Attention Deficit Hyperactivity Disorder [ADHD] Formulary Guidance [v1.0]

1. Introduction

These Guidelines are intended for routine use. However there will be instances where they are not suitable for the patient you are managing, where more bespoke treatment will be necessary. In such instances the rationale for prescribing away from formulary must be recorded.

Attention Deficit Hyperactivity Disorder (ADHD) is predominantly seen in childhood but may continue into adulthood and cause clinically significant impairments. Current tretaments for ADHD include a range of behavioural, social, psychological and pharmacological interventions and dietary advice. The management should be shared between primary and secondary care.
The principle diagnostic features are:

Inattention, hyperactivity and impulsive behaviours that are often disruptive and may become defiant and aggressive. In adults the hyperactivity and impulsiveness tend to decrease, but symptoms of inattention persist.

2. Diagnosis

The World Health Organisation system (ICD- 10) is widely used in Europe. A diagnosis of hyperkinetic disorder (severe ADHD) requires three difficulties to be present- hyperactivity, impulsivity and inattention.

The DSM - IV diagnostic criteria of the American Psychiatric Association has broader criteria: a diagnosis of ADHD can be made with either impulsivity- hyperactivity (the two problems are combined together) or inattention, as well as with both.

The health care professionals will look for alarm signals:

- The child who significantly under performs at school, despite having a normal intellect and no major specific learning difficulties.
- The child who has ADHD behaviour problems, which are considerably worse than, would be expected for the standard of parenting and home environment.

Differential diagnosis

- The normal active preschool child
- Intellectual disability
- Specific learning difficulties
- Autism Spectrum Disorder
- Epilepsy
- Depression
- Brain injury
- Family dysfunction

They may also use some objective pointers towards diagnosis such as:

- Rating scales by parents and teachers e.g., Conners Teacher and Parent Rating Scales
- Tests which measure length and type of mental process (Psychometric tests and profiles).

In adults and in patients with learning disabilities diagnosis may sometimes be based on impression and subsequent response to treatment

3. Pharmacological Treatment – Key Points

- ADHD medication is indicated in severe ADHD. If a child or adolescent needs treatment with medication for ADHD, methylphenidate, atomoxetine and dexamfetamine are all recommended as possible choices. When deciding which drug to use, doctors should consider the following:
    - whether the child or adolescent has other conditions such as epilepsy
    - the side effects of each drug
    - factors that might make it difficult for the person to take the medicine at the right time (for example, if it is difficult to take a dose during school hours)
    - the possibility that the medicine might be misused, or passed on to another person for misuse
    - the individual preference of the child or adolescent and/or their family or carer.

- Where more than one of the medicines is considered to be appropriate for a child or adolescent, their doctor should choose the cheapest one.

- Treatment with methylphenidate, atomoxetine or dexamfetamine should only be started after a specialist who is an expert in ADHD has thoroughly assessed the child or adolescent and confirmed the diagnosis. Once treatment has been started it can be continued and monitored by a GP.

Adults

- Young people continuing treatment into adulthood should be assessed to establish the need for continuing pharmacological treatment into adulthood.
- For adults with ADHD, drug treatment should be the first-line treatment unless psychological approaches are preferred.
- Pharmacological treatments for ADHD in adults should be initiated only under the guidance of a specialist with expertise in ADHD, ideally as part of a multidisciplinary team, following a thorough assessment as part of a comprehensive treatment programme that addresses psychological, behavioural and occupational needs. Those with co-morbide substance misuse should be managed by a specialist with knowledge of both areas.
- Before initiating drug treatment, confirm the diagnosis and carry out a full assessment of ADHD and associated co-morbidities, according to current national guidelines

Cognitive behavioural therapy may be considered when the service user has made an informed choice not to have drug treatment, or drug treatment is partially effective or not tolerated or ineffective.

4. Prescribing Advice

- No pharmacologic agent is currently licenced for adults newly diagnosed with ADHD.
- Methylphenidate and dexamfetamine are licensed for the treatment of ADHD in children and young people. Use in adults is off label, although tretament regimes are similar.
- Atomoxetine is licenced for continuation from adolescence into adulthood where treatment was initiated in childhood, not for initial treatment of ADHD in adults
- Informed consent to off-label treatment should be obtained and documented.
- Stimulants are controlled drugs and have the potential for misuse and diversion, either for subjective effects or effects on performance. The requirements of controlled drug legislation with respect to prescribing and supply must be followed.
- Before treatment, adults with ADHD should be offered written information about their condition and its assessment, risks and benefits of treatment, available services, psychological support and self help.
- During the titration phase, doses should be gradually increased until there is no further clinical improvement in ADHD symptoms, and side effects are tolerable.
- Following an adequate response, pharmacological treatment for ADHD should be continued for as long as it is clinically effective. If continued it should be reviewed as a minimum annually for adults and 6 monthly for children. During the review consider the benefits on core symptoms, compliance, adverse effects, missed doses and co-morbide conditions.
- Suspected side effects should be documented and reported via the yellow card scheme
- Following titration and dose stabilisation (usually over 4–6 weeks), continued prescribing and monitoring should continue under local shared care guidelines.
- Antipsychotics should not be used for treatment of ADHD in adults.

5. Baseline Assessments and Monitoring

NICE recommends that before starting drug treatment for ADHD, a full assessment should be completed and should include:

- full mental health and social assessment
- full history and physical examination, including:
  - assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms
  - heart rate and blood pressure (plotted on a centile chart)
  - weight and height, (for children using centile charts)
  - family history of cardiac disease and examination of the cardiovascular system.
  - an ECG if there is past medical or family history of serious cardiac disease, a history of sudden death in young dfamily members, or abnormal findings on examination.
- Risk assesment for substance misuse or drug diversion

Drug treatment should be reviewed annually. This should include:

- a comprehensive assessment of clinical need, benefits and side effects, taking into account the views of the person, family and close friends.
- the effect of missed doses
- the effect of planned dose reductions
- taking into account brief periods of no treatment
- the preferred pattern of use
- coexisting conditions, with the person treated or referred if necessary
- the need for psychological, social and occupational support for the person and their carers

During treatment, monitor weight and height (for children) at 3 and 6 months from initiation and every 6 months thereafter

Strategies to reduce weight loss should be recorded in the care plan.

Monitor heart rate and blood pressure at each dose change and routinely every 3 months. Reduce dose and review if any clinically significant changes are noticed.

Table 1: STIMULANT DRUG TREATMENT FOR ADHD

Methylphenidate and dexamphetamine are schedule 2 controlled drugs – prescription writing requirements apply

Drug, dose	Adverse effects	Therapeutic monitoring	Clinical relevant drug interactions
Methylphenidate ***Short acting*** • < 6years - unlicensed • >6 years – up to 60mg daily in divided doses ***Long acting*** Concerta XL • < 6years unlicensed • >6 years up to 54mg once daily Equasym XL • < 6years unlicensed • >6 years up to 60mg once daily Medikinet XL • < 6years unlicensed • >6 years up to 60mg once daily	• Insomnia • Lost appetite • GI upset • Headache • Hypertension • Reduced weight gain or weight loss • Tics • Rarely blood disorder including leucopenia and thrombocytopenia	**Secondary Care** • 6 monthly height & weight • 6 monthly BP & pulse • Annually discuss and consider with the patient/parent/carer interruption of treatment **Primary Care** • Side effects • Symptom control	• MAOI's risk of hypertensive crisis • Moclobemide risk of hypertensive crisis • Clonidine, serious adverse events reported (causality not established)
Dexamfetamine • 4-6yrs - 2.5mg daily (increase by 2.5mg daily at intervals of 1 week) • >6yrs - 5-10mg daily increasing by 5mg daily at weekly intervals to a maximum of 40mg	• Insomnia • Restlessness • Anorexia • GI symptoms • Tachycardia • Palpitations	**Secondary Care** • 6 monthly height & weight • 6 monthly BP & pulse • Annually discuss and consider with the patient/parent/carer interruption of treatment **Primary Care** • Side effects • Symptom control	• MAOI's risk of hypertensive crisis • Moclobemide risk of hypertensive crisis

Table 2: NON-STIMULANT DRUG TREATMENT FOR ADHD

Drug, dose	Adverse effects	Therapeutic monitoring	Clinical relevant drug interactions

Atomoxetine
• <6 years unlicensed
• Over 6 yrs -
  • >70 kg, 40 mg daily for 7 days increase according to response. Usual maintenance dose 80 mg daily; max. 100 mg daily
  • <70 kg, 500 micrograms/kg daily for 7 days then increased according to response to usual maintenance dose 1.2 mg/kg daily
	• GI Symptoms
	• Anorexia
	• Dry mouth
	• Palpitation, tachycardia
	• Increased blood pressure, postural hypotension
	• Restlessness, dizziness, headache
	• Urinary retention, enuresis
	• Sexual dysfunction, menstrual disturbance
	• Mydriasis, conjunctivitis
	• Dermatitis, sweating, weight changes
	• Less commonly suicidal ideation
	• Very rarely hepatic disorders.
		Secondary Care
		• 6 monthly height & weight
		• Perform comprehensive medical history including:
		  ○ concomitant medications,
		  ○ family history
		  ○ past and present co-morbid medical disorders or symptoms
		• Baseline evaluation of cardiovascular status, including blood pressure (BP) and pulse, results to be measured and recorded on centile chart or similar. The GP must be notified in writing of these results
		• Establish and confirm that evaluation shows an absence of severe cardiovascular or cerebrovascular disorder which would be expected to deteriorate if the patient experiences clinically important increases in blood pressure or in heart rate (e.g. 15-20mmHg increase in BP or 20 bpm increase in heart rate)
		• Confirm that initial findings from the patient's history and physical examination do not suggest any cardiovascular or cerebrovascular disease
		• Monitor & record BP & pulse at least every 6 months during treatment. These results must be sent to the GP.
		• Annually discuss and consider with the patient/parent/carer interruption of treatment
		
		Primary Care
		• Side effects
		• Symptom control
		• Record in medical record details of baseline cardiovascular assessment plus any subsequent BP & pulse measurements provided by Secondary Care
		• Where a previously stable dose has been changed by the Consultant, monitor & record BP & pulse 4 to 6 weeks after each dose adjustment and at least every 6 months during treatment.
		• If BP or pulse alters outside of recommendation from Consultant recheck BP & Pulse 3 times over a 2 week period.
		• • If patient develops symptoms that suggest cardiac disease contact Consultant Paediatrician for urgent advice and refer for prompt specialist cardiac evaluation.
			• MAOI's risk of hypertensive crisis
			
			• Increased risk of ventricular arrhythmias with
			Amiodarone
			Antidepressants, Tricyclics
			Antipsychotics
			Disopyramide
			Diuretics (hypokalaemia)
			Mefloquine
			Methadone
			Moxifloxacin
			Procainamide
			Sotalol

Table 3: METHYLPHENIDATE – COMPARISON OF PRODUCTS

	Immediate release	Modified Release		
	Methylphenidate generic and Ritalin®, Equasym®, or Medikinet®	**Concerta® XL**	**Equasym® XL**	**Medikinet® XL**
Strengths	5mg, 10mg, 20mg	18mg, 27mg, 36mg, 54mg	10 mg, 20 mg, 30 mg	10 mg, 20 mg, 30 mg, 40 mg
Product details	IR 3-4 hours duration	M/R 10-12 hours duration	M/R up to 8 hours duration	M/R Up to 8 hours duration
Release profile	Peak plasma Concentration in 1-2 hours.	22% IR:78% MR Initial peak plasma concentration in 1-2 hours. Second peak at 6-8 hours	30% IR: 70% MR Initial peak plasma concentration in 1-2 hours. Second peak at 4.5 hours	50% IR:50% MR Initial peak plasma concentration in 1-2 hours. Second phase of drug release 3 hours later resulting in a 3-4 hour plateau
Formulation	tablet	Capsule shaped tablet containing two layers of drug. Outer layer (overcoat) released first, followed by gradual release of drug from inner core. Empty tablet shell excreted	Capsule containing two types of pellets/beads which allow immediate release of drug, followed by gradual release over the day.	Capsule containing two types of pellets/beads which Allows immediate release of drug, followed by gradual release over the day.
Administration details	Tablets can be halved	Tablet must be swallowed whole, not chewed, crushed or broken	Capsule may be opened and contents mixed with soft foods.(stability unknown) Contents must be swallowed whole, not chewed, crushed or broken.	Capsule may be opened and contents mixed with soft foods.(stability unknown) Contents must be swallowed whole not chewed, crushed or broken. Ingestion with high fat content food delays absorption by approximately 1.5 hours.
Dose Comparison	5mg	-	-	-
	10mg		10mg	10mg
	15mg	18mg once daily	-	-
	20mg	-	20mg	20mg
	30mg	36mg once daily	30mg	30mg
	40mg	-	-	40mg
	45mg	54mg once daily	-	-
	60mg	72mg (licensed upto 54mg)	60mg	-