Shared care protocol for the use of methylphenidate, dexamfetamine & atomoxetine for the management of Attention-deficit hyperactivity disorder (ADHD)
Part 1: Children & adolescents; Part 2: Adults (ESSEX only)

PATIENT’S NAME:

PATIENT’S ADDRESS:

HOSPITAL NAME NHS NUMBER / PATIENT IDENTIFIER:

CONSULTANT ‘S NAME AND CONTACT NUMBER:

GP’s NAME:

Click here for SEPT prescribing guidelines on ADHD

What are key elements of the process to ensure good shared care arrangements are in place?

- It is imperative that the GP is contacted to discuss shared care arrangements before treatment is commenced to ensure that they are willing to jointly manage the patient’s therapy.
- It is reasonable to expect the hospital clinician to prescribe if the patient will have to regularly attend hospital for specialist monitoring.
- In addition, PCT policies on clinical effectiveness should be adhered to.
- The general practitioner should have sufficient information on the drug to either allow them to monitor the patient’s response to therapy and adjust dosages as required or know in what circumstances they should refer the patient back to the hospital clinician.
- Where the hospital clinician retains responsibility for monitoring drug therapy or making dosage adjustments, the general practitioner must be informed of any dose changes as soon as possible to avoid an incorrect dose being administered. Similarly if the GP changes the patient’s medication then the hospital clinician involved in the shared care agreement should be informed of any changes that the GP undertakes.
- If a GP is unhappy to participate in a shared care agreement, the PCT should be asked for assistance in facilitating suitable prescribing arrangements for the patient.
- Informing the patient’s usual community pharmacist of the medication will help ensure that supplies are available.
Part 1: Management of ADHD in children and adolescents

Pharmacological therapy is not indicated in all children with ADHD and the decision to use the drug is based on the Consultant’s evaluation of the child’s history and the duration and severity of symptoms.

A comprehensive treatment programme typically includes psychological, educational and social measures to stabilise children with a behavioural syndrome

SUMMARY OF CONSULTANT RESPONSIBILITIES

1. Contact the GP if the patient is referred for assessment by an alternative route other than GP referral.
2. Patient diagnosis and assessment of the need for pharmacological treatment with methylphenidate, atomoxetine or dexamfetamine.
3. Recommending the most appropriate treatment regime, pre-treatment monitoring and prescribing/monitoring for the 3-6 month trial of treatment (regular reviews will be required until a stable dose level is reached).
4. Discussion of benefits, adverse effects, and monitoring programme with the parents/carers and child. (Provide patient information booklets/leaflets relating to the prescribed medication).
5. Advising parents/carers that the treatment programme will be discontinued by the consultant if the monitoring programme is not complied with (and informing the GP in writing if appointments are not kept). – Appendix 1 section 6 of prescribing guidelines.
6. Liaising with the GP to agree to share the patients care after the final therapeutic dose and benefit from treatment is established (usually after 3-6 months trial of treatment) and providing the GP with enough information to do so.
7. GPs should only be asked to prescribe drugs, which are used in accordance with their product licence.
8. Assessing the patient’s continuing response to treatment after the trial. This will usually be done at 3-6 monthly intervals. For patients who take methylphenidate for more than one year, the Consultant should interrupt treatment at least once a year to determine whether continued treatment with methylphenidate is necessary.
9. Overall monitoring of disease status and drug therapy
10. Informing the school when the child is on any medication and whether it involves a lunchtime dose or not.
11. The Consultant will retain responsibility for monitoring drug therapy and making dosage adjustments. The GP will be informed of any dose changes as soon as possible (by fax if necessary) to avoid an incorrect dose being prescribed.
12. Evaluating adverse events noted by the GP or the patient/carer.
13. Deciding when to stop or withdraw treatment to assess progress. Treatment should be discontinued periodically in order to assess the patient’s condition and to check whether medication is still necessary. The decision to initiate such breaks in treatment should be made by the Consultant, as should the decision to either recommence treatment or discontinue permanently.
14. It is the Consultant’s decision to withdraw therapy.
15. The need for continuing treatment should be reviewed by the Consultant before the patient reaches the age of 18. In most cases, treatment should have been discontinued by the age of 18, but if treatment beyond this age is considered necessary, the Consultant should arrange for an appropriate referral.

SUMMARY OF GP RESPONSIBILITIES

1. Prescribe methylphenidate, atomoxetine or dexamfetamine in line with the respective product licences once the final therapeutic dose and benefit from treatment has been established (usually after the 3-6 month trial period).
2. To check that the patient is continuing to attend the Consultant clinic prior to re-authorisation of repeat prescriptions.
3. Monitor the patients overall health and well-being.
4. Symptomatic treatment of minor adverse events.
5. Inform consultant of any emerging side effects.
6. Alert the consultant if there is a significant change in behaviour or weight gain. The dosage may need to be reviewed.
7. Rarely other members in the family/carer may divert medication with increased requests for prescriptions. Please alert secondary care of such occurrences.

SUMMARY OF PARENT/CARER RESPONSIBILITIES

1. To provide written notification for further repeat prescriptions, giving the surgery at least 3 working days’ notice.
2. Informing the school when the child is on any medication and whether it involves a lunchtime dose or not.
3. To attend regular follow-up appointments (medication cannot be prescribed without regular follow-up).
4. To inform GP/Consultant of all medicines (including OTC preps) that the child is currently taking.
5. To report any unusual symptoms/adverse effects to GP/Consultant.
6. To ensure that the child takes the medication safely, appropriately and on time.
7. To safely store the medication.
8. To have read and understood the product's patient information leaflet.
Part 2: Management of ADHD into Adulthood (ESSEX ONLY)

As their brains mature, a significant proportion of adolescents will acquire the necessary skills to be able to manage without medication. However, some adolescents will still endure significant impairment due to ADHD, and will continue to need medication during the transition into adulthood, and during adult life.

SUMMARY OF COMMUNITY PAEDIATRICIAN AND/OR CAMHS RESPONSIBILITIES

- Inform, in writing, Adult Psychiatric services of the details and history of the patient (presentation, progress, compliance with medication, etc.) who is approaching his/her 18th birthday and who has been identified as someone who will require on-going support with ADHD.
- Inform, in writing, Adult Psychiatric Services the need for on-going medication. Atomoxetine should only be initiated in children and adolescence. Only adolescents who show clear improvement with Atomoxetine should be considered for on-going treatment as adults. Should on-going prescription of psychostimulants be considered necessary, the patient should be advised of the need for safe storage to prevent diversion and potential abuse. Patients should be reminded that although medication is not licensed in adult ADHD, it is, nevertheless, effective.
- Inform the GP regarding any decision to stop or alter the treatment plan prior to transition to adult services.

SUMMARY OF ADULT PSYCHIATRIC CLINIC RESPONSIBILITIES

- The Adult Psychiatric Outpatient clinic will accept patients who are approaching their 18th birthday and require on-going support and medication to manage their ADHD.
- The Adult Psychiatric outpatient clinic will review the patient regularly and liaise with the GP should treatment be varied or discontinued.
- Should medication no longer be considered necessary – it will, upon the advice of the clinic, be discontinued slowly and the patient’s on-going needs assessed by the CAS team of the adult CMHT.

SUMMARY OF GP RESPONSIBILITIES

- To check that the patient is continuing to attend the Consultant clinic prior to re-authorisation of repeat prescriptions.
- Monitor the patients overall health and well-being.
- Symptomatic treatment of minor adverse events.
- Contact the Consultant to discuss any significant changes in the patient.
- Inform Consultant of any emerging side effects.
- Inform the psychiatrist if there is suspicion of abuse of controlled drugs.
PREScribing Costs

(Costs based on March 2011 Drug Tariff)

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Cost / 30 days</th>
<th>Cost / 30mg dose or equiv. of methylphenidate* per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate standard release (generic)</td>
<td>£8.00 - £39.18 (5-20mg tds)</td>
<td>£19.59</td>
</tr>
<tr>
<td>Equasym XL® (methylphenidate modified release)</td>
<td>£25 - £70 (10-60mg od)</td>
<td>£35</td>
</tr>
<tr>
<td>Medikinet XL® (methylphenidate modified release)</td>
<td>£20.18 - £70.11 (10-60mg od)</td>
<td>£33.63</td>
</tr>
<tr>
<td>Atomoxetine (Strattera®)</td>
<td>£62.46 - £124.92 (10mg – 80 mg od)</td>
<td>N/A</td>
</tr>
<tr>
<td>Dexamphetamine</td>
<td>£15.90 - £63.60 (5-20mg od)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Summary of Main Features of Treatment Options for ADHD

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Atomoxetine</th>
<th>Methylphenidate Modified Release (Concerta XL® and Equasym XL®)</th>
<th>Dexamphetamine (Dexadrine®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of action</strong></td>
<td>24 hours</td>
<td>Concerta XL® -12 hours Equasym XL® - 8 hours</td>
<td>4- 24hours</td>
</tr>
<tr>
<td><strong>Adverse Reactions</strong></td>
<td>Transient abdominal pain and lost appetite. Cold/flu symptoms, anorexia, early morning awakening, irritability, mood swings, dizziness, somnolence, mydriasis, vomiting, constipation, dyspepsia, nausea, dermatitis, pruritus, rash, fatigue, weight decreased. Post-marketing experience – suicide-related adverse events, abnormal liver function tests, jaundice, hepatitis, seizures. Atomoxetine should not be used in patients with severe cardiovascular/cerebrovascular disorders in which clinical deterioration would be</td>
<td>Transient decreased appetite, nervousness, Insomnia, headache, stomach ache. Drowsiness, dizziness, dyskinesia. Abdominal pain, nausea and vomiting. dry mouth. Tachycardia, palpitations, arrhythmias, changes in blood pressure and heart rate .Rash, pruritus, urticaria, fever, arthralgia, alopecia. Cerebral arteritis, angina, hyperactivity, convulsions, psychosis, tics including Tourette syndrome, neuroleptic malignant syndrome, tolerance and</td>
<td>Insomnia, restlessness, irritability, euphoria, tremor, dizziness, headache and other symptoms of over-stimulation have been reported. Dry mouth, unwanted anorexia and other gastro-intestinal symptoms, sweating, convulsions and cardiovascular effects (tachycardia, palpitations, minor increases in blood pressure). Isolated reports of cardiomyopathy associated with chronic amphetamine use. Drug dependence. Intracranial haemorrhages and a toxic hypermetabolic state. Rhabdomyolysis and renal damage. Psychosis/psychotic reactions, night terrors, nervousness, abdominal</td>
</tr>
<tr>
<td>Special Precautions</td>
<td>Contraindications</td>
<td>Can be used in common ADHD comorbidities such as tics and Tourette's and marked anxiety</td>
<td>Evidence of abuse potential</td>
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<tr>
<td>Allergic reactions, hypertension, tachycardia, cardiovascular/cerebrovascular disease. Liver damage. Seizures. Suicidal thoughts/behaviour. Growth/development. Pre-screening monitoring required</td>
<td>Not to be used in combination with Monoamine Oxidase Inhibitors (MAOIs). Narrow angle glaucoma. Severe cardiovascular or cerebrovascular disorders</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Monitor growth, blood pressure and full blood count; history of drug or alcohol dependence; psychosis; epilepsy; avoid abrupt withdrawal; pregnancy; GI narrowing (m/r preps).</td>
<td>Anxiety or agitation; tics or a family history of Tourette's syndrome; hyperthyroidism, severe angina; cardiac arrhythmias; glaucoma; breast-feeding; in concomitant use, or use within the last two weeks, of monoamine oxidase inhibitors.</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Patients receiving guanethidine, mild hypertension or a family history of dystonias. Tics, epilepsy, monitor growth, impaired kidney function or unstable personality. Psychotic children. Avoid abrupt withdrawal.</td>
<td>During, or for 14 days after treatment with a Monoamine Oxidase Inhibitor (MAOI). History of drug abuse, symptomatic cardiovascular disease and/or moderate or severe hypertensive disease. Hyperthyroidism, hyperexcitability or glaucoma. Tourette's syndrome or similar dystonias. Prophyria. History of alcohol abuse.</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

Expected with increases in blood pressure or heart rate. See SPC for further details. Dependence, growth retardation, reduced weight gain, blood disorders including leucopenia and thrombocytopenia, muscle cramps, visual disturbances, exfoliative dermatitis, erythema multiforme. Cramps, decreased blood pressure, altered libido and impotence, growth retardation, hyperpyrexia, mydriasis, hyperflexia, chest pain, confusion, panic states, aggressive behaviour, delirium, visual disturbance, choreoathetoid movements, tics and Tourettes syndrome in pre-disposed individuals.
Annex 1: METHYLPHENIDATE drug fact sheet

Therapeutic Indications
- Methylphenidate is indicated as part of a comprehensive treatment programme for ADHD in children over the age of 6 years and adolescents where remedial measures alone prove insufficient.
- Treatment must be under the supervision of a specialist in childhood behavioural disorders.
- Methylphenidate does not have a licence for use in adulthood.

Dosage and Administration

Standard Release Methylphenidate (including Ritalin® and Equasym®)
- **Children over 6 years**: Begin with 5mg daily or twice daily (e.g. at breakfast and lunch), increasing the dose and frequency if necessary by weekly increments of 5-10mg in the daily dose.
- Doses above 60mg daily are not recommended.
- The total daily dose should be administered in divided doses. In some children rebound hyperactivity may occur if the effect of the drug wears off in the evening. An additional small evening dose of Methylphenidate may eliminate this difficulty but the need for this dose should be weighed against possible disturbances in falling asleep.

Concerta® XL
- **Children over 6 years of age and adolescents**: Starting dose is 18mg once daily. Dosage may be adjusted in 18mg increments to a maximum of 54mg/day taken once daily in the morning. In general, dosage adjustment may proceed at approximately weekly intervals.
- The recommended dose of Concerta® XL for patients who are currently taking methylphenidate (standard release) three times daily at doses of 15mg to 45 mg/day is provided in Table 1. Dosing recommendations are based on current dose regimen and clinical judgement.

Recommended Dose Conversion from other Methylphenidate Regimens to Concerta® XL

<table>
<thead>
<tr>
<th>Previous Methylphenidate (standard release) Daily Dose</th>
<th>Recommended Concerta® XL Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5mg three times daily</td>
<td>18mg once daily</td>
</tr>
<tr>
<td>10mg three times daily</td>
<td>36mg once daily</td>
</tr>
<tr>
<td>15mg three times daily</td>
<td>54mg once daily</td>
</tr>
</tbody>
</table>

- **Daily dosage above 54 mg is not recommended.** NB – there is no dosage recommendation for converting patients receiving 20mg TDS Methylphenidate Standard Release to Concerta® XL.
- Concerta XL® must be swallowed whole with the aid of liquids and must not be chewed, divided or crushed.

Equasym XL®
- **Children over 6 years of age**: Starting dose is 10mg once daily. Dose should be increased gradually if necessary to a maximum of 60mg daily.
- Patients currently using methylphenidate (standard release) may be switched to the milligram equivalent daily dose of Equasym XL®. (For example, 20mg Equasym XL® is regarded as equivalent to 10mg at breakfast and 10mg at lunchtime of standard release methylphenidate).
- Equasym XL® should be given in the morning before breakfast. The capsule may be swallowed whole with the aid of liquids, or alternatively, the capsule may be opened and the capsule contents sprinkled onto a small amount (tablespoon) of applesauce and given immediately, and not stored for future use. Drinking some fluids, e.g. water, should follow the intake of the sprinkles with applesauce. The capsule contents must not be crushed or chewed.
• Equasym XL® consists of an immediate release component (30% of the dose) and a modified release component (70% of the dose). Hence Equasym XL® 10mg yields an immediate-release dose of 3mg and an extended release dose of 7mg. The extended-release portion of each dose is designed to maintain a treatment response through the afternoon without the need for a midday dose. It is designed to deliver therapeutic plasma levels for a period, which is consistent with the school day rather than the whole day.

• If the effect of the medicinal product wears off too early in the late afternoon or evening, disturbed behaviour and/or inability to go to sleep may recur. A small dose of an immediate-release methylphenidate hydrochloride tablet late in the day may help to solve this problem. In that case, it could be considered that adequate symptom control might be achieved with a twice daily immediate release methylphenidate regimen. Treatment should not continue with Equasym XL if an additional late dose of immediate-release methylphenidate is required, unless it is known that the same extra dose was also required for a conventional immediate-release regimen at equivalent breakfast/lunchtime dose. The regimen that achieves satisfactory symptom control with the lowest total daily dose should be employed.

Contra-indications
Anxiety or agitation; tics or a family history of Tourette’s syndrome; hyperthyroidism, severe angina; cardiac arrhythmias; glaucoma; breast-feeding; in concomitant use, or use within the last two weeks, of monoamine oxidase inhibitors; sensitivity to methylphenidate or other components of the product.

Precautions and Warnings
• Before treatment, all patients should be screened to see if they have any problems with their blood pressure or heart rate. The family history of cardiovascular problems should also be checked. Any patients with these problems should not be treated without specialist evaluation.
• During treatment, blood pressure and heart rate should be monitored regularly. Any problems that develop should be investigated promptly.
• The use of methylphenidate could cause or worsen some psychiatric disorders such as depression, suicidal thoughts, hostility, psychosis and mania. All patients should be carefully screened for these disorders before treatment and monitored regularly for psychiatric symptoms during treatment.
• Do not use in children under 6 years old; monitor growth (if prolonged treatment), blood pressure; history of drug or alcohol dependence; psychosis; epilepsy (discontinue if increased seizure frequency); avoid abrupt withdrawal; pregnancy (manufacturer advises avoid unless potential benefit outweighs risk; toxicity in animals).
• Methylphenidate may cause drowsiness and dizziness, it is therefore advisable to exercise caution when driving, operating machinery, or engaging in other potentially hazardous activities.
• Equasym XL®/ Concerta XL® - patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this preparation.
• Equasym XL® - patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
• Concerta XL - Must be swallowed whole and therefore only given to patients who are able to swallow a tablet whole. Should not be given to patients with pre-existing severe GI narrowing or in patients with dysphagia.

Drug interactions
• Methylphenidate may inhibit the metabolism of coumarin anticoagulants, some anticonvulsants, phenylbutazone and antidepressants (tricyclic and selective serotonin reuptake inhibitors).
• Pressor agents and MAOIs may augment the effect of Methylphenidate (see contra-indications).
• Clonidine – serious adverse events have been reported in concomitant use, although no causality for the combination has been established.
• Decreased antihypertensive effect of guanethidine.
• Alcohol (abstinence is advised during treatment with methylphenidate).
• Clearance of Methylphenidate may be affected by changes in urinary pH (theoretical).

Very Common side effects include:
• Decreased appetite is a common but usually transient adverse effect of Methylphenidate.
• Nervousness and insomnia are the most common adverse reactions occurring at the beginning of treatment. They are usually controlled by reducing the dosage and omitting the drug in the afternoon or evening.
• Headache
• Stomach ache.

Common side effects include:
• Drowsiness, dizziness, dyskinesia.
• Abdominal pain, nausea and vomiting – may occur at the beginning of treatment and may be alleviated by taking the dose with food. Dry mouth.
• Tachycardia, palpitations, arrhythmias, changes in blood pressure and heart rate (usually an increase).
• Rash, pruritus, urticaria, fever, arthralgia, alopecia.

Rare side effects include:
Cerebral arteritis, angina, hyperactivity, convulsions, psychosis, tics including Tourette syndrome, neuroleptic malignant syndrome, tolerance and dependence, growth retardation, reduced weight gain, blood disorders including leucopenia and thrombocytopenia, muscle cramps, visual disturbances, exfoliative dermatitis, erythema multiforme.

Monitoring
• Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months.
• Height, weight and appetite should be recorded at least 6 monthly with maintenance of a growth chart
• Development of de novo or worsening of pre-existing psychiatric disorders should be monitored at every adjustment of dose and then at least every 6 months and at every visit.
• See appendix 1 of formulary section for full details

Withdrawal of therapy
• It is the specialist’s decision to withdraw therapy.
• There is a lack of information on the long term effects of methylphenidate. For patients who take methylphenidate for more than a year, doctors should interrupt treatment at least once a year to determine whether continued treatment with methylphenidate is necessary.
• Methylphenidate should be discontinued periodically to assess the patient’s condition.
• Drug therapy is usually discontinued during or after puberty.
• Careful supervision is required during drug withdrawal, since depression as well as renewed over-activity can be unmasked. Abrupt withdrawal should be avoided.
• If improvement of symptoms is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.
• None of the methylphenidate preparations is licensed for use in adults. The need for continuing treatment should therefore be reviewed by the specialist before the patient reaches the age of 18. In most cases, treatment should have been discontinued by the age of 18, but if treatment beyond this age is considered necessary, the specialist should arrange for an appropriate referral.

Prescription requirements and ‘Black Triangle Status’
• Methylphenidate is a schedule 2-controlled drug therefore prescriptions for this drug are subject to the full prescription requirements of the Misuse of Drugs Regulations 2001.
• Concerta XL® has black triangle status, which means that all suspected adverse reactions (including those considered not to be serious and where the causal link is uncertain) should be
reported to the CSM. It is not recommended to prescribe more than 1 months' supply at a time.

For full information consult the Summary of Product Characteristics (SPC) and the BNF.
Annex 2: ATOMOXETINE drug fact sheet

Therapeutic Indication
- Atomoxetine is indicated for the treatment of ADHD in children of 6 years and older and in adolescents as part of a comprehensive treatment programme. Treatment must be initiated by or under the supervision of a physician with appropriate knowledge and experience in treating ADHD.

Dosage and Administration*
- For oral use. Atomoxetine can be administered as a single daily dose in the morning, with or without food. Patients who do not achieve a satisfactory clinical response (tolerability or efficacy) when taking atomoxetine as a single daily dose might benefit from taking it as twice daily evenly divided doses in the morning and late afternoon or early evening.
- Atomoxetine may only be used in children of 6 years and older.
- **Dosing of children/adolescents up to 70kg body weight:** Atomoxetine should be initiated at a total daily dose of approximately 0.5 mg/kg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability to the recommended maintenance dose of approximately 1.2 mg/kg/day. No additional benefit has been demonstrated for doses higher than 1.2mg/kg/day. The safety of single doses over 1.8mg/kg/day and total daily doses above 1.8mg/kg have not been systematically evaluated.
- **Dosing of children/adolescents over 70 kg body weight:** Atomoxetine should be initiated at a total daily dose of 40mg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability to the recommended maintenance dose of 80mg (total daily dose). The maximum recommended total daily dose is 100mg. The safety of single doses over 120mg and total daily doses above 150mg have not been systematically evaluated.
- In some cases it might be appropriate to continue treatment into adulthood (assuming that treatment had been initiated prior to reaching adulthood).
- In patients with moderate hepatic insufficiency, the initial and target doses should be reduced to 50% of the usual doses. In severe hepatic insufficiency, the initial and target doses should be reduced to 25% of the usual doses. No adjustments are required in patients with renal insufficiency.

Contra-indications
- Hypersensitivity to atomoxetine or to any of the excipients.
- Atomoxetine should not be used in combination with monoamine oxidase inhibitors (MAOIs). Atomoxetine should not be used within a minimum of 2 weeks after discontinuing therapy with a MAOI. Treatment with a MAOI should not be initiated within 2 weeks after discontinuing atomoxetine.
- Atomoxetine should not be used in patients with narrow angle glaucoma, as in clinical trials the use of atomoxetine was associated with an increased incidence of mydriasis.
- Severe cardiovascular or cerebrovascular disorders.

Precautions and Warnings
- Although uncommon, allergic reactions, including rash, angioneurotic oedema, and urticaria, have been reported in patients taking atomoxetine.
- An increase in pulse and/or blood pressure has been reported. Atomoxetine should be used with caution in patients with hypertension, tachycardia, or cardiovascular or cerebrovascular disease. Pulse and blood pressure should be measured periodically while on therapy and during dose changes. Orthostatic hypotension has also been reported. Use with caution in any condition that may predispose patients to hypotension.
- Growth and development should be monitored during treatment with atomoxetine. Patients requiring long-term therapy should be monitored and consideration given to dose reduction or interrupting therapy in patients who are not growing or gaining weight satisfactorily.
- Clinical data do not suggest a deleterious effect of atomoxetine on cognition or sexual maturation, however, the amount of available long-term data is limited. Therefore patients...
requiring long-term therapy should be carefully monitored.

- Hostility and emotional lability were more frequently observed in clinical trials among children and adolescents treated with atomoxetine compared to those treated with placebo.

- Patients who are being treated for ADHD should be carefully monitored for the appearance of worsening of suicide related behaviour, hostility, and emotional lability.

- Atomoxetine is not indicated for the treatment of major depressive episodes and/or anxiety.

- Patients should be advised to use caution when driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected by atomoxetine.

- Pre-screening monitoring required

**CSM/MHRA WARNINGS**

The Commission on Human Medicines (formerly the Committee on Safety of Medicines has undertaken a Europe wide review of available data on the risks and benefits of Strattera® (atomoxetine). The review concluded that the overall balance of risks and benefits of Strattera® (atomoxetine) remains positive in the treatment of ADHD in children of 6 years and older and in adolescents. The following advice to prescribers has been issued:

- Seizures are a potential risk with Strattera® (atomoxetine) and therefore it should be introduced with caution in patients with a history of seizure. Discontinuation of Straterra® (atomoxetine) should be considered in any patient developing seizure or if there is an increase in seizure frequency. *(Advice issued Feb 06)*

- Reports of QT interval prolongation have been received in association with Strattera® (atomoxetine). Therefore, it should be used with caution in those with congenital or acquired long QT or a family history of QT prolongation. This risk may be increased if Straterra® (atomoxetine) is used concomitantly with other drugs that produce QT prolongation, drugs that can cause electrolyte disturbances and those that inhibit cytochrome P450 2D6. *(Advice issued Feb 06)*

- Due to concerns about an increased risk of suicidal thoughts and behaviour, patients should be monitored for signs of depression, suicidal thoughts or suicidal behaviour and referred for appropriate treatment if necessary. *(Advice issued Sept 05)*

- There is a risk of rare, but sometimes severe, hepatic disorders. Strattera® (atomoxetine) should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted. Due to the seemingly idiosyncratic nature of these reactions, routine liver monitoring of liver function is unlikely to be helpful in minimising the risk and is not recommended. Patients and carers and carers should be advised of the risk and told how to recognise symptoms; prompt medical attention should be sought in case of abdominal pain, unexplained nausea, malaise, darkening of urine or jaundice. *(Advice issued Feb 2005)*

- 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/cerebrovascular disorders. *(Advice issued Dec 2011)*

**Drug interactions**

- Atomoxetine should not be used with MAOIs (see above under contra-indications)

- The Summary of Product Characteristics (SPC) recommends that the following drugs be used with caution if co-administered with atomoxetine because of potential or theoretical drug interactions: CYP2D6 inhibitors (e.g. fluoxetine, paroxetine), salbutamol (high dose nebulised, or systemically administered), presser agents, drugs that affect noradrenaline (e.g. imipramine, venlafaxine, mirtazapine, pseudoephedrine, phenylephrine). See SPC for further details.

**Side Effects**

- Most common adverse effects in children and adolescents – abdominal pain and decreased appetite. These effects are usually transient.

- Other common adverse effects in children or adolescents were – cold/flu symptoms, anorexia, early morning awakening, irritability, mood swings, dizziness, somnolence, mydriasis (see contra-indications), vomiting, constipation, dyspepsia, nausea, dermatitis, pruritus, rash, fatigue, weight decreased.
• Post-marketing experience – suicide-related adverse events, abnormal liver function tests, jaundice, hepatitis, seizures. (See CSM Warnings above)

Pregnancy and Breastfeeding
• Atomoxetine should only be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.
• Atomoxetine should be avoided during breast-feeding.

Monitoring
• The patient’s blood pressure, heart rate and growth parameters should be monitored, especially in the early stages of treatment. Patients/careers should be advised of the risk of hepatic disorders, be told how to recognise symptoms and to seek prompt medical attention. Patients should be monitored for signs of depression, suicidal thoughts or suicidal behaviour and referred for appropriate treatment if necessary.
• See appendix 1 of formulary section for full details

Withdrawal of therapy
• In the study programme, no distinct withdrawal symptoms have been described. In cases of significant adverse effects, atomoxetine may be stopped abruptly; otherwise the drug may be tapered off over a suitable time period.
• It is the specialist’s decision to withdraw therapy.
• The patients need for therapy should reviewed by the time they are 18 years old and appropriate referral arrangements for continued care should be organised by the specialist.

Prescription requirements and ‘Black Triangle Status
• Atomoxetine is a Prescription Only Medicine (POM). It has black triangle status, which means that all suspected adverse reactions (including those considered not to be serious and where the causal link is uncertain) should be reported to the CSM.
• It is not recommended to prescribe more than one months supply at a time.

For full information consult the Summary of Product Characteristics (SPC) and the BNF.
Annex 3: DEXAMPHETAMINE drug fact sheet

Therapeutic Indication

- Dexamphetamine is indicated for children with refractory hyperkinetic states under the supervision of a physician specialising in child psychiatry.
- Not applicable for use in adulthood for the indication of children with hyperkinetic states. If used in adult patients, this would be a clinical decision by the prescriber to use the drug without licence.

Dosage and Administration

- In hyperkinetic states, the usual starting dose for children aged 3-5 years is 2.5mg a day, increased if necessary by 2.5 mg a day at weekly intervals; for children aged 6 years and over, the usual starting dose is 5-10 mg a day increasing if necessary by 5 mg at weekly intervals.
- The usual upper limit is 20mg a day though some older children have needed 40mg or more for optimal response.

Contra-indications

- Patient’s known to be intolerant of sympathomimetic amines.
- During, or for 14 days after treatment with a Monoamine Oxidase Inhibitor (MAOI).
- Those with a history of drug abuse.
- Patients with symptomatic cardiovascular disease and/or moderate or severe hypertensive disease.
- Patients suffering from hyperthyroidism, hyper excitability or glaucoma.
- Patients with de la Tourette syndrome or similar dystonias.
- Patients with porphyria.
- Patients with a history of alcohol abuse.

Precautions and Warnings

- Use with caution in patients receiving guanethidine, and patients with mild hypertension (monitor blood pressure) or a family history of dystonias.
- If tics develop, discontinue treatment with dexamphetamine.
- Caution is advised in patients with epilepsy (discontinue if convulsions occur).
- Height and weight should be carefully monitored in children as growth retardation may occur.
- Caution should be used when administering dexamphetamine to patients with impaired kidney function or unstable personality.
- In psychotic children, may exacerbate behavioural disturbances and thought disorder.
- Dexamphetamine may affect ability to drive or operate machinery.

Drug interactions*

The summary of product characteristics (SPC) lists the following drugs that may interact with dexamphetamine: adrenoreceptor blocking agents (e.g. propranolol), lithium, alpha methyltyrosine, disulfram, tricyclic antidepressants, MAOIs (see above under contra-indications), guanethidine (see above under precautions), phenothiazines, ethosuximide, phenobarbital, phenytoin, haloperidol, morphine. See SPC for more details.

Pregnancy & Lactation

- Dexamphetamine should be avoided in pregnancy, especially during the first trimester.
- Dexamphetamine passes into breast milk and use should be avoided during breast-feeding.

Side Effects

Insomnia, restlessness, irritability, euphoria, tremor, dizziness, headache and other symptoms of over-stimulation have been reported. Dry mouth, unwanted anorexia and other gastro-intestinal symptoms, sweating, convulsions and cardiovascular effects (tachycardia, palpitations, minor increases in blood pressure). Isolated reports of cardiomyopathy associated with chronic amphetamine use. Drug dependence. Intracranial haemorrhages, and a toxic hypermetabolic state.
(characterised by transient hyperactivity, hyperpyrexia, acidosis and death due to cardiovascular collapse) have been reported. Rhabdomyolysis and renal damage. Psychosis/psychotic reactions, night terrors, nervousness, abdominal cramps, decreased blood pressure, altered libido and impotence, growth retardation, hyperpyrexia, mydriasis, hyperflexia, chest pain, confusion, panic states, aggressive behaviour, delirium, visual disturbance, choreoathetoid movements, tics and Tourette’s syndrome in pre-disposed individuals.

Monitoring

- See appendix 1 of formulary section for full details

Withdrawal of therapy

- It is the specialist’s decision to withdraw therapy.
- Treatment should be stopped gradually since abrupt cessation may produce extreme fatigue, mental depression or renewed hyperactivity.
- The patients need for therapy should be reviewed by the time they are 18 years old and appropriate referral arrangements for continued care should be organised by the specialist.

Prescription requirements and ‘Black Triangle’ Status

- Dexamphetamine is a schedule 2-controlled drug therefore prescriptions for this drug are subject to the full prescription requirements of the Misuse of Drugs Regulations 2001. (see BNF for prescribing recommendations).
- As dexamphetamine is an old drug it does not have black triangle status – report all serious adverse reactions in adults and all serious and minor adverse reactions in children (under 18 years).
- It is not recommended to prescribe more than one month’s supply at a time.

*For full information consult the Summary of Product Characteristics (SPC) and the BNF.