# Atomoxetine Adult ADHD

**Part of the shared care protocol for Adult ADHD**
**Traffic light classification - AMBER 1**
**Information sheet for Primary Care Prescribers**

## Indications

Attention Deficit Hyperactivity Disorder (ADHD) in adults who are under the care of a specialist (Consultant Psychiatrist or Non-Medical Prescriber specializing in ADHD) as part of a comprehensive treatment program[1]. Atomoxetine is licensed in adults and recommended by NICE[1].

## Any patient groups to be excluded from shared care

- Treatment of ADHD in children and young people is covered by a separate shared care protocol.
- Adult patients who are not under the care of a specialist.

## Therapeutic Summary

Atomoxetine is a noradrenaline reuptake inhibitor, although the precise mechanism by which it works on ADHD is unknown. It is thought to increase brain levels of noradrenaline and dopamine, predominantly in the cortex rather than in sub-cortical regions.

## Medicines Initiation

Atomoxetine is a treatment option recommended by NICE for the management of ADHD in adults[1]. It may be considered for adults who cannot tolerate methylphenidate or lisdexamfetamine. It may also be considered if symptoms have not responded to separate 6-week trials of methylphenidate and lisdexamfetamine, having considered alternative preparations and doses[1].

Treatment with atomoxetine should only be initiated by a specialist with expertise in ADHD following a comprehensive assessment and diagnosis. It is recommended by NICE that prescribing and monitoring should be carried out under locally agreed shared care arrangements with primary care[1].

## Products available

Atomoxetine capsules – 10mg, 18mg, 25mg, 40mg, 60mg, 80mg or 100mg. Cost x 28 capsules = £48.49, £48.21, £47.92, £47.92, £48.20, £64.28 and £64.28 respectively[2,3].

Atomoxetine (Strattera®) oral solution – 4mg/mL. Cost x 300mL bottle = £85.00

As the unit cost of a dose of atomoxetine (except 80mg and 100mg capsule) is the same regardless of strength, twice daily dosing would double the cost of treatment with this medication and is therefore not recommended.

## Dosages and route of administration[2,4]

- Initiation, titration and stabilisation of the dose will be performed by the specialist.
- Atomoxetine is given orally, usually as a single daily dose in the morning, or in two divided doses (with the last dose no later than early evening) to minimize side-effects.

- **Up to 70kg body weight**: Initial dose 0.5mg/kg/day, increased after 7 days according to response. Maintenance dose 1.2mg/kg/day and maximum dose 1.8mg/kg/day.
- **Over 70kg body weight**: Initial dose 40mg/day, increased after 7 days according to response. Maintenance dose 80mg to 100mg/day. Higher daily doses (up to 120mg/day) may occasionally be undertaken by a specialist in cases of poor response to medication treatment. Note that doses >100mg/day in adults are not licensed.
- Atomoxetine can be taken with or without food.
- Atomoxetine capsules are not intended to be opened (it is an ocular irritant). In the event of the capsules content coming in contact with the eye, the affected eye should be flushed immediately with water, and medical advice obtained. Hands and any potentially contaminated surfaces should be washed as soon as possible.
- Hepatic impairment: for patients with moderate hepatic insufficiency (Child-Pugh Class B), initial and target doses should be reduced to 50% of the usual dose. For patients with severe hepatic insufficiency (Child-Pugh Class C), initial dose and target doses should be reduced to 25% of usual dose
- Renal impairment: Atomoxetine can be administered to ADHD patients with end-stage renal disease or lesser degrees of renal insufficiency using the usual dosing regimen. Atomoxetine may exacerbate hypertension in patients with end-stage renal disease.

**Duration of treatment**
Following an adequate treatment response, treatment with medication for ADHD should be continued for as long as it remains clinically effective. This should be reviewed at least every 12 months by the specialist[1].

In adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, treatment should be continued into adulthood[1].

**Monitoring Requirements and Responsibilities**
Pre-treatment/baseline assessments to be performed by the specialist and will include: Behavioural rating scales (e.g. SDQ, CAARS self and observer report), descriptive reports from partners/carers, medical history, assessment of mental health and social circumstances and review of physical health (including height, weight, baseline pulse and blood pressure)[1].

**Ongoing monitoring**
During dose titration and stabilisation, the appropriate monitoring will be performed by the specialist. When atomoxetine is being prescribed under a shared care agreement, the ongoing monitoring specified below will be performed by primary care and the results sent to the specialist for recording in the patient's notes.

Ongoing psychological response and assessment of continued need for atomoxetine will be performed by the specialist at least every 12 months.

| **Ongoing monitoring**[1,4] | **Frequency** |
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| Heart Rate and Blood Pressure | Baseline and six monthly.<br>Also before and after each dose change.<br>Refer to NICE guidelines for hypertension in adults[5]<br><br>Most patients taking atomoxetine experience a modest increase in heart rate (mean <10bpm) and/or increase in blood pressure (mean <5mmHg) that may not be clinically important.[4]<br>Approximately 6-10% of adults experience clinically important changes in heart rate (≥20bpm) or blood pressure (≥15-20mmHg). Of these, 27-32% had |

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| | sustained or progressive increases.[4] |
| Weight | Baseline then every 6 months.<br>Consider BMI monitoring of adults with ADHD if there has been weight change as a result of their treatment. |
| Development or worsening of psychiatric disorders | Baseline and six monthly.<br>Also before and after each dose change. |
| Development or worsening of tics | Baseline – collect family history and clinically evaluate for tics or Tourette's syndrome.<br>Six monthly.<br>Also before and after each dose change. |
| Medication related side-effects | At each visit. |
| ECG | Not recommended unless there is a clinical indication (e.g. family history of cardiomyopathy, cardiac illness, hypertension or concomitant treatment with a medicine that may pose an increased cardiac risk). |
| Routine blood tests | Not recommend unless there is a clinical indication. |

**Explicit criteria for review and discontinuation of the medicine[1,4]**

These recommendations do not replace the need for medical assessments that would be undertaken in response to these signs/symptoms. In any case of withholding/reducing doses, please discuss with the specialist and assess the need for a risk management plan and follow up appointments.

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| Sustained resting tachycardia (>120bpm) | Withhold/reduce dose and discuss with the specialist.<br>Arrange an ECG and prompt cardiology input if indicated. |
| Arrhythmia(suspected or confirmed) | Withhold/reduce dose if significant and discuss with the specialist.<br>Prompt cardiology input if indicated |
| A clinically significant increase in blood pressure (measured on 2 occasions) | Withhold/reduce dose if significant and discuss with the specialist.<br>Prompt cardiology input if indicated. |
| Patient fails to attend for physical monitoring | Arrange a further appointment in a timely manner.<br>If follow up appointments are not attended, do not provide further prescriptions and inform the specialist. |
| Reduced appetite and / or clinically significant weight change | Discuss with the specialist. May respond to dose reduction or altered timing. |
| Erectile or ejaculatory dysfunction in male patients | Possible side-effect of atomoxetine, discuss with the specialist. |
| Dysmenorrhoea | Possible side-effect of atomoxetine, discuss with the specialist. |
| Abdominal pain, unexplained nausea, malaise, or darkening of the urine | Withhold and discuss with the specialist. Consider rare possibility of liver injury from atomoxetine, check LFTs. |
| Jaundice or laboratory evidence of liver injury | Discontinue and discuss with the specialist. Atomoxetine should not be restarted[4]. |
| Development or worsening of psychiatric disorders (anxiety, agitation, depression, psychotic symptoms, mania, behavior changes, suicidal tendencies) | Discuss with the specialist. |
| Seizures in patients with no previous history | Consider urgent medical assessment.<br>Withhold and discuss with the specialist immediately. |

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| Increase in seizure activity in patients with previous history of seizures | Withhold and discuss with the specialist immediately. |

*For a full list of Side Effects refer to the BNF or Summary of Product Characteristics (SPC).*

Eli Lilly and Co Ltd issued a Dear Healthcare Professional letter on 5th December 2011 outlining important new safety information on Strattera® (atomoxetine) and risks of increased blood pressure and heart rate.[6] This was followed by publication of an MHRA Drug Safety Update in January 2012[7].

**Contraindications[2,4]**

- Severe cardiovascular disorders (e.g. severe hypertension, heart failure, arterial occlusive disease, angina, hemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, and potentially life-threatening arrhythmias).
- Severe cerebrovascular disorders (e.g. stroke or cerebral aneurysm)
- Concomitant Monoamine Oxidase Inhibitors (MAOIs). Atomoxetine should not be used in combination with MAOIs or 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.
- Patients with narrow-angle glaucoma - in clinical trials the use of atomoxetine was associated with an increased incidence of mydriasis.
- Patients with pheochromocytoma or a history of pheochromocytoma

**Precautions[2,4]**

Particular caution is needed in the following groups of patients:

- Patients with underlying medical conditions that could be worsened by increases in blood pressure and heart rate (e.g. hypertension, tachycardia, cardiovascular or cerebrovascular disease, including those with congenital or acquired long QT or a family history of QT prolongation (but see contraindications above).
- Patients with a history of psychosis, depression and/or suicidal behavior,
- In patients with moderate and severe hepatic insufficiency; the dose should be reduced.
- Patients with a history of seizures. 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.

**Pregnancy and Breast-Feeding**

There is limited experience of atomoxetine in pregnancy. It should be avoided in pregnancy unless potential benefit outweighs risk[2,4].

If appropriate, female patients should be advised to use effective contraception during treatment with atomoxetine. In the event of a female patient becoming pregnant whilst taking atomoxetine, or wishing to start a family she should be advised to contact the specialist as soon as possible.

Atomoxetine should be avoided in breast-feeding; it is not known whether atomoxetine is excreted in human milk.[4]

**Driving**

Patients must tell the DVLA if their ADHD or ADHD medication affects their ability to drive safely. Please refer to government advice on driving and psychiatric disorders[8].

**Clinically Relevant Medicine Interactions and their Management**[2,4]

- Monoamine Oxidase Inhibitors (MAOIs) including isocarboxazid, moclobemide, phenelzine and tranylcypromine – atomoxetine should not be used in combination with MAOIs or within 2 weeks of stopping a MAOI due to risk of hypertensive crisis.
- Atomoxetine is metabolised by the CYP2D6 pathway. Slower titration and lower final dosage of atomoxetine may be necessary in patients taking CYP2D6 inhibitors (e.g. fluoxetine, paroxetine, terbinafine).
- Atomoxetine should be used cautiously with antihypertensive medicines as it may increase blood pressure and therefore decrease the effectiveness of antihypertensive drugs.
- Potential for increased risk of QT interval prolongation when given with other QT prolonging medicines (e.g. neuroleptics, tricyclics, methadone, erythromycin) or in presence of electrolyte imbalance.
- Potential risk of seizures with other medicines known to lower seizure threshold (e.g. TCAs, neuroleptics, mefloquine, bupropion and tramadol).
- Potential additive pharmacological effects with other noradrenergic medicines (e.g. TCAs, venlafaxine, mirtazapine and decongestants such as pseudoephedrine).

*For a full list of contraindications, precautions and drug interactions refer to the BNF/ product SPC*

**Information Given to Patient**

- The patient must be warned to report immediately any abdominal pain, unexplained nausea, malaise, darkening of the urine or jaundice), or suicidal thinking and self-harm to the GP.[3,4]
- Written information sheets on the medicines used in ADHD can be found at the following sites:

http://www.choiceandmedication.org/nottinghamshirehealthcare/

http://www.rcpsych.ac.uk/mentalhealthinformation

**References**

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## Contacts


**Neurodevelopmental Specialist Service: Adult ADHD Service**
The Pines, Highbury Hospital, Bulwell, Nottingham, NG6 9DR
Tel: 01159 560893
Email: NeSS@nottshc.nhs.uk

**Pharmacy Services: Nottinghamshire Healthcare NHS Foundation Trust**
Wells Road Centre Pharmacy: 01159 555356
Highbury Hospital Pharmacy: 01158 542247
Millbrook Hospital Pharmacy: 01159 691300, ext 14124
Email: MI@nottshc.nhs.uk


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