Lisdexamfetamine: For treatment of adults with attention deficit hyperactivity disorder (ADHD)

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE
This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of lisdexamfetamine for adults with ADHD, where patient needs are complex, can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Specialist responsibilities

1. Discuss the benefits and side effects of treatment with the patient.
2. Initiate and stabilise treatment with lisdexamfetamine as part of a care package, or accept referral from CAMHS for continued treatment from childhood.
3. Notify the patient of any off-label unlicensed use, and gain appropriate informed consent (see overleaf).
4. Ask the GP whether he or she is willing to participate in shared care by emailing the shared care request letter, (continue to prescribe until GP has agreed to take over prescribing).
5. Continue to prescribe until GP has agreed to take over prescribing.
6. Communicate to the GP re-established regimen; follow up arrangements and when to refer back.
7. Communicate promptly with the GP when treatment is changed.
8. Monitor treatment as stated overleaf.
9. Notify GP of review date (at least annually), and give advice on stopping treatment. NB Drug holidays may not be possible, and on-going daily treatment may be required.
10. Have a mechanism in place to receive review of a patient from the GP in the event of rare or severe side-effects, significant deterioration in mental health, suicidal ideation, or cardiovascular problems.
11. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

Report adverse events to the MHRA on a Yellow Card on a Yellow Card, available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours).

General Practitioner responsibilities

1. Reply to the request for shared care as soon as practicable, preferably within 2 weeks, by emailing back the shared care letter. If declining the request please indicate the reason for declining.
2. Prescribe the lisdexamfetamine at the dose recommended, from the agreed date.
3. Adjust the dose as advised by the specialist.
4. Review patient annually, monitoring treatment as stated overleaf. Report significant findings to the specialist.
5. Report to & seek advice from the specialist on any aspect of patient care of concern to the GP that may affect treatment.
6. Refer back to specialist if the patient’s condition deteriorates, or if there are concerns over patient compliance.
7. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.

Report adverse events to the MHRA on a Yellow Card (www.mhra.gov.uk/yellowcard) and to the GP and appropriate Medicines Optimisation team (If in CWPT via the Clinical Governance Pharmacist - see Medicines Policy section 20).

Patient/carer’s role

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with lisdexamfetamine.
3. Inform specialist or GP of any other medication being taken, including over-the-counter products.
4. Inform specialist if any changes in symptoms or behaviour occur.
5. Report any adverse effects or warning symptoms to the specialist or GP whilst taking lisdexamfetamine.

Report any adverse effects or warning symptoms to the specialist or GP. The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card, available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours). The form can also be downloaded from www.mhra.gov.uk/yellowcard

BACK-UP ADVICE AND SUPPORT: See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care

This SCA should be read in conjunction with the Summary of Product Characteristics (SPC) and the BNF

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**SUPPORTING INFORMATION:**

**Licensed indications:** Lisdexamfetamine (Elvanse Adult®) is indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in adults. NICE Clinical Guideline 72, and the British Association for Psychopharmacology [BAP], both recommend drug treatment as the first line treatment for adults with ADHD with either moderate or severe levels of impairment.

**Before starting** drug treatment for adults with ADHD specialists should complete a full assessment & physical examination (including an assessment of history of exercise syncope, undue breathlessness & other cardiovascular symptoms; heart rate & blood pressure, weight, family history of cardiac disease & examination of the cardiovascular system (including an ECG if 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 substance misuse/drug diversion.

A young person with ADHD receiving treatment & care from CAMHS or paediatric services should be reassessed around school leaving age to establish the need for continuing treatment into adulthood. If treatment is necessary, arrangements should be made for a smooth transition to adult services. Complex ADHD adult patients will be retained within specialist adult mental health services, & non-complex ADHD adult patients will be discharged to primary care GP services – with full access to re-entry to mental health services if required, in addition to a package of specialist advice & support. After transition to adult services, a comprehensive assessment of the person with ADHD that includes personal, educational, occupational & social functioning, & assessment of any coexisting conditions, especially drug misuse, personality disorders, emotional problems & learning difficulties should be made.

Sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems. Adults: Sudden deaths, stroke, & myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

**Adult dosage & administration:** Lisdexamfetamine is a pharmacologically inactive prodrug. After oral administration, lisdexamfetamine is rapidly absorbed from the gastrointestinal tract & hydrolysed primarily by red blood cells to dexamfetamine.

**Initiation:** The starting dose for all patients is 30mg once daily in the morning. This may be increased at approximately weekly intervals by 20mg increments, to a maximum of 70mg once daily. The lowest effective dose should be administered.

**Following an adequate response,** drug treatment for ADHD should be continued for as long as it is clinically effective. Specialist to review complex ADHD patient treatment annually, reviewing clinical need, benefits & side effects, taking into account the views of the person & those of a spouse, parent, partner, close friends or carers wherever possible. The effect of missed doses, planned dose reductions & brief periods of no treatment should be taken into account & the preferred pattern of use reviewed. Drug treatment may have to be daily, & drug holidays may not be possible in adult patients since the pressures & demands of adult life are more constant than in childhood, & are not restricted to the educational environment. Coexisting conditions should be reviewed, & the person treated or referred if necessary. The need for psychological, social & occupational support for the person & their carers should be assessed.

Lisdexamfetamine may be taken with or without food. The capsules should be swallowed whole or opened, the contents dispersed in a glass of water (stir until completely dispersed) & the resulting solution swallowed immediately (a film of inactive ingredients may remain in the glass). Afternoon doses should be avoided (risk of insomnia). If there is a missed morning dose, wait until the following morning before administering the next dose. Treatment should be stopped if the symptoms do not improve after 1 month at an appropriate dose. Reduce the dosage if paradoxical aggravation of symptoms/other intolerable adverse events emerge.

**Lisdexamfetamine is a Schedule 2 Controlled Drug.** Prescribers must ensure compliance with controlled drug writing requirements - If uncertain please contact a pharmacist to clarify prescription requirements. Abuse liability- the SPC gives details of abuse liability studies which showed that lisdexamfetamine has less potential for abuse than dexamfetamine.

**Monitoring:** Routine blood tests & ECG are not recommended by NICE unless there is a clinical indication. Specialist: Baseline - weight, heart rate & blood pressure. Weight should be measured 3 months after start of treatment & annually thereafter as a minimum. Heart rate & blood pressure should be monitored before & after each dose change, & annually thereafter. An annual review of on-going mental health state, & on-going need for treatment. GP: Monitor & record blood pressure, heart rate, & weight annually as a minimum. Monitor for adverse drug reactions/interaction, & for any signs of drug misuse or diversion/emergence of psychiatric symptoms. Typically sustained resting tachycardia (increase of heart rate 20 beats per minute over normal) or 15-20 mmHg increase in systolic blood pressure measured on two occasions should prompt consideration of dose reduction & discussion or referral with the Specialist ADHD service. Emergence of symptoms such as palpitations, exercitional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of heart disease during ADHD treatment should undergo prompt specialist cardiac evaluation.

**Contraindications:** Hypersensitivity to sympathomimetic amines or any of the excipients: concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days after MAOI treatment, hyperthyroidism or thyrotoxicosis, agitated states, symptomatic cardiovascular disease, advanced arteriosclerosis, moderate to severe hypertension, glaucoma.

**Cautions:** In patients with a history of substance abuse or dependence; should not be used if there are known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate. Cardiomyopathy has been reported. All patients should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) & physical exam to assess for the presence of cardiac disease, & should receive further cardiac evaluation if findings suggest such disease. Patients who develop symptoms such as exercitional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation. Administration may exacerbate symptoms of behaviour disturbance & thought disorder in patients with pre-existing psychotic disorders. Take particular care in patients with comorbid bipolar disorder. Screen patients with comorbid depressive symptoms to determine if they are at risk for bipolar disorder before Lisdexamfetamine treatment is started. If treatment emergent psychotic or manic symptoms occur, consideration should be given to a possible causal role of the stimulant, & possible discontinuation of treatment. Patients beginning treatment for ADHD should be monitored for the appearance/worsening of aggressive behaviour or hostility. Clinical evaluation for tics & Tourette’s syndrome in children & their families should precede use. Growth should be monitored during treatment with stimulants, & patients who are
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not growing/gaining weight as expected may need to have their treatment interrupted. In the presence of new onset or worsening seizures, lisdexamfetamine should be discontinued. Difficulties with accommodation & blurring of vision have been reported with stimulant treatment. Use with caution in patients taking other sympathomimetic drugs.

**Patients with renal impairment** - Due to reduced clearance in patients with severe renal insufficiency (GFR 15 to <30 mL/min/1.73 m2 or CrCl <30 mL/min) the maximum dose should not exceed 50 mg/day. Further dosage reduction should be considered in patients undergoing dialysis.

**Side Effects:** NB the adult profile is slightly different to that in children/adolescents. **Very common:** decreased appetite, insomnia, headache, dry mouth, **common:** anorexia, psychomotor hyperactivity, dizziness, restlessness, tremor, tachycardia, palpitation, dyspnoea, diarrhoea, upper abdominal pain, nausea, hyperhidrosis, erectile dysfunction, irritability, fatigue, feeling jittery, increased blood pressure, decreased weight. See SPC for a full list of adverse effects that had a frequency occurrence of uncommon/rare or where the frequency was not known.

**Drug Interactions:** Amphetamines should not be administered during or within 14 days following the administration of monoamine oxidase inhibitors (MAOIs) because they can increase the release of norepinephrine & other monoamines. This can cause severe headaches & other signs of hypertensive crisis. A variety of toxic neurological effects & malignant hyperpyrexia can occur, sometimes with fatal outcomes. Chlorpromazine blocks dopamine & norepinephrine receptors, thus inhibiting the central stimulant effects of amphetamines. Haloperidol blocks dopamine receptors, thus inhibiting the central stimulant effects of amphetamines. The anorectic & stimulatory effects of amphetamines may be inhibited by lithium carbonate. Amphetamines potentiate the analgesic effect of narcotic analgesics. Amphetamines may decrease the effectiveness of guanethidine or other antihypertensive medications. Ascorbic acid & other agents & conditions (diets high in fruits & vegetables, urinary tract infections & vomiting) that acidify urine increase urinary excretion & decrease the half-life of amphetamine. Sodium bicarbonate & other agents & conditions (thiazide diuretics, diets high in animal protein, diabetes, respiratory acidosis) that alkalise urine decrease urinary excretion & extend the half-life of amphetamine. There are limited data on the possible interaction with alcohol. Amphetamines can cause a significant elevation in plasma corticosteroid levels. It may interfere with urinary steroid determinations. *In vitro* experiments with human microsomes indicate minor inhibition of CYP2D6 by amphetamine & minor inhibition of CYP1A2, 2D6, & 3A4 by one or more metabolites. Although the clinical significance of this interaction is likely to be minimal, consideration should be given when medications metabolised by these pathways are administered.

**Cost:** (July 2017) one year’s treatment at 50mg daily costs £894.25

**References:**
3. Drug position Statement Lisdexamfetamine. Coventry & Warwickshire Area Prescribing Committee 2013
4. ADHD Guidelines; British Association for Psychopharmacology Feb 2014