NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Shared Care Guideline

Dexamfetamine – Excessive sleepiness associated with narcolepsy

Executive Summary

- **Narcolepsy is a chronic, debilitating, life-long neurological disease characterised by excessive daytime sleepiness (EDS) in all patients.**
- **Dexamfetamine** is licensed for this indication. It is initiated by a Consultant Sleep Physician in the tertiary referral centre at Royal Papworth Hospital for patients following a diagnosis of narcolepsy.
- The usual starting dose is 10mg daily, given in divided doses, and dosage may be increased if necessary, by 10mg a day at weekly intervals to a suggested maximum of 60mg daily.
- **In elderly:** the recommended starting dose is 5mg daily, and increase by increments of 5mg at weekly intervals.
- **Efficacy Monitoring:** Specific monitoring for efficacy will be carried out by tertiary care on a regular basis.
- **If a patient fails to respond to dexamfetamine therapy**, this treatment will be stopped and patient reviewed for other treatment options.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document here.

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found here.

1. Scope

Cross boundary: Trust and general practice

2. Aim

To provide guidance in the prescribing and use of dexamfetamine for managing patients with a diagnosis of narcolepsy (with/without cataplexy).

3. Introduction

- Narcolepsy occurs in 1 in 2500 subjects and is a chronic, debilitating, life-long neurological disease characterised by excessive daytime sleepiness with peak incidence during the second and third decades of life.

- Narcolepsy may progress to include cataplexy (sudden loss of muscle tone), sleep paralysis, hypnagogic hallucinations and fragmented nocturnal sleep. Excessive, uncontrollable daytime sleepiness is experienced by all patients with narcolepsy, and is usually treated with stimulants such as dexamfetamine during the day to help keep patients awake

- Dexamfetamine Sulfate is used (licensed indication) for the treatment of narcolepsy in adult patients with or without cataplexy. At Papworth Hospital, Tertiary referral centre for sleep disorders, dexamfetamine is used to manage symptoms of narcolepsy, particularly excessive daytime sleepiness.The recommendation to start treatment will be made only by a specialist Consultant who will initiate dexamfetamine treatment.

- Dexamfetamine should only be used in patients who have had a complete evaluation of their excessive sleepiness and in whom a diagnosis of narcolepsy has been made in accordance with diagnostic criteria. Such an evaluation usually consists of, in addition to the patient's history, sleep measurement testing in a laboratory setting and exclusion of other possible causes of the observed hypersomnia.

4. Abbreviations

- CCG = Clinical Commissioning Group
- EDS = Excessive Daytime Sleepiness
- MAO = Mono Amine Oxidase
- NMS = Neuroleptic Malignant Syndrome
- RSSC = Respiratory Support and Sleep Centre

5. Dose and Administration

- Dexamfetamine is provided as 5 mg tablets

- The initial dose is usually 5 mg twice daily, with the first dose on rising and the second dose at lunchtime. The dose is then typically escalated by adding 5 to 10 mg per week until symptoms are controlled or 60 mg daily in divided doses is reached.

- The tablets may be swallowed whole with the aid of liquids, or alternatively, in cases of swallowing problems the tablets can be divided. The tablet score lines

enable division of the tablet into four parts. For division, the tablet is placed onto a hard surface with its cross- scored, convex side downwards and is then pushed carefully with the index finger at the centre of its top side. The tablet then breaks into four parts. Drinking some fluids, e.g. water, should follow the intake of the divided tablets.

- The effect of food on the absorption of dexamfetamine tablets has not been studied; therefore, a possible effect of food on absorption cannot be excluded. Hence, it is recommended that dexamfetamine tablets should be taken in a standardised manner in relation to the timing of meals, i.e. that doses should be given at the same times, relative to the time of meals, on each day, preferably with or immediately after meals.

Pre-treatment screening:

- Prior to prescribing, it is necessary to conduct a baseline evaluation of the patient's cardiovascular status including blood pressure and heart rate. A comprehensive history should document concomitant medications, past and present co-morbid medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death and accurate recording of pre-treatment height and weight

Cardiovascular status:

- Patients who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden cardiac or unexplained death or malignant arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further specialist cardiac evaluation if initial findings suggest such history or disease.
- Patients who develop symptoms such as palpitations, exceptional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of cardiac disease during dexamfetamine treatment should undergo a prompt specialist cardiac evaluation.
- Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded during dose titration and then at least every 6 months.
- Treatment with stimulants in general may lead to a minor increase in blood pressure (approx. 2-4 mm Hg) as well as an increase in heart rate (approx. 3-6 beats/minute).
  In a few patients, these values may be higher.
- Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate.
- The use of dexamfetamine is contraindicated in certain pre-existing cardiovascular disorders unless specialist cardiac advice has been obtained.
- In patients with *Pre-existing structural cardiac abnormalities:* Sudden death has been reported in association with the use of stimulants of the central nervous system at usual doses in children with structural cardiac abnormalities. Although some structural cardiac abnormalities alone may carry an increased risk of sudden death, stimulant products are not recommended in children, adolescents, or adults with known structural cardiac abnormalities.

Blood pressure should be monitored at appropriate intervals in all patients taking dexamfetamine, especially those with hypertension.

Psychiatric adverse events:

- Administration of stimulants may exacerbate symptoms of behaviour disturbance and thought disorders in patients with a pre-existing psychotic disorder.
- Particular care should be taken in using stimulants in patients with comorbid bipolar disorder because of concern for possible induction of a 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.
- Treatment emergent psychotic or manic symptoms, e.g. hallucinations, delusional thinking or mania in children or adolescents without a 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.

Special Populations:

- The safety and efficacy of dexamfetamine has not been established in children under the age of 6 years, and therefore it should not be used in this age group.

Epileptic patients:

- Should be used with caution in patients with epilepsy.
- It may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in the absence of seizures, and rarely in patients without a history of convulsions and no EEG abnormalities. If seizure frequency increases or new-onset seizures occur, dexamfetamine should be discontinued.

Pregnancy and Breast Feeding:

- Contra-indicated in pregnancy and breast feeding.

Availability:

- Dexamfetamine is available generically as 5mg tablets.

Further information can be found in the Summary of Product Characteristics:
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1516944577338.pdf

6. Adverse Effects

Very common (≥ 1 in 10)

- Decreased appetite, reduced weight gain and weight loss during prolonged use in children.

Common (≥ 1 in 100 and < 1 in 10)

- Arrhythmia

- Palpitations
- Tachycardia
- Abdominal pain and cramps, nausea, vomiting, and dry mouth (These effects usually occur at the beginning of treatment and may be alleviated by concomitant food intake)
- Changes in blood pressure and heart rate (usually increases)
- Arthralgia
- Vertigo, dyskinesia, headache, hyperactivity
- Abnormal behaviour, aggression, excitation, anorexia, anxiety, depression, irritability.

Rare (≥ 1 in 10000 and < 1 in 1000)

- Difficulties in visual accommodation, blurred vision, mydriasis
- Growth retardation during prolonged use in children
- Rash, urticarial
- Fatigue
- Angina pectoris.

Very Rare (<1/10,000)

- Anaemia, leukopenia, thrombocytopenia, thrombocytopenic purpura
- Cardiac arrest
- Tourette's syndrome
- Abnormal liver function ranging from hepatic enzyme elevations to hepatic coma
- Muscle cramps
- Convulsions, choreoathetoid movements, intracranial haemorrhage
- Hallucinations, psychosis / psychotic reactions, suicidal behaviour (Including completed suicide), tics, worsening of pre-existing tics
- Erythema multiforme, exfoliative dermatitis, fixed drug eruption
- Cerebral vasculitis and/or occlusion
- Cases of neuroleptic malignant syndrome (NMS) were observed. However, these reports were poorly documented and in most cases, patients were also receiving other medicinal products. Thus, the role of dexamfetamine in the development of NMS is unclear.

Not known (cannot be estimated from the available data)

- Cardiomyopathy, myocardial infarction
- Ischaemic colitis, diarrhoea
- Chest pain, hyperpyrexia, fatigue, sudden death
- Hypersensitivity including angioedema and anaphylaxis
- Acidosis
- Rhabdomyolysis
- Ataxia, dizziness, dysgeusia, concentration difficulties, hyperreflexia, stroke, tremor
- Confusion, dependence, dysphoria, emotional lability, euphoria, impaired cognitive test performance, altered libido, night terrors, obsessive-compulsive behaviour, panic states, paranoia, restlessness
- Renal damage

- Impotence
- Sweating, alopecia
- Cardiovascular collapse.

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1514526174825.pdf

7. Cautions

- To be used with caution in patients on guanethidine and patients with mild hypertension or a family history of dystonias. If tics develop, treatment with dexamfetamine should be discontinued.

- Caution should be used when administering dexamfetamine to patients with impaired kidney function or unstable personality.

- Drug dependence, with consumption of increasing doses to levels many times those
recommended, may occur as tolerance develops. At such levels, a psychosis which may be clinically indistinguishable from schizophrenia can occur.

- Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression.

- Due to the potential decreased appetite associated with dexamfetamine use, caution is advised in the presence of anorexia nervosa

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1514526174825.pdf

8. Contraindications

- 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 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, glaucoma, porphyria or hyper excitability.
- Patients with Gilles de la Tourette syndrome or similar dystonias.
- Dexamfetamine sulphate tablets include lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Dexamfetamine sulphate tablets include sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

9. Interactions

- Adrenoreceptor blocking agents (e.g. propanolol), lithium and α methyltyrosine may antagonise the effects of dexamfetamine. Disulfiram may inhibit metabolism and excretion.
- The concurrent use of tricyclic antidepressants may increase the risk of cardiovascular side effects.
- Concurrent use of MAOI's or use within the preceding 14 days may precipitate a hypertensive crisis.
- Concurrent use of beta-blockers may result in severe hypertension and dexamfetamine may result in diminished effect of other anti-hypertensives such as guanethidine.
- Phenothiazines may inhibit the actions of dexamfetamine.
- Amfetamines may delay the absorption of ethosuximide, phenobarbital and phenytoin.
- Acute dystonia has been noted with concurrent administration of haloperidol.
- Haloperidol blocks dopamine and norepinephrine re-uptake, thus inhibiting the central stimulant effects of amfetamines.
- The analgesic effect of morphine may be increased and its respiratory depressant effects decreased with concurrent use of morphine and dexamfetamine.
- Amfetamines potentiate the analgesic effects of meperidine.
- Concomitant administration of clonidine and dexamfetamine may result in an increased duration of action of dexamfetamine.
- Gastrointestinal acidifying agents (guanethidine, reserpine, glutamic acid HCl, ascorbic acid, fruit juices, etc.) lower absorption of dexamfetamine.

- Urinary acidifying agents (ammonium chloride, sodium acid phosphate, etc.) increase urinary excretion of dexamfetamine. Both groups of agents lower blood levels and efficacy of dexamfetamine.
- Gastrointestinal alkalizing agents (sodium bicarbonate, etc) increase the absorption of amfetamines.
- Urinary alkalizing agents (acetazolamide, some thiazides) increase the concentration of the non-ionized species of the amfetamine molecule, thereby decreasing urinary excretion. Both groups of agents increase blood levels and efficacy of amfetamines.
- Alcohol may exacerbate the CNS adverse reactions of psychoactive drugs, including dexamfetamine. It is therefore advisable for patients to abstain from alcohol during treatment.
- Chlorpromazine blocks dopamine and norepinephrine re-uptake, thus inhibiting the central stimulant effects of amfetamines, and can be used to treat amfetamine poisoning.

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1514526174825.pdf

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

- Laboratory tests are not required to monitor patient response to dexamfetamine administration
- Tachycardia and hypertension are potential adverse effects. Dexamfetamine should not be prescribed if the diastolic blood pressure is 100 mmHg or greater before treatment. The blood pressure should be monitored at appropriate intervals in all patients especially those with hypertension.
- Blood pressure should be monitored at appropriate intervals in all patients taking dexamfetamine, especially those with hypertension
- Patients should be advised that dexamfetamine is not a replacement for sleep and good sleep hygiene should be maintained. Steps to ensure good sleep hygiene may include a review of caffeine intake.

11. Shared Care Responsibilities

a. Hospital specialist:

The patient will be assessed by a consultant in the tertiary referral centre. If the patient is in agreement with the treatment plan then the hospital will undertake to:

- Send a letter to the GP requesting shared care for the patient.

- Evaluate patients for a history of drug abuse and account for any additional risks in these patients
- Provide information to the patient regarding the medicine
- Provide an initial one month supply of dexamfetamine tablets.
- Recommend an initial dose and how this may be titrated according to the response to treatment.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Inform GP of patients who do not attend clinic appointments and discuss patient's on-going treatment plan.
- Review the patient's progress on treatment. If the patient has failed to respond to treatment after a reasonable period then dexamfetamine therapy will be discontinued and other treatment options considered.
- Be available for advice to the general practitioner.
- Answer patient/carer enquiries on any aspect of this therapy.

b. General Practitioner:

- Agreement to shared care guideline by the GP.
- Continue to prescribe dexamfetamine once this has been initiated by the RSSC consultant specialist.
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.
- Monitor blood pressure on a regular basis.

c. Patient or parent/carer:

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment. Report any adverse effects to the hospital specialist or GP.
- Share any concerns they have in relation to their treatment.

12. Contact numbers for advice and support

Royal Papworth Hospital NHS Foundation Trust (Respiratory Support and Sleep Centre (RSSC) -Tertiary referral centre)		
Specialist	**Post**	**Telephone** (direct line)
Dr Ian E Smith	Director of RSSC and Consultant Sleep Physician	01480 364164
Dr Tim Quinnell	Consultant Sleep Physician	01480 364174
Dr Mike Davies	Consultant Sleep Physician	01480 364542
Dr Nick Oscroft	Consultant Sleep Physician	01480 364551
Dr M Mason	Consultant Sleep Physician	01480 364165

Mrs Netta Tyler	RSSC Directorate Pharmacist	01480 364762
Pharmacy Medicines Information Service		01480 364179
Pharmacy Medicines Helpline		01480 364739 (answerphone)

13. Equality and Diversity Statement

This document complies with the Royal Papworth Hospital NHS Foundation Trust service Equality and Diversity statement.

14. Disclaimer

It is your responsibility to check that this printed out copy is the most recent issue of this document.

15. Document Management

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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1514526174825.pdf