

Prescribing in attention deficit hyperactivity disorder (ADHD)

In England and Wales over £48 million is spent annually on medicines for attention deficit hyperactivity disorder (ADHD) (ePACT Apr - Jun 2016). Medicines optimisation projects in this area focus on quality of care, by ensuring that medication use is appropriate and safe. This includes ensuring correct monitoring of drug treatment and confirming that it is only continued where it remains clinically necessary and effective. There may also be scope for appropriate cost-effective prescribing of medication. This bulletin reviews the place in therapy of drug treatments for ADHD. It offers guidance and support material for organisations considering reviewing the prescribing of medicines for this condition as a medicines optimisation project.

Recommendations

- A diagnosis of ADHD should only be made after a full clinical and psychosocial assessment by a specialist psychiatrist, paediatrician (children and young people) or other appropriately qualified healthcare professional.
- Primary care practitioners should not make the initial diagnosis or start drug treatment in children or young people with suspected ADHD (a NICE 'Do not do' recommendation).
- ADHD should be considered in all age groups.
- Drug treatment for children, young people and adults with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions (or occupational needs in the case of adults).
- If prescribing under shared care agreements, ensure it is clear where responsibility for prescribing lies so patients are not prescribed treatments more than once.
- Drug treatment is not recommended for:
 - » Pre-school children (a NICE 'Do not do' recommendation).
 - » First-line treatment for school-age children and young people with moderate impairment (a NICE 'Do not do' recommendation). It should be reserved for those who have refused or responded insufficiently to non-drug interventions.
- Drug therapy should be the first-line treatment for:
 - » School-age children and young people with severe ADHD (hyperkinetic disorder) and severe impairment. Parents should also be offered a training/education programme.
 - » Adults with either moderate or severe impairment, unless the person would prefer a psychological approach.
- If there is a choice of more than one appropriate drug, the product with the lowest cost should be prescribed.
- Policy makers should consider the cost difference in primary care of the various modified release methylphenidate preparations when making formulary decisions.
- Atomoxetine has a flat pricing structure (most of the available strengths cost the same per capsule). The desired dosage should be given using the fewest number of capsules to maximise cost-effectiveness.

- Following an adequate treatment response, drug treatment should be continued for as long as it remains clinically effective. The need for continued drug treatment should be reviewed at least annually.
- Dietary supplementation with polyunsaturated fatty acids (PUFAs) is not recommended (a NICE 'Do not do' recommendation).
- Young people with ADHD should normally be transferred to adult services if they continue to have significant symptoms that require treatment. In some areas there is a need to address gaps in service provision for adults with ADHD.
- Side effects resulting from drug treatment for ADHD should be routinely monitored and documented. Clarity regarding responsibility for drug monitoring is essential. GP practices need robust systems to ensure monitoring is carried out and highlight where it has been missed.
- ADHD medicines cause side-effects that can affect a person's ability to drive. People should be advised not to drive until they are reasonably certain that their performance is not affected by the medicine.
- It is an offence to drive with more than a specified amount of amphetamines (e.g. dexamfetamine, lisdexamfetamine) in the body. Provided driving is not impaired, a 'statutory defence' to avoid prosecution can be raised if the medication was prescribed and has been taken as advised.
- Before prescribing ADHD medication the risk of substance misuse and drug diversion should be assessed.
- Methylphenidate, dexamfetamine and lisdexamfetamine are schedule 2 controlled drugs. Prescribers should be familiar with the requirements of controlled drug legislation governing their prescription and supply.
- Different versions of methylphenidate modified-release preparations can have different release profiles and may not have the same clinical effect. Prescribers should specify the brand to be dispensed.

Background

ADHD is a common neurodevelopmental disorder characterised by inappropriate levels of activity and impulsivity and an impaired ability to sustain attention.¹ Those affected have difficulty regulating their activities to conform to expected norms, and often fail to achieve their potential. Many have comorbid difficulties such as developmental delays, specific learning problems and other emotional and behavioural disorders. Severe ADHD may be diagnosed as hyperkinetic disorder, which is characterised by a more severe disturbance with significant hyperactivity.²

Although ADHD begins in childhood, research has shown that it can continue through to adulthood for some. Approximately 15% of children with ADHD retain the diagnosis by age 25. A much larger proportion (65%) are in partial remission, with persistence of some symptoms associated with continued impairment.³ In adults, social and occupational problems can be caused by difficulties in concentrating, paying attention to detail and completing tasks, together with impulsivity and an inability to plan ahead. Moreover, ADHD is commonly associated with mental health, addiction or behavioural problems.³

Treatment for people with ADHD is usually provided across primary and secondary (or tertiary) care. Specialist mental health or paediatric teams provide diagnostic services and initiate/stabilise medications where they are part of the treatment plan. Once stabilised, drug treatment it is often continued in primary care in accordance with locally agreed shared care arrangements.⁴

Psychological interventions

Psychological interventions for children and young people with ADHD can include behavioural interventions and parent training, cognitive training and social skills training. The main aim of these interventions is to improve the daily functioning of the child or young person by improving their behaviour and their family and peer relationships.⁴

Psychological interventions for adults with ADHD are less developed. The focus of research to date has been on cognitive behavioural therapy (CBT). CBT can address developing skills such as to attend, organise and plan.⁴

Licensed medicines for ADHD

Drug therapy in ADHD is used for the control of symptoms but is not curative.⁵ In the UK methylphenidate, atomoxetine, lisdexamfetamine dimesylate and guanfacine are licensed for the management of ADHD in children and young people from the age of six years.⁶⁻¹⁰ Dexamfetamine is licensed for hyperkinetic states from three years of age, although NICE do not recommend drug treatment in pre-school children.^{4,11} Some modified release methylphenidate products are also licensed for use in adults with persisting symptoms, where they were initiated in childhood and showed clear benefit.^{7,12-14} Atomoxetine and lisdexamfetamine dimesylate are both licensed for initiation in adults, where the presence of ADHD symptoms in childhood are confirmed.^{8,15} Guanfacine is licensed for six to 17 year olds for whom stimulants are not suitable. It is not licensed for use in combination with stimulants or for adults with ADHD.¹⁰

Methylphenidate, dexamfetamine and lisdexamfetamine dimesylate are central stimulant drugs. Stimulants act principally on dopamine and noradrenaline reuptake inhibition, and presynaptic release.¹ Lisdexamfetamine dimesylate is a pro-drug of dexamfetamine. It is longer acting than dexamfetamine and is dosed once daily, in contrast to two to four times a day for dexamfetamine.¹⁶ Atomoxetine, a non-stimulant drug, is a selective noradrenaline reuptake inhibitor.¹ Guanfacine is a selective alpha2-adrenergic receptor agonist.¹⁷ It is also a non-stimulant drug and has actions and uses similar to those of clonidine.¹⁸ It was launched in the UK in February 2016 as the prolonged-release product Intuniv®.^{10,17}

Unlicensed medicines

Other medicines that have been used for ADHD include bupropion, clonidine, modafinil and imipramine.⁴ Although all of these drugs are available in the UK, none are licensed for use in ADHD. A modified release mixed amphetamine salt (Adderall®) is licensed in the United States for treating ADHD.² It is not available as a licensed product in the UK. The use of unlicensed medication for ADHD should only be considered in the context of tertiary services, and will not be discussed further here.⁴

Dietary interventions

There has been much interest in dietary interventions as treatments for ADHD. They include supplementing the diet with substances thought to be deficient, such as polyunsaturated fatty acids (PUFAs). Exclusion of substances thought to be harmful, such as artificial colouring and additives, has also been undertaken.⁴ More recently there has been interest in evidence for 'few food' diets. Such diets are a type of restriction/elimination diet, where certain foods are either restricted or removed completely.¹⁹

National guidance

Diagnosis and treatment

NICE have published guidance on the diagnosis and management of ADHD (CG72, September 2008, last updated February 2016) and a Technology Appraisal (TA) on methylphenidate, atomoxetine and dexamfetamine for ADHD in children and adolescents (TA98, March 2006).^{20,21} NICE advise that ADHD should be considered in all age groups, with symptom criteria adjusted for age-appropriate changes in behaviour.²⁰ A diagnosis of ADHD should only be made after a full clinical and psychosocial assessment by a specialist psychiatrist, paediatrician (children and young people) or other appropriately qualified healthcare professional. Primary care practitioners should not make the initial diagnosis or start drug treatment in children or young people with suspected ADHD (a NICE 'Do not do' recommendation).

- For pre-school children parent-training/education programmes are the first-line treatment. Drug treatment is not recommended in this group (a NICE 'Do not do' recommendation).
- For school-age children and young people with moderate impairment parent-training/education

programmes are usually the first-line treatment. CBT and/or social skills training may also be offered. Drug therapy is not indicated as the first-line treatment in this group (a NICE 'Do not do' recommendation). It should be reserved for those who have refused non-drug interventions, or whose symptoms have not responded sufficiently to psychological treatments.

- For school-age children and young people with severe ADHD (hyperkinetic disorder) and severe impairment, drug therapy is the first-line treatment. Parents should also be offered a training/education programme. Other psychological treatment such as CBT and/or social skills training may be offered.
- For adults with either moderate or severe impairment drug therapy should be the first-line treatment unless the person would prefer a psychological approach. Drug treatment should be started only under the guidance of a psychiatrist, nurse prescriber specialising in ADHD, or other clinical prescriber with training in the diagnosis and management of ADHD. CBT may also be considered.

Drug treatment for children, young people and adults with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions (or occupational needs in the case of adults).²⁰

Choice of drug therapy

In children and young people for whom drug treatment is appropriate, NICE recommend methylphenidate, atomoxetine and dexamfetamine as options, within their licensed indications. The decision regarding which product to use should be based on specific criteria, such as the presence of comorbid conditions, outlined in NICE CG72.²⁰ Methylphenidate is generally the first-line choice, followed-by atomoxetine.^{1,22}

Following a decision to start drug treatment in adults with ADHD, methylphenidate should normally be tried first. Atomoxetine or dexamfetamine should be considered in adults unresponsive or intolerant to an adequate trial of methylphenidate (this should usually be about six weeks). Caution should be exercised when prescribing dexamfetamine to those likely to be at risk of stimulant misuse or diversion.²⁰

Prescribers should be familiar with the pharmacokinetic profiles of all the modified-release and immediate-release preparations available for ADHD to ensure that treatment is tailored effectively to the individual.²⁰ Selecting and tailoring treatments will usually be the remit of the specialist.

If there is a choice of more than one appropriate drug, the product with the lowest cost (taking into account the cost per dose and number of daily doses) should be prescribed.²⁰

Antipsychotics are not recommended for the treatment of ADHD in children, young people or adults (a NICE 'Do not do' recommendation).²⁰

Lisdexamfetamine dimesylate and guanfacine

NICE TA98 and CG72 both pre-date the availability of lisdexamfetamine dimesylate and licensed guanfacine in the UK. NICE have published 'Evidence summary: new medicine' documents on both medicines.^{16,17} They state that local decision makers will need to consider the available evidence as well as cost and individual patient factors, when making decisions about using these treatments for ADHD.

The Scottish Medicines Consortium (SMC) have accepted both lisdexamfetamine dimesylate and guanfacine prolonged release for use in NHS Scotland.²³⁻²⁵ The All Wales Medicines Strategy Group (AWMSG) have recommended lisdexamfetamine for use in NHS Wales.^{26,27} However they state that the case for cost-effectiveness for guanfacine has not been proven and they do not recommend its use in NHS Wales.²⁸

Duration of drug therapy

Despite a large body of literature supporting the short-term benefits of stimulant medication in children with ADHD, there is still uncertainty regarding balance of risks and benefits of long-term

drug treatment.⁴ The evidence for long-term benefit of medication beyond symptom control (e.g. improved social functioning, academic achievement and employment status) is limited and inconsistent. Therefore, an individualised approach to clinical decisions about starting, continuing, and stopping of ADHD medication is needed.²⁹

Following an adequate treatment response, NICE advise that drug treatment be continued for as long as it remains clinically effective. The need for continued drug treatment should be reviewed at least annually. This should involve a comprehensive assessment of clinical need, benefits and side effects. The effect of missed doses, planned dose reductions and brief periods of no treatment should be evaluated. NICE state that drug holidays, although not routinely recommended, may be considered.⁴ The Medicines and Healthcare products Regulatory Agency (MHRA) have recommended that methylphenidate treatment be interrupted at least yearly to determine if continuation is needed.^{30,31} This type of comprehensive review will generally remain within the remit of the specialist overseeing the person's care. Primary care prescribers can have a role in ensuring such reviews have taken place.

Dietary interventions

NICE recommend that healthcare professionals stress the value of a balanced diet, good nutrition and regular exercise for children, young people and adults with ADHD. They do not advise elimination of artificial colouring and additives from the diet as a generally applicable treatment. Rather, they advise referral to a dietitian for advice on diet if there is a clear link (from a food diary) between behaviour and a particular type of food or drink. NICE state that there is no evidence about the long-term effectiveness or potential harms of a 'few food' diet for children with ADHD, and only limited evidence of short-term benefits.^{4,19}

Dietary fatty acid supplementation is not recommended for the treatment of ADHD in children and young people (a NICE 'Do not do' recommendation).⁴

Clinical effectiveness

Methylphenidate, atomoxetine and dexamfetamine

NICE undertook a systematic literature search for CG72 to identify randomised controlled trials (RCTs) that assessed the efficacy and/or safety of pharmacological treatments for ADHD. For pre-school children NICE found no evidence that drug treatment is effective in the treatment of ADHD.⁴

Methylphenidate and atomoxetine were found to be the only drugs with clear RCT evidence of clinical effectiveness in reducing ADHD symptoms in school-age children, young people and adults. When compared with placebo, the size of clinical effect was found to be largest for methylphenidate. Two studies that involved head-to-head comparisons of these treatments gave conflicting results.⁴

For CG72 NICE found one small study that indicated a clinical improvement in ADHD symptoms in adults taking dexamfetamine, compared with placebo. No high-quality RCTs investigating dexamfetamine use in children were identified. The recommendation to consider treatment with dexamfetamine in children is based on lower-level evidence from crossover trials.⁴

Since the publication of CG72 a number of Cochrane reviews have been published on drug treatments for ADHD in children and adolescents, and in adults. The conclusions of these reviews are all generally compatible with NICE's recommendations.³²⁻³⁵

Evidence summaries for lisdexamfetamine dimesylate and guanfacine prolonged release can be found in their respective NICE new medicine evidence summaries, available at <https://www.nice.org.uk/advice/esnm19/chapter/key-points-from-the-evidence> and <https://www.nice.org.uk/advice/esnm70/chapter/Key-points-from-the-evidence>

Polyunsaturated fatty acids (PUFAs)

NICE systematically reviewed the literature regarding PUFAs in children and young people with ADHD. They concluded that there was evidence of no clinically important difference between PUFAs

and control in terms of ADHD symptoms and academic performance.¹⁹ A Cochrane review similarly concluded that there is little evidence of benefit for the symptoms of ADHD in this group.³⁶

Transition to adult services

Young people with ADHD receiving treatment and care from child and adolescent mental health services (CAMHS) or paediatric services should normally be transferred to adult services if they continue to have significant symptoms that require treatment. Others that may require access to adult ADHD services include those with significant impairment who either went undiagnosed in childhood, or who were diagnosed in childhood but are not currently receiving treatment.⁴

The transfer between child and adult services occurs at a time of increased vulnerability for the young person, who is likely to be making decisions about their future and experiencing change.³⁷ There is a risk that young people may disengage from treatment if the transition is not smooth and if services are unable to liaise effectively.³⁸ NICE have recently published guidelines on the transition from children's to adults' services for young people.³⁹ The guideline reinforces the need for a smooth and gradual transfer, with integrated working between child and adult services. It recommends that practitioners should usually start planning for adulthood from age 13 or 14. The point of transfer should not be based on a rigid age threshold and should occur at a time of relative stability for the young person. NICE recommend identifying a single practitioner with whom the young person has a meaningful relationship as a 'named worker', to coordinate their transition care. This person could be, for example, a nurse, youth worker/existing keyworker or a named GP.³⁹

Although the need for transitional care is recognised by the NICE guidelines, many localities lack clear protocols for transition from child and adolescent to adult services.^{37,38} It has been noted that in reality, ADHD in adults is under-recognised and that services for adults with ADHD are patchy, with few areas having properly commissioned services.^{3,37,40} Anecdotally this can result in people failing to receive necessary treatment, or in GPs being asked to continue to prescribe ADHD medication without formal arrangements for care being in place.

Those planning and developing transitional care need to consider what services exist locally for adults. NICE advise undertaking a gap analysis. This is to identify and respond to the needs of young people who have been receiving support from children's services, including child and adolescent mental health services, but who are unable to get support from adult services.³⁹ GPs could support this process by gathering data on the size of the issue locally. For example, providing CCGs with (anonymised) data on the number of adults, and the number of soon to be adults (e.g. 16-17 years), that practices prescribe ADHD medication for could help in building a business case for adult ADHD services, where they are lacking.

Safety

Side-effects and monitoring

Common side effects of stimulant medications include insomnia, decreased appetite, nervousness, headaches, cardiovascular effects and gastrointestinal problems such as nausea, vomiting and abdominal pain.^{7-9,41} Psychosis and hallucinations are less common side-effects of stimulants and atomoxetine.^{7-9,43,42}

Atomoxetine can cause decreased appetite, headaches, cardiovascular effects and gastrointestinal problems. Somnolence occurs very commonly.⁸ Less common adverse effects of atomoxetine that parents and carers should be counselled on include suicidal ideation and hepatic disorders.²⁰

The most frequently reported adverse-effects of guanfacine prolonged release include somnolence, headache, fatigue, upper abdominal pain, and sedation. Serious adverse reactions commonly reported include hypotension, weight increase, bradycardia and syncope (uncommon).¹⁰ After discontinuation, in particular after abrupt cessation of treatment, rebound hypertension and tachycardia may occur.¹⁷

Many side-effects are more pronounced at the beginning of treatment and improve with time.¹ Sleep problems caused or worsened by stimulant medicines should be addressed with good sleep hygiene and behavioural approaches first-line. Where these are inadequate melatonin is sometimes used.⁴³ (see PrescQIPP bulletin 108 on melatonin available at www.prescqipp.info/resources/viewcategory/391-melatonin-spot-list)

The height and weight of children and young people treated with ADHD medication should be plotted regularly on a growth chart. Height should be measured every six months and weight should be measured at three and six months after initiation and six monthly thereafter. If growth is significantly affected the option of a planned break in treatment over school holidays should be considered to allow 'catch-up' growth to occur. Adults should also be monitored for weight loss.²⁰

Cardiovascular side-effects including tachycardia, palpitations, and increased heart rate and blood pressure can occur with stimulant medications and atomoxetine.^{7-9,41} Guanfacine commonly causes bradycardia, hypotension, and orthostatic hypotension.¹⁰ The pre-drug treatment assessment undertaken by the specialist must include a careful assessment of cardiovascular risk status and relevant family history.²⁰ The MHRA have emphasised the importance of such assessments and of ongoing cardiovascular monitoring during treatment with methylphenidate and atomoxetine.^{30,31,44} NICE advise that heart rate and blood pressure be monitored and recorded on a centile chart before and after each dose change and routinely every three months. Routine blood tests and ECGs are not recommended unless there is a clinical indication.²⁰

Both guanfacine and atomoxetine should be used cautiously where there is a risk of QT interval prolongation.^{8,10}

Side effects resulting from drug treatment for ADHD should be routinely monitored and documented.²⁰ Clarity regarding responsibility for drug monitoring in ADHD treatment is essential. Locally agreed shared care protocols are used to define responsibilities and provide information on indications for specialist consultation. GP practices need robust systems to ensure monitoring is carried out and highlight where it has been missed.

Driving

Methylphenidate, dexamfetamine, lisdexamfetamine, atomoxetine and guanfacine can all cause side-effects that can affect a person's ability to drive. Anyone prescribed these medicines who may drive should be advised of this. They should not drive (or operate hazardous machinery) until they are reasonably certain that their performance is not affected by the medicine. They must avoid driving if they are affected.⁷⁻¹¹ It is an offence to drive whilst impaired through drugs, regardless of whether or not the drugs are being used legitimately.⁴⁵

Under legislation introduced in 2015 it is now also an offence to drive with more than a specified amount of certain drugs in the body, whether driving is impaired or not. The drugs specified include amphetamines (e.g. dexamfetamine, lisdexamfetamine). Provided driving is not impaired, a 'statutory defence' to avoid prosecution can be raised if the amphetamine was prescribed and has been taken as advised. It may be helpful for the person to keep evidence (such as a repeat prescription slip) with them while driving to show that they are taking the medication in accordance with medical advice.^{45,46}

Risk of misuse and diversion

Concerns exist regarding the misuse of stimulants to achieve a 'high' or for other reasons, such as to aid weight loss.⁴⁷ Before prescribing ADHD medication the risk of substance misuse and drug diversion (where the drug is passed on to others for non-prescription use) should be assessed.²⁰

Dexamfetamine has a greater potential for diversion and misuse than the other ADHD medications.⁴ Atomoxetine (a non-stimulant medication) does not appear to be associated with substance misuse. Extended-release formulations (which are less prone to misuse and diversion⁴⁷) or atomoxetine may be preferred where there are concerns.²⁰ Lisdexamfetamine dimesylate, a longer-acting pro-drug of dexamfetamine may also be a more appropriate choice in these circumstances. However, confirmation

of the theoretical decreased abuse potential of this agent is required in longer-term studies and evaluation of clinical experience.¹⁶ Guanfacine prolonged release is another agent with which there is less clinical experience in the UK. It is currently thought likely to have a low abuse potential.⁴⁸

Other prescribing considerations

- Different versions of methylphenidate modified release preparations can have different release profiles and may not have the same clinical effect. Prescribers should specify the brand to be dispensed (see methylphenidate modified release preparations below).⁴⁹
- Methylphenidate, dexamfetamine and lisdexamfetamine are schedule 2 controlled drugs.⁴⁹ Prescribers should be familiar with the requirements of controlled drug legislation governing their prescription and supply.²⁰
- The need for taking medication at school may be avoided by the use of modified release preparations (of methylphenidate) or by using longer acting medicines (such as atomoxetine or lisdexamfetamine). This can avoid potential issues with schools having to store and administer controlled drugs. It may also improve adherence and reduce stigma.²⁰
- Where more flexible dosing regimens are necessary or where dexamfetamine is prescribed, doses of medication may be needed during the school day. Schools should have a policy and clear procedures for managing medicines, including controlled drugs.⁵⁰
- Patients intending to travel abroad for more than three months carrying any amount of schedule 2 (or 3 or 4 Part I) controlled drugs require a personal export/import licence. This is not required for those travelling for less than three months. In this case patients are advised to carry a letter from the prescribing doctor.⁴⁹
- Atomoxetine has a flat pricing structure (most of the available strengths cost the same per capsule). Where possible, doses should be optimised to provide the desired dose at the lowest cost (i.e. with the fewest capsules).
- Atomoxetine is taken as a single daily dose in the morning, although it can be taken twice daily in evenly divided doses.⁸ Divided doses are more costly and less convenient, so should only be used where single daily doses are unsuitable, e.g. due to tolerability.
- Some areas have also devised and agreed local protocols for making minor dosage adjustments to atomoxetine doses in primary care in order to improve cost-effectiveness. An example of such a project can be found in the sharepoint section of the PrescQIPP website: <https://www.prescqipp.info/innovation-hub/innovation/atomoxetine-dose-optimisation-northamptonshire-prescribing-advisory-group-npag-showcased-october-2016>

Methylphenidate modified release preparations

Concerta XL® consists of an immediate release component (22% of the dose) and a modified release component (78% of the dose). The percentage immediate release/percentage modified release split for Equasym® XL is 30/70, and for Medikinet® XL is 50/50.⁴⁹ Other pharmacokinetic parameters also vary, including the release profiles and duration of action. These differences may be useful in helping clinicians individualise a person's ADHD treatment. Matoride XL® tablets and Xenidate XL® tablets are recent additions to the UK market, and have been granted marketing authorisation on the basis of bioequivalence to Concerta XL® tablets as the licensed reference product as opposed to clinical studies. In order to demonstrate bioequivalence, pharmacokinetic trials need to show that the upper and lower limits of the 90% confidence intervals for both the maximal concentration after dosing (C_{max}) and the area under curve of plasma level vs. time (AUC) do not fall outside of the range of 80%-125% of the value for the reference product.⁵¹

Policy makers should consider the cost difference in primary care of the various modified release methylphenidate preparations when making formulary decisions. Including Xenidate XL® or Matoride XL® tablets on formularies where Concerta XL® would have been considered appropriate could release savings when new patients are initiated on treatment. There may also be scope to review

and consider switching the medication of those already established on Concerta XL®. Organisations considering a review of prescribing of Concerta XL® prescribing should ensure that the principle, process and switching methodology is agreed locally by all key stakeholders, including local specialists and GPs. Changes to medication should only be made in the context of individual review, and should be communicated and monitored appropriately.

Costs

There are significant cost differences between the various medications for ADHD (see table 1). If there is a choice of more than one appropriate drug, NICE advise that the product with the lowest cost (taking into account the cost per dose and number of daily doses) should be prescribed.²⁰ Prescribing decisions about choice of therapy in ADHD are generally made by the specialist, in partnership with the patient (or their parent/carer).

Table 1. Preparations and costs of ADHD medicines. Costs are shown for the licensed dose range in six to 17 year olds

Drug	Product name	Type/strength of formulation	Licensed total daily dose (for 6 - 17 yrs)	Cost of 28 days treatment
Methylphenidate	Methylphenidate (generic)	Tablet 5mg, 10mg, 20mg	5mg-60mg ⁴⁹	£2.83-£30.58 ⁵²
	Medikinet®	Tablet 5mg, 10mg, 20mg	5mg-60mg ⁵³	£2.83-£30.58 ⁵⁴
	Tranquilyn®	Tablet 5mg, 10mg, 20mg	5mg-60mg ⁴⁹	£2.83-30.58 ⁵⁵
	Ritalin®	Tablet 10mg	5mg-60mg ⁶	£6.23-£37.41 ⁵⁴
	Concerta XL®	Modified release tablet 18mg, 27mg, 36mg, 54mg	18mg-54mg ⁷	£29.11-£68.71 ⁵⁴
	Matoride XL®	Modified release tablet 18mg, 36mg, 54mg	18mg-54mg ¹²	£23.29-£56.45 ⁵⁴
	Xenidate XL®	Modified release tablet 18mg, 36mg, 54mg	18mg-54mg ⁵⁴	£18.92-£44.66 ⁵⁴
	Medikinet XL®	Modified release capsule 5mg, 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	5mg-60mg ^{13,14,56}	£22.44-£62.83 ⁵⁴
	Equasym XL®	Modified release capsule 10mg, 20mg, 30mg	10mg-60mg ⁵⁷	£23.33-£65.33 ⁵⁴
Atomoxetine	Strattera®	Capsule 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg	10mg-100mg ⁸ (a)	£53.09-£70.79 ⁵²
	Strattera®	Oral solution 4mg/ml	10mg-100mg ⁵⁸ (a)	£19.83-£198.33 ⁵²
Dexamfetamine	Dexamfetamine (generic)	Tablet 5mg	2.5mg-20mg ⁴⁹ (b)	£24.75-£99.00 ⁵²
	Amfexa®	Tablet 5mg	5mg-20mg ⁴¹ (b)	£18.56-£74.26 ⁵⁵
	Dexamfetamine (generic)	Oral solution sugar free 5mg/5ml	2.5mg-20mg ⁵⁹ (b)	£16.03-£128.23 ⁵²

Drug	Product name	Type/strength of formulation	Licensed total daily dose (for 6 - 17 yrs)	Cost of 28 days treatment
Lisdexamfetamine	Elvanse® (c)	Capsule 20mg, 30mg, 40mg, 50mg, 60mg, 70mg	20mg-70mg ⁹	£54.62-£83.16 ⁵⁴
	Elvanse Adult®	Capsule 30mg, 50mg, 70mg	Only licensed for adults ¹⁵	£62.40-£89.10 ⁵⁴
Guanfacine	Intuniv®	Modified-release tablet 1mg, 2mg, 3mg, 4mg	1mg-7mg ¹⁰ (c)	£56.00-£141.68 ⁵⁴

(a) = Lower dose range (10mg) based on the example of a 20kg six year old.

(b) = Reference cited states the usual maximum dose is 20mg, although doses up to 40mg have been required.

(c) = Not licensed for children <25kg.

Atomoxetine oral solution can be particularly costly at higher doses. The SMC recommend restricting its use to those who cannot swallow capsules.⁶⁰

Savings

Across England and Wales over £48 million is spent annually on medicines for ADHD (ePACT Apr - Jun 2016).

Savings may be achieved by:

- Considering formulary choice of methylphenidate prolonged release. For example, if 50% of Concerta XL® prescribing was for Xenidate XL® instead, **this could release annual savings of almost £2.8 million across England and Wales. This equates to £4,591 per 100,000 patients.**
- Optimising atomoxetine doses (i.e. using the fewest number of capsules to get the desired dosage). A 10% reduction in spend on atomoxetine **would result in savings of approximately £800,000 across England and Wales. This equates to £1,212 per 100,000 patients.**

Although not quantifiable, savings may be achieved by:

- Ensuring those prescribed ADHD medicines fit appropriate criteria for treatment. In primary care this may mean checking that shared care arrangements are in place and that the person prescribed the medicine meets the shared care protocol criteria.
- Reducing harm from medication by ensuring it is correctly monitored, in line with a shared care protocol.
- Ensuring it is only continued where it remains clinically effective. In primary care this could mean confirming that periodic reassessment of continued benefit has been undertaken with the specialist.

NICE present a number of wider potential benefits and savings from implementing their guidance on ADHD,⁶¹ and on transitional care.⁶² They include:

- A reduction in broader societal costs, such as parental absence from work and related productivity losses.
- A reduction in the costs of special education services, and costs of other social services, including the youth justice system.⁶¹
- Reduced risk of young people falling between services and needing care, or treatment, for crisis that could have been avoided.
- Improved health and care outcomes for young people from effective transition.⁶²

- An increase in the productivity and performance of adults with ADHD, at work, after starting drug treatment.
- Potential discount on contributions to the NHS Litigation Authority schemes, including Clinical Negligence Scheme for Trusts (CNST). Compliance with NICE guidance is one of the criteria indicating good risk reduction strategies.⁶¹

Summary

ADHD is a common neurodevelopmental disorder that begins in childhood, with symptoms persisting into adulthood for many. It is associated with problems in social, academic, family, mental health and employment functioning.³ Medicines for ADHD require careful initiation by a specialist and should form part of a comprehensive treatment plan.²⁰ Primary care prescribers have a key role in the safe provision and monitoring of stabilised ADHD medication. In some areas there is a need to address gaps in service provision for adults with ADHD. Providing safe, effective care for people with ADHD for as long as it is clinically necessary has the potential to deliver positive outcomes for the individual and their family, as well as broader societal benefits.

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Additional PrescQIPP resources



Briefing



Data pack



Audit

Available here: <https://www.prescqipp.info/category/327-prescribing-in-adhd>

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