHD – be based on comprehensive assessment – always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions. • Drug treatment is not indicated as the first-line treatment for all school-age children and adolescents with ADHD. It should be reserved for those with severe symptoms and impairment, or for those with moderate levels of impairment who have refused non-drug interventions or whose symptoms have not responded sufficiently to parent-training/education programmes or group psychological treatment. • Consider dexamfetamine in children of 6 years and older and adolescents when symptoms are unresponsive to a maximum tolerated dose of methylphenidate or atomoxetine. • Consider Elvanse® (lisdexamfetamine) in children of 6 years and older and adolescents when response to previous methylphenidate treatment is considered clinically inadequate. • GPs may continue prescribing and monitoring drug treatment under shared care arrangements. • If improvement of symptoms is not seen after appropriate dose adjustment, dexamfetamine / lisdexamfetamine will be discontinued. Drug treatment in adults • NICE recommends pharmacological intervention as the first-line treatment for adults with ADHD with moderate to severe levels of impairment. • Consider Elvanse Adult® (lisdexamfetamine) in adults unresponsive to or intolerant to an adequate trial of methylphenidate or where the treatment response is considered clinically inadequate. • GPs may continue prescribing and monitoring drug treatment under shared care arrangements. • If improvement of symptoms is not seen after appropriate dose adjustment, Elvanse Adult® (lisdexamfetamine) will be discontinued.
Pharmacological Summary	• Dexamfetamine and lisdexamfetamine have a dual action, both of which increase synaptic noradrenaline and dopamine availability: 1. Blockade of reuptake of dopamine and noradrenaline by competitive inhibition of the dopamine active transporter (DAT) and noradrenaline transporter (NAT). 2. Promotion of release of dopamine and noradrenaline by competitive inhibition of the intraneuronal vesicular monoamine transporter (VMAT). • Dexamfetamine is readily absorbed by the small intestine and rapidly distributed to body tissues. Lisdexamfetamine is a pharmacologically inactive prodrug with similar pharmacokinetics to that of dexamfetamine. After absorption by the small intestine, lisdexamfetamine is hydrolysed primarily by red blood cells to active dexamfetamine.

Individuals' Responsibilities	
Specialist's Responsibilities	1. Confirm the diagnosis of ADHD following full assessment, drawing upon information from all sources and first-hand observation of the patient. 2. Before starting drug treatment, children, adolescents and adults with ADHD should have a full pre-treatment assessment, which should include:

	– a full mental health and social assessment – a full history and physical examination, including: o assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms o heart rate and blood pressure (plotted on a centile chart for children and adolescents) o height and weight (plotted on a growth chart for children and adolescents) o family history of cardiac disease and examination of the cardiovascular system – an electrocardiogram (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. 3. Initiation of dexamfetamine / lisdexamfetamine therapy and supply of the medicine for one further month after the dose has been stabilised before considering shared care. 4. Ensure that the patient has an adequate supply of medication until GP prescribing can be agreed and arranged. 5. Review the patient at regular intervals 4-weekly initially and then as necessary, but all patients should be seen once a year by the Specialist. 6. Review the patient promptly if requested to do so by the GP. 7. Review the need for treatment at school leaving age and if necessary arrange transition to adult services. 8. Monitor heart rate and blood pressure before and after any dose change, and monitor height and weight before treatment and then 3 months and 6 months into treatment (see below). It is recommended that these measurements are recorded on a centile chart or other appropriate monitoring chart to detect clinically-informed increases. 9. Adjusting treatment as appropriate e.g. varying dosage or timing, and informing the GP of any changes in writing. 10. Continuing supply of dexamfetamine / lisdexamfetamine for children under 6 years old. 11. Inform and decide with GP any action if patient misses an appointment. 12. If requested to provide a prescription once shared care has been agreed, undertake steps to ensure the medicine is not being diverted or misused, by contacting the primary care surgery for example. 13. Stopping treatment when appropriate. Baseline tests: Height, weight, blood pressure and heart rate (height does not need to be measured in adults). Patient Information to be received by the GP from the Specialist: • Details of patient follow-up, including Care Plan. • The Specialist's review letter - sent after initial assessment and following each further appointment and including any changes to the patient's medication regimen. • The specialist should specify the brand of lisdexamfetamine to be prescribed. • When dose titration has been completed and the treatment is stable, the GP should be asked by the Specialist to continue prescribing and monitoring under a shared care arrangement. A copy of this Shared Care Guideline should then be sent to the GP.
General Practitioner's Responsibilities	1. The GP must reply in writing to the request for shared care within two weeks if unwilling to participate in shared care. 2. Arrange to see the patient on a regular basis to monitor their health and well-being. This includes undertaking any necessary physical health monitoring to ensure that monitoring requirements are maintained beyond Specialist review appointments (see below). 3. Report and discuss with Specialist any adverse effects of medication, possible drug interactions or deteriorating behaviour.

	4. Upon acceptance of shared care, provide the patient with monthly prescriptions of dexamfetamine / lisdexamfetamine. 5. To be mindful of the possibility of drug diversion or misuse if asked to provide a prescription at less than monthly intervals. 6. To only continue prescriptions if monitoring compliance and results are satisfactory. 7. To ensure no drug interactions with concomitant medicines. Maintenance physical health monitoring: Height and weight measured every 6 months (height does not need to be measured in adults). Heart rate and blood pressure measured every 3 months. Dexamfetamine / lisdexamfetamine can cause tachycardia and elevated blood pressure. If there is a **persistent** increase above baseline there should be a discussion with secondary care on whether medication should be reduced or referral made to paediatrics for an opinion to ensure that there are no other medical reasons for **the persistent** elevation. Further information on monitoring blood pressure in children can be found at http://www.gosh.nhs.uk/health-professionals/clinical-guidelines/blood-pressure-monitoring Patient Information to be received by the Specialist from the GP: • Details of any adverse effects experienced by the patient. • Any relevant medical information, including any test results. • Any changes to the patient's medication regimen. • Notification of patient's failure to attend regularly for monitoring.
Joint Responsibilities of GP and Specialist	It is the joint responsibility of the GP and Specialist to ensure the patient/parent/carer are aware of their responsibilities: 1. To attend appointments. 2. To have the recommended tests. 3. To inform the GP if health problems arise. 4. To be aware of side effects listed in the patient information leaflet supplied with the medication and report any relevant symptoms.
When and How to Discontinue Treatment (Only on the advice of the Specialist, except in the case of significant adverse effects)	• Discontinue if insufficient treatment response after one month following appropriate dose adjustment. • The SPC for dexamfetamine states that treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression. This may also occur with higher doses of lisdexamfetamine.
Information given to the patient	A pharmaceutical company patient information leaflet (PIL) will be provided with each supply. NICE website address for further information is www.nice.org.uk. www.choiceandmedication.org/swyp
Contact Details	To be included in Specialist's letter

Product Information	
The information in this Shared Care Guideline should be used in conjunction with the latest edition of the BNF and Summary of Product Characteristics	
Dosage and Administration	Dexamfetamine: • Child 6–18 years – initially 2.5mg 2-3 times daily, increased if necessary at weekly intervals by 5 mg daily; usual max. 1 mg/kg (up to 20mg) daily (40mg daily has been required in some children). • Adult over 18 years [unlicensed use] – initially 5mg twice daily, increased at weekly intervals according to response; max. 60mg daily. • Maintenance dose given in 2–4 divided doses. • Use with caution in patients with impaired renal function. Lisdexamfetamine: • Child 6-18 years – Elvanse® initially 30mg once daily in the morning, increased

	if necessary at weekly intervals by 20mg; max. 70mg daily. • Adult over 18 years – Elvanse Adult® initially 30mg once daily in the morning, increased if necessary at weekly intervals by 20mg; max. 70mg daily. • Swallow whole or mix contents of capsule in yoghurt or a glass of water or orange juice; contents should be dispersed completely and consumed immediately. • In severe renal impairment (GFR <30mL/min/1.73m^2), maximum daily dose is 50mg.
Adverse Effects and their Suggested Management	<u>Very common (≥ 1 in 10):</u> Appetite decreased and weight loss – This is most common at the start of treatment. It usually settles after a couple of weeks. Weight gain and growth should be monitored. If there is notable weight loss or lack of weight gain consider stopping treatment. Headache – Patients should be advised to try a mild analgesic such as paracetamol. Insomnia – This is most common at the start of treatment. It usually settles after a couple of weeks. It is continues, it may be appropriate to reduce the dose or change the dosage regimen. <u>Common (≥ 1 in 100 to < 1 in 10):</u> Abdominal pain – This is most common at the start of treatment. It usually settles after a couple of weeks. The dose can be taken with or after food. Constipation – Patients should be advised to maintain a good fluid intake, a fibrous diet, and exercise regularly. If not responsive to such interventions, patients may require a mild laxative. Dizziness – Patients should be advised to avoid standing up quickly. If they feel dizzy, they should try to lie down. Patients should be advised not to drive (if applicable). Dry mouth – Patients should be advised that frequent sips of water, sugar-free boiled sweets, chewing gum or citrus fruits will often help. Fatigue – Patients should be advised not to drive (if applicable). Irritability – This is most common at the start of treatment. It usually settles after a couple of weeks. It is continues, it may be appropriate to reduce the dose or change the dosage regimen. Nausea and vomiting – This is most common at the start of treatment. Patients should be advised to try taking the dose with or after food. Palpitations and tachycardia – These should be investigated, and the treatment may need to be discontinued. <u>Uncommon (≥ 1 in 1000 to < 1 in 100):</u> Agitation, allergic reactions, anxiety, bruxism, depression, drowsiness, dyspnoea, logorrhoea, mania, rashes, tics, tremor, sexual dysfunction, pyrexia. <u>Rare (≥ 1 in 10,000 to < 1 in 1000):</u> Angle-closure glaucoma, growth restriction.
Precautions and Contra-indications	Precautions: • Anorexia. • Mild hypertension (contra-indicated if moderate or severe). • Psychosis or bipolar disorder. • Monitor for aggressive behaviour or hostility during initial treatment. • History of drug or alcohol abuse (this is a contra-indication for dexamfetamine treatment). • Tics and Tourette's disorder – discontinue if tics occur. • History of epilepsy – discontinue if seizures occur. • Susceptibility to angle-closure glaucoma. • Special precautions in children – Monitor height and weight as growth restriction may occur during prolonged therapy. Drug-free periods may allow catch-up in growth but withdraw slowly to avoid inducing depression or renewed hyperactivity. • Driving – may affect performance of skilled tasks such as driving.

	Contra-indications: • Hypersensitivity to sympathomimetic amines or any of the excipients. • During or within 14 days following the administration of a MAOI. • Symptomatic cardiovascular disease (including moderate to severe hypertension and advanced arteriosclerosis). • Hyper-excitability or agitated states. • Hyperthyroidism. • Glaucoma. • Specific to dexamfetamine – structural cardiac abnormalities, history of drug or alcohol abuse, porphyria, Tourette's Disorder or similar dystonias. Pregnancy – Dexamfetamine use is contra-indicated in pregnancy as prenatal exposure is associated with significantly lower birth weight, prematurity, and increased morbidity in both mother and child. There is no adequate clinical data regarding pregnancies exposed to lisdexamfetamine, and it should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus. Breast-feeding – Dexamfetamine is excreted in human milk and so dexamfetamine / lisdexamfetamine should not be used.
Clinically-relevant Drug Interactions and their Suggested Management	• Alkalising agents may decrease the excretion of amfetamines. If these agents must be used together, patients should be monitored closely for excessive amfetamine effects. • Antiepileptics: Amfetamines may decrease the plasma concentrations of ethosuximide, phenobarbital and phenytoin. This possible interaction may be minimised by separating the administration of the medications by at least two hours. • Antihypertensives: Amfetamines may diminish the antihypertensive effect of antihypertensives. Monitor response to antihypertensive medications when starting, stopping, or changing the dose of concomitant amfetamines. • Antipsychotics may antagonise the effect of amfetamines. Monitor effectiveness of amfetamine therapy when altering concurrent antipsychotic therapy. • Lithium may antagonise the effect of amfetamines. Monitor effectiveness of amfetamine therapy in patients who are concurrently receiving lithium. • MAOIs may enhance the hypertensive effect of amfetamines and precipitate hypertensive crisis. Amfetamine use is contra-indicated during or within 14 days following the administration of a MAOI. • Opioid analgesics: The analgesic effect of opioid analgesics may be enhanced and their respiratory depressant effects increased with concurrent amfetamine use. Monitor analgesic response in patients receiving an amfetamine. A lower opioid dose may be required to provide appropriate analgesia. • Tricyclic Antidepressants: Concurrent use of tricyclic antidepressants may enhance the stimulatory effect of amfetamines, and potentiate their cardiovascular and adverse effects. Monitor the stimulant and cardiovascular response to amfetamines closely in patients who are also receiving a tricyclic antidepressant.

References	
References	• SPC for dexamfetamine tablets. • SPC for Elvanse® • SPC for Elvanse Adult® • NICE Technology Appraisal No 98. – Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. • NICE clinical guideline No 72. – Attention deficit hyperactivity disorder - Diagnosis and management of ADHD in children, young people and adults