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EFFECTIVE SHARED CARE AGREEMENT

31 Dec 1969

Lisdexamfetamine dimesylate (Elvanse®▼)

For attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.

INTRODUCTION

[*Insert details of responsible healthcare body/group*] recommends that shared care agreements are suitable for patients newly initiated on lisdexamfetamine dimesylate (Elvanse).

This shared care agreement outlines responsibilities for managing the prescribing of lisdexamfetamine dimesylate (Elvanse) for the treatment of attention deficit hyperactivity disorder (ADHD) and how they are to be shared between the secondary care specialist and primary care physician (GP) / primary care prescriber. (Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.)

Lisdexamfetamine dimesylate is indicated as part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate for example, a ≥50% worsening in ADHD symptoms or the occurrence of an adverse event. Lisdexamfetamine dimesylate is not indicated in all children with ADHD and the decision to use the drug must be based on a very thorough assessment of the severity and chronicity of the childs symptoms in relation to the childs age and potential for abuse, misuse or diversion.

Diagnosis of ADHD should be made according to DSM-IV criteria or the guidelines in ICD-10 and should be based on a complete history and evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptom (eg. both impaired attention and overactivity should be evident in more than one setting home, classroom, clinic, etc).

NICE published its evidence summary Lisdexamfetamine for ADHD in May 2013 (*http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM19.jsp).*

This shared care agreement for lisdexamfetamine dimesylate (Elvanse) has been agreed by:

[*signature*] .....

[*signature*] .....

[*date*] .....

SUPPORTING INFORMATION

Licensed indication

Lisdexamfetamine dimesylate is indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.

Diagnosis should be made according to DSM-IV criteria or the guidelines in ICD-10 and should be based on a complete history and evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptom.

Lisdexamfetamine dimesylate is not indicated in all children with ADHD and the decision to use the drug must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age and potential for abuse, misuse or diversion.

Appropriate educational placement is essential, and psychosocial intervention is generally necessary. The use of lisdexamfetamine dimesylate should always be used in this way according to the licensed indication.

Dosage and administration

Dosage should be individualised according to the therapeutic needs and response of the patient. Careful dose titration is necessary at the start of treatment:

- For all patients, either starting treatment for ADHD or switching from another medication, the starting dose is 30 mg taken once daily in the morning.
- The dose may be increased by 20 mg increments, at approximately weekly intervals. Lisdexamfetamine dimesylate should be administered orally at the lowest effective dosage.
- The maximum recommended dose is 70 mg/day; higher doses have not been studied.

Lisdexamfetamine dimesylate may be taken once-daily with or without food. The capsule may be swallowed whole, or the capsule opened and the entire contents dissolved in a glass of water.

In the event of a missed dose, dosing can resume the next day. Afternoon doses should be avoided because of the potential for insomnia.

The least amount of lisdexamfetamine dimesylate feasible should be prescribed or dispensed in order to minimise the risk of possible overdose by the patient. (The prolonged release of dexamfetamine after administration of lisdexamfetamine dimesylate should be considered when treating patients with overdose.)

Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a 1 month period. If paradoxical aggravation of symptoms or other intolerable adverse events occur, the dosage should be reduced or discontinued.

Dexamfetamine clearance is reduced in the elderly so dose adjustment may be required.

Long-term use

Pharmacological treatment of ADHD may be needed for extended periods. The physician who elects to use lisdexamfetamine dimesylate for extended periods (over 12 months) should re-evaluate its usefulness at least yearly, and consider trial periods off medication to assess the patient's functioning without pharmacotherapy, preferably during times of school holidays.

Adults

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood. (Note: safety and efficacy have not been established for the routine continuation of treatment beyond 18 years of age).

Children Under 6 years

Lisdexamfetamine dimesylate should not be used in children under the age of 6 years. Safety and efficacy in this age group has not been established.

Elderly

Dexamfetamine clearance is reduced in the elderly so dose adjustment may be required.

Patients with renal or hepatic impairment

No studies have been conducted in patients with renal or hepatic impairment. There was no relationship between creatinine clearance and amfetamine pharmacokinetics in elderly subjects. Dosage reduction may be required in renally impaired patients.

Storage

Shelf life is 2 years. Do not store above 25.

Contraindications

- Hypersensitivity to sympathomimetic amines or any of the excipients listed in the SPC
- Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days after MAOI treatment (hypertensive crisis may result)
- Hyperthyroidism or thyrotoxicosis
- Agitated states
- Symptomatic cardiovascular disease
- Advanced arteriosclerosis
- Moderate to severe hypertension
- Glaucoma

Special warnings and precautions

Abuse and dependence

Stimulants including lisdexamfetamine dimesylate have a potential for abuse, misuse, dependence, or diversion for non-therapeutic uses that physicians should consider when prescribing this product. Stimulants should be prescribed cautiously to patients with a history of substance abuse or dependence.

Tolerance, extreme psychological dependence, and severe social disability have occurred with the abuse of stimulants. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression. Changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amfetamines may include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Cardiovascular adverse events

Sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems

Children and adolescents: Sudden death has been reported in children and adolescents taking CNS stimulants,

including those with structural cardiac abnormalities or other serious heart problems. Stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems.

Adults: Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. 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.

Hypertension and other cardiovascular conditions

Stimulant medications cause a modest increase in average blood pressure (about 2 - 4 mmHg) and average heart rate (about 3 - 6 bpm); all patients should be monitored for larger increases. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia.

The use of lisdexamfetamine dimesylate is contraindicated in patients with symptomatic cardiovascular disease and also in those patients with moderate to severe hypertension.

Cardiomyopathy

Cardiomyopathy has been reported with chronic amfetamine use and with lisdexamfetamine dimesylate.

Assessing cardiovascular status in patients being treated with stimulant medications

All patients who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram or echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

Psychiatric adverse events

Pre existing psychosis

Administration of stimulants may exacerbate symptoms of behaviour disturbance and thought disorder in patients with pre existing psychotic disorders.

Bipolar illness

Particular care should be taken in using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible induction of mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Emergence of new psychotic or manic symptoms

Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of

treatment may be appropriate.

Aggression

Aggressive behaviour or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD including lisdexamfetamine dimesylate. Stimulants may cause aggressive behaviour or hostility. Patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behaviour or hostility.

Tics

Stimulants have been reported to exacerbate motor and phonic tics and Tourette's syndrome. Therefore, clinical evaluation for tics and Tourette's syndrome in children and their families should precede use of stimulant medications.

Long-term suppression of growth (height and weight)

Stimulants have been associated with a slowing of weight gain and a reduction in attained height. Growth should be monitored during treatment with stimulants, and patients who are not growing or gaining weight as expected may need to have their treatment interrupted. Height, weight, and appetite should be recorded at least 6 monthly.

In a controlled study of patients aged 6 to 17 years the mean (SD) changes in body weight after seven weeks were -2.35 (2.084) kg for lisdexamfetamine dimesylate, +0.87 (1.102) kg for placebo, and -1.36 (1.552) kg for methylphenidate hydrochloride.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizure, in patients with prior EEG abnormalities in absence of seizures, and very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of new onset or worsening seizures, the drug should be discontinued.

Visual disturbance

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

Side-effects

Tabulated summary of adverse reactions

Adverse reactions observed with lisdexamfetamine dimesylate treatment mainly reflect side effects commonly associated with stimulant use. Very common adverse reactions include decreased appetite, insomnia, dry mouth, headache, weight decreased and upper abdominal pain.

The following table presents all adverse reactions based on clinical trials and spontaneous reporting.

System Organ Class	Adverse Reaction	Children (6 to 12 years)	Adolescents (13 to 17 years)	Adults
Immune System Disorders	Anaphylactic reaction	Frequency not known	Frequency not known	Frequency not known
	Hypersensitivity	Uncommon	Frequency not known	Uncommon

Metabolism and Nutrition Disorders	Decreased appetite	Very common	Very common	Very common
	Anorexia	Common	Common	Common
Psychiatric Disorders	*Insomnia	Very common	Very common	Very common
	Agitation	Uncommon	Uncommon	Common
	Anxiety	Uncommon	Uncommon	Common
	Logorrhea	Uncommon	Uncommon	Uncommon
	Libido decreased	Not applicable	Not reported	Common
	Depression	Uncommon	Uncommon	Uncommon
	Tic	Common	Uncommon	Uncommon
	Affect lability	Common	Common	Uncommon
	Dysphoria	Uncommon	Frequency not known	Uncommon
	Euphoria	Frequency not known	Uncommon	Uncommon
	Psychomotor hyperactivity	Common	Uncommon	Common
	Dermatillomania	Uncommon	Uncommon	Uncommon
	Psychotic episodes	Frequency not known	Frequency not known	Frequency not known
	Mania	Uncommon	Frequency not known	Uncommon
	Hallucination	Uncommon	Uncommon	Frequency not known
	Aggression	Common	Uncommon	Frequency not known
Nervous System Disorders	Headache	Very common	Very common	Very common
	Dizziness	Common	Common	Common
	Restlessness	Uncommon	Uncommon	Common
	Tremor	Uncommon	Common	Common
	Somnolence	Common	Uncommon	Uncommon
	Seizure	Frequency not known	Frequency not known	Frequency not known
	Dyskinesia	Frequency not known	Frequency not known	Uncommon
Eye Disorders	Vision blurred	Uncommon	Frequency not known	Uncommon
	Mydriasis	Common	Uncommon	Frequency not known
Cardiac Disorders	Tachycardia	Uncommon	Common	Common
	Palpitation	Uncommon	Common	Common

	Cardiomyopathy	Frequency not known	Frequency not known	Frequency not known
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea	Uncommon	Common	Common
Gastrointestinal Disorders	Dry mouth	Common	Common	Very common
	Diarrhoea	Common	Common	Common
	Upper abdominal pain	Very common	Common	Common
	Nausea	Common	Common	Common
	Vomiting	Common	Common	Uncommon
Hepatobilary Disorders	*Eosinophilic Hepatitis	Frequency not known	Frequency not known	Frequency not known
Skin and Subcutaneous Tissue Disorders	Hyperhidrosis	Uncommon	Frequency not known	Common
	Urticaria	Uncommon	Uncommon	Uncommon
	Rash	Common	Uncommon	Uncommon
	*Angiodema	Frequency not known	Frequency not known	Frequency not known
	*Stevens-Johnson Syndrome	Frequency not known	Frequency not known	Frequency not known
Reproductive System and Breast Disorders	Erectile dysfunction	Not applicable	Uncommon	Common
General Disorders and Administration Site Conditions	Irritability	Common	Common	Common
	Fatigue	Common	Common	Common
	Feeling jittery	Uncommon	Uncommon	Common
	Pyrexia	Common	Uncommon	Uncommon
Investigations	Blood pressure increased	Uncommon	Common	Common
	*Weight decreased	Very common	Very common	Common

The following definitions apply to the frequency terminology used above: Very common (≥ 1/10) Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to <1/100) Rare (≥ 1/10,000 to < 1/1,000) Very rare (< 1/10,000) Frequency not known (cannot be estimated from the available data). An asterisk (*) indicates that additional information on the respective adverse reaction is provided in the SPC and below.

Description of selected adverse reactions

Insomnia

Includes insomnia, initial insomnia, and middle insomnia.

Weight decreased

In a 4 week controlled trial of lisdexamfetamine dimesylate in children aged 6 to 12 years, mean weight loss from baseline to endpoint was 0.4, 0.9, and 1.1 kg, for patients assigned to receive 30 mg, 50 mg, and 70 mg of lisdexamfetamine dimesylate respectively, compared to a 0.5 kg weight gain for patients receiving placebo. Higher doses were associated with greater weight loss with 4 weeks of treatment. Careful follow- up for weight in children aged 6 to 12 years who received lisdexamfetamine dimesylate over 12 months suggests that continuous treatment (i.e., treatment for 7 days per week throughout the year) slows growth rate measured by body weight as demonstrated by an age- and sex normalised mean change from baseline in percentile of -13.4 over 1 year. The average percentiles at baseline (n=271) and 12 months (n=146) were 60.9 and 47.2, respectively.

In a 4 week controlled trial of lisdexamfetamine dimesylate in adolescents aged 13 to 17 years, mean weight loss from baseline to endpoint was 1.2, 1.9, and 2.3 kg for patients assigned to receive 30 mg, 50 mg, and 70 mg of lisdexamfetamine dimesylate respectively, compared to a 0.9 kg weight gain for patients receiving placebo. Careful follow-up for weight in adolescents aged 13 to 17 years who received lisdexamfetamine dimesylate over 12 months suggests that continuous treatment (i.e., treatment for 7 days per week throughout the year) slows growth rate measured by body weight as demonstrated by an age and sex normalised mean change from baseline in percentile of -6.5 over 1 year. The average percentiles at baseline (n=265) and 12 months (n=156) were 66.0 and 61.5, respectively.

Eosinophilic hepatitis

No cases were reported in the clinical studies.

Angioedema

No cases were reported in the clinical studies.

Stevens-Johnson syndrome

No cases were reported in the clinical studies.

Lisdexamfetamine dimesylate can cause dizziness, drowsiness and visual disturbances including difficulties with accommodation, diplopia and blurred vision. These could have a moderate influence on the ability to drive and use machines. Patients should be warned of these possible effects and advised that if affected, they should avoid potentially hazardous activities such as driving or operating machinery.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive.
- Do not drive until you know how the medicine affects you.
- It is an offence to drive while under the influence of this medicine.
- However, you would not be committing an offence (called 'statutory defence') if:

- The medicine has been prescribed to treat a medical problem and
- You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
- It was not affecting your ability to drive safely.

Monitoring

Growth, psychiatric, and cardiovascular status should be continually monitored.

- Blood pressure and pulse to be recorded on a centile chart at each adjustment of dose and at least every six months.
- Height, weight, and appetite to be recorded at least six-monthly with maintenance of a growth chart.
- Development of de novo or worsening of pre-existing psychiatric disorders to be monitored at every adjustment of dose and then at least every six months and at every visit.
- Patients to be monitored for the risk of diversion, misuse, and abuse of lisdexamfetamine dimesylate.

Interactions

Agents whose blood levels may be impacted by lisdexamfetamine dimesylate

Extended release guanfacine: In a drug interaction study, administration of an extended release guanfacine in combination with lisdexamfetamine dimesylate induced a 19% increase in guanfacine maximum plasma concentrations, whereas, exposure (area under the curve; AUC) was increased by 7%. These small changes are not expected to be clinically meaningful. In this study, no effect on dexamfetamine exposure was observed following co administration of extended release guanfacine and lisdexamfetamine dimesylate.

Extended release venlafaxine: In a drug interaction study, administration of 225 mg extended release venlafaxine, a CYP2D6 substrate, in combination with 70 mg lisdexamfetamine dimesylate induced a 9% decrease in the Cmax and 17% decrease in the AUC for the primary active metabolite o-desmethylvenlafaxine and a 10% increase in Cmax and 13% increase in AUC for venlafaxine. Dexamfetamine may be a weak inhibitor of CYP2D6. Lisdexamfetamine has no effect on the AUC and Cmax of the composite of venlafaxine and o-desmethylvenlafaxine. These small changes are not expected to be clinically meaningful. In this study, no effect on dexamfetamine exposure was observed following co-administration of extended release venlafaxine and lisdexamfetamine dimesylate.

In vitro enzyme inhibition

In vitro experiments with human microsomes indicate minor inhibition of CYP2D6 by amfetamine and minor inhibition of CYP1A2, 2D6, and 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.

Agents and conditions that alter urinary pH and impact the urinary excretion and half-life of amfetamine

Ascorbic acid and other agents and conditions (diets high in fruits and vegetables, urinary tract infections and vomiting) that acidify urine increase urinary excretion and decrease the half-life of amfetamine. Sodium bicarbonate and other agents and conditions (thiazide diuretics, diets high in animal protein, diabetes, respiratory acidosis) that alkalinise urine decrease urinary excretion and extend the half-life of amfetamine.

Monoamine oxidase inhibitors

Amfetamine should not be administered during or within 14 days following the administration of monoamine oxidase inhibitors (MAOI) because it can increase the release of norepinephrine and other monoamines. This can cause severe headaches and other signs of hypertensive crisis. A variety of toxic neurological effects and malignant hyperpyrexia can occur, sometimes with fatal outcomes.

Agents whose effects may be reduced by amfetamines

Antihypertensives: Amfetamines may decrease the effectiveness of guanethidine or other antihypertensive medications.

Agents whose effects may be potentiated by amfetamines

Amfetamines potentiate the analgesic effect of narcotic analgesics.

Agents that may reduce the effects of amfetamines

Chlorpromazine: Chlorpromazine blocks dopamine and norepinephrine receptors, thus inhibiting the central stimulant effects of amfetamines.

Haloperidol: Haloperidol blocks dopamine receptors, thus inhibiting the central stimulant effects of amfetamines.

Lithium carbonate: The anorectic and stimulatory effects of amfetamines may be inhibited by lithium carbonate.

Use with alcohol

There are limited data on the possible interaction with alcohol.

Drug/laboratory test interactions

Amfetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amfetamine may interfere with urinary steroid determinations.

Fertility, pregnancy and lactation

Fertility

The effect of lisdexamfetamine dimesylate on human fertility has not been investigated.

Pregnancy

There are no adequate and well controlled studies of lisdexamfetamine dimesylate in pregnant women. Dexamfetamine, the active metabolite of lisdexamfetamine, crosses the placenta.

The physician should discuss treatment with female patients who have started menstruation. Lisdexamfetamine dimesylate should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus.

Breast-feeding

Amfetamines are excreted in human milk. Lisdexamfetamine dimesylate should not be used during breast-feeding.

RESPONSIBILITIES AND ROLES

Primary care

Primary care physician to reply to the request from secondary care for shared care as soon as possible taking into

account the extent of the care they are asked to be involved in eg. prescribing of lisdexamfetamine dimesylate, monitoring of treatment and/or patient's condition.

If in agreement, the primary care physician is to prescribe lisdexamfetamine dimesylate at the dose at which the patient has been stabilised after communication with the secondary care specialist.

Primary care physician to ensure a full understanding of their responsibilities for managing patients with ADHD on lisdexamfetamine dimesylate, including side-effects in line with the SPC.

Primary care physician to report to and receive advice from the secondary care specialist on any aspect of patient care that is of concern.

Primary care physician to refer the patient back to the secondary care specialist if the patient's condition deteriorates and/or they experience any adverse events. Particular attention should be paid to symptoms of:

- Abuse and misuse (eg. severe dermatoses, insomnia, irritability, hyperactivity, personality changes)
- Psychosis or mania; aggressive behaviour
- Exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease
- Tics
- Seizures

Primary care physician to report to the secondary care specialist immediately if the patient is pregnant or thinks they may be pregnant.

Primary care physician to ensure that monoamine oxidase inhibitors (MAOI) are not taken with lisdexamfetamine dimesylate. Caution is to also be exercised when considering prescribing:

- Extended- release guanfacine, extended-release venlafaxine, ascorbic acid and other agents that acidify urine, sodium bicarbonate and other agents that alkalinise urine, antihypertensives, narcotic analgesics, chlorpromazine, haloperidol, lithium carbonate. (For more information please refer to the SPC.)

Primary care physician to check that the patient is attending their six monthly specialist ADHD clinics and thus continued prescription is required.

Primary care physician to report any adverse events to the specialist and the MHRA - http://yellowcard.mhra.gov.uk/. Lisdexamfetamine dimesylate is a black triangle product.

Secondary care - specialist

Secondary care specialist to confirm diagnosis of ADHD according to DSM-IV criteria or the guidelines in ICD-10 based on a complete history and evaluation of the patient.

Lisdexamfetamine dimesylate is indicated when response to previous methylphenidate treatment is considered clinically inadequate. Secondary care specialist to assess response to methylphenidate treatment in consultation with the parent/carer/patient. It may include but is not limited to:

- the continued presence of some residual symptoms
- inadequate duration of action
- inconsistent day-to-day symptom control

Secondary care specialist to confirm absence of:

- Hypersensitivity to sympathomimetic amines or any of the excipients listed in the Summary of Product Characteristics (SPC)
- Concomitant use of monoamine oxidase inhibitors (MAOI) or within 14 days after MAOI treatment (hypertensive crisis may result)
- Hyperthyroidism or thyrotoxicosis
- Agitated states
- Symptomatic cardiovascular disease
- Advanced arteriosclerosis
- Moderate to severe hypertension
- Glaucoma

Secondary care specialist to establish if patient drives or operates machinery and advise accordingly.

Prior to prescribing, secondary care specialist to:

- Conduct baseline evaluation of cardiovascular status (including blood pressure and heart rate)
- Document concomitant medications, past and present co-morbid medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death
- Record pre-treatment height and weight on a growth chart
- Consider the potential for abuse, misuse or diversion

Secondary care specialist to initiate lisdexamfetamine dimesylate for the licensed indication in accordance with the Summary of Product Characteristics (SPC). (Treatment must be initiated under the supervision of an appropriate specialist in childhood and/or adolescent behavioural disorders.)

Dose to be titrated according to the therapeutic needs and response of the patient.

- Starting dose (for all patients) = 30mg taken once daily in the morning (avoid afternoon doses because of risk of insomnia)
- Dose may be increased by 20mg increments, at approximately weekly intervals
- Maximum recommended dose = 70mg/day
- In the event of a missed dose, dosing can resume the next day

Treatment must be stopped if symptoms do not improve after appropriate dosage adjustment over a 1-month period. If paradoxical aggravation of symptoms or other intolerable adverse events occur dosage should be reduced or discontinued.

Secondary care specialist to follow local policy on notifying professionals responsible for the childs development. Where appropriate, parents/carers and class teachers are to be given information about lisdexamfetamine dimesylate, for example, monitoring the effects and side effects of treatment.

Secondary care specialist to discuss with the parent/carer/patient the benefits and possible common and uncommon side-effects of lisdexamfetamine dimesylate as listed in the patient information leaflet. Special attention should be

paid to notifying the doctor immediately if the patient experiences:

- Changes to their mood or how they feel (psychiatric status)
- Any problems with their heart chest pains, palpitations, shortness of breath (cardiovascular status)

Secondary care specialist to provide parent/carer (patient) with lisdexamfetamine dimesylate patient information leaflet.

Secondary care specialist to review patient weekly / fortnightly after initiation of lisdexamfetamine dimesylate to assess for effectiveness and tolerability. Further follow up should then take place in the specialist led clinic every 6 weeks until patient is demonstrably stable on medication that is, free from significant side-effects and has consistent day-to-day control of symptoms. Once patient is stablised for a period of three months, secondary care specialist to review patient every 6 months thereafter.

Treatment must be stopped if symptoms do not improve after appropriate dosage adjustment over a 1-month period. If paradoxical aggravation of symptoms or other intolerable adverse events occur dosage should be reduced or discontinued.

Secondary care specialist to only consider transferring prescribing responsibility to primary care following initial dose titration and when the patient has been stabilised on medication free from significant side-effects and consistent day-to-day control of symptoms for a period of 3 months.

Whilst the patient is under the care of the general practitioner, the secondary care specialist is to continue to review the patient every 6 months and advise the general practitioner if subsequent dose adjustments are required or in the event of adverse reactions.

Secondary care specialist to discuss and agree with the patient's GP the possibility of a shared care arrangement for management of the patient's clinical condition with lisdexamfetamine dimesylate. They are to inform the GP that a draft document setting out a possible shared care arrangement for their agreement will be provided.

Secondary care specialist to ensure that arrangements are in place for GP to obtain advice and support where needed and respond promptly when issues arise, eg. adverse events, deterioration in condition, pregnancy.

Secondary care specialist to review the patient at least every 6 months and monitor the patients growth, psychia tric, and cardiovascular status:

- Blood pressure and pulse to be recorded on a centile chart at each adjustment of dose and at least every six months
- Height, weight, and appetite to be recorded at least six-monthly with maintenance of a growth chart
- Development of de novo or worsening of pre-existing psychiatric disorders to be monitored at every adjustment of dose and then at least every six months and at every visit
- Patients to be monitored for the risk of diversion, misuse, and abuse

If the patient is under a shared care agreement, a letter/email should be sent to the GP after each clinic visit notifying the GP of any changes in medication regime, adverse effects and results of the patients routine monitoring.

If considered appropriate, secondary care specialist to give patient (parent/carer) a copy of the shared care agreement to give to their community pharmacist.

Secondary care specialist to report any adverse events to the MHRA - http://yellowcard.mhra.gov.uk/.

Lisdexamfetamine dimesylate is a black triangle product.

Patient's role (or that of parent/carer)

Parent/carer (patient) to notify the specialist or GP of any other medication being taken, including over-the-counter products.

Parent/carer (patient) to share any concerns in relation to treatment with lisdexamfetamine dimesylate and report if he/she does not have a clear understanding of the treatment.

Prior to taking lisdexamfetamine dimesylate, parent/carer to notify the GP or secondary care specialist if patient:

- is taking a medicine called a monoamine oxidase inhibitor (MAOI) used for depression, or has taken an MAOI in the last 14 days
- has a thyroid problem
- feels unusually excited, over-active, or un-inhibited
- has ever had heart problems, high blood pressure or increased pressure in the eye (glaucoma)
- has ever abused prescription medicines or street drugs
- has had kidney problems
- has had fits (seizures, convulsions, epilepsy) or any abnormal brain scans (EEGs)
- has started periods girls only
- has hard-to-control and repeated twitching of any parts of the body or he/she repeats sounds and words
- has a mental health problem
- drives a vehicle or operates machinery

Patient (parent/carer) to present rapidly to the GP or secondary care specialist should their condition significantly worsen or they experience any adverse reactions, particularly if:

- Their mood or how they feel changes
- They feel any problems with their heart chest pains, palpitations, shortness of breath

Parent/carer (patient) to respond in timely manner to specialist recall for appointment for six monthly review.

Patient / carer to notify the specialist or GP if the patient becomes pregnant, thinks she is pregnant, or is planning to have a baby.