Lisdexamfetamine Adult ADHD

Part of the shared care protocol for Adult ADHD
Traffic light classification - AMBER 1
Information sheet for Primary Care Prescribers

Indications

Attention Deficit Hyperactivity Disorder (ADHD) in adults who are under the care of a specialist (Consultant Psychiatrist or Non-Medical Prescriber specialising in ADHD) as part of a comprehensive treatment program[1]. Lisdexamfetamine is recommended by NICE as a first line treatment for adult ADHD[1].

Any patient groups to be excluded from shared care

Treatment of ADHD in children and young people is covered by a separate shared care protocol.
Adult patients who are not under the care of a specialist.

Therapeutic Summary

Pharmacologically inactive prodrug. After oral administration lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and hydrolysed to dexamfetamine. Amfetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. The mode of therapeutic action of amfetamine in ADHD is not fully established, however is thought to be due to its ability to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extra neuronal space.

Medicines Initiation

NICE guidance (2018), suggests prescribing lisdexamfetamine as first line pharmacological treatment of adults with ADHD. Treatment with lisdexamfetamine should only be initiated by a specialist with expertise in ADHD following a comprehensive assessment and diagnosis[1]. It is recommended by NICE that prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care[1].

Products available[2,3]

Lisdexamfetamine capsules (Elvanse® Adult) – 30mg, 50mg and 70mg. Cost x 28 capsules = £58.24, £68.60 and £83.16 respectively.

It is advised to prescribe Lisdexamfetamine by brand due to differences in licensing between Elvanse® Adult and Elvanse®

N.B: Manufacturer advises swallow whole or mix contents of capsule with soft food such as yoghurt or in a glass of water or orange juice; contents should be dispersed completely and consumed immediately[2].

Lisdexamfetamine 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.

Dosages and route of administration[2,4]

- Initiation, titration and stabilisation of dose will be performed by the specialist.
- The starting dose is 30mg taken once daily (orally) in the morning.
- The dose may be increased in steps of 20mg, every week if required.
- The maximum recommended dose is 70mg/day; higher doses have not been studied.
- In patients with severe renal insufficiency (GFR 15 to <30 mL/min/1.73 m^2 or CrCl <30 mL/min) the maximum dose should not exceed 50 mg/day. Further dosage reduction should be considered in patients undergoing dialysis.

Duration of treatment

Following an adequate treatment response, treatment with medication for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least every 12 months by the specialist[1].

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, treatment should be continued into adulthood[1].

Monitoring Requirements and Responsibilities

Pre-treatment/baseline assessments to be performed by the specialist and will include: Behavioural rating scales (e.g. SDQ, CAARS self and observer report), descriptive reports from partners/carers, medical history, assessment of mental health and social circumstances and review of physical health (including height, weight, baseline pulse and blood pressure)[1].

Ongoing monitoring

During dose titration and stabilisation, the appropriate monitoring will be performed by the specialist. When lisdexamfetamine is being prescribed under a shared care agreement, the on-going monitoring specified below will be performed by primary care and the results sent to the specialist for recording in the patient's notes.

On-going psychological response and assessment of continued need for lisdexamfetamine will be performed by the specialist at least every 12 months.

Ongoing monitoring[1,4]	**Frequency**[1]
Heart Rate and Blood Pressure	Baseline and six monthly. Also before and after each dose change. Refer to NICE guidelines for hypertension in adults[5]
Weight	Baseline then every 6 months. Consider BMI monitoring of adults with ADHD if there has been weight change as a result of their treatment.
Development or worsening of psychiatric disorders	Baseline and six monthly. Also before and after each dose change.
Development or worsening of tics	Baseline – collect family history and clinically evaluate for tics or Tourette's syndrome. Six monthly. Also before and after each dose change.
Medication related side-effects	At each visit
Risk of diversion, misuse and abuse	At each visit
ECG	Not recommended unless there is a clinical indication (e.g. family history of cardiomyopathy, cardiac illness,

	hypertension or concomitant treatment with a medication that may pose an increased cardiac risk).
Routine blood tests	Not recommend unless there is a clinical indication.

Explicit criteria for review and discontinuation of the medicine[1,2,4]

These recommendations do not replace the need for medical assessments that would be undertaken in response to these signs/symptoms. In any case of withholding/reducing doses, please discuss with the specialist and assess the need for a risk management plan and follow up appointments.

Sustained resting tachycardia (>120bpm)	Withhold/reduce dose and discuss with the specialist Arrange an ECG, prompt cardiology input if indicated.
Arrhythmia (suspected or confirmed)	Withhold/reduce dose if significant and discuss with the specialist Prompt cardiology input if indicated.
A clinically significant increase in blood pressure (measured on 2 occasions)	Withhold/reduce dose if significant and discuss with the specialist Prompt cardiology input if indicated
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 the specialist.
Tics	Stimulants have been reported to exacerbate motor and phonic tics and Tourette's syndrome. Discuss with the specialist if tics are new or significantly impairing function. Observation over a period of 3 months may be required before a clinical decision can be made. Dose reduction or switch to atomoxetine may be considered.
Insomnia	Ensure the dose is taken in the morning. Monitor changes in sleep pattern (consider a sleep diary) and discuss with the specialist. May respond to dose reduction or timing adjustment.
Reduced appetite and / or clinically significant weight change	Discuss with the specialist. May respond to dose reduction or altered timing.
Development or worsening of psychiatric disorders (anxiety, agitation, depression, psychotic symptoms, mania, behaviour changes, suicidal tendencies)	Discuss with the specialist.
Anaemia related symptoms (e.g. paleness, lethargy)	Seek medical attention, rarely related to lisdexamfetamine.
Abnormal bruising / bleeding / severe sore throat / skin lesions or severe infection	Seek immediate medical attention, rarely related to lisdexamfetamine.
Seizures in patients with no previous history	Consider urgent medical assessment. Withhold and discuss with the specialist
Increase in seizure activity in patients with previous history of seizures	Withhold and discuss with the specialist
Suspected drug misuse and diversion	Discuss with the specialist

For a full list of Side Effects refer to the BNF or Summary of Product Characteristics (SPC).

Contraindications[2,4]

- Advanced atherosclerosis, moderate or severe hypertension, symptomatic cardiovascular disease, known serious structural cardiac abnormalities and cardiomyopathy
- Hyperthyroidism or thyrotoxicosis
- Agitated states
- Glaucoma
- Hypersensitivity to sympathomimetic amines or any excipients as listed in the SPC
- Concomitant use of MAOIs or within 14 days of MAOI treatment

Precautions[2,4]

- Bipolar disorder
- Psychotic disorders
- History of cardiovascular disease
- History of substance abuse
- May lower the seizure threshold
- Susceptibility to angle-closure glaucoma
- Tics
- Tourette syndrome
- With other sympathomimetic medications

Pregnancy and Breastfeeding

There are no adequate and well controlled studies of lisdexamfetamine in pregnant women. Dexamfetamine, the active metabolite of lisdexamfetamine, crosses the placenta. Lisdexamfetamine should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus[2,4].

If appropriate, female patients should be advised to use effective contraception during treatment with lisdexamfetamine. In the event of a female patient becoming pregnant whilst taking lisdexamfetamine, or wishing to start a family she should be advised to contact the specialist as soon as possible.

Lisdexamfetamine should be avoided in breast-feeding[2,4].

Driving

Patients must tell the DVLA if their ADHD or ADHD medication affects their ability to drive safely. Please refer to government advice on driving and psychiatric disorders[6].

Patients should be warned about the potential of lisdexamfetamine 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)[2].

Clinically relevant medicine interactions and their management[2,4]

- Monoamine Oxidase Inhibitors (MAOIs) including isocarboxazid, moclobemide, phenelzine and tranylcypromine - lisdexamfetamine should not be used in combination with MAOIs or within 2 weeks of stopping a MAOI due to risk of hypertensive crisis.
- Selegiline/Rasigiline – avoid concomitant use due to risk of hypertensive crisis.

- Guanfacine plasma concentrations are increased by lisdexamfetamine; this is not expected to be clinically meaningful.
- Venlafaxine. Conversion to the active metabolite o-desmethylvenlafaxine may be reduced by lisdexamfetamine; this is not expected to be clinically meaningful.
- Agents that acidify urine increase urine excretion and decrease the half-life of amfetamine include ascorbic acid and thiazide diuretics.
- Agents that alkalinise urine decrease urinary excretion and extend the half-life of amfetamine include sodium bicarbonate.
- Agents that may reduce the effects of lisdexamfetamine: chlorpromazine, haloperidol and lithium carbonate.
- Amfetamines may decrease the effectiveness of guanethidine or other antihypertensives.
- Amfetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening.
- Serotonin syndrome has rarely occurred in association with the use of amfetamines when given in conjunction with serotonergic medications.

For a full list of contraindications, precautions and drug interactions refer to the BNF/product SPC.

Information Given to Patient
Written information sheets on the medicines used in ADHD can be found at the following sites:

- http://www.choiceandmedication.org/nottinghamshirehealthcare/
- http://www.rcpsych.ac.uk/mentalhealthinformation

References

1. Attention deficit hyperactivity disorder: Diagnosis and management. NICE Clinical Guideline 87 (March 2018). Available from: http://www.nice.co.uk/guidance/ng87
2. Joint Formulary Committee. *British National Formulary* (online) London:BMJ Group and Pharmaceutical Press. https://www.medicinescomplete.com/mc/bnf/current/ [Accessed on 02/03/2021].
3. The Electronic Drug Tariff https://www.drugtariff.nhsbsa.nhs.uk/#/00798052-DC/DC00798043/Home [Accessed on 02/03/2021].
4. Elvanse Adult 30mg, 50mg, 70mg capsules – Shire Pharmaceuticals ltd. Summary of product characteristics (last updated 12/11/2020) https://www.medicines.org.uk/emc/product/2979 [Accessed on 02/03/2021].
5. Hypertension in adults: diagnosis and management. NICE Clinical Guideline 136 (August 2019). https://www.nice.org.uk/guidance/ng136
6. DVLA. Attention deficit hyperactivity disorder (ADHD) and driving. https://www.gov.uk/adhd-and-driving [Accessed on 02/03/2021]

Contacts

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Version Control - Adult ADHD Lisdexamfetamine Information Sheet			
Version	Author(s)	Date	Changes
1.1	**Hannah Godden**, Mental Health Interface and Efficiencies Pharmacist, Nottingham and Nottinghamshire CCGs/ Nottinghamshire Healthcare NHS Foundation Trust	May 2021	-Clarification about brand prescribing added to products available section -Removed references to Elvanse®
1.0	Based on draft document developed by Dr B Houghton, Professor Chris Hollis and John Lawton. Reviewed and updated by: -**Dr Kiran Jeenkeri**, Consultant Psychiatrist and Clinical Director IDD Services, Nottinghamshire Healthcare NHS Foundation Trust -**Jackie Dziewanowska**, Neurodevelopmental Disorder Nurse Consultant and Neurodevelopmental Service Clinical Lead, Nottinghamshire Healthcare NHS Foundation Trust -**Hannah Godden**, Mental Health Interface and Efficiencies Pharmacist, Nottingham and Nottinghamshire CCGs/ Nottinghamshire Healthcare NHS Foundation Trust	March 2021	