Frimley Health and Care

Approved for use in Frimley North Places:
Heatherwood and Wexham Park Hospitals
Bracknell Forest, Slough and Royal Borough of Windsor and Maidenhead

Prescribing Guidelines	
Name of medicine	Methylphenidate, dexamfetamine, atomoxetine, lisdexamfetamine, guanfacine and unlicensed drugs
Indication	Children with ADHD (attention deficit hyperactivity disorder) with transition to adult services in Berkshire
Author(s): Ozma Tahir **Contributions by**: Dr Carsten Vogt **Organisation(s):** Berkshire Healthcare Foundation Trust	
Date ratified by Frimley Health MOB (FH MOB):	22nd September 2021

Berkshire West Integrated Care System

Berkshire West Integrated Care System
Representing
Berkshire West Clinical Commisioning Group
Royal Berkshire NHS Foundation Trust
Berkshire Healthcare NHS Foundation Trust
Berkshire West Primary Care Alliance

Prescribing Guidelines

Prescribing arrangement for the management of patients transferring from ***Secondary Care to Primary Care***

Prescribing arrangements for the use of methylphenidate, dexamfetamine, atomoxetine, lisdexamfetamine, guanfacine and unlicensed drugs in children with ADHD (attention deficit hyperactivity disorder) with transition to adult services in Berkshire

For the latest information on interactions and adverse effects, always consult the latest version of the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Approval and Authorisation

Approved by	Job Title	Date
BHFT Drugs and Therapeutics Committee	M Irani, Medical Director, Chair	July 2021
BW Area Prescribing Committee	G Braham, Chair	September 2021

Change History

Version	Date	Author	Reason
V 1.0	November 2013	Kiran Hewitt/ Katie Sims	New document
V 2.0	November 2017	Ozma Tahir	Review - Replaces version 1: Prescribing Arrangements for the use of methylphenidate, dexamfetamine, lisdexamfetamine and atomoxetine in child ADHD (attention deficit hyperactivity disorder) with transition to Adult services in Berkshire
V 2.1	March 2018	Ozma Tahir	Update to formulary position in Berkshire East for lisdexamfetamine, atomoxetine and dexamfetamine
V 2.2	October 2019	Ozma Tahir	NICE update September 2019 re ECG requirement before prescribing atomoxetine (and other QT prolonging medicines), subsequently removed.
V 3.0	May 2021	Ozma Tahir	Review. Inclusion of guanfacine as amber status in line with NICE recommendations.

This prescribing guideline remains open to review considering any new evidence.

This guideline should only be viewed online and will no longer be valid if printed off or saved locally

Acknowledgements: *Leicestershire Partnership Trusts Medicines Strategy Group, for sharing and allowing reproduction of parts of their ADHD shared care agreement.*

Useful information about ADHD and other mental health conditions can be found at the BHFT "choice and medication" website:
www.choiceandmedication.org.uk/berkshirehealthcare

BHFT Medicines Information Service, Prospect Park Hospital - Tel: 0118 960 5075
Email: medicines.information@berkshire.nhs.uk

Principles of Prescribing Arrangement

These prescribing Guidelines are a local policy to enable General Practitioners to accept responsibility for the prescribing and monitoring of medicines, treatments or devices in primary care, in agreement with the initiating specialist service.

This guideline provides a framework for the seamless transfer of care for a person from a hospital or specialist service setting to general practice, where this is appropriate and, in the patient's, best interest. People should never be placed in a position where they are unable to obtain the medicines they need because of a lack of communication between primary and secondary care.

It is important to note, in line with the General Medical Council guidance on prescribing, doctors are responsible for prescriptions they sign, and their decisions and actions when they supply and administers medicines and devices; or authorise or instruct others to do so.

Transfer of care

Transfer of clinical responsibility to primary care should only be considered where the patient's clinical condition is stable or predictable.

Referral to the GP should only take place once the GP has agreed to this in **each individual case**, and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that supply arrangements have been finalised. The secondary care provider must supply an adequate amount of the medication to cover this transition period. The patient should then be informed to obtain further prescriptions from the GP.

Clinicians should clearly explain what a shared care arrangement means for the patient and why it might be an option in their case. The patient or their carers should have the opportunity to ask questions and explore other options if they don't feel confident that shared care will work for them. They should be fully involved in, and in agreement with, the decisions to move to a shared care model for their on-going care. **Importantly, patients should never be used as a conduit for informing the GP that the prescribing is to be transferred.**

Patient consent

The best interest, agreement and preferences of the patient should be at the centre of the decision to begin shared care and their wishes followed wherever possible. Patients should be able to decline shared care if, after due consideration of the options, they decide that it is not in their best interests. Involvement of carers may be critical, especially in circumstances when it is not possible for the patients to make a decision e.g. mental capacity; where appropriate they should be included in the discussion about shared care.

Background – Attention Deficit Hyperactivity Disorder

Attention deficit hyperactivity disorder (ADHD) is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically observed in individuals at a comparable level of development and which interferes with functioning and/or development[2]. A diagnosis of ADHD should be made only after a comprehensive assessment by a specialist with expertise in ADHD[3].

Symptoms include:

- Inattention, for example, not listening when spoken to, not following through on instructions given, avoiding tasks which require prolonged mental effort, easily distractable etc.
- Hyperactivity and impulsivity e.g. fidgetiness, not being able to remain seated, unable to play quietly, talking excessively, interrupting others etc.

To attain ADHD diagnosis, several symptoms should be present before the age of 12 years and that these are present in two or more settings.

There are three types of ADHD:

- **Predominantly inattentive;** Some hyperactive-impulsive symptoms may also be present, but these are not clinically significant in relation to the inattentive symptoms.
- **Predominantly hyperactive-impulsive;** Some inattentive symptoms may also be present, but these are not clinically significant in relation to the hyperactive-impulsive symptoms.
- **Combined;** Both inattentive and hyperactive-impulsive symptoms are clinically significant, with neither predominating in the clinical presentation.

Appropriate psychological, psychosocial and behavioural interventions should be put in place as well as considering drug treatments. Around 65% of patients with ADHD continue to meet full criteria or have achieved only partial remission by adulthood. It is appropriate to continue treatment started in childhood in adults whose symptoms remain disabling.

Link to Patient UK information: ADD or Attention Deficit and Hyperactivity Disorder - Patient | Patient

NICE Clinical Guideline 87 states that 'Healthcare providers should ensure continuity of care for people with ADHD'. Also, that after titration and dose stabilisation, prescribing and monitoring of ADHD medication should be carried out under Shared Care Protocol arrangements with primary care.

The BHFT CAMH Service is commissioned to provide a service to children aged up to and including 18 years of age.

Clear guidelines are necessary to clarify the roles of primary and secondary care providers when using more specialist medicines that are categorised as amber, red, green, brown or non-formulary drugs in the NHS Berkshire traffic light system. This document sets out these responsibilities from initial referral to the Child and Adolescent Mental Health Service (CAMHS) ADHD Pathway through to on-going treatment maintenance, support and ultimately, referral to Adult ADHD services if necessary.

Formulary Status and Prescribing Guidance

According to NICE Guidelines[4]:

1. Offer methylphenidate (either short or long acting) as the first line pharmacological treatment for children aged 5 years and over and young people with ADHD.

2. Consider switching to lisdexamfetamine for children aged 5 years and over and young people who have had a 6-week trial of methylphenidate at an adequate dose and not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.

3. Consider dexamfetamine for children aged 5 years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile.
   Note that this is an off-label use for some people aged 6 to 17. See NICE's information on prescribing medicines.

4. Offer atomoxetine or guanfacine to children aged 5 years and over and young people if:
   - they cannot tolerate methylphenidate or lisdexamfetamine **or**
   - their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.

Choice of Medicine (with link to SPC)	**Place in therapy**	**Formulary status Berkshire West**
Methylphenidate IR	1st line	Amber Modified release options on BHFT Formulary: - Xenidate XL® (equivalent to Concerta XL®) - Equasym XL® - Medikinet XL®
Lisdexamfetamine	2nd line	Amber
Dexamfetamine	3rd line	Amber
Atomoxetine	3rd line	Amber
Guanfacine	3rd line	Amber

Prescribing Information

Refer to BNF for Children and SPC for full prescribing information (links above in table). See Appendix 1 for dosing and release profiles.

Misuse/Toxicity

All stimulants can cause tolerance and dependence so there is a risk of abuse and/or diversion (i.e. theft/sale of medication to others). Prescribers must take care when prescribing to patients who have a known history of substance misuse. Patients have been known to increase their dose of stimulant to higher than the maximum licensed doses.

Symptoms of chronic intoxication with amfetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, personality changes and even psychosis.

If extra prescriptions are requested by the patient or their carer, then the prescriber must inform either the GP or Consultant Psychiatrist (depending on who the request goes to) of this immediately to prevent duplication of requests.

If a patient is suspected of misusing stimulants, they should be referred back to their Consultant Psychiatrist, for consideration of alternate treatment.

Pregnancy & Lactation

The safety of these drugs in pregnancy and lactation **cannot be guaranteed**. If a patient taking any of these drugs reports a pregnancy or is planning a pregnancy, refer to the specialist for guidance and advice. Alternatively, call the Medicines Information Service on 0118 960 5075.

Responsibilities

Specialist Team Responsibilities (CAMHs)

The service offers medication choice for children aged 6 years and over and young people.

Initial Consultation

1. To determine diagnosis of Attention Deficit Hyperactivity Disorder following full assessment
2. Carry out a full pre-drug treatment assessment including:
    - a full mental health and social assessment
    - a full history and physical examination, including:
        - past and present medical and psychiatric disorders or symptoms
        - Baseline height, weight, blood pressure, heart rate.
        - documentation of concomitant medicines
        - assessment for risk of substance misuse and drug diversion

    - **Cardiac Examination**
      The main cardiac condition of concern from this age group is rhythm abnormalities such as malignant arrhythmias. If rhythm abnormalities are present, clinically, this would be picked up through assessment of the rate and rhythm of the pulse. Details of what should be included in the cardiac examination can be found in appendix 2.

3. At the time of diagnosis, clinicians from the ADHD Specialist Care Pathway provide young people and carers with psycho-education and information about the comprehensive management of ADHD including non-psychopharmacological interventions and psychopharmacological interventions.

They will be advised that more useful information about medications for ADHD can be found at the BHFT "choice and medication" website:
www.choiceandmedication.org.uk/berkshirehealthcare
Or can be accessed via the Berkshire Healthcare NHS Foundation Trust internet site at
www.berkshirehealthcare.nhs.uk
(Click on "Medicines")

GPs can call BHFT Medicines Information Service, Prospect Park Hospital for advice about mental health medicines on 0118 960 5075 (open between 9am and 1pm, Monday to Friday) or by Email: medicines.information@berkshire.nhs.uk

A. **All medication for ADHD should only be initiated by a healthcare professional with training and expertise in diagnosing and managing ADHD.**

NICE[1] state; 'An electrocardiogram is not needed before starting stimulants, atomoxetine or guanfacine if cardiovascular history and examination are normal and the person is not on medicine that poses an increased cardiovascular risk'. However, where there are cardiovascular risk factors (including family history), the GP will be requested to provide an ECG.

For further information regarding the drug initiation process, see appendix 6: drug initiation protocol.

B. **Within 4 weeks of initial prescription** (and usually within first 2 weeks – this could be in the form of a telephone review):

- Review efficacy of medication prescribed,
- Monitor for side-effects. Those patients prescribed atomoxetine should be closely monitored for agitation, irritability, suicidal thinking, self-harming behaviour and unusual changes in behaviour, particularly during the initial months of treatment of after a change in dose. Parents or carers should also be warned about the potential for liver damage in rare cases with atomoxetine (usually presenting as abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice).
- Adjust dose if necessary, or switch to alternative if treatment deemed ineffective
- Height, weight, blood pressure and pulse check at follow-up appointment.

6. **When the patient is stable** refer to GP for shared care when both parties consider it is clinically appropriate to do so.

7. Provide support and advice regarding all aspects of medication to the GP.

8. Review progress if requested by GP e.g. change in behaviour; treatment resistance, increased sedation, significant growth delay etc. Notify the GP of the results of any patient reviews, including changes in prescribed dose, and ensure the patient has sufficient medication until the GP has received this information.

9. Receive and respond to feedback from shared care GP as appropriate, e.g. progress/status of the child and in particular noting any dose changes/alterations/discontinuation etc. of treatment under the shared care agreement.

10. Liaise with the child's; school, residential placements and respite care homes as appropriate and ensure that information on drug treatment is given as appropriate to the patient, carers and teachers.

11. At least annually, review and monitor progress. This would include monitoring of physical parameters/ psychiatric symptoms and inform the GP of the outcome. Ideally timed so that patient is reviewed every 3months, alternating between GP and CAMHs specialist.

12. Because BHFT make recommendations in a cost-effective manner, changes of specified brands should only be initiated by the secondary care specialist to prevent potential adverse effects when switching brands. Different brands of modified release methylphenidate are not interchangeable.

Drug Holidays

These should be discussed with and initiated by the specialist. 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. Drug holidays may reduce adverse events without causing a deterioration of ADHD symptoms over time.

The effect of missed doses planned dose reductions and brief periods of no treatment should be considered and the preferred pattern of use should also be reviewed. Coexisting conditions should be reviewed, and the child or young person treated or referred if necessary. The need for psychological and social support for the child or young person and for the parents or other carers should be assessed.

Drug holidays are not advised for guanfacine in view of discontinuation symptoms.

Trial withdrawal

There should be a discussion with the patient at annual reviews to consider whether the medication is still needed, especially where treatment has continued for 24 months. If there has not already been a trial off medication, consider withdrawal of medication (except if review by specialist has led to an increase in dose). This should be offered and discussed with the patient and the outcome recorded. Consideration must be given to patient choice.

Methylphenidate, dexamfetamine and lisdexamfetamine can generally be withdrawn by treatment discontinuation but monitor for signs of withdrawal (e.g. extreme tiredness, becoming even more hyperactive, eating more and depression).

Atomoxetine withdrawal
Reduce the dose at weekly intervals and discontinue over a four-week period.

Guanfacine withdrawal
Blood pressure and pulse may increase following discontinuation of guanfacine. In post-marketing experience, hypertensive encephalopathy has been very rarely reported upon abrupt discontinuation of treatment.

To minimise the risk of an increase in blood pressure upon discontinuation, **the total daily dose should be tapered in decrements of no more than 1 mg every 3 to 7 days**. Blood pressure and pulse should be monitored when reducing the dose or discontinuing treatment.

If two or more doses are omitted unintentionally, then guanfacine should be re-titrated from the start again.

If by the age of 17yrs and 6 months, the patient is not stable after trial withdrawal and is foreseen to continue with medication treatment into adulthood, the transition to the adult ADHD service is to be made (see appendix 5).

Tertiary Care Specialist Advice and Unlicensed Use of Medicines

In children and young people whose ADHD is unresponsive to methylphenidate, lisdexamfetamine, dexamfetamine, atomoxetine and guanfacine, further treatment should follow referral to tertiary services.

The use of medication not included in recommendations, or unlicensed for ADHD (such as bupropion, clonidine, modafinil and imipramine) should only be considered in the context of tertiary services. Advice from a tertiary service should be sought for Clonidine for children with ADHD and sleep disturbance, rages or tics, atypical antipsychotics in addition to stimulants for people with ADHD and coexisting pervasive aggression, rages or irritability.

Transition to Adult Services

- The transition process applies to all CAMHs patients on prescribed ADHD treatment (i.e. methylphenidate, atomoxetine, dexamfetamine, lisdexamfetamine and guanfacine), (see appendix 5; transition protocol).
- Transition process to commence at 17yrs 6 months, in preparation for transfer at 18 years.
- If the patient has psychiatric co-morbidity requiring on going managed care with CMHT care pathways, transition should be made to CMHT as usual. (Note, the CMHT will not continue the prescription for ADHD treatment, this will be continued by GP)
- CAMHS clinician confirms that efficacy has been demonstrated by drug free trial in last one year; patient wishes to remain on medication and patient will remain registered with Berkshire GP in 19th year.
- Adult ADHD service undertakes initial assessment of on-going need and offer medication monitoring and supervision
- If GP unable to continue prescribing, drug treatment will stop when discharged from CAMHs

Transfer of Prescribing Responsibilities

- Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stable or predictable.
- Communicate to the patient's GP to request a transfer of prescribing responsibilities; detailing the drug, formulation, dose, and frequency to be prescribed, along with details of how to refer to the CAMHS team should the patient develop a problem with their treatment.

Disease Monitoring

- The patient will be reviewed by the Specialist Team when necessary. The time interval will differ depending on the individual patient.
- Communicate to the GP all necessary monitoring that needs to be carried out in primary care (detailed below).

Primary Care Team Responsibilities (General Practitioner)
Pre-Referral to secondary care specialist service:
• Referral from the community to CPE from either health, education, or social care professionals (for example, GPs, paediatricians, educational psychologists, SENCOs, social workers, Primary Mental Health Care Worker).

- The person making the referral to secondary care must inform the child or young person's GP.

- Because symptoms of ADHD can be mimicked by a number of physical conditions such as thyrotoxicosis, or side effects of medical treatment for physical conditions (e.g. high dose salbutamol in asthma) or associated with physical conditions such as neurofibromatosis, and tuberosclerosis, the referrer/GP should provide as much medical information as possible at the initial referral including:
    - details of any diagnosis or history where caution is needed for potential medication treatment, such as history of exercise syncope, undue breathlessness, and other cardiovascular symptoms
    - past and present medical and psychiatric symptoms including currently prescribed medications and allergies. Records of any previous physical assessments including cardiovascular system examination, weight, blood pressure and heart rate.
    - Information that suggests risk of substance misuse and drug diversion should be included in the referral.

- Refer to Paediatric Cardiologist if there is past medical or family history of serious cardiac disease such as malignant arrhythmias, a history of sudden death in young family members who are under the age of 40, abnormal findings on previous cardiac examination **before medical intervention for ADHD** (see appendix 2). Any abnormal findings should be sent to the CAMHS psychiatrist as well as GP.

General Practitioner Responsibilities – Maintenance

1. Issue repeat prescriptions after stabilisation. Methylphenidate, Dexamfetamine and Lisdexamfetamine are controlled drugs (CDs).

2. Sustained release methylphenidate preparations need to be prescribed by brand as they are NOT interchangeable due to different release profiles. Changes of specified brands should only be initiated by the secondary care specialist to prevent potential adverse effects when switching brands.

3. Continue any required monitoring as per specialist recommendations (will be dependent on the drug prescribed).

4. To evaluate annually the benefit of treatment, symptom control, adverse effects, and the need to continue. Provide feedback to the specialist as appropriate, as to the progress/status of the child and in particular notifying of intention to discontinue and adverse effects of treatment. Ideally timed so that patient is reviewed every 3 months, alternating between GP and CAMHs specialist.

5. To make urgent arrangements to be seen by the specialist in the event of any of the following.
    - Failure to thrive/retardation of growth
    - Persistent sleep disturbance
    - Persistent problems with poor attention/deterioration in behaviour
    - Pronounced change in mental state

6. To refer patients for prompt specialist cardiac evaluation if symptoms develop such as palpitations, exertional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of heart disease.

7. To be alert for signs of diversion, misuse, or abuse of methylphenidate.

8. Where a change in medication or dose is required, for example if a drug/dose has not been tolerated, the following procedure will be followed:
    a. GP/Patient to contact Clinical Nurse Specialist who will liaise with Consultant to decide on a suitable alternative dose.
    b. Clinical Nurse Specialist will send a written request featuring the prescriber's advice to ask GP, including which prescriber gave the advice, to issue a prescription, detailing individual patient plan including dose titration or the need to discontinue treatment (where applicable).
    c. Written requests from NMP's will not require approval from a doctor for requests as stated in 8.b.
9. Report adverse events to the CHM/MHRA.
10. Report adverse events to the consultant sharing the care of the patient.

Monitoring

Parameter	Frequency	Target Results	Action (for GP) on variance
Cardiovascular	Monitor heart rate and blood pressure and compare with the normal range for age before and after each dose change and every 6months.	Stability	Sustained resting tachycardia, arrhythmia or clinically significant increase in systolic b.p. should prompt dose reduction and referral to other (e.g. cardiac) where appropriate. Approx. 10% patients on atomoxetine may develop more significant rises in b.p. and heart rate with clinical implications. See MHRA warning [4].
Height and weight	Measure height every 6 months in children and young people. Measure weight every 3 months in children 10 years and under. measure weight at 3 and 6 months after starting treatment in children over 10 years and young people, and every 6 months thereafter, or more often if concerns arise		Discuss concerns with specialist. Consider monitoring BMI and changing the drug if weight loss persists.
FBC LFTs (atomoxetine)	If there is a specific concern/symptom of hepatic problem.	Results within normal limits	Discontinue if neutropenia develops and discuss with appropriate specialist.

			Atomoxetine may require dose reduction/discontinuation if laboratory or clinical evidence of abnormal hepatic function.
Behaviour including self-harming	At each appointment	Able to cope with daily living	If unexpected change in behaviour is noted review is indicated.
Mental state including emergence of psychotic symptoms, irritability, tics, suicidal thinking or anxiety/panic symptoms	3-12 monthly depending on actual presentation (by GP or if specialist has been referred to)		Discuss with secondary care specialist as necessary

Patient's role (or that of carer)
• Ask the specialist or GP for information if he or she does not have a clear understanding of the treatment. • Tell the specialist or GP of any other medication being taken, including over-the-counter products. • Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP • Adhere to treatment as advised by the specialist.

Communication – Contact Details

Contact Details - Child and Adolescents	
Slough – CAMHs: Upton Hospital, Fir Tree House Albert Street Slough, Berkshire, SL1 2BJ Tel: **01753 635645/46** Fax: 01753 635623	**Reading - CAMHs:** Science and Technology Building University of Reading Earley Gate Whiteknights Road RG6 6BZ Tel: 01182070930 Fax: 01183131413
Bracknell - CAMHs: Wokingham Community Hospital 41 Barkham Road Clinic Building Wokingham Berkshire RG41 2RE Tel: **0118 9495060/5177** Fax: 0118 9492944	**Wokingham CAMHs**: Wokingham Community Hospital 41 Barkham Road Clinic Building Wokingham Berkshire RG41 2RE Tel: **0118 9495060/5177** Fax: 0118 9492944
Windsor & **Maidenhead -CAMHs:** 1st Floor Nicholsons House Nicholsons Walk Maidenhead Berkshire SL6 1LD Tel: **01628 640300** Fax: 01628 640301	**Newbury- CAMHs**: Lower Henwick Farmhouse Turnpike Road Thatcham Berkshire RG18 3AP Tel: **01635 295555** Fax: 01635 295590
Wherever possible, queries regarding medications are best addressed to the patient's CAMHS consultant or ADHD Practitioner. However, GPs and other clinicians can access urgent medical advice about a young people on ADHD medications or other clinical enquiries by contacting the CAMHS Common Point of Entry (CPE) on 03003650300 (9am-5pm) and requesting to be called back by the on-call CAMHS Consultant.	

References

1. NHS England. 2018. *Responsibility for prescribing between Primary & Secondary/Tertiary Care. Accessed via https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ on 16/3/2018.*

2. Patient UK Professional article for ADHD: ADD or Attention Deficit and Hyperactivity Disorder - Patient | Patient Published 10/03/2020.

3. Maudsley Prescribing Guidelines 14th edition 2021.

4. NICE Guidelines: Attention deficit hyperactivity disorder: diagnosis and management. NG87 Published: 14 March 2018 Last updated: 13 September 2019 Recommendations | Attention deficit hyperactivity disorder: diagnosis and management | Guidance | NICE

5. MHRA UK Public Assessment Report. Atomoxetine: a review of the effects on heart rate and blood pressure. May 2012.
6. SPCs (Summary of Product Characteristics) for Equasym XL, MedikiNet XL, Concerta XL, Strattera, Elvanse and Ritalin. Accessed online 20 May 2021. Available online www.emc.medicines.org.uk
7. BNF and Childrens BNF Accessed online 20th May 2021.
8. 'Practitioner Review: Current best practice in the management of adverse effects during treatment with ADHD medications in children and adolescents.' Cortese et al. Journal of Child Psychology and Psychiatry. 54:3 (2013), pp227-246.
9. London Medicines Evaluation Network. Extended-release methylphenidate – a review of the pharmacokinetic profiles available. May 2016. Authored by Martin Bradley.

Appendix 1: Dosing/ cost information

Drug (with links to SPC)	Action	Dosage (BNF)	BNF[6] Prices (28/30 days - op)
Methylphenidate IR Generic methylphenidate	CNS stimulant. Schedule 2 controlled drug. Onset: 20-60 min Duration: 2-4 hours	For Child (4–)5 years Initially 2.5 mg twice daily, increased in steps of 2.5 mg daily if required, at weekly intervals, increased if necessary up to 1.4 mg/kg daily in 2–3 divided doses, discontinue if no response after 1 month, if effect wears off in evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose). Treatment may be started using a modified-release preparation. **- For Child 6–17 years** Initially 5 mg 1–2 times a day, increased in steps of 5–10 mg daily if required, at weekly intervals, increased if necessary up to 60 mg daily in 2–3 divided doses, increased if necessary up to 2.1 mg/kg daily in 2–3 divided doses, the licensed maximum dose is 60 mg daily in 2–3 doses, higher dose (up to a maximum of 90 mg daily) under the direction of a specialist, discontinue if no response after 1 month, if effect wears off in evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose). Treatment may be started using a modified-release preparation.	**15mg/day** = £9.09 **100mg/day** = £54.60
Methylphenidate modified release	Dose titration should start at the lowest possible dose. This is achieved by starting patients on immediate release methylphenidate 5mg once or twice daily and increasing dose by 5-10mg every week before moving to a modified release preparation.		

Xenidate XL®	CNS stimulant. Schedule 2 controlled drug. Onset: 30min – 2h Duration: 12hours IR:22% ER:78%	18mg – 54mg once daily Start at 18mg daily. Adjust at weekly intervals. 18mg Xaggitin XL® = 18mg Concerta XL® = 15mg Ritalin®	**18mg/day** = £31.19 **27mg/day** = £36.81 **36mg/day** = £42.45 **54mg/day** = £36.80 **108mg/day** = £73.60
Medikinet XL® capsules	CNS stimulant. Schedule 2 controlled drug. Onset: 20-60 min Duration: up to 8 hours IR:50% ER:50%	10mg – 60mg once daily. Start at 10mg daily. Adjust at weekly intervals.	**20mg/day** = £30.00 **30mg/day** = £35.00 **40mg/day** = £57.72 **50mg/day** = £62.52 **60mg/day** = £67.32 ***100mg/day*** = *£113.02*
Equasym XL® capsules	CNS stimulant. Schedule 2 controlled drug. Onset: 20-60 min Duration: 8 hours IR:30% ER:70%	10mg to 60mg once daily Start at 10mg daily. Adjust at weekly intervals.	**10mg/day** = £25.00 **20mg/day** = £30.00 **30mg/day** = £35.00 ***60mg/day*** = *£70.00* ***100mg/day*** = *£130.00*
Lisdexamfetamine Elvanse®	CNS stimulant Schedule 2 controlled drug Onset: 3.5 hours Duration: unclear	30mg once daily (morning), increased weekly to 50mg then 70mg if necessary. Can be started at 20mg if consid	**30mg/day** = £58.24 **50mg/day** = £68.60 **70mg/day** = £83.16
Atomoxetine Strattera®	Selective Noradrenaline reuptake inhibitor (not a controlled drug) Onset of action: may	**For Child 6–17 years (body-weight up to 70 kg)** Initially 500 micrograms/kg daily for 7 days, dose is increased according to response; maintenance 1.2 mg/kg daily, total daily dose may be given either as a single dose in the morning or in 2 divided doses	**60mg/day and less** = £48.20 **80-100mg/day** = £64.28 ***Liquid***

	take 4-6 weeks Can be given as a single dose in the morning OR twice daily – last dose no later than early evening.	with last dose no later than early evening, high daily doses to be given under the direction of a specialist; maximum 1.8 mg/kg per day; maximum 120 mg per day. **For Child 6–17 years (body-weight 70 kg and above)** Initially 40 mg daily for 7 days, dose is increased according to response; maintenance 80 mg daily, total daily dose may be given either as a single dose in the morning or in 2 divided doses with last dose no later than early evening, high daily doses to be given under the direction of a specialist; maximum 120 mg per day.	***4mg/1ml (300mls) £85.00***
Dexamfetamine	CNS stimulant Schedule 2 controlled drug Onset: 20-60 min Duration: 3-6 hours	Initially 2.5 mg 2–3 times a day, increased in steps of 5 mg once weekly if required. Usual maximum 1 mg/kg daily, up to 20 mg daily (40 mg daily has been required in some children); maintenance dose to be given in 2–4 divided doses.	**10mg/day** = £49.46 **60mg/day** = £238.68 ***Liquid 5mg/5ml (500ml) = £114.49***
Guanfacine Intuniv®	Selective alpha2A-adrenergic receptor agonist. Non-stimulant.	Start with 1mg daily, then increase dose weekly by not more than 1mg increments according to response. The recommended maintenance dose range is 0.05-0.12 mg/kg/day.	**1mg/day** = £60.00 **4mg/day** = £81.60

Appendix 2:

ADHD Treatment and Cardiac Concerns:

When to refer, when to do an ECG, when to do nothing.

This guideline is to guide the appropriate assessment, investigation, and referral for cardiology opinion, of paediatric patients with ADHD in whom treatment is being considered.

Reference is made to the guidance produced by the National Institute for Health and Clinical Excellence - NICE clinical guideline 87, '**Attention deficit hyperactivity disorder,** Diagnosis and management of ADHD in children, young people and adults, September 2008.'

For those in whom treatment (Methylphenidate, Atomoxetine, Dexamfetamine) is being considered, we suggest:

A full history and physical examination, including:

- assessment of history of
  - Symptoms
    - exercise syncope
    - undue breathlessness, not obviously due to a respiratory cause
    - chest pains
    - palpitations
  - Past medical and family history
    - past medical or family history of serious cardiac disease
    - a history of sudden cardiac death in family members aged <40 years
- examination of the cardiovascular system, including:
  - height
  - weight
  - heart rate
  - blood pressure (plot on a centile chart - http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.pdf).

An electrocardiogram (ECG) should be performed if there are:

- positive features in the history
- abnormal findings on cardiac examination (murmur, abnormal pulses, radio-femoral delay, hypertension).

- The ECG should be done in a recognised electrophysiology department
- if the treatment may affect the QT interval (NICE 2018)

The patient should not be started on medication and should be referred to a Paediatrician with Expertise in Cardiology if there is:

- a positive history for cardiovascular symptoms
- a past medical history of serious cardiac disease or family history of sudden cardiac death in people under 40 years
- **Sustained** resting tachycardia, greater than maximum heart rate for age on 2 separate occasions (see table below).
- BP>95th percentile
- Abnormal cardiovascular examination
- Abnormal ECG
- blood pressure that is classified as hypertensive for adults (see NICE's guideline on hypertension in adults)
- shortness of breath on exertion compared with peers

Monitoring of treatment and consideration of onward referral

- Monitor heart rate and blood pressure and record on a centile chart before and after each dose change, and every 3-12 months.
- Palpitations, arrhythmia, **sustained** resting tachycardia (see table below), or systolic blood pressure rising to greater than the 95th percentile, measured on two separate occasions, should prompt dose reduction and/or stoppage, but are **not necessarily indications for referral** to a Paediatrician with a Cardiology Interest.

Age – related Heart Rate Ranges[1]

Age	Heart Rate Range
<1 yr	80 – 180
1 – 2 yrs	100 – 160
2 – 4 yrs	80 – 140
4 – 6 yrs	80 – 120
6 – 8 yrs	70 – 115
8 – 12 yrs	70 – 110
>12yrs	60 – 110

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[1] *Advanced Paediatric Life Support: The Practical Approach (APLS) 5th Edition,* Advanced Life Support Group, John Wiley & Sons, 2011.

Appendix 3 Drug Initiation Protocol

Drug Initiation Protocol
Baseline assessment

D1. Before starting medication, people with ADHD should have a full assessment, which should include:

• a review to confirm they continue to meet the criteria for ADHD and need treatment
• a review of mental health and social circumstances, including:
- presence of co-existing mental health and neurodevelopmental conditions
- current educational or employment circumstances
- risk assessment for substance misuse and drug diversion
- care needs
• a review of physical health, including:
- a medical history, conditions that may be contraindications for specific medicines
- current medication
- height and weight (measured and recorded against the normal range for age, height and sex)
- baseline pulse and blood pressure (measured with an appropriately sized cuff and compared with the normal range for age)
- an ECG if the treatment may affect the QT interval (for example, tricyclics and monoamine oxidase inhibitors).

D2. Refer for a cardiology opinion before starting medication for ADHD if any of the following apply:

• history of congenital heart disease or previous cardiac surgery
• history of sudden death in a first-degree relative under 40 years, which could suggest a family history of cardiomyopathy or channelopathy
• 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 (fleeting occasional 8 bumps are usually ectopic and do not need investigation)
• chest pain suggesting cardiac origin
• signs of heart failure
• blood pressure consistently above the 95th centile for age and height.

Allergies

Prior to commencing ADHD medications for drug naïve individuals, any food allergies or intolerances should be elicited in order to exclude products that may contain the known allergen. Further enquiries regarding product composition can be obtained via the information help desk at Prospect Park Pharmacy.
Example: Gluten intolerance
1) The manufactures of Medikinet can confirm that both the controlled release capsules and immediate release tablets are gluten free and there is no risk of cross contamination during the manufacturing process.

2) The manufactures of Concerta XL cannot specifically state that the product does not contain gluten as they cannot confirm that there is no cross contamination during the manufacturing process. Gluten is not listed in the product ingredients.

3) Novartis confirmed that although the Ritalin does not come into contact with gluten in the process of manufacturing, it does contain wheat starch at less than 100ppn wheat gluten. According to Celiac UK this is classified as a low gluten product.

Immediate release (IR) or sustained release, OROS (Osmotic controlled Release Oral System) ?
Is there any evidence in terms of efficacy and adverse effects?
IR methylphenidate versus OROS methylphenidate
• No evidence was identified for all-cause mortality, suicide or suicidal ideation, cardiac mortality, cardiac events, substance misuse, increase in seizures, liver damage, tremor, congenital defects, sexual dysfunction and psychotic symptoms for follow up to 12 weeks. No evidence was identified for follow up over 12 weeks.
• At 4 weeks the total number of children reporting any adverse event was not clinically different between the groups (1 study, low quality). Differences in appetite, insomnia and tics at 3-4 weeks (1 study very low quality) were not clinically important between the 37 groups.
Answer: No
When to use IR?
1. Titrating in slower steps
Ensure that dose titration is slower and monitoring more frequent if any of the following are present in people with ADHD:
• neurodevelopmental disorders [for example, autism spectrum disorder, tic disorders, learning disability (intellectual disability)].
• mental health conditions [for example, anxiety disorders (including obsessive–compulsive disorder), schizophrenia or bipolar disorder, depression, personality disorder, eating disorder, post-traumatic stress disorder, substance misuse]
• physical health conditions (for example, epilepsy or acquired brain injury).
IR: tailoring to need and flexibility;
- Addition in the afternoon to 8 h OROS
- Co-existing conditions where careful monitoring and slow titration required.

2. Treatment is tailored effectively to the individual needs of the child, young person or adult.
- Flexibility around more drug free periods during the day.
- Adjunct when effect of OROS wears off.

3. To optimise effect (for example, 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).

When to use OROS or sustained release medications ?
1 Sustained and smoother cover during the day
- Less variation in blood level concentrations
2. Convenience
- Fewer times to administer during the day
3. Administration
- Difficulties swallowing tablets
- Forgetting to take IR tablets during the day
4. Treatment is tailored effectively to the individual needs of the child, young person or adult.
5. Improving adherence

6. reducing stigma (because there is no need to take medication at school or in the workplace)
7. reducing problems of storing and administering controlled drugs at school
8. the risk of stimulant misuse and diversion with immediate-release preparations

Matched Biphasic Release Methylphenidate Preparations
According to the London Medicines Evaluation Network the newer preparations Matoride XL and Xenidate XL have been granted replicate marketing authorisation to Concerta XL on the basis that they have satisfied the criteria for an equivalent release profile for the Concerta XL product. It would seem appropriate for Matoride XL or Xenidate XL to be considered as alternatives to Concerta XL when initiation of Concerta XL is appropriate in an individual patient. As per BNF advice, prescribers should specify the brand when prescribing Matoride XL or Xenidate XL to ensure the correct product is dispensed. Xenidate XL is preferred to Matoride XL because it offers dose increases of 9mg steps with a 27 mg tablet (18-27-36-45-54). Matoride XL does not provide a 27 mg tablet and thus only offers 18 mg step increases (18-36-54).

Cost efficiencies
The NHS indicative price for Xenidate XL is almost half as much as Concerta XL (see BNF).

Concerta XL 18mg tablets (Janssen-Cilag Ltd)

	Size	Unit	NHS indicative price	Drug tariff	Drug tariff price
• Methylphenidate hydrochloride 18 mg	30	tablet (POM)	£31.19	Part VIIIA Category C	£31.19

Xenidate XL 18mg tablets (Mylan)

Active ingredients	Size	Unit	NHS indicative price	Drug tariff	Drug tariff price
• Methylphenidate hydrochloride 18 mg	30	tablet (POM)	£15.57	Part VIIIA Category C	£31.19

Switching stable patients to different biphasic release Methylphenidate Preparations
Switching a stable patient from Concerta XL to another matched biphasic release preparation is not recommended. The patient should remain on whichever brand they were initiated on if they are stable. There are many reports in this country and abroad where patients were seriously destabilised after a local switch in brand. Destabilising a patient can have huge financial implications – e.g. repeat appointments, drug costs, education/job losses etc. that could far outweigh any cost-savings from switching.

Using SR 5mg Dose Increases
When considering dose increases of Medikinet XL in 5 mg steps, a detailed assessment of the effectiveness of drug cover over time is required and consideration should be taken whether alternative modified-release preparations with different biphasic release profiles are more appropriate to use.

Appendix 4: Transition of care from Specialist CAMHS ADHD pathway to adult ADHD services

ADHD Transition protocol:

- All ADHD cases, when the YP turns 17 should be prepared for transition to adult services such that when they turn 18 they are either transitioned to Adult mental health services or to the care of the GP

- Preparation for Transition:

A. In the first six months:

1. Re assessment/re-evaluation if they will still meet the criteria for ADHD, offer medication breaks. DIVA is a useful tool to use. http://www.divacenter.eu/DIVA.aspx
2. Update the initial ADHD assessment report, with the information gathered since e.g. new information regarding family history of cardiac disease may have been documented, update of any medical condition since diagnosis etc.
3. Evaluate the need for concurrent referral to CMHT or other agencies
4. Adult ADHD team members will endeavour to attend the CAMHS ADHD team meeting once a quarter, that complex transition cases could be discussed.

B. In the second six months:

- Initiate the referral to Adult ADHD team: when the YP is around 17 and half years old, referral to ADHD team, using ADHD transition referral form
- Inform the GP about the transition and request GP for physical checks, as per the shared cared protocol with adult services, so that the physical check results are available for the adult services when YP is seen first time by the adult team
- Transition groups: Whilst the YP waits for the transition, they will have opportunity to attend the transition group. Aim of the transition group will be to socialise the YP to adult ADHD service, psych education of ADHD in adult and inform the YP about the available resources they can access (in the education services, voluntary sectors etc). (The details for the group is yet to be formalised, we also plan to use Skype for YP who are not able to attend the meeting, and also use Sharon platform)

- Once referral is accepted by the Adult ADHD team, YP will be discharged from the CAMHS
- First appointment with the Adult ADHD team will be with in the 6 months to one year of the referral

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