PrescQIPP
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Prescribing in attention deficit hyperactivity disorder (ADHD)

This bulletin reviews the place in therapy of drug treatments for ADHD. Medicines optimisation in this area focuses on the 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 is also scope for appropriate cost-effective prescribing of medication.

Recommendations

- Primary care clinicians are most likely to be the first practitioners to see children, young people and adults with signs and symptoms of ADHD and should refer these patients to the appropriate specialist.
- Primary care practitioners should not make the initial diagnosis or start drug treatment in children, young people or adults with suspected ADHD.
- Drug treatment for children, young people and adults with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural and environmental interventions.
- Commissioners should consider the cost difference in primary care of the various ADHD medications when making formulary decisions across healthcare systems.
- Commissioners and Providers should agree local shared care protocols for ADHD medication. Regional Medicines Optimisation Committee (RMOC) shared care protocols should be used where available.
- If prescribing under shared care agreements, ensure it is clear where responsibility for prescribing and ongoing monitoring lies.
- Different versions of methylphenidate modified release preparations can have different release profiles and may not have the same clinical effect, therefore, prescribers should specify the brand to be dispensed. However, commissioners should consider the cost difference in primary care of the 'branded generic' formulations equivalent to Concerta® XL tablets when making formulary decisions.
- Atomoxetine is available as a generic formulation and preparations have a flat pricing structure (most of the available strengths cost the same per capsule). Maximising cost-effectiveness involves prescribing generically and ensuring that the required dosage is given using the fewest number of capsules.
- Side effects resulting from drug treatment for ADHD should be routinely monitored for and documented. Who is responsible for drug monitoring should be set out clearly in shared care arrangements.

Recommendations

- ADHD medicines may cause side-effects that can affect a person's ability to drive. Adults 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 amfetamine (e.g. dexamfetamine, lisdexamfetamine) in the body. Provided driving is not impaired, a 'statutory defence' to avoid prosecution can be raised if the medication is prescribed and has been taken as advised.
- The stimulants methylphenidate, dexamfetamine and lisdexamfetamine are Schedule 2 controlled drugs. Before prescribing ADHD medication the risk of substance misuse and drug diversion should be assessed, particularly with the shorter acting formulations.
- 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.

Background

ADHD is a behavioural disorder characterised by inattention, hyperactivity and impulsivity, which can lead to functional impairment such as psychological, social, educational or occupational difficulties. While these symptoms tend to co-exist, some people are predominantly hyperactive and impulsive, while others are principally inattentive. ADHD is more commonly diagnosed in males than in females.[1]

ADHD begins in childhood. Symptoms of ADHD tend to be noticed at an early age and may become more noticeable when a child's circumstances change, such as when they start school.[2] Most cases are diagnosed when children are six to twelve years old.[3] The estimated global prevalence of ADHD in children is around 5%, while studies based on US populations estimate the rate at between 8% and 10%.[4] The symptoms of ADHD usually improve with age, but many adults who were diagnosed with the condition at a young age continue to experience problems. By the age of 25, an estimated 15% of adults diagnosed with ADHD as children still have a full range of symptoms, and 65% still have some symptoms that affect their daily lives.[2]

The symptoms of ADHD in children and young people are well defined. The main signs of inattentiveness include:[2]

- Having a short attention span and being easily distracted
- Appearing forgetful or losing things
- Appearing to be unable to listen to or carry out instructions
- Having difficulty organising tasks.

While the main signs of hyperactivity and impulsiveness include:

- Constantly fidgeting
- Being unable to concentrate on tasks
- Excessive physical movement and excessive talking
- Being unable to wait their turn
- Acting without thinking
- Interrupting conversations.

These symptoms can cause significant problems in a child's life, such as underachievement at school, poor social interaction with other children and adults, and problems with discipline.[3]

In adults, the symptoms of ADHD can be more difficult to define. The way in which inattentiveness, and hyperactivity and impulsiveness affect adults can be very different from the way they affect children. For example, hyperactivity tends to decrease in adults, while inattentiveness tends to get worse as the pressures of adult life increase.[3] In the UK, the prevalence of ADHD in adults is estimated at 3% to 4% with a male to female ratio of approximately three to one.[4]

Adult symptoms of ADHD also tend to be far more subtle than childhood symptoms and can include:[2]

- Carelessness and lack of attention to detail
- Continually starting new tasks before finishing old ones
- Poor organisational skills
- Continually losing or misplacing things
- Forgetfulness
- Restlessness and edginess
- Difficulty keeping quiet, and speaking out of turn
- Blurting out responses and often interrupting others
- Mood swings, irritability and a quick temper
- Extreme impatience
- Taking risks in activities, often with little or no regard for personal safety or the safety of others – for example, driving dangerously.

The aims of treatment are to reduce functional impairment, severity of symptoms, and to improve quality of life. Drug treatment should be initiated by a specialist trained in the diagnosis and management of ADHD. Following dose stabilisation, continuation and monitoring of drug treatment can be undertaken by the person's general practitioner under a shared care arrangement.[1]

In 2021, the National Institute for Health and Care Excellence (NICE) published a revised Clinical Knowledge Summary[4] to support the clinical guidance *Attention deficit hyperactivity disorder: diagnosis and management* [NG87] which was revised in 2019.[5] The Scottish Intercollegiate Guidelines Network (SIGN) guidelines *Management of attention deficit and hyperkinetic disorders in children and young people* published in 2009, were withdrawn in September 2019.[6]

Diagnosis

ADHD is suspected if there are at least six (five in adults) inattention symptoms and/or at least six (five in adults) hyperactivity-impulsivity symptoms that have:

- Started before 12 years of age.
- Occurred in two or more settings such as at home, school, social situations, or work.
- Been present for at least six months.
- Clearly interfered with, or reduced the quality of social, academic or occupational functioning.
- Other causes for symptoms excluded, such as learning difficulties, anxiety, depression, or by other psychiatric diagnoses.[4]

The formal diagnosis and treatment of ADHD should be carried out by a specialist, which may include a specialist paediatrician, a child psychiatrist, Child and Adolescent Mental Health Services (CAMHS), or an adult psychiatrist, depending on the age of the person and local service provision. The school's special educational needs coordinator (SENCO) or social services may also be involved. Those with

symptoms that are causing only a moderate impairment to their ability to function socially and at work or school, can initially be managed in primary care with self-help, simple behavioural management, or parent support programmes.[4]

Treatment

The treatment options offered by a specialist depend on the person's age and the degree of functional impairment and may include:[4]

- Parent education/support programmes.
- Psychological treatment: Including cognitive behavioural therapy (CBT) and/or social skills training.
- Environmental modifications: These are changes made to the physical environment that can help reduce the impact of ADHD symptoms on a person's day-to-day life. The modifications should be specific to the person's circumstances, and may involve changes to seating arrangements, lighting and noise, reducing distractions, optimising work or education by having shorter periods of focus with movement breaks, and reinforcing verbal requests with written instructions.[1]
- Eating a balanced diet and taking regular exercise: Healthcare professionals should stress the value of a balanced diet, good nutrition and regular exercise for children, young people and adults with ADHD. Eliminating artificial colourings and additives from the diet is not recommended unless there appears to be a link between certain foods or drinks and a person's ADHD symptoms.[5] Ask about foods or drinks that appear to influence hyperactive behaviour as part of the clinical assessment of ADHD in children and young people, and:

  1. If there is a clear link, advise parents or carers to keep a diary of food and drinks taken and ADHD behaviour.
  2. If the diary supports a relationship between specific foods and drinks and behaviour, offer referral to a dietitian.
  3. Ensure that further management (for example, specific dietary elimination) is jointly undertaken by the dietitian, mental health specialist or paediatrician, and the parent or carer and child or young person.[5]

  Do not advise or offer dietary fatty acid supplementation for treating ADHD in children and young people.[5] A systemic review which assessed a range of non-drug treatments for ADHD found that omega fatty acids did not produce a statistically significant effect on ADHD symptoms compared with the control group.[7]
- Medication treatment - see information below.

Medication treatment

Medication should be started in people with ADHD whose symptoms are still causing significant impairment in at least one area of function, despite environmental modifications. People with ADHD and anxiety disorder, tic disorder, or autism spectrum disorder should be offered the same treatment options as other people with ADHD.[1]

Where people with ADHD experience an acute psychotic or manic episode:[5]

- Any medication for ADHD should be stopped.
- Consider restarting or starting new ADHD medication after the episode has resolved, taking into account the individual circumstances, and the risks and benefits of the ADHD medication.

Medication choices

Children and young people

The NICE guidance for Attention deficit hyperactivity disorder: diagnosis and management [NG87] advises on the treatment of ADHD for children aged five years and over acknowledging that medicines for treating ADHD are off-label in children aged five and under.[5]

Methylphenidate (either short or long acting) remains the first-choice drug treatment for children aged five years and over and young people with ADHD.[5,8]

A switch to lisdexamfetamine can be considered following a six week trial of methylphenidate at an adequate dose, where not enough benefit has been derived in terms of reduced ADHD symptoms and associated impairment.[5]

Lisdexamfetamine is a prodrug of dexamfetamine, and has also been approved for use by the Scottish Medicines Consortium (SMC)[9] and the All Wales Medicines Strategy Group (AWMSG)[10] as part of a comprehensive treatment programme for ADHD in children aged six years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.

Dexamfetamine can be considered in children aged five years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer duration of effect.[1,5] This is an unlicensed use of dexamfetamine.[5]

Atomoxetine or guanfacine can then be offered if a child aged five years and over and young people if:

- They cannot tolerate methylphenidate or lisdexamfetamine or
- Their symptoms have not responded to separate six-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.[5]

Guanfacine is licensed in children and adolescents aged 6 to 17 years old in whom stimulants are not suitable, not tolerated or ineffective.[1] Atomoxetine is licensed in children of six years and older, in adolescents and in adults as part of a comprehensive treatment programme, and has been approved for use by the SMC.[11,12]

Adults (continuation from childhood and newly diagnosed)

Lisdexamfetamine or methylphenidate should be offered as first-line treatment for adults with ADHD.[5]

There is evidence to support amfetamines as the most effective group of drugs for treating adults with ADHD in the short-term.[13]

A switch to the alternative drug can be considered for adults who have had a six week trial at an adequate dose but have not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.[5]

Dexamfetamine can be considered for those adults whose ADHD symptoms are responding to lisdexamfetamine, but who cannot tolerate the longer duration of effect.[1,5]

Lisdexamfetamine has been approved for use by the SMC[14] and the AWMSG[15] as part of a comprehensive treatment programme for ADHD in adults.

Atomoxetine can then be offered to adults if:

- They cannot tolerate lisdexamfetamine or methylphenidate or
- Their symptoms have not responded to separate six week trials of lisdexamfetamine and methylphenidate having considered alternative preparations and adequate doses.[5]

License considerations in adults with ADHD

Dexamfetamine, guanfacine and immediate release methylphenidate preparations are not licensed for use in adult ADHD.[1,5] Lisdexamfetamine and atomoxetine are licensed for use in adults with ADHD only if continued from childhood.[4] Of the modified release methylphenidate preparations available, Concerta® XL, Delmosart® PR, Matoride® XL, Medikinet® XL, Ritalin® XL, Xaggitin® XL, Xenidate® XL are licensed for use in adult ADHD only if continued from childhood.[16-22] Only Medikinet® XL and Ritalin® XL preparations are additionally licensed for use in adults with ADHD who are new to treatment.[19,20] Equasym® XL and Addepta® XL are not licensed for use in adults with ADHD.[23,24]

Methylphenidate modified-release preparations

Healthcare professionals initiating medication for ADHD should:

- Be familiar with the pharmacokinetic profiles of the short- and long-acting preparations available for ADHD.[5]
- Ensure that treatment is tailored effectively to the individual needs of the person.[5]
- Take account of variations in bioavailability or pharmacokinetic profiles of different preparations to avoid reduced effect or excessive adverse effects.[5]
- Prescribe by brand name since different versions of modified-release preparations may not have the same clinical effect.[1]

Modified-release once-daily preparations are recommended when prescribing methylphenidate for reasons including:[5]

- Improved adherence: ADHD may lead to people having difficulty remembering to take medication.
- Reduced stigma: Because there is no need to take medication at school or in the workplace.
- Reduced problems of storing and administering controlled drugs at school.
- Reduced risk of stimulant misuse and diversion with immediate-release preparations, e.g. for cognitive enhancement or appetite suppression.

Immediate-release preparations may be suitable if more flexible dosing regimens are needed (e.g. a modified-release preparation of methylphenidate in the morning and an immediate-release preparation of methylphenidate at another time of the day to extend the duration of effect), or during initial titration to determine correct dosing levels.[5]

All the modified-release methylphenidate preparations include an immediate-release component as well as an extended-release component. This allows for rapid onset of action while avoiding the need to take further doses during the day to maintain effect.

The biphasic release profiles of these products are, however, not all equivalent and contain different proportions of the immediate-release and modified-release component (see table 1).[25]

The separate release profiles of the Equasym® XL, Medikinet® XL, Ritalin XL® and Concerta® XL allows prescribers a choice of preparations to match a person's needs. For example, Concerta® XL may be preferable for people with evening symptoms due to the larger proportion of sustained release component and longer duration of effect, whereas the other products may be preferred in people that might have a potential to suffer from insomnia, due to higher proportions of immediate-release component.[25]

Delmosart® prolonged-release, Matoride® XL, Xaggitin® XL and Xenidate® XL have been granted replicate marketing authorisations to Concerta® XL on the basis that they have satisfied the criteria for equivalent release profile for the reference Concerta® XL product. It would seem appropriate for these branded generics to be considered as alternatives to Concerta® XL (when initiation of Concerta® XL is appropriate).[25]

Table 1: Methylphenidate modified-release preparations

Preparation[1]	Available strengths[1]	Dose conversion[25]	Release profile[25]
Modified-release capsule			
Medikinet® XL capsules	5mg, 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	When converting from immediate-release methylphenidate, the total daily dose can be converted 1:1 to Medikinet® XL.	Consists of an immediate-release component (50% of the dose) and a modified-release component (50% of the dose).
Equasym® XL capsules	10mg, 20mg, 30mg	When converting from immediate-release methylphenidate, the total daily dose can be converted 1:1 to Equasym® XL.	Consists of an immediate-release component (30% of the dose) and a modified-release component (70% of the dose).
Ritalin® XL capsules	10mg, 20mg, 30mg, 40mg, 60mg	When converting from immediate-release methylphenidate, the total daily dose can be converted 1:1 to Ritalin® XL.[20]	Consists of an immediate-release component (50% of the dose) and a modified-release component (50% of the dose).
Modified-release tablet			
Concerta® XL tablets	18mg, 27mg, 36mg, 54mg	Total daily dose of 15 mg of immediate-release formulation is considered equivalent to Concerta® XL 18 mg once daily.	Consists of an immediate-release component (22% of the dose) and a modified-release component (78% of the dose).
Delmosart® prolonged-release tablets	18mg, 27mg, 36mg, 54mg	Total daily dose of 15 mg of immediate-release formulation is considered equivalent to 18 mg once daily.	Has been approved based on bioequivalence data compared to Concerta® XL tablets. They therefore have a release profile similar to Concerta® XL.
Matoride® XL tablets	18mg, 36mg, 54mg		
Xaggitin® XL tablets	18mg, 27mg, 36mg, 54mg		
Xenidate® XL tablets	18mg, 27mg, 36mg, 54mg		

Initiation

In September 2019, NICE amended the recommendation on assessment for people starting medication for ADHD to indicate that an electrocardiogram (ECG) is not needed before starting stimulants, atomoxetine or guanfacine if cardiovascular history and examination are normal and the person is not on medication that poses an increased cardiovascular risk.[5]

Before starting medication for ADHD, people with ADHD should have a full assessment, which should include:[5]

- A review to confirm they continue to meet the criteria for ADHD and need treatment.
- A review of mental health and social circumstances, including:
  1. Presence of coexisting mental health and neurodevelopmental conditions.
  2. Current educational or employment circumstances.
  3. Risk assessment for substance misuse and drug diversion.
  4. Care needs.
- A review of physical health, including:
  1. A medical history, taking into account conditions that may be contraindications for specific medicines.
  2. Current medication.
  3. Height and weight (measured and recorded against the normal range for age, height and sex).
  4. Baseline pulse and blood pressure (measured with an appropriately sized cuff and compared with the normal range for age).
  5. A cardiovascular assessment. An ECG is not needed before starting stimulants, atomoxetine or guanfacine, unless the person has a co-existing condition that is being treated with a medicine that may pose an increased cardiac risk, or has a history of, e.g.
     - Congenital heart disease or previous cardiac surgery
     - Sudden death in a first-degree relative under 40 years suggesting a cardiac disease
     - Shortness of breath on exertion compared with peers
     - Fainting on exertion or in response to fright or noise
     - Palpitations that are rapid, regular and start and stop suddenly
     - Chest pain suggesting cardiac origin
     - Signs of heart failure
     - A murmur heard on cardiac examination
     - Blood pressure that is classified as hypertensive for adults.

Educational Risk Minimisation Materials are included in the electronic medicines compendium for some medicines. They include prescribing checklists which should be used before prescribing the medicine and for ongoing monitoring. They aim to help reduce the risk associated with using the medicine. The risk minimisation materials for ADHD medication should be referred to before prescribing and when monitoring treatment.

Patient counselling

Tables 2 and 3 describe how the medicines are taken, common side effects, key counselling points, and sources of further information. Refer to the BNF or Summary of Product Characteristics for further information.

Patients should avoid abrupt withdrawal of medication.[1]

Patients can be signposted to the information on ADHD in adults available from the Royal College of Psychiatrists[26,27] and to Medicines in Children leaflets highlighted in table 2.

Table 2: ADHD medication patient counselling and prescribing considerations

Drug	Common side effects[3]	Counselling points and prescribing considerations
Methylphenidate	• A small increase in blood pressure and heart rate • Loss of appetite • Trouble sleeping • Headaches • Stomach aches • Mood swings • Feeling aggressive, irritable, depressed, anxious or tense	Can impair a person's ability to drive.[1] Carefully monitor for the risk of diversion, misuse and abuse of methylphenidate.[1] Is a Schedule 2 controlled drug therefore prescribers should be familiar with the requirements of controlled drug legislation governing prescription, supply and travel abroad.[1] Signpost to patient sources of information.[3,28]
Lisdexamfetamine	• Decreased appetite • Aggression • Drowsiness • Dizziness • Headaches • Diarrhoea • Nausea and vomiting	Aggression is common in children aged six to twelve years, uncommon in adolescents and frequency is unknown in adults.[29] Monitor for aggressive behaviour or hostility during initial treatment.[1] In the event of a missed dose, dosing can resume the next day. Afternoon doses should be avoided because of the potential for insomnia.[29] Can impair a person's ability to drive.[1] People whose driving is not impaired by amfetamines should be advised to carry suitable evidence that the drug is prescribed and that it is taken according to the instructions given by the prescriber (e.g. a repeat prescription form).[1,30] Provided driving is not impaired, a 'statutory defence' to avoid prosecution can be raised if the medication is prescribed and has been taken as advised. People should be advised that it is an offence to drive with more than a specified amount of amfetamine in the body.[30] Monitor for the risk of diversion, misuse, and abuse.[29] Is a Schedule 2 controlled drug therefore prescribers should be familiar with the requirements of controlled drug legislation governing prescription, supply and travel abroad.[1] Signpost to patient sources of information.[3,31]

Drug	Common side effects[3]	Counselling points and prescribing considerations
Dexamfetamine	• Decreased appetite • Mood swings • Agitation and aggression • Dizziness • Headaches • Diarrhoea • Nausea and vomiting	Monitor for aggressive behaviour or hostility during initial treatment.[1] Can impair a person's ability to drive.[1] People whose driving is not impaired by amfetamines should be advised to carry suitable evidence that the drug is prescribed and that it is taken according to the instructions given by the prescriber (e.g. a repeat prescription form).[1,30] Provided driving is not impaired, a 'statutory defence' to avoid prosecution can be raised if the medication is prescribed and has been taken as advised. People should be advised that it is an offence to drive with more than a specified amount of amfetamine in the body.[30] Is a Schedule 2 controlled drug therefore prescribers should be familiar with the requirements of controlled drug legislation governing prescription, supply, and travel abroad.[1] Monitor for the risk of diversion, misuse, and abuse of dexamfetamine. The risk is generally greater for short acting stimulants than for corresponding long-acting products.[32] Signpost to patient sources of information.[3]
Atomoxetine	• A small increase in blood pressure and heart rate • Trouble sleeping • Headache • Dizziness • Nausea and vomiting • Stomach aches • Irritability	Has a minor influence on the ability to drive.[33] Suicidal ideation: Patients and carers should be aware of the risk and should be vigilant for any change in behaviour, suicidal thoughts, agitation, aggression, emotional lability, or depression.[4] Hepatic disorders: Patients and carers should be aware of the risk and should be advised on the symptoms (abdominal pain, unexplained nausea, malaise, dark urine, or jaundice), suggesting liver damage, and encouraged to seek prompt medical help if this occurs.[4] Signpost to patient sources of information.[3,34]
Guanfacine	• Tiredness or fatigue • Headache • Abdominal pain • Dry mouth	Inform prescriber if two or more consecutive doses are missed and consider dose re-titration.[35] Can cause syncope, hypotension and bradycardia (increased risk of dizziness and syncope).[1,35] Somnolence and sedation may occur, predominantly during the first two to three weeks of treatment and with dose increases; manufacturer advises to consider dose reduction or discontinuation of treatment if symptoms are clinically significant or persistent.[1] Therefore, guanfacine may have a moderate to severe influence on the ability to drive and use machines.[35] Signpost to patient sources of information.[3,36]

Table 3: How to take the ADHD medication

Drug	How to take the ADHD medication
Methylphenidate	Immediate-release methylphenidate tablets • Can be given when more flexible dosing regimens are required, or during initial dose titration. A combination of modified-release and immediate-release preparations taken at different times of the day can be used to extend the duration of effect. • If effect wears off in the evening (with rebound hyperactivity) a dose at bedtime may be appropriate. The pros and cons of a small evening dose versus disturbances in falling asleep should be considered, therefore establish the need with a trial bedtime dose).[1] Medikinet® XL Capsules • The dose is taken once daily taken in the morning with or after breakfast.[1,19] • Medikinet® XL has to be taken with or after a meal in order to obtain sufficiently prolonged action and to avoid high plasma peaks.[19,25] • The capsule contents can be sprinkled on a tablespoon of apple sauce or yoghurt (then swallowed immediately without chewing).[1,19] Equasym® XL Capsules • The dose is taken once daily in the morning before breakfast.[1] • Ingestion together with food with a high fat content delays absorption of Equasym® XL.[23] • The capsule contents can be sprinkled on a tablespoon of apple sauce (then swallowed immediately without chewing).[23] Ritalin XL® Capsules • The dose is taken once daily taken in the morning with or without food.[20] • The capsule contents can be sprinkled onto a small amount (tablespoon) of soft food which should not be warm (e.g. apple sauce, jam, spread, yoghurt) and given immediately.[20] Concerta® XL Tablets • The dose is taken once daily taken in the morning with or without food.[1,16] • The tablet membrane may pass through gastro-intestinal tract unchanged.[1,16]
Lisdexamfetamine	• The dose is taken once daily in the morning.[1,29] • The capsule contents can be mixed with soft food such as yoghurt or in a glass of water or orange juice.[1,29]
Dexamfetamine	• The tablets can be divided to aid swallowing (a sugar free oral solution is also available but is not as cost-effective as dividing a tablet).[1,32] • The effect of food on the absorption of dexamfetamine from Amfexa® Tablets has not been studied; therefore, a possible effect of food on absorption cannot be excluded. It is recommended that Amfexa® 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.[32] • The dose should be given once or twice daily based on the course of symptoms at different times of the day. Dexamfetamine should not be taken too late after lunch time to avoid disturbances of sleep.[32]

Drug	How to take the ADHD medication
Atomoxetine	• Take either as a single dose in the morning or in two divided doses with last dose no later than early evening.[1,33]
Guanfacine	• The dose is taken once daily either morning or evening.[1,35] • Can be taken with or without food, however, avoid administration with high fat meals (as this may increase absorption). Do not crush, chew or break tablets as this increases the rate of guanfacine release.[1,35]

Shared care and ongoing monitoring

The NICE guideline on ADHD: diagnosis and management [NG87] recommends that after titration and dose stabilisation, prescribing and monitoring of ADHD medication should be carried out under shared care protocol arrangements with primary care.[5]

Commissioners and providers should agree local shared care protocols for ADHD medications. The RMOCs document, Shared Care for Medicines Guidance – A Standard Approach, defines the principles for a national system of shared care for medicines. A number of shared care protocols are being developed for ADHD medication in adults and children in support of this approach. Currently, shared care protocols are available for **adults with ADHD** only for:[37]

- Dexamfetamine
- Lisdexamfetamine
- Methylphenidate
- Atomoxetine
- Guanfacine

The protocols state that:[37]

- Specialists initiating treatment should prescribe the maintenance treatment for at least four weeks and until optimised; and should prescribe sufficient medication to enable transfer to primary care.
- Primary care should respond to the request from the specialist for shared care in writing within 14 days.

Each protocol also describes the monitoring requirements and actions to take in the event of an adverse reaction.[37]

Parents and carers should be encouraged to oversee ADHD medication for children and young people.[5] For adults, the symptoms of ADHD may lead to people having difficulty adhering to treatment plans therefore consider how a person's adherence to treatment can be supported, for example:[5]

- Is the person remembering to order and collect medication?
- Are there clear dosage instructions on the label?
- Are clear instructions about how to take the medication given in picture or written format, which may include information on dose, duration, adverse effects and the dosage schedule (the instructions should stay with the medication, for example, a sticker on the side of the packet)?
- Is the medication being taken as part of their daily routine (e.g. before meals or after brushing teeth)?
- Would the person benefit from reminders to take medication regularly (e.g. apps, alarms)?

People with ADHD who are taking drug treatment should have a specialist review at least annually to assess their need for continued treatment.[5]

Prescribers should be familiar with the requirements of controlled drug legislation governing the prescription and supply of stimulants.[5]

Height and weight

For people taking medication for ADHD:[5]

- Measure height every six months in children and young people.
- Measure weight every three months in children ten years and under.
- Measure weight at three and six months after starting treatment in children over ten years and young people, and every six months thereafter, or more often if concerns arise.
- Measure weight every six months in adults.
- Plot height and weight of children and young people on a growth chart and ensure a review by the healthcare professional responsible for treatment.

If weight loss is a clinical concern, consider the following strategies:[5]

- Taking medication either with or after food, rather than before meals.
- Taking additional meals or snacks early in the morning or late in the evening when stimulant effects have worn off.
- Obtaining dietary advice.
- Consuming high-calorie foods of good nutritional value.
- Taking a planned break from treatment.
- Changing the medication.

If a child or young person's height over time is significantly affected by medication (that is, they have not met the height expected for their age), consider a planned break in treatment over school holidays to allow 'catch-up' growth.[5]

Consider monitoring BMI of adults with ADHD if there has been weight change as a result of their treatment and changing the medication if weight change persists.[5]

Cardiovascular

Heart rate and blood pressure should be monitored and compared with the normal range for age before and after each dose change and every six months.[5] Tables containing normal heart rates and normal blood pressures for children can be found on the Great Ormond Street Hospital website.

Routine blood tests (including liver function tests) or ECGs should not be offered to people taking medication for ADHD unless there is a clinical indication.[5]

If a person taking ADHD medication has sustained resting tachycardia (more than 120 beats per minute), arrhythmia, or a clinically significant increase in systolic blood pressure measured on two occasions, reduce their dose and refer them to a paediatric hypertension specialist or adult physician.[5]

If a person taking guanfacine has sustained orthostatic hypotension or fainting episodes, reduce their dose or switch to another ADHD medication.[5]

Tics

Tics are fast, repetitive muscle movements that result in sudden and difficult to control body jolts or sounds.[38] If a person taking stimulants develops tics, consider whether:

- The tics are related to the stimulant (tics naturally wax and wane) and
- The impairment associated with the tics outweighs the benefits of ADHD treatment.

If tics are stimulant related, reduce the stimulant dose, or consider changing to, e.g. guanfacine or atomoxetine.[5]

Seizures

If a person with ADHD develops new seizures or a worsening of existing seizures, review their ADHD medication and stop any medication that might be contributing to the seizures. After investigation, cautiously reintroduce ADHD medication if it is unlikely to be the cause of the seizures.[5]

Sleep

Monitor changes in sleep pattern (for example, with a sleep diary) and adjust medication accordingly.[5]

Stimulant diversion

Healthcare professionals and parents or carers should monitor changes in the potential for stimulant misuse and diversion, which may come with changes in circumstances and age.[5]

Particularly consider the risk of diversion, misuse, and abuse of dexamfetamine since the risk is generally greater for short acting stimulants than for corresponding long-acting products.[32]

Transfer to adult services

A young person with ADHD receiving treatment and care from CAMHS or paediatric services should be reassessed at school-leaving age to establish the need for continuing treatment into adulthood. If treatment is necessary, arrangements should be made for a smooth transition to adult services. Precise timing of arrangements may vary locally but should usually be completed by the time the young person is 18 years.[5]

After transition to adult services, adult services healthcare professionals should carry out a comprehensive assessment of the person with ADHD that includes personal, educational, occupational and social functioning, and assessment of any co-existing conditions, especially drug misuse, personality disorders, emotional problems and learning difficulties.[5]

Review of medication

A healthcare professional with training and expertise in managing ADHD should review ADHD medication at least once a year and discuss with the person with ADHD (and their families and carers as appropriate) whether medication should be continued. The review should include a comprehensive assessment of the:[5]

- Preference of the child, young person or adult with ADHD (and their family or carers as appropriate).
- Benefits, including how well the current treatment is working throughout the day.
- Adverse effects.
- Clinical need and whether the medication has been optimised.
- Impact on education and employment.
- Effects of missed doses, planned dose reductions and periods of no treatment.
- Effect of medication on existing or new mental health, physical health or neurodevelopmental conditions.
- Need for support and type of support (e.g. psychological, educational, social) if medication has been optimised but ADHD symptoms continue to cause a significant impairment.

Consideration should be given to trial periods of stopping medication or reducing the dose when assessment of the overall balance of benefits and harms suggests this may be appropriate. If the decision is made to continue medication, the reasons for this should be documented.[5]

Costs

There are significant cost differences between the various medications for ADHD (see table 4).[39,40] Commissioners should consider the cost difference in primary care of the various ADHD medications when making formulary decisions across healthcare systems.

Table 4: Drug treatment costs for ADHD medications

Drug		Brand, formulation, and strengths	Licensed dose range for 6-17 years old[1]	Dose range for adults	Cost for 28 days[39,40]
Methylphenidate: Immediate-release formulations		Generic methylphenidate tablets 5mg, 10mg, 20mg Medikinet® tablets 5mg, 10mg, 20mg Tranquilyn® tablets 5mg, 10mg, 20mg	5mg 1-2 times a day, increased if necessary up to a total of 60mg daily in 2-3 divided doses	Not licensed	Generic methylphenidate tablets, Medikinet® or Tranquilyn® tablets £2.83 - £30.58
		Ritalin® tablets 10mg			5mg - 60mg £6.24 - £37.41
Methylphenidate: Modified-release formulations	Modified-release capsules	Medikinet® XL capsules 5mg, 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	10mg - 60mg once daily taken in the morning[20]	10mg - 80mg daily, two divided doses (taken morning and lunchtime)[41]	10mg - 60mg once daily £22.44 - £62.83 5mg - 40mg twice daily £44.87 - £107.74
		Equasym® XL capsules 10mg, 20mg, 30mg		Not licensed	10mg - 60mg once daily £23.33 - £65.33
		Ritalin XL® capsules 10mg, 20mg, 30mg, 40mg, 60mg		10mg - 80mg once daily taken in the morning[20]	10mg - 60mg once daily £22.33 - £62.52 10mg - 80mg once daily £22.33 - £107.20

Drug		Brand, formulation, and strengths	Licensed dose range for 6-17 years old[1]	Dose range for adults	Cost for 28 days[39,40]
Methylphenidate: Modified-release formulations	Modified-release tablets	Concerta® XL tablets 18mg, 27mg, 36mg, 54mg	18mg - 54mg once daily in the morning	18mg - 54mg once daily in the morning	18mg - 54mg once daily £29.11 - £68.71
		Delmosart® prolonged-release tablets 18mg, 27mg, 36mg, 54mg			18mg - 54mg once daily £14.53 - £34.34
		Matoride® XL tablets 18mg, 36mg, 54mg			18 mg - 54mg once daily £14.54 - £34.35
		Xaggitin® XL tablets 18mg, 27mg, 36mg, 54mg			18 mg - 54mg once daily £14.54 - £34.35
		Xenidate® XL tablets 18mg, 27mg, 36mg, 54mg			18 mg - 54mg once daily £14.53 - £34.34
Amfetamines	Lisdexamfetamine	Elvanse® capsules 20mg, 30mg, 40mg, 50mg, 60mg, 70mg Elvanse Adult® capsules 30mg, 50mg, 70mg	20mg - 70mg daily in the morning	30mg - 70mg daily in the morning	20mg - 70mg once daily £54.62 - £83.16 30mg - 70mg once daily £58.24 - £83.16
	Dexamfetamine	Generic dexamfetamine 5mg tablets	5mg - 20mg daily in two to four divided doses	Not licensed	2.5mg twice daily - 5mg four times daily £24.73 (half 5mg tablet twice daily) - £98.92
		Amfexa® tablets 5mg, 10mg, 20mg	5mg - 20mg daily in one to two divided doses (taken morning and lunchtime)[32]		5mg once daily - 10mg twice daily £18.56 - £74.26
		Generic dexamfetamine 5mg/5ml oral solution sugar free	5mg - 20mg daily in two to four divided doses		2.5mg twice daily - 5mg four times daily £106.86 - £427.43

Drug		Brand, formulation, and strengths	Licensed dose range for 6-17 years old[1]	Dose range for adults	Cost for 28 days[39,40]
Selective noradrenaline reuptake inhibitor	Atomoxetine*	Generic atomoxetine capsules 10mg, 18mg, 25mg, 40mg, 60mg, 80mg 100mg	Body weight up to 70kg: 500 micrograms/kg - 1.2 mg/kg daily Body weight 70kg and above: 40mg - 80mg daily	40mg - 100mg daily	40mg - 100mg once daily £18.74 - £30.01
		Atomaid® capsules 10mg, 18mg, 25mg, 40mg, 60mg, 80mg 100mg			40mg - 100mg once daily £19.19 - £25.61
		Strattera® capsules 10mg, 18mg, 25mg, 40mg, 60mg, 80mg 100mg			40mg - 100mg once daily £53.09 - £70.79
		Strattera® oral solution 4mg/1ml			40mg - 100mg once daily £79.33 - £198.33
Selective alpha2-adrenergic receptor agonist	Guanfacine	Intuniv® modified-release tablets 1mg, 2mg, 3mg, 4mg	For child 6 - 12 years (body weight 25kg and above): 1mg - 4mg once daily For adolescent 13 -17 years (body weight 34kg and above): 1mg – 7mg once daily See BNF or SPC for exact dose range depending on child's body weight[1,35]	Not licensed[35]	1mg - 7mg once daily £56.00 - £141.68

*Patients who do not achieve a satisfactory clinical response when taking as a single daily dose might benefit from taking it as twice daily evenly divided doses in the morning and late afternoon or early evening.[33]

Costs and savings

In England, Scotland and Wales, approximately £78 million is spent annually on the prescribing of medication for ADHD [NHSBSA Sept-Nov21, and Public Health Scotland Sept-Nov21].

Savings may be achieved by:

- Undertaking regular medication review to determine whether treatment:
  - Remains clinically necessary and effective?
  - Is causing harm or producing intolerable adverse effects?

Reducing doses or stopping prescribing where clinically appropriate and in discussion with the person could release savings. For example, reducing the dose or deprescribing in 10% of clinically appropriate patients could release **savings of £6.6 million in England, £260,582 in Wales and £915,533 in Scotland.** [NHSBSA Sept-Nov21, and Public Health Scotland Sept-Nov21]. **This equates to £11,124 per 100,000 population.**

- Including a cost-effective alternative to Concerta® XL on the local formulary (Delmosart® prolonged-release tablets, Matoride® XL prolonged-release tablets, Xaggitin® XL prolonged-release tablets and Xenidate® XL prolonged-release tablets). If 50% of Concerta® XL prescribing was for one of the branded generic preparations instead, this **could release annual savings of £3.2million in England, £151,894 in Wales, £246,503 in Scotland** [NHSBSA Sept-Nov21, and Public Health Scotland Sept-Nov21]. **This equates to £5,143 per 100,000 population.**
- Prescribing atomoxetine capsules generically could **release annual savings of £99,297 in England, £2,085 in Wales and £29,469 in Scotland over 12 months** [NHSBSA Sept-Nov21, and Public Health Scotland Sept-Nov21]. Additional savings could be made by optimising atomoxetine doses (i.e. using the fewest number of capsules to achieve the desired dosage) which would also be more convenient for patients.
- Prescribing Ritalin® 10mg tablets generically as methylphenidate 10mg tablets, **could release annual savings of £70,686 in England, £2,828 in Wales and £6,393 in Scotland over 12 months** [NHSBSA Sept-Nov21, and Public Health Scotland Sept-Nov21].

Summary of actions to consider

- Primary care practitioners should not make the initial diagnosis or start drug treatment in children, young people or adults with suspected ADHD.
- It should be clear from shared care agreements where responsibility for prescribing and ongoing monitoring of medication lies, within a comprehensive treatment plan that includes psychological, behavioural and environmental interventions.
- For cost-effective prescribing, consider the cost difference of the 'branded generic' formulations equivalent to Concerta® XL tablets, and the generic availability and flat pricing structure of atomoxetine. It can be challenging to fully engage with this cohort of patients; therefore, any switching of products needs to be done in a very considered way, e.g. it may be better to explain these changes to gain acceptance and understanding rather than just sending a template letter. Also consider follow up with patients who are known to have difficulty adhering to treatment plans.
- Ensure that all modified-release preparations of methylphenidate are prescribed by brand.
- Use the template clinical audit tool to ensure that ongoing monitoring and documentation of patient parameters is being carried out as per shared care agreements. Checklists found in the medication risk minimisation materials for ADHD medication found in the electronic medicines compendium should be followed.
- Drug treatment should be continued for as long as it remains clinically effective (bearing in mind licensing restrictions). The need for continued drug treatment should be reviewed at least annually.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-302-prescribing-in-adhd/
Implementation tools	
Data pack	https://data.prescqipp.info/views/B302_PrescribinginADHD/FrontPage?%3Aembed=y&%3Aiid=1&%3AisGuestRedirectFromVizportal=y

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