North East Hampshire and Farnham Clinical Commissioning Group

Sussex Partnership NHS Foundation Trust

SHARED CARE PRESCRIBING GUIDELINE

LICENSED MEDICATIONS FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDHOOD

NOTE: to be used by practices participating in the locally commissioned service- 12 monthly physical medication review monitoring for CNS stimulants, atomoxetine and guanfacine

Prescribing classification: Amber with shared care

NOTES to the GP

Amber drugs: *Prescribing to be initiated by a consultant / specialist but with the potential to transfer to primary care. The expectation is that this agreement should provide sufficient information to enable primary care prescribers to be confident to take clinical and legal responsibility for prescribing these drugs.*

The questions below will help you confirm this:

- *Is the patient's condition predictable?*
- *Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care agreement?*
- *Have you been provided with relevant clinical details including monitoring data?*

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of the final page to the requesting consultant / specialist. Until the requesting consultant / specialist has received a signed copy of the page 14 indicating that shared care has been agreed all care (including prescribing) remains with the consultant / specialist.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant / specialist within 14 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, which will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your Medicines Management pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the specialist.

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

Adapted from original West Coastal Sussex CCG & Sussex Partnership Effective Shared Care Agreement

Valid from: April 2019 Approved by: NEHF CCG Medicines Optimisation Board
Review date: April 2021 Date: May 2019

1. Link to the relevant SPC website:

Link to the relevant SPC at www.medicines.org.uk

Methylphenidate:

Xaggitin XL®: https://www.medicines.org.uk/emc/product/2704
Concerta XL®: https://www.medicines.org.uk/emc/product/6872
Equasym XL®: https://www.medicines.org.uk/emc/search?q=%22Equasym%22
Medikinet Tablets®: https://www.medicines.org.uk/emc/search?q=medikinet
Medikinet XL® capsules: https://www.medicines.org.uk/emc/search?q=medikinet
Ritalin®: https://www.medicines.org.uk/emc/product/1035

Dexamfetamine:

Immediate release: https://www.medicines.org.uk/emc/search?q=%22Dexamfetamine+%22

Lisdexamfetamine: https://www.medicines.org.uk/emc/search?q=%22lisdexamfetamine+dimesylate%22
Atomoxetine: https://www.medicines.org.uk/emc/search?q=%22atomoxetine+hydrochloride%22
Guanfacine: https://www.medicines.org.uk/emc/search?q=%22guanfacine+hydrochloride%22

2. Criteria for use, including licence status

The diagnosis of ADHD is made by a Child Psychiatrist or a Specialist Paediatrician after a comprehensive assessment which includes clinical observations both in clinic as well as in a school setting and the completion of questionnaires by carers and teachers, such as the Conner's questionnaires. If there is significant co-morbidity such as learning difficulties or other mental health problems, a full multidisciplinary assessment is advised. If medication is indicated as part of the treatment package, an initial prescription for treatment is given by the specialist for a trial period of at least one month.

Methylphenidate:

- If improvement of symptoms is not observed after appropriate dosage adjustment over the one month period, the drug should be discontinued by the specialist. The medication may be stopped abruptly; there is no tailing off necessary.
- The drug may be discontinued periodically to assess the child's condition as advised by the specialist.

Atomoxetine:

- This is considered a third line treatment for ADHD after methylphenidate and lisdexamfetmaine. Reasons for switching to atomoxetine are: excessive anxiety (particularly if worsened by stimulants), poor effectiveness of stimulants, worsening tics, sleep disturbance, appetite disturbance and any other unacceptable side effects with methylphenidate.
- ADHD symptoms can show an improvement by the first week of commencing atomoxetine and the maximum therapeutic effect can be seen from four weeks onwards. However, it can take up to three months in some patients to see the full desired effect.
- If improvement of symptoms is not observed after appropriate dosage adjustment the drug should be discontinued by the specialist. The medication may be stopped abruptly; there is no tailing off necessary.
- The drug may be discontinued periodically to assess the child's condition as advised by the specialist.

Lisdexamfetamine:

- This is used as an additional step between methylphenidate and atomoxetine.
- If improvement of symptoms is not observed after appropriate dosage adjustment the drug should be discontinued by the specialist. Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression.
- The drug may be discontinued periodically to assess the child's condition as advised by the specialist

Guanfacine:

- Guanfacine is considered as an option after the use of stimulant medications (3rd line). Both Methylphendiate and lisdexamfetamine should be trialled prior to guanfacine use unless clear clinical reason(s) not to do so are present.
- If improvement of symptoms is not observed after appropriate dosage adjustment the drug should be discontinued by the specialist. Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression.

- The drug may be discontinued periodically to assess the child's condition as advised by the specialist

Dexamfetamine:

- Dexamfetamine is considered third/fourth line treatment for ADHD after other stimulants and atomoxetine/guanfacine.
- If improvement of symptoms is not observed after appropriate dosage adjustment over the one month period, the drug should be discontinued by the specialist. Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue and mental depression

It is the specialist's responsibility for stopping medications for the treatment of ADHD or to agree aftercare when the patient reaches 18 years of age.

All children and families with a child taking licensed ADHD medications should receive psychological and / or educational interventions with a view to improving the symptoms of ADHD and allowing children to reduce their need for medication. The extent of these interventions and the level of need will be assessed and agreed with the individual clinician and family.

Explanations given to the family about medication are important. For example children should not be told that the medication is the only thing that can control their behaviour. Explanations should always seek to foster healthy development trajectories for children.

Prescriptions should be written in accordance with the Misuse of Drugs Regulations 2001.

Some clinicians use methylphenidate, dexamfetamine and lisdexamfetamine on school days only where the effect sought may relate mainly to education and this is recognised practice.

Methylphenidate, Dexamfetamine and Lisdexamfetamine:
Methylphenidate, dexamfetamine, and lisdexamfetamine are stimulant drugs used in the treatment of severe Attention Deficit Hyperactivity Disorder (ADHD), Attention Deficit Disorder (ADD) and Hyperkinetic Disorder (HKD) as part of a comprehensive treatment approach when remedial measures alone prove insufficient. Methylphenidate is licensed in children of 6 years old and over.

Lisdexamfetamine is licensed in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate. Lisdexamfetamine therapy is indicated by Sussex Partnership Trust and North East Hampshire and Farnham Clinical Commissioning Group after the trial of at least two preparations of modified release methylphenidate, unless a previous adverse reaction to methylphenidate has ruled out further use.

Atomoxetine:
Atomoxetine is licensed for the treatment of attention deficit hyperactivity disorder (ADHD) in children aged 6 years and over, and in adolescents as part of a comprehensive treatment plan.

(Comprehensive treatment programme – defined to include psychological, education & social measures).

3. Dose & administration

Methylphenidate:
Plain – Ritalin® and Medikinet®: Child 4-5 years old (unlicensed), initially 2.5 mg twice daily, increased in steps of 2.5 mg daily if required, at weekly intervals

For Children over 6 years initially 5mg once, or twice daily with or after breakfast and lunch, increasing if necessary in weekly intervals of 5-10mg in 2 to 3 divided doses. The maximum licensed dose for methylphenidate is 60mg daily, with 90mg daily used in some specialist centres, which is supported by NICE (NICE NG 87 March 2018).

In some children rebound hyperactivity may occur if the effect of the drug wears off in the evening. An additional dose later in the day may eliminate this difficulty but may disturb sleep.

Equasym XL®: Child 6* years or over, initially 10mg once daily (in the morning before breakfast), increasing if necessary in weekly intervals to a maximum of 60mg daily. For children 4-5 years 10mg daily (in the morning with breakfast) could be considered but this is unlicensed.

Medikinet XL®: Child 6* years or over, initially 10mg once daily (in the morning with breakfast), adjusted according to response at weekly intervals to a maximum of 60mg daily. For children 4-5 years old Medikinet XL 5mg once daily (in the morning before breakfast) could be considered, with this being unlicensed

Concerta XL®, Xaggitin XL® Matoride XL® & Xenidate XL®: Child 6* years or over initially 18mg once daily (in the morning), increasing if necessary in weekly increments of 18mg up to a maximum licensed dose of 54mg once daily. For children 4-5 years 18mg daily (in the morning with breakfast) could be considered but this is unlicensed.

Branded Concerta XL® Generics – all are considered by MHRA as being bioequivalent to Concerta® XL preparations

Branded Generic	Doses Available
Xaggitin XL® -preferred choice	**18mg, 27mg, 36mg & 54mg**
Delmosart XL®	18mg, 27mg, 36mg & 54mg
Matoride XL®	18mg, 36mg & 54mg
Xenidate XL®	18mg, 27mg, 36mg & 54mg

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Note: SPfT endorses Xaggitin XL® as a suitable 12 hour MPH option for new patients and for switching appropriate existing Concerta XL® patients due to its cost effectiveness (50% reduction in acquisition costs), same doses available and pilot studies suggesting ease of switching.

A 15mg dose of all other formulations of methylphenidate is considered equivalent to Concerta XL® 18mg and branded generic versions of this. The unlicensed dose of Concerta XL® 72mg is therefore equivalent to the licensed maximum 60mg dose of Ritalin®, Medikinet®, Equasym XL® or Medikinet XL®.

Atomoxetine:
Atomoxetine is licensed in children from the age of 6 years.

Dosing in children/adolescents up to 70kg body weight:
Initially a total daily dose of approximately 0.5mg/kg per day. This should be maintained for a minimum of 7 days, before titrating upwards according to clinical response and tolerability. Maintenance dose is approximately 1.2mg/kg per day (depending on the patient's weight and available dosage strengths of atomoxetine).

No additional benefit has been demonstrated for doses higher than 1.2mg/kg/day. The safety of doses above 1.8mg/kg has not been systematically evaluated.

Dosing of children/adolescents over 70 kg body weight:
Initial dose of 40mg per day. This should be maintained for a minimum of 7 days, before titrating upwards according to clinical response and tolerability. Maintenance dose is 80mg per day.

Maximum licensed dose is 100mg/day; however no additional benefit has been demonstrated for doses higher than 80mg. The safety of single doses over 120mg and total daily doses above 150mg have not been systematically evaluated.

Notes:

- Atomoxetine should be administered as a single daily dose in the morning with or without food.
- For adolescents whose ADHD symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood. However, start of treatment with atomoxetine in adults is not appropriate.

Dexamfetamine (Amfexa® & generic versions):
The usual starting dosage for children aged 3-5 years is 2.5mg a day, increased if necessary by 2.5mg a day at weekly intervals; for children aged 6 years and over, the usual starting dose is 2.5mg 2 to 3 times per day increasing if necessary by 5mg per day at weekly intervals. The usual upper limit is 20mg a day though some older children have needed 40mg or more for optimal response. Maintenance dose should be given in 2 to 4 divided doses.

If prescribing dexamfetamine as Amfexa® please note that this is licensed from 6 years and above and the starting dose is 5mg once or twice daily increasing if necessary by 5mg daily at weekly intervals. Usual maximum dose is 20mg daily.

Lisdexamfetamine (Elvanse®):

Lisdexamfetamine is a pro-drug formulation of dexamfetamine, which is converted to free dexamfetamine by enzymes present on red blood cells. The starting dose in children of 6 years and over, is 30mg once daily taken in the morning, which can be increased in dose by 10-20mg increments, at minimum intervals of one week up to a maximum of 70mg once daily.

Guanfacine:
Guanfacine is to be initially prescribed at 1mg daily (morning or evening), which can be increased by 1mg at a minimum interval of 1 week up to a maximum dose of 7mg once daily, with the lowest effective dose to be used for maintenance treatment. The usual maximum dose is 4 mg in children and 4-7 mg in adolescents, based on weight - Adolescent subjects must weigh ≥ 34kg, with those titrated up to 7mg daily being ≥ 58.5kg.

Depending on the patient's response and tolerability to guanfacine the recommended maintenance dose range is 0.05-0.12 mg/kg/day.

When initiating guanfacine the Summary of Product Characteristics (SmPC) recommends that monitoring weekly blood pressure and pulse are conducted for the first 4 weeks.

Guanfacine should be avoided being taken with high fatty foods/meals as this can considerably increase the plasma concentration.

4. Cautions

Methylphenidate, Dexamfetamine, and Lisdexamfetamine:
Cardiovascular:
The use of stimulants of the central nervous system has been associated in reports of sudden death at usual doses in children, some of whom had structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone may carry an increased risk of sudden death, stimulant products are not recommended in children or adolescents with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant medicine.

If consideration is being given for a patient to commence stimulant therapy they should have a careful history (including assessment for a family history of sudden cardiac or unexplained death or malignant arrhythmia) and a physical examination to assess for the presence of cardiac disease. Such patients should receive further specialist cardiac evaluation if initial findings suggest such history or disease. If a patient develops symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of Stimulant clinical trial data analyses in children and adolescents with ADHD witnessed that patients using such medications may commonly experience changes in diastolic and systolic blood pressure of over 10 mmHg relative to controls. The clinical consequences of these cardiovascular effects in children and adolescents are not known.

Caution is advised in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate.

Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months.

Psychiatric:
Stimulants should be used with caution in patients with history of tics, Tourette's syndrome and porphyria. In psychotic children, stimulants may exacerbate behavioural disturbances and thought disorder.

Treatment emergent psychotic or manic symptoms, e.g. hallucinations, delusional thinking or mania in children or adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant and discontinuation of treatment may be appropriate.

Patients with new onset suicidal ideation or behaviour during stimulant treatment for ADHD should be evaluated immediately by their physician. Consideration should be given to the exacerbation of an underlying psychiatric condition and to a possible causal role of stimulant therapy. Treatment of an underlying psychiatric condition may be necessary and consideration should be given to a possible discontinuation of the stimulant medication.

Careful supervision is required during drug withdrawal since this may unmask depression as well as chronic over-activity.

Development or worsening of psychiatric disorders should be monitored at every adjustment of dose, then at least every 6 months, and at every visit; discontinuation of treatment may be appropriate.

Growth:
Suppression of growth (weight gain and/or height) has been reported with long term use of stimulants in children, therefore careful monitoring is required.

Growth should be monitored during stimulant treatment with height, weight and appetite recorded on a centile chart at baseline, after every dose increase and at least every 6 months.

Seizures:
Caution should be exercised when prescribing stimulants in patients with epilepsy. Stimulants may lower the convulsive threshold. If seizure frequency increases or new-onset seizures occur, stimulant medication should be discontinued.

Abuse Potential:
Stimulants should be used with caution in patients with known drug or alcohol dependency because of a potential for abuse, misuse or diversion. Patients should be carefully monitored for the risk of diversion, misuse and abuse of stimulant medication.

Specific administration instructions:
Patients should be informed that Concerta XL® and Matoride XL® must be swallowed whole and must not be chewed, divided or crushed. Equasym XL® and Medikinet XL® capsules can be opened and the contents sprinkled on to apple sauce if desired. The capsule contents should not be crushed or chewed.

Lisdexamfetamine (Elvanse®) may be swallowed whole, or the capsule opened and the entire contents dissolved in a glass of water. If the contents include any compacted powder, a spoon may be used to break apart the powder in the water. The contents should be stirred until completely dispersed. The patient should consume the full glass of water immediately; it should not be stored. The active ingredient dissolves completely once dispersed; however, a film containing the inactive ingredients may remain in the glass once the water is consumed.

Atomoxetine:
Cardiovascular:
There have been reports of sudden death in children and adolescents who were taking atomoxetine at usual doses with existing structural cardiac abnormalities. Although some serious structural cardiac abnormalities alone carry an increased risk of sudden death, atomoxetine should only be used with caution in children or adolescents with known serious structural cardiac abnormalities and in consultation with a cardiac specialist.

Atomoxetine can affect heart rate and blood pressure. Most patients taking atomoxetine experience a modest increase in heart rate (mean <10 bpm) and/or increase in blood pressure (mean <5 mm Hg) that may not be clinically important.

MHRA advice in January 2012 states that atomoxetine causes clinically important increases in blood pressure or heart rate, or both, in a small proportion of patients. Atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders. Thorough pre-treatment screening and regular monitoring of cardiovascular status is recommended. Specialist cardiac evaluation and advice should be sought if pre-treatment findings suggest cardiac disease or history, or if symptoms suggesting cardiac disease are found during treatment.

It is recommended that heart rate and blood pressure be measured and recorded on a centile chart before treatment is started and, during treatment, after each adjustment of dose and then at least every 6 months to detect possible clinically important increases.

Atomoxetine can cause prolongation of the QT interval and so should be used with caution in patients with congenital or acquired long QT or a family history of QT prolongation.

As orthostatic hypotension has also been reported, atomoxetine should be used with caution in any condition that may predispose patients to hypotension or conditions associated with abrupt heart rate or blood pressure changes.

Psychiatric:
Suicide-related behaviour has been reported in patients treated with atomoxetine. Patients who are being treated for ADHD should be carefully monitored for the appearance or worsening of suicide-related behaviour.

Treatment-emergent psychotic or manic symptoms (e.g., hallucinations, delusional thinking, mania or agitation in children and adolescents without a prior history of psychotic illness or mania) have been reported following exposure to atomoxetine at usual doses. Atomoxetine may also exacerbate pre-existing psychotic or manic symptoms. If such symptoms occur, consideration should be given to a possible causal role of atomoxetine, and discontinuation of treatment should be considered.

Patients should be closely monitored for the appearance or worsening of aggressive behaviour, hostility or emotional lability. Hostility (predominantly aggression, oppositional behaviour and anger) and emotional lability were more frequently observed in clinical trials among children and adolescents treated with atomoxetine compared to placebo.

Patient/parents should be warned to report immediately the appearance or worsening of any of these behaviours or symptoms, being particularly vigilant when starting treatment and with increased doses.

Growth:
Growth and development should be monitored during treatment with atomoxetine. Height, weight and appetite should be recorded on a centile chart at baseline, after very dose change and at least at six monthly intervals. Patients requiring long-term therapy should be monitored and consideration should be given to dose reduction or interrupting therapy in patients who are not growing or gaining weight satisfactorily.

Seizures:
Atomoxetine can lower the seizure threshold. Atomoxetine should be introduced with caution in patients with a history of seizure. Discontinuation of atomoxetine should be considered in any patient developing a seizure or if there is an increase in seizure frequency where no other cause is identified.

Hepatotoxicity & allergy:
Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted. Very rarely, liver toxicity, manifested by elevated hepatic enzymes and bilirubin with jaundice, has been reported.

Allergic reactions have been reported in patients, although uncommon (including rash, oedema, and urticaria).

Guanfacine:
Hypotension, bradycardia and syncope
Guanfacine can cause syncope, hypotension and bradycardia. Syncope may involve risks of falls or accidents, which could result in serious harm. Hence prior to initiation of treatment, patient's cardiovascular status including heart rate and blood pressure parameters, family history of sudden cardiac death/unexplained death, should be assessed to identify patients at increased risk of hypotension, bradycardia, QT-prolongation and risk of arrhythmia.

Monitoring of heart rate and blood pressure parameters should continue on a weekly basis during dose titration and stabilisation and at least every 3 months for the first year, taking into consideration clinical judgement. 6 monthly monitoring should follow thereafter, with more frequent monitoring following any dose adjustment.

Caution is advised when treating patients with guanfacine who have a history of hypotension, heart block, bradycardia, or cardiovascular disease, or who have a history of syncope or a condition that may predispose them to syncope, such as hypotension, orthostatic hypotension, bradycardia, or dehydration. Caution is also advised when treating patients with guanfacine who are being treated concomitantly with antihypertensives or other medicinal products that can reduce blood pressure or heart rate or increase the risk of syncope.

QTc interval
Guanfacine should be prescribed with caution in patients with a known history of QT prolongation, risk factors for torsade de pointes (e.g. heart block, bradycardia, hypokalemia) or patients who are taking medicinal products known to prolong the QT interval. These patients should receive further cardiac evaluation based on clinical judgement

Sedation and somnolence
Guanfacine can cause somnolence and sedation predominantly at the start of treatment, which if experienced typically lasts at least 2-3 weeks.

It is therefore recommended that patients will be closely monitored weekly during dose titration and stabilisation, and every 3 months during the first year, taking into consideration clinical judgement.

Before guanfacine is used with any other centrally active depressants (such as alcohol, sedatives, phenothiazines, barbiturates, or benzodiazepines) the potential for additive sedative effects should be considered. Patients should be advised not to drink alcohol whilst taking guanfacine.

Effects on height, weight and Body Mass index (BMI)
Children and adolescents treated with guanfacine may show an increase in their BMI.

Therefore, monitoring of height, weight and BMI should be done prior to initiation of therapy and then every 3 months for the first year, taking into consideration clinical judgement. Six monthly monitoring should follow thereafter, with more frequent monitoring following any dose adjustment.

5. Contraindications

Methylphenidate, dexamfetamine, and lisdexamfetamine:
Known hypersensitivity to methyphenidate, dexamfetamine, lisdexamfetamine or any of the other product ingredients.

Marked anxiety and tension, hyperthyroidism/thyrotoxicosis, hyper-excitability or agitated states, family history or diagnosis of Tourette's syndrome, history of drug or alcohol abuse, glaucoma, pregnancy and breastfeeding.

Diagnosis or history of severe depression, anorexia nervosa or anorexic disorders, suicidal tendencies, psychotic symptoms, mania, schizophrenia, severe mood disorders, or psychopathic or borderline personality disorder

Stimulants should not be used in combination with monoamine oxidase inhibitors (MAOIs).Stimulant medication should not be used within two weeks after discontinuing therapy with a MAOI. Treatment with an MAOI should not be initiated within two weeks of discontinuing stimulant therapy.

Unless specialist cardiac advice has been obtained: in pre-existing cardiovascular disorders, including moderate to severe hypertension and advanced arteriosclerosis, heart failure, arterial occlusive disease ,angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, phaechromocytoma, potentially life-threatening arrhythmias, and dysfunction of cardiac ion channels

Atomoxetine:
Known hypersensitivity to atomoxetine, or any of the other product ingredients.

Atomoxetine should not be used in combination with monoamine oxidase inhibitors (MAOIs). Atomoxetine should not be used within two weeks after discontinuing therapy with a MAOI. Treatment with an MAOI should not be initiated within two weeks of discontinuing atomoxetine.

Atomoxetine should not be used in patients with severe cardiovascular or cerebrovascular disorders whose condition would be expected to deteriorate if they experienced increases in blood pressure or heart rate that could be clinically important.

Phaechromocytoma.

Atomoxetine should not be used in patients with narrow angle glaucoma.

If the patient develops jaundice and/or other signs of liver injury, then atomoxetine should be immediately discontinued and not restarted.

Guanfacine:
Known hypersensitivity to guanfacine, or any of the other product ingredients.

6. Side effects

Methylphenidate, dexamfetamine, and lisdexamfetamine:

Very Common (frequency estimate >10%) side effects include:

- Insomnia, nervousness and headache
- Decreased appetite and weight loss (lisdexamfetamine)

Common (frequency estimate 1% to 10%) side effects include:

- Abdominal pain, nausea, vomiting, diarrhoea, dry mouth, appetite suppression (usually transient), weight loss, anorexia

- Drowsiness, dizziness, dyskinesia
- Tachycardia, palpitations, arrhythmias, changes in BP and heart rate
- Rash, pruritis, urticaria, fever, alopecia, arthralgia and muscle tightness

Less Common (frequency estimate 0.1% to 1%) side effects include:
- Hypersensitivity reactions, constipation, tremor, blurred vision and dry eyes
- Psychotic symptoms, suicidal ideation and irritability
- Chest pain

Atomoxetine:
Very Common (frequency estimate >10%) side effects include:
- Decreased appetite (usually transient), headache, somnolence, abdominal pain, nausea and vomiting (usually transient).

Common (frequency estimate 1% to 10%) side effects include:
- Anorexia (loss of appetite), irritability, mood swings, insomnia, dizziness, constipation, dyspepsia, dermatitis, rash, fatigue, lethargy, weight loss (0.5kg average), greatest during initiation and at higher doses, increased blood pressure.

Less Common (frequency estimate 0.1% to 1%) side effects include:
- Early morning awakening, syncope, migraine, peripheral coldness, allergic reaction, palpitations and sinus tachycardia

Post marketing reports of psychosis, suicidal ideation, seizure, QT prolongation, abnormal liver function tests and hepatitis have all been reported.

Guanfacine:
Very Common (frequency estimate >10%) side effects include:
- Somnolence, headache, abdominal pain & fatigue

Common (frequency estimate 1% to 10%) side effects include:
- Sedation, dizziness, lethargy, bradycardia, hypotension, constipation, dry mouth, vomiting, diarrhoea, nausea, decreased appetite, depression, anxiety, insomnia & nightmares

Less Common (frequency estimate 0.1% to 1%) side effects include:
- Hypersensitivity, agitation, hallucinations, convulsions, syncope, tachycardia, sinus arrhythmia, pallor, dyspepsia, pruritus & chest pain

7. Interactions
Methylphenidate, dexamfetamine and lisdexamfetamine:
- Methylphenidate may possibly enhance anticoagulant effect of coumarins.
- Risk of hypertensive crisis when stimulants given with MAOIs and moclobemide. amfetamine should not be administered during or within 14 days following the administration of monoamine oxidase inhibitors (MAOI) as it can increase the release of norepinephrine and other monoamines. This can cause severe headaches and other signs of hypertensive crisis. A variety of toxic neurological effects and malignant hyperpyrexia can occur, sometimes with fatal outcomes.
- Methylphenidate possibly inhibits metabolism of SSRIs and tricyclics and so contribute to increase risk of side effects from these medications.
- Stimulants may decrease the effect of drugs used to treat hypertension.
- Because a predominant action of stimulants is to increase extracelluar dopamine levels, caution is recommended when administering stimulants with dopaminergic drugs, including antipsychotics.
- Seizures are a potential risk with stimulant medication. Caution is advised with concomitant use of medicinal drugs which are known to lower the seizure threshold (such as antidepressants, neuroleptics, mefloquine, bupropion, or tramadol).
- QT interval prolongation is an increased risk when stimulants are administered with other QT prolonging drugs (such as antipsychotics, anti-arrhythmics, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium) and drugs that cause electrolyte imbalance (such as thiazide diuretics).
- Methylphenidate possibly increases plasma concentration of phenytoin, phenobarbital and primidone.
- Alcohol may exacerbate adverse CNS effects therefore it is advisable to abstain from alcohol during treatment.
- Ascorbic acid and other agents and conditions (diets high in fruits and vegetables, urinary tract infections and vomiting) that acidify urine increase urinary excretion and decrease the half-life of amfetamine. Sodium bicarbonate and other agents and conditions (thiazide diuretics, diets high in animal protein, diabetes, respiratory acidosis) that alkalinise urine decrease urinary excretion and extend the half-life of amfetamine.

Atomoxetine:
- Risk of hypertensive crisis when given with MAOIs and moclobemide

- Combining with potent cytochrome P450 inhibitors particularly CYP2D6 inhibitors *(e.g., fluoxetine, paroxetine, quinidine, terbinafine):* In patients receiving treatment with these drugs, atomoxetine exposure may be 6-to 8-fold increased as atomoxetine is primarily metabolised by CYP2D6. Slower titration and lower final dosage of atomoxetine may be necessary in those patients who are also taking CYP2D6 inhibitor drugs.
- Atomoxetine should be administered with caution to patients being treated with high dose nebulised or systemically administered salbutamol (or other beta$_2$ agonists) because the action of salbutamol on the cardiovascular system can be potentiated, increases in heart rate and blood pressure.
- QT interval prolongation is an increased risk when atomoxetine is administered with other QT prolonging drugs (such as antipsychotics, anti-arrhythmics, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium), drugs that cause electrolyte imbalance (such as thiazide diuretics) and drugs that inhibit CYP2D6.
- Seizures are a potential risk with atomoxetine. Caution is advised with concomitant use of medicinal drugs which are known to lower the seizure threshold (such as antidepressants, neuroleptics, mefloquine, bupropion, or tramadol).
- Because of possible effects on blood pressure, atomoxetine should be used cautiously with pressor agents.
- Drugs that affect noradrenaline should be used cautiously when co-administered with atomoxetine because of the potential for additive or synergistic pharmacological effects. Examples include antidepressants, such as imipramine, venlafaxine, and mirtazapine, or decongestant pseudoephedrine.

Guanfacine

- Caution should be used when guanfacine is administered to patients taking ketoconazole and other moderate and strong CYP3A4/5 inhibitors such as macrolide antibiotics, ciprofloxacin, diltiazem, verapamil, fluconazole and grapefruit juice. Co-administration of guanfacine with moderate and strong CYP3A4/5 inhibitors elevates plasma guanfacine concentrations and increases the risk of adverse reactions such as hypotension, bradycardia, and sedation. Such prescribing often requires a decrease in the dose of guanfacine within the recommended dose range.
- Patients taking guanfacine concomitantly with a CYP3A4 inducer are likely to require an increase in the dose of guanfacine within the recommended dose range. Examples of such inducers are; carbamazepine, phenobarbital, phenytoin, modafinil, rifampicin, oxcarbazepine and St. John's Wort
- When guanfacine is co-administered with valproic acid, patients should be monitored for potential additive central nervous system (CNS) effects and consideration should be given to the monitoring of serum valproic acid concentrations. This is due to the potential of increased plasma levels of valproic acid. Adjustments in the dose of valproic acid and guanfacine may be indicated when co-administered.
- Caution should be used when guanfacine is administered concomitantly with antihypertensive medicinal products, due to the potential for additive pharmacodynamic effects such as hypotension and syncope.
- Caution should be used when guanfacine is administered concomitantly with CNS depressant medicinal products (e.g. alcohol, sedatives, hypnotics, benzodiazepines, barbiturates, and antipsychotics) due to the potential for additive pharmacodynamic effects such as sedation and somnolence.
- Guanfacine should not be administered with high fat meals due to increased exposure, as it has been shown that high fat meals have a significant effect on the absorption of guanfacine.

8. Any further information (e.g. supporting therapies)

Methylphenidate, Dexamfetamine and Lisdexamfetamine:

If improvement of symptoms is not observed after the appropriate dosage adjustment over one month, it should be discontinued.

Following updated MHRA guidance on the use of methylphenidate in ADHD, issued in March 2009, treatment with stimulant medication should be interrupted at least once a year to determine whether continuation is needed (e.g. by stopping the drug for up to two weeks each year). Drug treatment should usually be discontinued by late adolescence.

Lisdexamfetamine at oral doses up to 100mg has been shown in one abuse liability study to have less 'drug liking effects' than immediate release dexamfetamine 40mg. However oral doses of 150mg and above had comparable 'drug liking effects' to immediate release dexamfetamine 40mg. Another study on IV administration witnessed doses of up to 50mg producing drug liking effects greater than placebo, but less than IV administration of immediate release dexamfetamine 20mg.

All children and families with a child taking stimulant medication should be considered for psychosocial interventions, which may help to reduce the need for medication.

Explanations given to the family about the medication are important and this might include leaflets for parents and suitable discussion with the child emphasising the benefits of drug treatment on schoolwork.

Prescriptions should be written in accordance with the Misuse of Drugs Act.

Clinicians may prescribe stimulant medication on schooldays only where the effect sought relates mainly to education. This is recognised practice.

Atomoxetine:
ADHD symptoms can show an improvement by the first week of commencing atomoxetine and the maximum therapeutic effect can be seen from four weeks.

In response to adverse effects, atomoxetine can be discontinued without titrating down the dose otherwise it should be tapered off over a suitable time period.

If improvement of symptoms is not observed after appropriate dosage adjustment over a 10-week period, the drug should be discontinued by the CAMHS / ADHD specialist.

Consideration should be given to periodically discontinuing atomoxetine in order to assess child's condition and ongoing need for medication.

Following updated MHRA guidance on the use of atomoxetine in ADHD, issued in January 2012, patients taking atomoxetine for extended periods (i.e. >1 year) should have their treatment reviewed at least once a year by a specialist to determine whether continuation is needed.

Drug treatment should usually be discontinued by late adolescence.

If a treatment break is deemed appropriate, consideration should be given to the length of any break. It may take up to five days for atomoxetine to be eliminated. Following any treatment break it may take four weeks before the full benefit from atomoxetine is again observed.

Sussex Partnership Trust and North East Hampshire and Farnham Clinical Commissioning Group have agreed that prescribing of guanfacine should be restricted to those who are compliant with medication and unable to take stimulants (either ineffective or not tolerated), but require a quicker onset of action than that realised with atomoxetine (3-4 weeks vs 8-12 weeks for maximal effect) due to a crisis situation.

10. References

McCarthy S, Wilton L, Murray ML et al. The epidemiology of pharmacologically treated attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care. BMC Paediatr. 2012;12:78

National Institute of Health and Clinical Excellence. NICE NG87. Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. 2018. Full guideline. Accessed via https://www.nice.org.uk/guidance/ng87/resources/attention-deficit-hyperactivity-disorder-diagnosis-and-management-pdf-1837699732933

Drug Tariff. Figures accessed from https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariffCosts correct as of 03/04/19 (inc VAT).

RESPONSIBILITIES and ROLES

	Consultant / Specialist responsibilities
1	To assess the patient and establish a diagnosis of attention-deficit hyperactivity disorder, to determine a management strategy and communicate this to the family and GP. The diagnosis must clearly be demonstrated through a detailed report outlining the current problems, developmental history and presence of "core signs" of ADHD. These must meet the diagnostic criteria of the DSM-IV. Almost 50% of children who have ADHD may have other co-morbid conditions which include autistic spectrum/Asperger's syndrome, dyslexia, dyspraxia and oppositional-defiant difficulties. Recognising these conditions is important to ensure comprehensive planning is made.
2	Consider and discuss treatment with the parents / responsible adult for the children who meet the criteria laid down in NICE guidance. This should include a discussion of the reasons for treatment, the possible side effects and the lack of information in relation to longer term outcomes including effectiveness and adverse effects. **Following reports of suicidal thoughts and behaviour with atomoxetine, the CSM has advised that patients and their carers should be informed about the risk and told to report clinical worsening, suicidal thoughts or behaviour, irritability, agitation or depression. In addition, the CSM has advised that patients and their carers should be advised of the risks of hepatic disorder and told how to**

	recognise symptoms.
3	Ensure baseline monitoring of height, weight, BP, pulse rate have been performed plus any additional relevant investigations such as ECG in case of family history of arrhythmia or sudden death.
4	Initiation and stabilisation of drug treatment. **12 hour Modified release methylphenidate should be prescribed as Xaggitin XL®**. The GP is not expected to enter into a shared care agreement until the patient is stabilised on the medication and the parents at this stage are instructed to communicate directly with the clinic. If the decision to switch treatment due to side effects/ poor response is made by the specialist then another shared care agreement should be made between the specialist and the GP once the patient has stabilised on the medication
5	Set the review interval and criteria. The Specialist must ensure contact four weeks after initiation of treatment to assess if being effective. An appointment should be arranged three months after initiation of treatment to undertake necessary monitoring (see point 6 below). Once a child's treatment is stabilised, face to face 12 monthly reviews are provided by the Specialist. Specialist ADHD nurses, junior doctors and other staff are closely involved with the monitoring of the patients. When junior / middle grade doctors are helping the Specialists in the clinic, changes should be made after discussion with the Specialist only, and should be clearly stated in a letter to the GP.
6	To review the patient and monitor the following (if relevant to specific drug) usually on a six monthly basis (though well-established adolescents & adults may be seen annually. A move to annual monitoring must be communicated to the primary care prescriber), act on the results appropriately and communicate these results to the primary care prescriber: • Height, weight and appetite, recorded at baseline, following dosage changes & 6 monthly. Recorded on a growth centile chart. Similar for the next three points. • Weight recorded at baseline and every 3 months for children 10 years and under. Recorded on a growth centile chart. • 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. Recorded on a growth centile chart. • Blood pressure and pulse for all age groups, recorded at baseline, following dosage adjustments and 6 monthly. • Do not conduct blood tests (e.g. LFTs) or ECGs to people taking medication for ADHD unless there is a clinical indication. • As stimulant medications are controlled drugs, the specialist or parents should inform the school concerning any medication for these indications. In order to assess the effects of the drug on the child's emotional, physical or behavioural states the specialist should request further information from the school about the child's behaviour. • To counsel and refer patients if appropriate to primary care or if serious to A&E who develop symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea, or other symptoms suggestive of heart disease for cardiac evaluation. To monitor for the development of new, or the worsening of pre-existing, psychiatric symptoms following initiation and dose changes and at every visit.
	For guanfacine only; during the first year of treatment it is recommended that a patient should be assessed at least every 3 months for: • Signs and symptoms of somnolence & sedation, hypotension and bradycardia • Weight increase/risk of obesity
	Parents/carers and patients must be informed to report missing of more than one dose to the prescriber, with particular reference to missed doses of guanfacine
7	Supply the medication until the dose is stabilised. Prescribing may be transferred to the GP under shared care once the patient is stabilised on medication. The GP will not be asked to prescribe the drug outside its licensed indications.
8	Request agreement of shared care with primary care prescriber: a detailed clinic letter highlighting relevant patient information should be sent to the GP requesting shared care including: - Information that all conditions in point 2 & 3 have been discussed and appropriately actioned - the date of the next follow up review Shared care should only be requested if the patient is stable. Once shared care is agreed advise the patient that their next 6 monthly review will take place with their GP
9	To collate (including on centile charts) and review the physical medication monitoring results received from the patient's GP practice by fax every 12 months (received 6 months after the specialist review detailed in point 6) and advise the GP of any required actions. The bottom section on the faxed results form received from the patient's GP practice should be completed and the form faxed back to the practice after each GP physical medication review.
10	A written letter should be sent to the GP after each clinic visit notifying the GP of changes in the medication regime, adverse effects and results of the patient's routine monitoring. The GP must be notified of non-attendance at clinic. (**NOTE**: patients that regularly do not attend their 6 monthly reviews are not appropriate

	for shared care)
11	Keep the GP fully informed about the patient's condition and medication. The specialist will be available to answer queries from the GP and carers.
12	Stop or modify the dosage as appropriate
13	Advise the GP when the treatment is being discontinued. The specialist will provide necessary supervision and support during the drug discontinuation phase.
14	Liaison with other members of the multidisciplinary team responsible for the child's development and education. The parents and class teachers should be given information about atomoxetine in particular the monitoring and side effects.
15	Evaluate adverse drug reactions reported by the GP or carer.
16	The appropriateness of medication into adulthood should be carefully reviewed. If the drug is to be continued beyond the age of 18, the specialist will seek to make appropriate arrangements
17	Continue supply of medication for children under six years.
18	Explain to the patient / carer their roles

	General Practitioner responsibilities
1	Some GPs may feel able to make a diagnosis of ADHD. Psychoeducation and parent training can take place in primary care for children who have mild or moderate ADHD. Other GPs will initiate referral to a specialist on suspicion of ADHD.
2	GPs should be aware that almost 50% of children who have ADHD may have other co-morbid conditions which include autistic spectrum/Asperger's syndrome, dyslexia, dyspraxia and oppositional-defiant difficulties. Recognising these conditions is important to ensure comprehensive planning is made.
3	Children who are severely affected by ADHD should be referred to secondary care without delay. These children will require medication early as part of the treatment package.
4	Monitor patient's overall health and well being
5	Continued prescription of treatment, once patient is stabilised on medication and shared care is agreed, at the appropriate intervals given the nature of the drug and the family involved. As it is not necessary for a doctor to see the child more than every 3-6 months, unless there are specific indications, repeat prescriptions can be issued without necessarily seeing the child on each occasion.
6	To check that stable patients are attending their 12 monthly specialist ADHD clinics and thus continued prescription is required.
7	To carry out a physical medication review monitoring the following on a 12 monthly basis (the patient will be reviewed 6 monthly in line with the product license, with reviews alternating between GP 12 monthly review and specialist 12 monthly review): o Height weight and appetite o Blood pressure and pulse Results of the above tests should be communicated to the consultant for reviewing and collating in hospital records: to support this a template is available on DXS and attached as Appendix 1. After reviewing the monitoring results received the specialist will advise the GP of any required actions. The practice should communicate to the specialist after every physical medication review. This will enable the specialist to know if the patient is not attending GP follow up which may highlight a safeguarding concern for example.
8	To report adverse effects to the specialist.
9	To inform the consultant via the numbers below if the patient does not attend their 12 monthly physical medication review for advice in particular in relation to appropriate continued prescription. **Children's Neurodevelopmental Disorder's Team: Aldershot community CAMHS team** **SPNT.Aldershot-CAMHS@nhs.net Tel: 01252 335600**
10	To record any changes in therapy in the prescribing record on receipt of such communication from secondary care and act upon these
11	To provide symptomatic management of minor adverse effects.
12	If prescribing modified release methylphenidate this must be by 'Brand' to avoid the risk of the wrong formulation being dispensed. **Xaggitin XL® is the 12 hour lasting preparation of choice.**
13	When prescribing stimulant medication to look out for signs of diversion (transfer of the medicine from the individual for whom it was prescribed to one for whom it is not prescribed), misuse, and abuse.
14	To interrupt treatment at least annually on the recommendation of the specialist.
15	Referral back to specialist if any problems arise.
16	Ensure that if care of the patient is transferred to another prescriber that the new prescriber is made aware of the ESCA.

	Patient's / Carer's role
1	Ask the consultant / specialist or primary care prescriber for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with any medication covered by this agreement
3	Tell the consultant / specialist or primary care prescriber of any other medication being taken, including over-the-counter products.
4	Read the patient information leaflet included with your medication and report any side effects or concerns you have to the consultant / specialist or primary care prescriber.
5	Inform the specialist of more than one consecutive missed dose by patient, for those patients taking guanfacine.
6	To attend 6 monthly appointments (both in primary and secondary care)
7	Arrange blood tests as per consultant / specialist request
8	To be aware of side effects and report to their consultant / specialist or primary care prescriber any relevant symptoms such as: palpitations, exertional chest pain, unexplained fainting, shortness of breath, development of new or worsening of pre-existing psychiatric symptoms.

BACK-UP ADVICE AND SUPPORT

	Name / position	Telephone	Email
	Children's Neurodevelopmental Disorder's Team: Aldershot community CAMHS team	01252 335600	SPNT.Aldershot-CAMHS@nhs.net

North East Hampshire and Farnham Clinical Commissioning Group

Sussex Partnership NHS Foundation Trust

Shared Care Prescribing Guideline

Licensed Medications for the Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in Childhood

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 12 months

Consultant: Address: Contact Number	**Agreement to shared care, to be signed by GP, Consultant and carer.** **Consultant Signature:** …….. **Date:**
GP: Address: Contact Number	**GP Signature:** …… **Date:**
Main Carer: Contact Number:	**Main Carer:** …… **Date:**
Key worker if appropriate: Contact Number:	

If shared care is agreed and GP has signed above please return a copy of this page to the requesting consultant or alternatively email to: SPNT.Aldershot-CAMHS@nhs.net

Adapted from original West Coastal Sussex CCG & Sussex Partnership Effective Shared Care Agreement

North East Hampshire and Farnham Clinical Commissioning Group

Sussex Partnership NHS NHS Foundation Trust

Appendix 1

ADHD Shared Care Protocol Follow Up Sheet – 12 monthly physical medication review monitoring

Patient name/ Date of Birth **NHS Number/ Hospital number**		**GP Practice / email address**	
Height (cm)	**Weight (kg)**	**Pulse**	**BP**
Previous: _____ Date: _____ Current:_____ Date: _____	Previous: _____ Date: _____ Current:_____ Date: _____	Previous: _____ Date: _____ Current:_____ Date: _____	Previous: _____ Date: _____ Current:_____ Date: _____
Appetite (please circle)	Good	Moderate	Poor
Medication (name/s and current dosage)			
Does this child require an early review at the Behavioural Clinic (Planned review 12 monthly)	Yes/No If Yes- Why?		

On completion please email to the Children's Neurodevelopmental Disorder's Team: Aldershot community CAMHS team**. SPNT.Aldershot-CAMHS@nhs.net Tel: 01252 335600**