Dexamfetamine for ADHD Children and Young People

Part of the shared care protocol for ADHD in Children and Young People
Traffic light classification- AMBER 1
Information sheet for Primary Care Prescribers

Licensed Indications

Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 to 17 who are under the care of a specialist (Consultant Psychiatrist, Community Paediatrician or Non-Medical Prescriber specializing in ADHD) as part of a comprehensive treatment program when response to previous methylphenidate treatment is considered clinically inadequate[1]. It is recommended by NICE for patients whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile[2].

Any patient groups to be excluded from shared care

Patients ≥ 18 years old – see separate Nottinghamshire APC shared care protocol and medication information sheets for adult ADHD
Children < 6 years old – unlicensed, not recommended by NICE[2]

Therapeutic Summary

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 noradrenaline and dopamine into the presynaptic neuron and increase the release of these monoamines into the extra neuronal space.

Medicines Initiation

NICE guidance (2018), suggests considering dexamfetamine for children aged 5 years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile. Treatment with dexamfetamine should only be initiated by a specialist with expertise in ADHD following a comprehensive assessment and diagnosis[2]. NICE recommend that GPs should continue prescribing and monitoring medication treatment under shared care arrangements[2].

Products available

Dexamfetamine tablets (Amfexa), 5mg, 10mg, 20mg (30 tablets - £19.89, £39.78, £79.56 respectively[3]). Generic tablets also available.

Dexamfetamine is a Schedule 2 Controlled Drug (CD). As such, prescriptions must conform to specific CD prescription writing criteria and each prescription should be for no longer than 30 days treatment.

Dosages and route of administration

The recommended starting daily dose is 5 mg once or twice daily (e.g. at breakfast and lunch), increasing if necessary by weekly increments of 5 mg in the daily dose according to tolerability and degree of efficacy observed. The maximum daily dose in children and adolescents is usually 20mg, although doses of 40mg may in rare cases be necessary`. The decision to give Amfexa once or twice daily should be based on the course of symptoms at different times of the day.

The tablets may be swallowed whole with the aid of liquids, or alternatively, in cases of swallowing problems the tablets can be divided.
Dosage may be altered by specialists to reflect the child's current physical condition, symptoms or social demands. The patient should require no extra monitoring than already described in this guidance if dosage is adjusted by the specialist in this way.
As a child grows, the dose of dexamfetamine will need to be amended to ensure the treatment remains at steady state. A patient's weight and height should be monitored as described under "Ongoing monitoring", and dosage may be increased if required as per the section above; "dosage and route of administration". Increases in medication dose due to growth of the patient should be viewed as a patient's treatment being "stable".

Where a patient has been switched between medications (i.e. lisdexamfetamine to dexamfetamine) further monitoring may be required, as per specialist instruction.

Duration of treatment
Following an adequate treatment response, medication treatment for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least annually by the specialist[2].

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood[2]. It is the specialist's responsibility to transfer care to the appropriate adult service if ADHD treatment is deemed appropriate to continue into adulthood. See the Nottinghamshire Area Prescribing Committee shared care protocol and medication information sheets for adult ADHD at: https://www.nottsapc.nhs.uk/shared-care/.

Monitoring Requirements and Responsibilities
Pre-treatment assessment to be performed by specialist and will include:
Behavioural rating scales (e.g. SDQ, Conners') and descriptive reports from parents and teachers, medical history, physical examination (including height and weight) and evaluation of cardiovascular status (including heart rate, blood pressure) as a baseline.

For children where there is a first degree relative who has suffered from severe cardiac disease (e.g. myocardial infarction, arrhythmia) or sudden death of unknown cause before the age of 40 years, or in children who have a history of cardiac disease themselves, these patients should have further cardiac screening in the form of an ECG and echocardiogram. Cardiology expertise may be required in deciding if it is safe to start medication.

Ongoing monitoring – monitoring will be performed by the specialist within the first 3 months. Further physical monitoring will be performed by primary care (see below) and the results sent to the specialist for recording in the patients notes. Ongoing psychological response and assessment of continued need for dexamfetamine will be performed by the specialist at 3 months and 6 months and then at least annually.

If the child / young person fails to attend for physical monitoring, despite attempts to re-appoint, do not issue any further prescriptions, contact the patient/carer and inform the specialist. The patient should be informed of this policy when treatment begins.

Ongoing monitoring[2]	Frequency[2]
Heart Rate and Blood Pressure	Six monthly.

	Also before and after each dose change (note that increases in dose due to growth should be viewed as a patient being "stable" on their medication, and should require no extra monitoring). Compare with previous measurements. Information on blood pressure and heart rate monitoring in children (including centile reference tables) is available on the Nottinghamshire Area Prescribing Committee website.[6] Refer to paediatric hypertension specialist if blood pressure is consistently above the 95th centile for age and height.
Weight and appetite	Following initiation, at three months and six months, then: • Every 3 months in children 10 years and under. • Every 6 months in children over 10 years and young people Plot on a growth chart (link: http://www.rcpch.ac.uk/growthcharts). If weight loss or reduced weight gain this should be discussed with the specialist.
Height	Six monthly. Plot on a growth chart. If growth is affected significantly this should be discussed with the specialist.
Medication related side-effects*	At each visit.
Risk of diversion, misuse/abuse	At each visit
ECG, LFTs, FBC	Not recommended unless there is a clinical indication.

Explicit criteria for review and discontinuation of dexamfetamine

- 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.
- In the event of treatment emergent psychotic or manic symptoms (hallucinations, delusional thinking, mania without prior history), consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate.
- In the presence of new onset or worsening seizures the dexamfetamine should be discontinued.

For a full list of Side Effects refer to the BNF/BNFC or Summary of Product Characteristics (SPC)[1].

IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE SPECIALIST TEAM.

Contraindications

- Hypersensitivity to dexamfetamine
- Hypersensitivity to sympathomimetic amines or any of the excipients
- Concomitant use of MAOIs or within 14 days of MAOI treatment
- Phaeochromocytoma
- Hyperthyroidism or thyrotoxicosis
- Agitated states
- Symptomatic cardiovascular disease
- Advance arteriosclerosis
- Moderate to severe hypertension
- Glaucoma
- Severe depression, anorexic disorders, suicidal ideation, psychotic symptoms, uncontrolled bipolar disorder, schizophrenia
- Cerebrovascular events
- Gilles de la Tourrettes

Precautions

- Stimulants have a potential for abuse, misuse, dependence, or diversion for non-therapeutic uses that physicians should consider when prescribing the product. Use caution in prescribing to patients with a history of substance abuse or dependence.
- Sudden death has been reported in children and adolescents taking CNS stimulants, including those with structural cardiac abnormalities or other serious heart problems. Not for use in children or adolescents with 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 of a stimulant medication.
- Stimulants may exacerbate symptoms of behaviour disturbance and thought disorder in patients with pre-existing psychotic disorders.
- Particular care should be taken in treating ADHD patients with comorbid bipolar disorder because of concern for possible induction of mixed/manic episodes in such patients.
- Treatment emergent pyschotic or manic symptoms can be caused by stimulants at usual doses. If these occur, consider the potential role of the stimulant, and discontinuation of treatment may be appropriate.
- Stimulants have been associated with a slowing of weight gain and a reduction in attained height. Monitor growth during treatment with stimulants.
- Stimulants may lower the convulsive threshold in patients with prior history of seizure. In the presence of new onset or worsening seizures the medication should be discontinued.
- Due to reduced' clearance 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.

Pregnancy and Breastfeeding[1]

There is a limited amount of data from the use of dexamfetamine in pregnant women. Children of mothers who are dependent on amfetamine have been shown to be at an increased risk of premature birth and reduced birth weight. Results of studies in animals suggest that high doses of dexamfetamine may elicit reproductive toxicity; the use during pregnancy is not recommended[4].

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

Amfetamines are excreted in breast milk and should not be used in those who are breastfeeding[4].

Clinically relevant medicine interactions and their management[1]

- Monoamine Oxidase Inhibitors (MAOIs) including isocarboxazid, moclobemide, phenelzine and tranylcypromine - dexamfetamine should not be used in combination with MAOIs or within 2 weeks of stopping a MAOI due to risk of hypertensive crisis.
- Anticonvulsants: dexamfetamine may increase plasma levels of phenytoin and possibly primidone and phenobarbital.
- Coumarins: dexamfetamine may enhance the anticoagulant effect of warfarin. May require an increased frequency of INR monitoring.
- Dexamfetamine may enhance the effect of some antidepressants (SSRIs and tricyclics).
- Agents that may reduce the effects of dexamfetamine: chlorpromazine, haloperidol and lithium carbonate.
- 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.
- 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.

Information Given to Patient

- The specialist will provide relevant, written information to people with ADHD and their families and carers about diagnosis, assessment, support groups, self-help, psychological treatment, medication treatment and possible side-effects.
- The patient must be warned to report immediately any abdominal pain, unexplained nausea, malaise, darkening of the urine, jaundice, or suicidal thinking and self-harm to the GP.[2,4]
- An information leaflet for parents and carers is available from Choice and Medication.

Patient Roles and Responsibilities

1. The patient will report any suspected adverse reactions to the GP for assessment.
2. The patient will report to their GP or specialist any new onset nausea, vomiting, abdominal discomfort, dark urine and jaundice as these could be adverse effects of dexamfetamine.
3. The patient will report to their GP or specialist signs of clinical worsening, suicidal thoughts or self-harming behaviour, irritability, psychotic symptoms, agitation, or depression as these can be adverse effects of dexamfetamine.
4. The patient will attend all follow-up appointments with GP and specialist. If they are unable to attend any appointments they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.

Community Pharmacist Roles and Responsibilities

Community pharmacists are well placed to stress the value of a balanced diet, good nutrition and regular exercise for all patients with ADHD. Community pharmacists can offer support to help improve treatment adherence in patients with ADHD.

References

1. Amfexa 5mg, 10mg, 20mg tablets, Flynn Pharma Ltd. Summary of product characeteristics [07/2016] available at https://www.medicines.org.uk/emc/product/7403/smpc, accessed 02.12.2019
2. Attention deficit hyperactivity disorder: Diagnosis and management. NICE Clinical Guideline 87 (March 2018). Available: http://www.nice.co.uk/guidance/ng87

3. BNFC Online, Available from https://www.medicinescomplete.com, accessed [02.12.2019]
4. The Electronic Drug Tariff. Available from http://www.ppa.org.uk/ppa/edt_intro.htm [accessed 02.12.2019]
5. Graham J et al. European guidelines on managing adverse effects of medication for ADHD. Eur Child Adolesc Psychiatry (2011),20:17-37. On-line at http://www.springerlink.com/content/y667034856017253/fulltext.pdf
6. Nottinghamshire Area Prescribing Committee. September 2020. Blood pressure and heart rate monitoring in children. Information Sheet for Primary Care Prescribers. Available from https://www.nottsapc.nhs.uk/media/1627/bp_and_hr_monitoring_for_children.pdf.

Version Control - **Children and Young people ADHD - Dexamfetamine 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	April 2021 (interim update)	-Added standard header & version control -Added link to Notts APC guideline on blood pressure and heart rate monitoring in children -Removed link to NUH guideline on blood pressure monitoring in children -Updated information about transition of care and Notts APC adult ADHD shared care protocol -Updated wording of pregnancy&breastfeeding and interactions sections in line with adult information sheet
1.0	Dr Katherine Martin, Dr Amy Taylor (Community Paediatrics, Nottingham University Hospitals) Dr Esther Corker (Community Paediatrics), Sherwood Forest Hospitals Nick Sherwood, Mental Health Interface and Efficiencies Pharmacist, Nottinghamshire CCGs/Nottinghamshire Healthcare NHS Foundation Trust	December 2019	