LINCOLNSHIRE CLINICAL COMMISSIONING GROUPS in association with UNITED LINCOLNSHIRE HOSPITALS TRUST AND LINCOLNSHIRE PARTNERSHIP FOUNDATION TRUST

SHARED CARE GUIDELINE: Methylphenidate, atomoxetine, dexamfetamine and lisdexamfetamine in the management of Attention Deficit Hyperactivity Disorder (ADHD)

The shared care protocol covers the initiation and review of treatment in children and adolescents with ADHD. THIS PROTOCOL DOES NOT COVER THE INITIATION OF NEW TREATMENT IN ADULT PATIENTS.

The protocol however can be extended to cover the ongoing therapy for existing patients once they have reached 18 years of age.

General Principles

Shared Care Responsibilities:

In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF*, 68, September - March 2015, p. 5)

Aims:

(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost or high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further copies of any guideline in this series are available from members of the Greater East Midlands Commissioning Support Unit (GEMS) Prescribing & Medicines Optimisation Team.

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Principles of shared care

The General Medical Council published their Good Practice In Prescribing And Managing Medicines and which came into effect 25th February 2013. A section of the guidance provides recommendations for the sharing of care which applies to any instance when care is shared between different services.

Good practice recommendation 35.

- Decisions about who and who should take responsibility for continuing care or treatment after initial diagnosis or assessment should be based on patients best interest rather than on convenience or the cost of the medicine and associated monitoring or follow-up

Good practice recommendation 36.

- Shared care requires the agreement of all parties including the patient. Effective communication and continuing liaison between all parties to a shared care agreement is essential.

Good practice recommendation 37.

- If you prescribe at the recommendation of another doctor, nurse or other healthcare professional, you must satisfy yourself that the prescription is needed, appropriate for the patient and within the limits of your competence.

Good practice recommendation 38.

- If you delegate assessment of a patients' suitability for a medicine, you must be satisfied that the person to whom you delegate has the qualifications, experience, knowledge and skills to make the assessment. You must give them enough information about the patient to carry out the assessment required

Good practice recommendation 39.

- In both cases, you will be responsible for any prescription you sign.

Good practice recommendation 40.

- If you recommend that a colleague, for example a junior doctor or general practitioner, prescribes a particular medicine for a patient, you must consider their competence to do so. You must satisfy yourself that they have sufficient knowledge of the patient and the medicine, experience (especially in the case of junior doctors) and information to prescribe. You should be willing to answer their questions and otherwise assist them in caring for the patient, as required

Good practice recommendation 41

- If you share responsibility for a patient's care with a colleague , you must be competent to exercise your share of clinical responsibility.

You should:

a) Keep yourself informed about the medicines that are to be prescribed for the patient
b) Be able to recognise serious and frequently occurring adverse side effects
c) Make sure appropriate clinical monitoring arrangements are in place and that the patient and the healthcare professionals involved understand them
d) Keep up to date with relevance guidance on the use of the medicines and on the management of the patient's condition

Good practice recommendation 42

- In proposing a shared care arrangement, specialists may advise the patient's general practitioner which medicine to prescribe. If you are recommending a new or rarely prescribed medicine you should specify the dosage and means of administration and agree a protocol for treatment. You should explain the use of unlicensed medicines and departures from

authoritative guidance or recommended treatments and provide both the general practitioner and the patient with sufficient information to permit the safe management of the patient's condition.

Good practice recommendation 43

- If you are uncertain about your competence to take responsibility for the patients continuing care you should seek further information or advice from the clinician with whom the patient's care is shared or from another experienced colleague. If you are still not satisfied you should explain this to the other clinician and to the patient and make appropriate arrangements for their continuing care.

Introduction

In September 2008 the National Institute for Health and Clinical Excellence (NICE) published its clinical guideline 72 on diagnosis and management of Attention Deficit Hyperactivity Disorder (ADHD) in children, young people and adults.

The main conclusions from the guideline in relation to the pharmacological management of the condition are:

- Diagnosis should only be made by a specialist psychiatrist, paediatrician or other healthcare professional with training and expertise in the diagnosis of ADHD. Diagnosis should be made according to DSM-IV criteria or the guidelines in ICD-10.
- In pre-school age children – drug treatment is not recommended. Healthcare professionals should offer parents or carers of pre-school children with ADHD a referral to apparent-training/education programme as first-line treatment.
- In school age children with moderate ADHD and moderate impairment – drug treatment should be reserved for those with moderate impairment where non-drug interventions have been refused or where there are persisting significant impairment following parent-training/education programme or group psychological treatment.
- In school age children and young people with severe ADHD and severe impairment – offer drug treatment first line – also offer parents a group based training programme.
- Drug treatment should only be started by a healthcare professional with expertise in ADHD.
- Treatment should be based on comprehensive assessment.
- Drug treatment should always be part of comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions.
- **GPs may continue prescribing and monitoring drug treatment under shared care arrangements**.
- Do not use antipsychotics for the management of ADHD in children and young people.
- Methylphenidate, atomoxetine and dexamfetamine are recommended, within their licensed indications, as options for the management of ADHD.
- Drug choice is the responsibility of the healthcare professional with expertise in ADHD and should be based on:
    - ❖ Co-morbidities e.g. tics, tourettes syndrome, epilepsy.
    - ❖ Different adverse effects of drug treatments
    - ❖ Potential problems with compliance e.g. arrangements for midday dose to be administered at school.
    - ❖ Potential risk of drug diversion and misuse
    - ❖ Preferences of child/young person and their parent/carer.
- NICE advises:
    - ❖ Consider methylphenidate for ADHD without significant co morbidity
    - ❖ Consider methylphenidate for ADHD with co morbid conduct disorder

- ❖ Consider methylphenidate or atomoxetine in the presence of tics, Tourettes syndrome, anxiety disorder, and stimulant misuse or stimulant diversion.
- ❖ Consider atomoxetine if methylphenidate has been tried and has been ineffective at the maximum tolerate dose or the child/young person is intolerant to low or moderate doses of methylphenidate.
- ❖ If there is a choice of more than one drug use the drug with the lowest overall cost.

- If using methylphenidate, consider:
  - ❖ Modified- release preparations for convenience, their pharmacokinetic profile, improving adherence, reducing stigma(because the drug does not need to be taken at school) and reducing problems of storing and administering controlled drugs in schools.
  - ❖ Immediate-release preparations if more flexible dosing is required or during initial titration to determine correct dosing levels

- Consider dexamfetamine when symptoms are unresponsive to the maximum tolerated dose of methylphenidate or atomoxetine.

Lisdexamfetamine

- Lisdexamfetamine was launched in the UK in 2013 licensed to be used as part of a comprehensive treatment programme for the treatment of attention deficit disorder in children aged over 6 years of age when response to previous methyphenidate treatment is considered to be clinically inadequate. Lisdexamfetsamine is a prodrug that is converted in the blood to dexamfetamine. Lincolnshire's Prescribing and Clinical Effectiveness Forum (PACEF) has approved lisdexamfetamine for use within its licensing authorisation as an option for treatment.

Drug Details

Approved generic name - **Methylphenidate**
Brand Name - Concerta XL, Equasym XL, Medikinet, Medikinet XL, Ritalin
Form and strength: standard release and modified release preparations

Approved generic name – Atomoxetine
Brand Name - Strattera
Form and strength: 10mg, 18mg, 25mg, 40mg, 60mg and 80mg capsules

Approved generic name - Dexamfetamine
Form and strength: 5mg tablets

Approved generic name - Lisdexamfetamine
Brand name – Elvanse
Form and strength: 30mg,50mg and 70mg capsules

Specialist Responsibilities

The specialist secondary/tertiary care service will:

1. Provide a comprehensive baseline ~~physical~~ assessment as stipulated in NICE guidance to include:
    - A full mental health and social assessment
    - A full history and physical examination, including:
        - ❖ Assessment of history of exercise syncope, undue breathlessness and other cardiovascular symptoms
        - ❖ Heart rate and blood pressure (plot on centile chart)
        - ❖ Height and weight (plot on growth chart)
        - ❖ Family history of cardiac disease and examination of the cardiovascular system
    - An electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination..
    - Risk assessment for substance misuse and drug diversion.

2. Routine blood tests and ECGs are not recommended unless there is a clinical indication.
3. Interpret or arrange interpretation of electrocardiogram (ECG) if applicable.
4. Initiate therapy following full discussion with the patient/carer of different treatment options, benefits and risks. **The choice of initial drug treatment and any changes to the choice of treatment is the responsibility of the specialist service.**
5. Provide relevant, age appropriate, written information to the child/young person/parent/carer about diagnosis, assessment, support, self-help, psychological treatment, drug treatment and possible side effects.
6. Liaise with GP, School and any other agency involved with the child/young person, providing a comprehensive treatment programme for the child/young person. This must include frequency of specialist review following stabilisation and be aware of ongoing issues relating to prescribing when reaching young adulthood.
7. Titrate dose according to schedule adjusting dose as appropriate and undertake monitoring of clinical response and side effects. **In certain circumstances agreement may be reached between the specialist service and the GP for the GP to continue to titrate the dose according to response.**
8. **During titration ensure the:**
    - Gradual increase of the dose until there is no further improvement in symptoms, behaviour, education and or relationships and side effects are tolerable. Methylphenidate and dexamphetamine should be titrated over 4-6weeks.
    - Parents and teachers record symptoms and side effects at each dose change (for example on conners'10- item scale
    - Review progress regularly (for example, weekly telephone contact and at each dose change).
    - Dose titration is slower if tics or seizures are present
    - Dose reduction is considered if side effects become troublesome
9. After titration and dose stabilisation carry out prescription and monitoring under locally agreed shared care arrangements with primary care
10. Send a letter to the GP, once a patient is stabilised on treatment suggesting that shared care should be considered for this patient. This letter should contain the following information.
    - Patient details including name, address date of birth and NHS number.
    - Details of treatment including drug name, dose, date treatment commenced and any further dose titration that is required (if applicable).

- Details and the results of any investigations/ base line checks that have been carried out prior to commencement of treatment. This should include blood pressure, pulse rate, weight and height.
- Date of patient's last clinic visit and date of next clinic visit.
- Name and contact details of consultant, key worker (if appropriate) and main carer.

Appendix A is an example of the letter but format and content may vary depending on which specialist service is responsible for the treatment.

11. Specialist review should be undertaken either by an ADHD specialist **or, if agreed by the person with ADHD and their specialist, in primary care under a locally agreed shared care arrangement** after titration and dose stabilisation
12. Review the patient at least annually to assess their need for continued treatment The annual specialist review of drug treatment should include a comprehensive assessment of the following
    - Routine monitoring of height, weight, blood pressure and heart rate.
    - Clinical need, benefits and side effects.
    - The views of the person and those of a parent, carer, teacher, spouse, partner and close friends as appropriate.
    - The effect of missed doses, planned dose reductions and brief periods of no treatment should be taken into account and the preferred pattern of use should also be reviewed.
    - Coexisting conditions should be reviewed, and the person treated or referred if necessary.
    - The need for psychological, social and occupational support for the person and their parents or carers (as appropriate) should be assessed
13. Issue a letter/clinic report to the GP after each review appointment providing a summary of review findings, confirmation of continuing treatment or treatment changes, confirmation that relevant monitoring has taken place or an explanation as to why it has been deemed necessary unnecessary, assessment of the child/young person's progress and confirmation that further prescriptions should be issued and the time of the next review.
14. Respond to any request from the GP to review the patient due to adverse effects of therapy.
15. Report any adverse effects of therapy to the Medicines and Health care products Regulatory Agency (MHRA)
16. Remain alert for the potential for misuse of methylphenidate and dexamfetamine, by observing the frequency and quantity of prescriptions issued and be alert to changes in family circumstances
17. Advise the GP on continuing or stopping the medication following medical review of the patient and associated drug therapy.
18. Notify the GP if the patient is failing to attend for appropriate monitoring and advise GP on appropriate action. If the patient and their family fail to attend on two consecutive occasions the specialist will contact the patient's GP and advise them not to issue any further prescriptions and the patient will be discharged from the specialist service.
19. For patients aged 17-18 years manage withdrawal of treatment prior to discharge or refer to appropriate adult services. Reassess a young person treated in CAMHS or paediatric services at school leaving age to determine if treatment needs to be continued. If it does arrange for transition to adult services (usually by age 18) giving details of the anticipated treatment and services required.
20. Will inform the patient's GP if the ongoing responsibility for patient care is to be transferred to another consultant/ specialist service and to ensure both parties are aware of this change

Methylphenidate, dexamfetamine and lisdexamfetamine are schedule 2 controlled drugs and therefore all controlled drug prescription writing legislation set down in the section of "Controlled Drugs and Drug dependence" in the British National Formulary (BNF) applies.

GP Responsibilities

The GP will:

1. Prior to referral to the specialist service determine the severity of behavioural and/ or inattention problems suggestive of ADHD and how they affect the child or young person and their parents or carers. If problems are having an adverse impact on development or family life and persist with at least moderate impairment following either a period of up to 10 weeks watchful waiting or referral into a parent training/education programme then refer to secondary care either a paediatrician, child psychiatrist or specialist from the Children & Adolescents Mental Health Service. CAMHS.
2. Refer directly to secondary care if the behavioural and /or inattention problems are associated with severe impairment.
3. Notify the consultant in writing, without undue delay whether or not they agree to share care.
4. Provide any information requested by the specialist in relation to previous history of QTC prolongation or concurrent medication.
5. Prescribe the drug therapy as part of the shared care agreement once patient is stabilised. In certain circumstances the GP, following a request from the consultant specialist may agree to further titrate the dose according to the patient's response.
6. Monitor the patients overall health and well-being on a needs led basis.
7. Monitor patients for side effects including heart rate, BP and weight as stipulated in monitoring section of the NICE clinical guideline 72. (see monitoring section page 14)
8. Monitor those patients prescribed atomoxetine for signs of depression,
9. Monitor patient's suicidal thoughts or behaviour. If warning signs are detected treatment should be discontinued and urgent advice sought from specialist.
10. Remain alert for the potential for misuse of methylphenidate and dexamfetamine, by observing the frequency and quantity of prescriptions issued and be alert to changes in family circumstances.
11. Report adverse effects of therapy to the consultant and the medicines and health care products Regulatory Agency (MHRA).
12. Act on advice provided by the consultant if patient does not attend for appropriate monitoring. If the patient and their family fail to attend on two consecutive occasions then the GP will be advised not to issue any further prescriptions.
13. Can re-refer patients and their families back to secondary care following discontinuation of treatment as outlines in point 11 if the family can show they are willing to engage with both the specialist service and the monitoring requirements for the proposed treatment.
14. Alert the specialist if there are any concerns about the patient's response to treatment or the ability of the patient to tolerate treatment.
15. Alert the specialist if there are any issues identified relating to poor concordance/compliance e.g. irregularities in the collection of repeat prescriptions.

Referral Criteria

The patients will be stabilised on a suitable dose of methylphenidate, atomoxetine, dexamfetamine or lisdexamfetamine before prescribing responsibility is transferred to the GP.
The specialist service will continue to supply treatment until the GP is prepared to accept responsibility for shared care.

Licensed Indications

Methylphenidate hydrochloride, atomoxetine, dexamfetamine and lisdexamfetamine are all licensed for the treatment of Attention Deficit Hyperactivity Disorders.
Their license states that treatment should be initiated by a specialist physician experienced in managing the condition or in the case of dexamfetamine use should be under specialist supervision.There are licensing variations between the various substances and products. Refer to summary of product characteristics for further details. **Methylphenidate, dexamfetamine and lisdexamfetamine are not licensed for the management of ADHD in adults aged over 18 years. Atomoxetine, methylphenidate and lisdexamfetamine are not licensed for use in children under the age of 6 years of age.**

Recommended Dosage and Administration

Methylphenidate

Standard formulations e.g. generic methylphenidate or branded products Ritalin or Medikinet require careful dose titration.
Child 6-18 years. - The recommended starting dose is 5mg daily or twice daily increasing as necessary in weekly increments of 5-10mg to an effective dose. Usual maximum recommended dose is 60mg in two or three divided doses. Dose may be increased beyond the licensed daily dose of 0.7mg/kg up to 2.1mg/kg daily in 2-3 divided doses (up to a maximum of 90mg daily), under the direction of a specialist. Discontinue if no response after 1 month.
At higher doses monitor carefully for adverse effects.
Adults over 18 years – unlicensed use. 5mg three times daily increased if necessary at weekly intervals according to response. Maximum dose 100mg daily in 2-3 divided doses.
Modified release formulations – vary in the ration of immediate release to extended release methylphenidate that they contain, and also have differing pharmacokinetic profiles resulting in some delivering higher levels of methylphenidate at the start of the day and some provide a therapeutic effect lasting that of a school day 8 hours where others provide an effect lasting up to 12 hours.
Concerta XL – The formulation is 22% immediate release and 78% extended release. For those patients who have not previously taken methylphenidate the starting dose is for a child 6-18 years, 18mg once daily. Dose should be carefully titrated in increments of 18mg once a week to a maximum daily dose of 54mg/day taken as a single daily dose in the morning. If patients have previously taken methylphenidate Concerta XL please refer to manufactures information for equivalent doses. Discontinue if no response after 1 month
Equasym XL - This contains immediate release and extended release methylphenidate in the ratio 30:70. . For those patients who have not taken methylphenidate before the starting dose is for a child 6-18 years, 10mg once daily in the morning increasing gradually at weekly intervals if necessary, usual maximum 60mg daily but may be increased to 2.1mg/kg daily (max 90mg)- unlicensed dose) under direction of specialist. For those patients currently on immediate release methyphenidate careful dose titration will be required when switching to a modified release formulation. Discontinue if no response after 1 month

Medikinet XL - This formulation consists of 50% extended release and 50% immediate release methylphenidate. In those patients not currently taking methylphenidate the starting dose for child 6-18 years is 10mg once daily in the morning with or after breakfast increasing gradually to a maximum of 100mg. if required. For those patients currently on immediate release methyphenidate careful dose titration will be required when switching to a modified release formulation.

Atomoxetine
Child over 6 years of age and adolescent with body weight under 70kg, initially 500micrograms/kg daily for seven days then increased according to response to usual maintenance dose of 1.2mg/kg

daily, but may be increased to 1.8mg/kg daily (maximum dose 120mg daily – unlicensed) under direction of a specialist.
Child and adolescent with body weight over 70kg, initially 40mg daily for seven days then increased according to response to usual maintenance dose of 80mg daily ; but may be increased to 1.8mg/kg/day up to a maximum dose of 120mg daily (unlicensed) under the direction of a specialist. These higher doses should only be used after review of poor response to drug treatment and in consultation with a tertiary or regional centre. At higher does monitor carefully for adverse effects. Total daily dose can be given either a single dose in the morning or in two divided doses with the last dose given no later then early evening.
Atomoxetine is now licensed for use in adults when the presence of symptoms of ADHD that were pre-existing in childhood are confirmed. Initiation of treatment in adults is not covered under this shared care protocol.

Dexamfetamine
Child 6-18 years initially 2.5mg 2-3 times daily increased if necessary at weekly intervals by 5mg usual max 1mg/kg (up to 20mg) daily.
Maintenance dose is given in 2-4 divided doses.
Use in adults is unlicensed.
Lisdexamfetamine dimesylate
Children aged 6 years or older initially 30mg once daily in the morning. The lowest effective dose should be used. The dose can be increased by 20mg increments at approximately weekly intervals to a maximum recommended daily dose of 70mg. Treatment should be stopped if the symptoms do not improve after appropriate dosage adjustment over a one month period.
Use in adults is unlicensed.

Background Pharmacology

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most commonly diagnosed behavioural disorders of childhood, affecting 1-5% of school aged children. Its basic symptoms include developmentally inappropriate levels of attention, concentration, activity, distractibility and impulsivity. It causes problems in at home, in school, with peer relationships and may have long term adverse effects on self confidence, academic performance, vocational success and social development.
Drugs licensed for the treatment of this disorder should be used as part of a comprehensive treatment programme.
Drugs used can be divided into two groups.
Central Nervous Stimulants
Methylphenidate – is a central nervous stimulant.
Dexamfetamine - is a sympathomimetic amine with a central stimulant and anorectic activity. On set of action is 60-90 minutes with peak serum concentration being reached 3 hours after oral administration.
Lisdexamfetamine dimesylate is a pharmacologically inactive prodrug of dexamfetamine. After oral administration lisdexamfetamine is rapidly absorbed from the gastrointestinal tract and hydrolysed primarily by red blood cells to dexamfetamine.
Both methylphenidate and dexamfetamine are controlled drugs and subject to the requirements of the misuse of drugs regulations. As a prodrug of dexamfetamine it is expected that lisdexamfetamine will also be classed as a schedule 2 controlled drug. In the interim the Home Office and the Royal Pharmaceutical Society have advised that Lisdexamfetamine should be treated as a schedule 2 CD
All three drugs potentially have a resale value as drugs of abuse. These are all amphetamine related substances and are effective in increasing attention and concentration and reducing impulsive and

restless behaviours. Secondary effects include increased school performance, improved peer relations and reduced aggression

Noradrenalin uptake inhibitor.

Atomoxetine is a highly selective and potent noradrenaline reuptake inhibitor, although the precise mechanism by which it works on ADHD is unknown. It is not a psychostimulant and is not an amphetamine derivative.

It is effective in increasing attention and concentration and reducing impulsive and restless behaviours. It may also improve sleep and have an effect on early morning behaviours. It provided 24 hour control of ADHD symptoms.

Adverse Effects(please refer to BNF and product SPC for more details)

Methylphenidate

Abdominal pain, nausea, vomiting, diarrhoea, dyspepsia, dry mouth, anorexia, reduced weight gain, tachycardia, palpitation, arrhythmias, changes in blood pressure, cough, nasopharyngitis, tics (very rarely tourettes syndrome), insomnia, nervousness, asthenia, depression, irritability, aggression, headache, drowsiness, dizziness, movement disorders, fever, arthralgia, rash, pruritus, alopecia, growth restriction. Less commonly constipation, dyspnoea, abnormal dreams, confusion, suicidal ideation, urinary frequency, haematuria, muscle cramps, epistaxis, rarely angina, sweating and visual disturbances. Very rarely hepatic dysfunction, myocardial infarction, cerebral arteritis, psychosis, seizures, neuroleptic malignant syndrome, tolerance and dependence, blood disorders including leucopenia and thrombocytopenia, angle-closure glaucoma, exfoliative dermatitis and erythema multiforme, supraventricular tachycardia, bradycardia and convulsions also reported.

Atomoxetine

Anorexia, dry mouth, nausea, vomiting, abdominal pain, constipation, dyspepsia, flatulence, palpitation, tachycardia, increased blood pressure, postural hypotension, hot flushes, sleep disturbances, dizziness, headache, fatigue, lethargy, drowsiness, irritability, tremor, rigors, urinary retention, enuresis, prostatis, sexual dysfunction, menstrual disturbances, conjunctivitis, dermatitis, pruritus, rash, sweating, weight changes, less commonly suicidal ideation, aggression, hostility, emotional lability, cold extremities, mydriasis, very rarely angle-closure glaucoma also reported hepatic disorders, psychosis, hypoaesthesia, anxiety, depression, seizures and Raynaud's phenomenon.

Dexamfetamine

Nausea, diarrhoea, dry mouth, abdominal cramps, anorexia (increased appetite also reported) weight loss, taste disturbance, ischaemic colitis, palpitations, tachycardia, chest pain, hypertension, hypotension, cardiomyopathy, myocardial infarction, cardio vascular collapse, cerebral vasculitis, stroke, , headache, restlessness, depression, hyperreflexia, hyperactivity, impaired concentration, ataxia, anxiety,aggression, dizziness, confusion, sleep disturbances, dysphoria, euphoria, irritability, nervousness, malaise, obsessive-complusive behaviour, paranoia, psychosis, panic attack, tremor, seizures, neuroleptic malignant syndrome, anhedonia, growth restriction in children, pyrexia, renal impairment, sexual dysfunction, acidosis, rhabdomyolysis, mrdriasis, visual disturbances, alopecia, rash , sweating, urticarial, central stimulants have provoked choreoathetoid movements and dyskinesia tics and Tourette syndrome in predisposed individuals, very rarely angle closure glaucoma.

Lisdexamfetamine

Nausea, decreased appetite, vomiting, diarrhoea, dry mouth, abdominal cramps, dyspnoea, sleep disturbances, tics, aggression, headache, dizziness, drowsiness, mydriasis, labile mood, weight loss, pyrexia, malaise, growth restriction in children. Less commonly anorexia, tachycardia, palpitation, hypertension, logorrhoea, anxiety, paranoia, restlessness, depression, dysphoria, dermatillomania, mania, hallucination, sweating, tremor, visual disturbance, sexual dysfunction, rash. Very rarely angle closure glaucoma also reported cardiomyopathy, euphoria, seizures, central stimulants have

provoked choreoathetoid movements and dyskinesia and Tourette syndrome in predisposed individuals.
As a black triangle drug all adverse reactions should be reported through the yellow card system accessible online at www.mhra.gov.uk/yellowcard.

Drug Interactions (please refer to BNF and product SPC for more details)

Methylphenidate

Monoamine Oxidase Inhibitors (MAOIs) contraindicated in those being treated with MAOI's or those who have had treatment in preceding two weeks due to risk of hypertensive crisis.
Warfarin – may increase the anticoagulant effect
Anticonvulsants – may increase plasma levels of phenobarbitone, primidone.
Alcohol – may increase CNS effects of methylphenidate.
Anti- hypertensives – may decrease effectiveness.
Halogenated anaesthetics – risk of sudden blood pressure increase during surgery. If surgery planned methyphenidate should not be used on day of surgery.
Dopaminergic drugs – caution recommended if using with dopamine antagonists such as antipsychotics or dopamine agonists such as tricyclic antidepressants as action of methyphenidate is to increase extracellular dopamine levels.
Centrally acting alpha-2 agonists e.g. clonidine - serious adverse reactions have been reported including sudden death – avoid concomitant use.

Atomoxetine

Monoamine Oxidase Inhibitors (MAOIs) Atomoxetine should not be used in combination with a MAOI. It should not be used within a minimum of two weeks after discontinuing therapy with a MAOI and treatment with an MAOI should not be initiated within two weeks after discontinuing treatment with atomoxetine.
Increases risk of ventricular arrhythmias with tricyclic antidepressants, methadone, amiodarone, disopyramide, parenteral erythromycin, moxifloxacin, and mefloquine, antipsychotics that increase the QTC interval, sotalol and diuretics.
Use with caution in patients on concomitant drugs that may lower the seizure threshold e.g. antidepressants, mefloquine, bupropion, tramadol and neuroleptics.

Dexamfetamine

Tricyclic antidepressants may increase risk of cardiovascular adverse effect.
Beta-blockers used concurrently may result in severe hypertension.
Lithium may antagonise effects of dexamfetamine.
Concurrent use of MAOIs or use within the preceding fourteen days may precipitate a hypertensive crisis.
Antihistamines may delay absorption of ethosuximide, phenobarbitone and phenytoin.
Acute dystonia has been noted with concurrent administration of haloperidol.
Phenothiazines may inhibit the actions of dexamfetamine.
Alcohol can increase CNS effects of dexamfetamine and patients should be advised to abstain from alcohol during treatment.

Lisdexamfetamine

Ascorbic acid can acidifly urine , increase urinary excretion of lisdexamfetamine and reducing its half-life.
Sodium bicarbonate and other agents that alkalise the urine decrease urinary excretion and can prolong the half life.
Monamine oxidase inhibitors (MAOI's) should not be administered during or within 14 days of MAOI's as can increase the release of norepinephrine and other monoamines leading to severe headaches and other signs of hypertensive crisis.

Antihypertensives – may decrease effectiveness of guanethidine and other antihypertensive medications.
Could potentiate the analgesic effect of narcotic analgesics.
Chlorpromazine and haloperidol inhibit central stimulant effects of amphetamines.
Lithium may block anorectic and stimulatory effects of amphetamines.
May elevate plasma corticosteroid levels.

Precautions (please refer to Summary of product characteristics and current edition of the BNF for more detail)

Methylphenidate

Should be used with caution in patients with history of epilepsy (discontinue or seek specialist advice if increased seizure frequency), psychotic disorders anxiety or agitation, tics or a family history of Tourette sundrome, susceptibility to angle-closure glaucoma; avoid abrupt withdrawal.

Atomoxetine

Should be used with caution in patients whose underlying medical condition could be worsened by increases in blood pressure and heart rate , such as patients with hypertension, tachycardia or cardiovascular or cerebrovascular disease. Patients who develop symptoms such as palpitations, extertional chest pain , unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease during atomoxetine treatment should undergo a prompt specialist cardiac evaluation.
Atomoxetine should only be used with caution in those with congenital or acquired long QTC or a family history of QTC prolongation. The risk increases if atomoxetine is used concomitantly with other drugs that produce QTC prolongation, drugs that cause electrolyte disturbances and those that inhibit cytochrome P450 2D6.
Patients should be monitored for the appearance of, or worsening of suicide related behaviour, hostility, psychotic or manic symptoms and emotional lability.
Seizures are a potential risk therefore atomoxetine should be introduced with caution in patients with a history of seizure. Discontinuation should be considered in any patient developing seizure or if thee is an increase in seizure frequency.
Should be discontinued in patients with jaundice or laboratory evidence of liver injury and should not be restarted. Patients and carers should be advised of risk of hepatic disorders and told how to recognise symptoms.
Hepatic impairment - halve dose in moderate impairment, quarter dose in sever impairment.
Pregnancy - no information available avoid use unless potential benefit outweighs risk.

Dexamfetamine

Use with caution in patients with anorexia, mild hypertension (contra-indicated if moderate or severe) psychosis or bipolar disorder, monitor for aggressive behaviour or hostility during initial treatment, history of epilepsy discontinue if seizures occur), tics and Tourette's syndrome (use with caution) – discontinue if tics occur, monitoring growth in children and susceptibility to angle closed glaucoma. Avoid abrupt withdrawal, data on safety and efficacy of long-term use not complete, acute porphyria. Special caution for use in children- monitor height and weight as growth restriction may occur in prolonged therapy. (Drug free periods may allow catch up in growth but withdraw slowly to avoid inducing depression or renewed hyperactivity)

Lisdexamfetamine

Use with caution in those with anorexia, history of cardiovascular disease or abnormalities including mild hypertension, heart failure, recent MI and ventricular arrhythmia. Evaluate cardiovascular status before starting treatment.
Use with caution in those with psychotic disorders, bipolar disorder, monitor for aggressive behaviour or hostility during drug treatment, history of drug or alcohol abuse, may lower seizure threshold (discontinue if seizures occur) tics and Tourettes syndrome (use with caution and discontinue is tics occur.

Use with caution in those with susceptibilioty to angle-closure glaucoma, avoid abrupt withdrawal, acute porphyria.
Special caution for use in children- monitor height and weight as growth restriction may occur in prolonged therapy. (Drug free periods may allow catch up in growth but withdraw slowly to avoid inducing depression or renewed hyperactivity)
Renal impairment.

Contraindications(please refer to Summary of product characteristics and current edition of the BNF for more detail)

Methylphenidate –
Not to be used in patients with severe depression, suicidal ideation, anorexia nervosa, drug or alcohol dependence, psychosis, uncontrolled bipolar disorder, hyperthyroidism or thyrotoxicosis , cardiovascular disease (including heart failure, cardiomyopathy, severe hypertension, arterial occlusive disease, angina, and arrhythmias), structural cardiac abnormalities, phaeochromocytoma, glaucoma, vasculitis, cerebrovascular disorders.
Hypersensitivity or intolerance to methylphenidate or excipients
Pregnancy - no information available avoid use unless potential benefit outweighs risk.
Breast feeding – limited information available – avoid..

Atomoxetine –
Do not use in patients with narrow angle glaucoma
Should not be used if patient concurrently taking monoamine oxidase inhibitors (MAOIs).
Hypersensitivity or intolerance to atomoxetine or excipients
Should not be used in patients with pheochromocytoma or history of pheochromocytoma.
Should not be used in patients with severe cardiovascular or cerebrovascular disorders.
Pregnancy - no information available avoid use unless potential benefit outweighs risk.
Breast feeding – avoid use present in milk in animal studies.

Dexamfetamine –
Not to be used in patients with marked anxiety disorders,hyperexcitability, psychosis, history of drug or alcohol abuse, cardiovascular disease (including moderate to severe hypertension), structural cardiac abnormalities, advanced arteriosclerosis, hyperthyroidism, glaucoma and in pregnancy and breast feeding.
Contra-indicated in Tourettes syndrome but is used with caution by specialists. Any prescribing in this situation is unlicensed.
Hypersensitivity or intolerance to dexamfetamine or excipients.

Lisdexamfetamine-
Not to be used in those with symptomatic cardiovascular disease including moderate to severe hypertension and advanced arteriosclerosis, hyperexcitability or agitated states, hyperthyroidism.
Not to be used if breast feeding.
Pregnancy – manufacturer advises use only if potential benefit outweighs risk.

Monitoring

Responsibility of specialist service prior to commencement of treatment

Children and young people with ADHD should have a full pre-treatment assessment which 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 centile chart)
- Height and weight (plotted on growth chart)
- Family history of cardiac disease and examination of the cardiovascular system.
- An ECG if there is a past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination.
- Risk assessment for substance abuse and drug diversion
- Enquiry about history of seizures or tics.

Monitoring required during drug treatment –.
Blood pressure and heart rate should be monitored before and after each dose change, and every three months. **If sustained tachycardia, arrhythmia or systolic BP greater than 95th centile (or a clinically significant increase) is measured on 2 occasions contact paediatrician for advice and consider dose reduction.**
Height should be monitored every 6 months.
Weight should be measured at 3 & 6 months after treatment started and then 6 monthly thereafter.
Both height and weight measurements should be plotted on growth centile chart and should be regularly reviewed by the specialist responsible for treatment.

During treatment NICE states that people taking methylphenidate, dexamfetamine or atomoxetine, do not need routine blood tests and ECGs unless there is a clinical need.
For children and young people taking methylphenidate and dexamfetamine, healthcare professionals/parents and carers should monitor changes in the potential for drug misuse and diversion which may come with changes in circumstances and age .In these situations modified release methylphenidate or atomoxetine may be preffered.
In young people sexual dysfunction and dysmenorrhoea should be monitored as potential side effects of atomoxetine.

Reference values for blood pressure measurements
The Journal of hypertension 27(9):1719-1742 September 2009 contains reference blood pressure charts for children and adolescents. This can be accessed via The British Hypertension Society website following the link below:
http://www.bhsoc.org/resources/children-young-people/
Appendix B contains the Nottinghamshire Guideline for the assessment and management of Hypertension in Paediatric Patients which also contains reference tables for blood pressure centiles by gender, age and height percentiles.

Management of adverse effects.
Atomoxetine

At normal doses atomoxetine can be associated with treatment emergent psychotic or manic symptoms e.g. hallucinations, delusional thinking, mania or agitation) in children or adolescents without a previous history. If such symptoms occur contact consultant medical team urgently for advice and consider discontinuing or withdrawing treatment.
Patients and their carers should be informed of risk of suicidal thoughts/behaviour and advised to contact the specialist team for urgent advice if these occur or if there is worsening of irritability, agitation or depression.
Development of seizures. Discontinue treatment and seek urgent advice from specialist.
Hepatic disorders. Be alert to possibility of jaundice or laboratory evidence of liver injury. If either occurs discontinue treatment and seek urgent specialist advice. In these circumstances treatment must not be restarted. Patients and carers should be advised of risk of liver damage and be told how to recognise symptoms. Prompt medical attention should be sought in case of abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice.

Indication of Likely Cost of Therapy in Primary Care

Approximate annual cost at licensed dose.

Methylphenidate

Methylphenidate 5-60mg in one to two divided doses £37 -£396
Medikinet 5-60mg in one to two divided doses £37 - £394
Ritalin -5-60mg in one to two divided doses £41-£481
Concerta XL 18-54mg once daily £375-£884
Equasym XL 10-60mg once daily £300-£840
Medikinet XL 10-60mg once daily £289 - £808

Atomoxetine

Strattera 10/18/25/40/60mg one tablet daily £812

Dexamfetamine

Dexedrine 2.5mg-40mg daily, £160-£2,574
Lisdexamfetamine 30-70mg daily £758 - £1,081

Guide prices from September 2015 edition of MIMS

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References:

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8. Summary of product characteristics. Elvanse 30mg,50mg & 70mg hard capsules. Shire Pharmaceuticals Limited. Updated 28th February 2013.
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Appendix A Invitation to shared care.

Shared Care Protocol for treatment of Attention Deficit Hyperactivity Disorder in Childhood

Section 1: Agreement for transfer of prescribing to GP

Patient details/addressograph

Name ……
Address ……
……
DOB …… Hospital No ……

Drug name and dose:

The following tests, investigations have been carried out:

Blood pressure: Date:
Pulse: Date:
Weight: (including centiles) Date:
Height: (including centiles) Date:
Diagnosis of ADHD made on (date):
Medication started on (date):
Patient stabilised on (drug/dose):
Patient's last clinic visit on (date):
Patient's next clinic visit on: then every months

Consultant: Address: Contact Number:	**Agreement to shared care, to be signed by GP and Consultant before transfer of care to GP.** **Consultant Signature:** …… **Date:**
GP Address: Contact Number:	
Main Carer / parent / guardian: Contact Number:	**GP Signature:** …… **Date:**
Key worker if appropriate: Contact Number:	

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant. The GP should then discuss alternative arrangements with the responsible consultant.

Hypertension

Title of Guideline (must include the word "Guideline" (not protocol, policy, procedure etc)	Guideline for the assessment and management of Hypertension in Paediatric Patients
Contact Name and Job Title (author)	David Broodbank ST7 Paediatrics Corinne Langstaff Paediatric Nephrology Consultant
Directorate & Speciality	Family Health – Paediatric Nephrology
Date of submission	September 2013
Date on which guideline must be reviewed (this should be one to three years)	September 2016
Explicit definition of patient group to which it applies (e.g. inclusion and exclusion criteria, diagnosis)	Children and Young People presenting to Nottingham Children's Hospital With Hypertension
Abstract	This guideline describes the Assessment and Management of Hypertension in Paediatric patients.
Key Words	Hypertension, High Blood Pressure, Child, Young Person, Renal,
Statement of the evidence base of the guideline – has the guideline been peer reviewed by colleagues? **Evidence base: (1-5)**	2a
Consultation Process	Children's Renal Unit guideline review, Paediatric Clinical Guidelines Group
Target audience	Clinicians and healthcare professionals caring for children and young people treated for Hypertension at Nottingham University Hospitals NHS Trust
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.	

1a	meta analysis of randomised controlled trials
1b	at least one randomised controlled trial
2a	at least one well-designed controlled study without randomisation
2b	at least one other type of well-designed quasi-experimental study
3	well –designed non-experimental descriptive studies (ie comparative / correlation and case studies)
4	expert committee reports or opinions and / or clinical experiences of respected authorities
5	recommended best practise based on the clinical experience of the guideline developer

Version Number	Date Produced	Author
Hypertension Guideline V1	May 2008	Dr D Wood, Dr S Rhodes
V2	Sept 2013	Dr David Broodbank Dr Corinne Langstaff

Document History

Major changes from previous guideline:

1. Inclusion of definitions of hypertension in line with 4th report
2. Reduction in detail regarding presentation, history and examination
3. Clarification of section on lifestyle management
4. Inclusion of section on management of hypertensive crisis
5. Update of centile charts as per 4th report and inclusion of centile charts for neonates.
6. Addition of section on specific anti-hypertensive agents
7. Addition of separate algorithms for patients with acute severe / symptomatic hypertension and asymptomatic hypertension

1. Introduction

Hypertension in children is common, occurring in 5% of the paediatric population. Although often asymptomatic, a significant proportion of children will have an underlying cause so investigation is usually justified. The measurement of blood pressure itself in children is challenging and hypertension will only be identified if children have their blood pressure checked appropriately. The long-term health risks for hypertensive children and adolescents can be substantial and so it is important to seek out and treat hypertension.

2. Definitions (Fourth Report[1])

- **Hypertension:** Average systolic blood pressure (SBP) and / or diastolic blood pressure (DSP) greater or equal to the 95th percentile for age, sex and height on three or more occasions.

- **Severe Hypertension** (also described as stage 2 hypertension)**:** Average of 3 readings SBP and / or DSP >5mmHg above the 99th percentile.

- **Prehypertension (or high normal blood pressure):** Average SBP and /or DSP greater or equal to the 90th percentile but below the 95th percentile.

- **Adolescents (aged 10-19 years)** with blood pressure above 120/80mmHg should be considered prehypertensive.

- **White Coat Hypertension:** A patient with BP levels above the 95th percentile in clinic or hospital, who is normotensive outside a clinical setting. Ambulatory BP monitoring (ABPM) is usually required to make this diagnosis.

3. Presentation

Hypertension may present as an asymptomatic incidental finding, during screening in at risk groups or as:

- Congestive cardiac failure
- Headache
- Cerebrovascular incident
- Hypertensive encephalopathy
- Facial nerve palsy
- Failure to thrive

The history and examination needs to seek out these features and also look for features of any of the above causes. This guideline is not intended to provide and exhaustive list of all the clinical features of the many causes of hypertension.

4. Investigation

Investigations are aimed at identifying the cause of hypertension if this is not already known, assessing the presence of any co-morbidities and identifying any end-organ damage. Investigations will be directed by clinical findings but below is a suggested scheme:

All Children

- **To identify a cause**
  - Urinalysis for protein / blood / infection
  - Full blood count
  - U&Es, creatinine
  - Renal ultrasound (with renal vessel doppler if available)
  - Thyroid function tests
  - Urine catecholamines
  - Plasma renin and aldosterone (sample should be taken directly to the laboratory for immediate separation and freezing. Do not put in pod.)

- **To identify co-morbidities**
  - Fasting lipids
  - Glucose

- **To assess for end-organ damage**
  - ECG
  - Echocardiogram (presence of left ventricular hypertrophy, may also identify a cause eg. Coarctation of aorta)
  - Retinal examination (in those with severe or long standing hypertension)
  - (U&Es and urinalysis are also part of the end-organ assessment)

If indicated

  - Urine pregnancy test
  - Urine toxicology screen
  - Urine steroid profile

Renovascular disease should be considered in children if peripheral renin/aldosterone is elevated or basic renal imaging is suggestive. It should also be considered if hypertension remains difficult to control despite the use of two agents, even if other investigations are normal. These cases should be discussed with paediatric nephrology.

If possible, blood and urine samples should be taken prior to commencing treatment. However, treatment should not be delayed unnecessarily.

5. Management

5.1 Goals of Therapy

1. To reduce blood pressure to <95th percentile
2. To reduce blood pressure to <90th percentile in those with co-morbidities
3. To consider aggressive blood pressure control (<50th percentile) in some patient groups (e.g. those with chronic kidney disease)

5.2 Lifestyle advice

This may be all that is required in prehypertensive children and should be given to all children with hypertension

- Dietary advice regarding healthy eating (including reducing salt intake). All children with hypertension and pre-hypertension should be referred to a dietician.
- Regular physical activity (30-60 minutes/day)
- Weight reduction if overweight or obese (see management of obesity in children and young people guidelines)
- Interventions to improve sleep if sleep apnoea identified.
- Advice regarding alcohol, caffeine and drugs

Note that lifestyle interventions are more successful if the whole family participate.

5.3 Pharmacological Intervention indicated in:-

- Symptomatic hypertension
- Secondary hypertension
- Hypertension with associated target-organ damage
- Diabetes (types 1 and 2)
- Persistent hypertension despite non pharmacologic measures

Selection of an appropriate anti-hypertensive depends upon the age of the patient, the clinical scenario and the presence of any contraindications. This guidance intends to highlight some important points about each drug class but is not intended to replace a full clinical assessment or the advice contained within the BNFc. Paediatric nephrology is

General Principles

- Once daily dosing regimes are preferable when possible to aid compliance
- Younger children (<1 yr) may need multiple daily dosing to increase dose flexibility e.g. propranolol rather than atenolol or captopril rather than enalapril.
- Doses should be commenced at the starting dose in the BNFc and then gradually titrated until the desired blood pressure is achieved (see goals of therapy).
- In infants or those with impaired cardiac function it may be necessary to initiate antihypertensive medication in hospital with BP monitoring – these patients should be discussed with a paediatric nephrologist.

Calcium Channel Blockers (eg. nifedipine, amlodipine)

- Can be used as first or second line agents in most cases of hypertension if not contraindicated (eg. diabetes mellitus (nifedipine))
- Amlodipine tablets can be dispersed in a known volume of water and a proportion taken. This avoids the need to order expensive special medications which also have a short shelf life.
- Nifedipine has a short half-life and so can lead to relatively large fluctuations in BP. Amlodipine is therefore preferable for long term treatment, though

modified release preparations of nifedipine are an acceptable alternative in patients able to swallow tablets.
- Patients under 6 years of age may have an increased ability to clear amlodipine. Dividing the daily dose into two divided doses in this age group may therefore improve efficacy, though this has not been robustly demonstrated to be beneficial.

Beta Blockers (eg propranolol, atenolol)
- Can be used as first or second line agent in most cases of hypertension if not contraindicated (eg. asthma, portal hypertension)
- Cases of phaeochromocytoma need concurrent alpha-blockade

ACE Inhibitors (eg.captopril, enalapril, lisinopril)
- Good first line agent in cases of chronic kidney disease providing renal artery stenosis has been excluded.
- Electrolytes and creatinine must be checked 7 – 10 days after initiating or increasing an ACE inhibitor dose because of the risk of renal impairment and hyperkalaemia
- Counsel teenage girls regarding the contraindication in pregnancy
- Counsel regarding the importance of stopping medication whilst unwell with diarrhoeal or vomiting illnesses
- Enalapril and lisinopril tablets can be crushed and made into a suspension. This removes the need for expensive Special Preparations.
- Angiotensin 2 receptor blockers (eg. Losartan) may provide an alternative in those who are unable to tolerate ACE inhibitors or can be used in addition.

Diuretics (eg.furosemide)
- May be the most appropriate treatment for hypertension in the context of fluid overload –for example, glomerulonephritis.
- Counsel regarding the importance of stopping medication whilst unwell with diarrhoeal or vomiting illnesses

6. **Algorithms for management of specific categories of hypertensive child:**

6.1 Hypertensive crisis (seizures, encephalopathy or cardiac failure)

6.2 Symptomatic (eg. Headaches, facial nerve palsy) **or severe hypertension** (Average SBP and / or DSP >5 mmHg above the 99th percentile).

6.3 Asymptomatic hypertension (Average systolic blood pressure (SBP) and / or diastolic blood pressure (DSP) greater or equal to the 95th percentile for age, sex and height on three or more occasions).

6.1 Hypertensive crisis : seizures, encephalopathy or cardiac failure

These children will require admission to an HDU or PICU setting (or another appropriately equipped ward e.g. tertiary nephrology ward) for close blood pressure monitoring and intravenous anti-hypertensives.

Admit to high dependency area for:

- Neurological observations
- *Consider* intra-arterial blood pressure monitoring
- **Consider intracerebral pathology which might be causing raised intracranial pressure – if suspected, investigate and DO NOT aim to lower blood pressure until this cause has been excluded.**

⇩

Use IV treatment to reduce BP **slowly:**

1/3 of total BP reduction over the first 12 hours

Next 1/3 total BP reduction over second 12 hours

Final 1/3 of BP reduction over next 24 hours

If blood pressure drops suddenly then treat with fluid bolus

⇩

Convert to oral agents as BP improves

Intravenous Options:

- **Labetalol**
- **Sodium Nitroprusside**

See PICU pharmacopeia for dosing regimes and BNFc for cautions / contraindications

Special considerations;
If proven / suspected phaeochromocytoma consideration should be given to alpha-blockade and patients should be managed in conjunction with paediatric oncologist.

6.2 Symptomatic hypertension and/or acute severe hypertension:

Average SBP and / or DSP >5 mmHg above the 99th percentile

Admit to a ward able to monitor blood pressure frequently

- Discuss management with a paediatrician experienced in the management of acute severe hypertension
- **Ensure hypertension NOT secondary to intracerebral pathology in which case lowering BP could be dangerous**

↓

Set a BP threshold for PRN treatment appropriate for the patient e.g. 10 mm Hg above 95th percentile on 2 occasions 15 mins apart

↓

Control BP

- Use Nifedipine up to 250 micrograms/kg/dose (maximum dose: 5 mg) if not contraindicated* (nb frequent small doses are safest)
- Aim to **reduce blood pressure slowly** (1/3 of the blood pressure reduction over the first 12 hours of treatment)
- Ensure immediate medical review if the blood pressure drops markedly or the patient becomes symptomatic
- Consider **fluid overload** as the cause of hypertension in which case a diuretic may be a more appropriate treatment

↓

Re-check BP every 30 minutes
Consider second dose of nifedipine if BP remains raised above threshold
Discuss with paediatric nephrologist if unable to control BP

↓

Once BP improving:

- Convert to a long acting anti-hypertensive (see below)
- Investigations as above

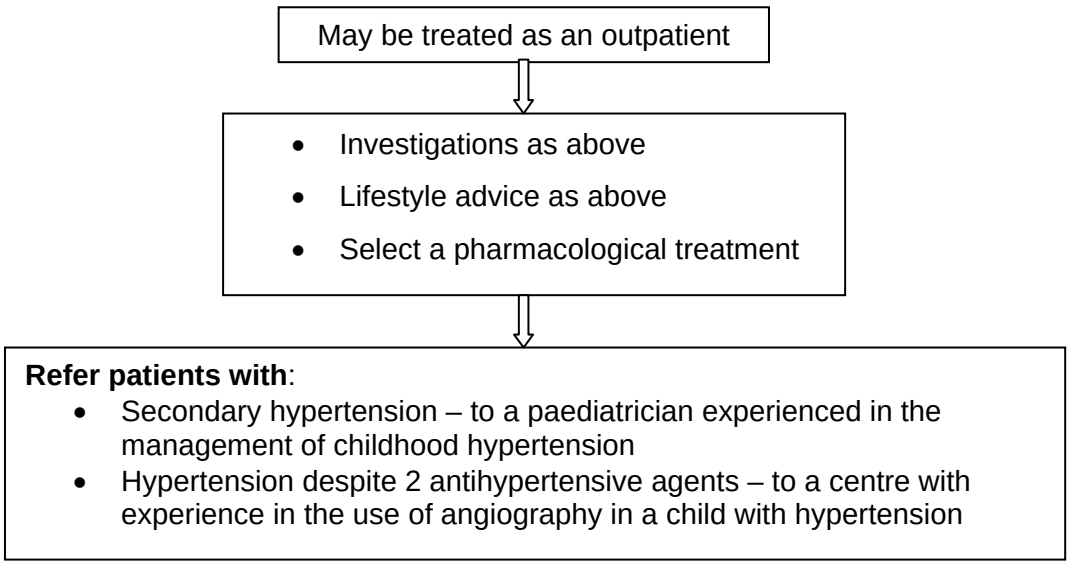
***Nifedipine contraindications:**

- Shock
- Advanced aortic stenosis
- Encephalopathy / cranial hypertension

Cautions

- Impaired cardiac function
- Diabetes (may affect blood sugars)

6.3 **Asymptomatic hypertension** : Average systolic blood pressure (SBP) and / or diastolic blood pressure (DSP) greater or equal to the 95th percentile but less than 5 mm over the 99th percentile for age, sex and height on three or more occasions.



7. Audit Points

1. Is blood pressure being measured correctly in inpatient and outpatient situations?
2. Have patients had appropriate investigations to elicit secondary causes of hypertension?
3. Have investigations been undertaken prior to commencing treatment if appropriate?
4. Is blood pressure being maintained within the recommended parameters?
5. Has an appropriate choice of antihypertensive agent been made?

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Appendix 1
Blood pressure centiles by gender, age and height percentile

TABLE 3. BP Levels for Boys by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for boys with height percentiles given in Table 3 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z scores given by: 5% 1.645; 10% 1.28; 25% 0.68; 50% 0; 75% 0.68; 90% 1.28; and 95% 1.645, and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

TABLE 4. BP Levels for Girls by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

* The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
For research purposes, the SDs in Table B1 allow one to compute BP *Z* scores and percentiles for girls with height percentiles given in Table 4 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height *Z* scores given by: 5% 1.645; 10% 1.28; 25% 0.68; 50% 0; 75% 0.68; 90% 1.28; and 95% 1.645 and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

Appendix 2 - Neonatal blood pressure centiles

Post-conceptual age	50th percentile	95th percentile	99th percentile
44 weeks			
SBP	88	105	110
DBP	50	68	73
MAP	**63**	**80**	**85**
42 weeks			
SBP	85	98	102
DBP	50	65	70
MAP	**62**	**76**	**81**
40 weeks			
SBP	80	95	100
DBP	50	65	70
MAP	**60**	**75**	**80**
38 weeks			
SBP	77	92	97
DBP	50	65	70
MAP	**59**	**74**	**79**
36 weeks			
SBP	72	87	92
DBP	50	65	70
MAP	**57**	**72**	**77**
34 weeks			
SBP	70	85	90
DBP	40	55	60
MAP	**50**	**65**	**70**
32 weeks			
SBP	68	83	88
DBP	40	55	60
MAP	**49**	**64**	**69**
30 weeks			
SBP	65	80	85
DBP	40	55	60
MAP	**48**	**63**	**68**
28 weeks			
SBP	60	75	80
DBP	38	50	54
MAP	**45**	**58**	**63**
26 weeks			
SBP	55	72	77
DBP	30	50	56
MAP	**38**	**57**	**63**

This table provides estimated values for blood pressures after two weeks of age in infants from 26 to 44 weeks post conceptual age. The 95th and 99th percentile values are intended to serve as a reference to identify infants with persistent hypertension that may require treatment.
SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure.
Reproduced from: Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management, and outcome. Pediatr Nephrol

Appendix 3 90th and 95th percentiles of mean day- and night-time systolic and diastolic BP, stratified according to gender and height

	Systolic BP				Diastolic BP			
	Day		Night		Day		Night	
BOYS Height (cm)	90th pct	95th pct	90th pct	95th pct	90th pct	95th pct	90th pct	95th pct
120	120.6	123.5	103.7	106.4	79.1	81.2	61.9	64.1
125	121.0	124.0	104.9	107.8	79.3	81.3	62.2	64.3
130	121.6	124.6	106.3	109.5	79.3	81.4	62.4	64.5
135	122.2	125.2	107.7	111.3	79.3	81.3	62.7	64.8
140	123.0	126.0	109.3	113.1	79.2	81.2	62.9	65.0
145	124.0	127.0	110.7	114.7	79.1	81.1	63.1	65.2
150	125.4	128.5	111.9	115.9	79.1	81.0	63.3	65.4
155	127.2	130.2	113.1	117.0	79.2	81.1	63.4	65.6
160	129.2	132.3	114.3	118.0	79.3	81.3	63.6	65.7
165	131.3	134.5	115.5	119.1	79.7	81.7	63.7	65.8
170	133.5	136.7	116.8	120.2	80.1	82.2	63.8	65.9
175	135.6	138.8	118.1	121.2	80.6	82.8	63.8	65.9
180	137.7	140.9	119.2	122.1	81.1	83.4	63.8	65.8
185	139.8	143.0	120.3	123.0	81.7	84.1	63.8	65.8

	Systolic BP				Diastolic BP			
	Day		Night		Day		Night	
GIRLS Height (cm)	90th pct	95th pct	90th pct	95th pct	90th pct	95th pct	90th pct	95th pct
120	118.5	121.1	105.7	109.0	79.7	81.8	64.0	66.4
125	119.5	122.1	106.4	109.8	79.7	81.8	63.8	66.2
130	120.4	123.1	107.2	110.6	79.7	81.8	63.6	66.0
135	121.4	124.1	107.9	111.3	79.7	81.8	63.4	65.8
140	122.3	125.1	108.4	111.9	79.8	81.8	63.2	65.7
145	123.4	126.3	109.1	112.5	79.8	81.8	63.0	65.6
150	124.6	127.5	109.9	113.1	79.9	81.9	63.0	65.5
155	125.7	128.5	110.6	113.8	79.9	81.9	62.9	65.5
160	126.6	129.3	111.1	114.0	79.9	81.9	92.8	65.4
165	127.2	129.8	111.2	114.0	79.9	81.9	62.7	65.2
170	127.5	130.0	111.2	114.0	79.9	81.8	62.5	65.0
175	127.6	129.9	111.2	114.0	79.8	81.7	62.3	64.7

Appendix 4 - Measuring Blood Pressure

Manual blood pressure measurement using a sphygmomanometer is the gold standard. Blood pressure may be measured using an automated oscillometric device or a manual cuff and auscultation. Oscillometric devices may overestimate blood pressure so any high blood pressure measured this way should be checked manually. The use of a Doppler technique is preferable in very young children as the Korotkov sounds are less reliably heard in this group.

- **Cuff size:-**The largest cuff which can fit on the arm should be used. The cuff should be 2/3 the length of the upper arm and the bladder should be 80-100% the circumference of the arm. Errors due to too large a cuff are unlikely but if the cuff is too small blood pressure can be overestimated.

- **Environment:-**The child should be rested for at least 5 minutes. The brachial artery should be at the level of the heart and blood pressure should be measured in the right arm when possible. The sphygmomanometer should also be at the level of the heart.

- **Technique:-**The brachial artery should be palpated to obtain an approximate systolic BP. Auscultation should then be performed with the first Korotkov sound (K1) being taken as systolic BP. Diastolic BP is recorded at the disappearance of Korotkov sounds (K5) In some children this may not occur in which case the muffling of sounds (K4) may be recorded.

- **Doppler:-**The Doppler probe is placed over the brachial artery and the cuff inflated until the signal disappears. The point at which the signal returns is the systolic blood pressure. The diastolic pressure cannot be identified with this method.

- **Automated:-**Oscillometric devices have the advantage of reducing inter-observer error and were also used in the construction of the centile charts. However, they still require the correct size cuff and **any child with a BP above the 90th centile should have it re-checked manually**. Not all oscillometric machines have been validated in children. Note that the default maximum pressure is usually 200mmHg which is too high for a child. **The maximum pressure should be set at 20 – 30 mmHg above baseline prior to use.**

- **Ambulatory:-** Ambulatory blood pressure monitoring is helpful to determine true blood pressure. This is available in a number of centres including Nottingham, Sheffield and Leicester. Results should be reviewed by a clinician experienced in interpretation of 24 hour blood pressure monitoring.

Appendix 5 - Causes of Hypertension

Hypertension may be either primary (no underlying cause identified and formerly known as essential) or secondary to an underlying cause. Of those with an underlying cause the majority will be renal or reno-vascular in nature. Hypertension in children should be investigated with primary hypertension being a diagnosis of exclusion.

The causes of hypertension can be considered by age of presentation:

Newborn – 1 year	1-5 years	5-10 years	10-20 years
• Renal artery stenosis • Renal vein or artery thrombosis • Congenital renal disease (ARPKD, dysplasia etc) • Aortic coarctation • Neuroblastoma • Wilm's tumour • Bronchopulmonary dysplasia • Patent ductus • Intraventricular haemorrhage • Hydrocephalus • Drugs	• Renal artery stenosis • Middle aortic syndrome • Glomerulonephritis • Renal vein thrombosis • Phaeochromocytoma • Neuroblastoma • Cystic kidney disease • Corticosteroids • Monogenic hypertension (e.g. Liddle's syndrome) • Wilm's tumour • Brain tumour	• Reflux nephropathy • Glomerulonephritis • Cystic renal disease • Renal artery stenosis • Middle aortic syndrome • Endocrine tumours • Wilm's tumour • Other parenchymal renal disease e.g. nephronpthisis • Primary hypertension • Brain tumour	• Primary Hypertension • Reflux nephropathy • Glomerulonephritis • Renal artery stenosis • Endocrine tumours • Monogenic hypertension • Pregnancy • Drugs inc oral contraceptive pill • Brain tumour • Intracerebral bleed