Clinical guidelines for the treatment of ADHD in adults

Background

The NICE clinical guideline on the diagnosis and management of ADHD in children, young people and adults, states that following a decision to start drug treatment in adults with ADHD, methylphenidate should normally be tried first. If methylphenidate is ineffective or unacceptable, atomoxetine or dexamfetamine can be tried. This clinical guideline pre-dated the arrival of lisdexamfetamine on the market, which now has a licence to treat ADHD in adults. A recent questions and answers paper prepared in August 2015 reconfirmed the first-line role of methylphenidate in treating adults with ADHD.

NICE clinical guidelines state that following a decision to start drug treatment in adults with ADHD, methylphenidate should normally be tried first even though the methylphenidate preparations currently available in the UK are not licensed for use in adults. The SPCs for Concerta XL, Matoride XL and Medikinet XL (10-60mg) say they can be used in adolescents whose symptoms persist into adulthood and who have shown clear benefit from treatment, so it may be appropriate to continue treatment into adulthood.

Methylphenidate is effective in reducing ADHD core symptoms and in producing clinical improvement in adults with ADHD when assessed against investigator rating scales. Improvement in symptoms is dose dependent and sustained release and immediate release methylphenidate preparations have similar efficacy in adults. A naturalistic follow up study showed that treatment of ADHD in adults for more than 2 years was associated with better functioning than treatment for 2 years or less. Co-morbidity at baseline is a predictor of poorer outcome.

There is a positive correlation between dropout rate and the dose of methylphenidate. Women, newly diagnosed patients, patients with a substance use disorder and subjects with high educational degrees seem to have a higher risk of non-adherence. Methylphenidate is associated, on average, with only small elevations in blood pressure and heart rate. Increased risk of sudden death or ventricular arrhythmia has not been demonstrated in large population based studies.

Proposed adult ADHD prescribing guidance

1. Use methylphenidate first-line:

- Initial treatment should begin with low doses - 5 mg three times daily of an immediate-release preparation (or modified release equivalent)
- The dose should be titrated against symptoms and side effects over 4–6 weeks
- The dose should be increased according to response up to a maximum of 100 mg/day (immediate release equivalent) Note - this is an unlicensed dose in under 18s, but is recommended maximum in the latest NICE ADHD guidelines at the time of publication
- Modified-release preparations should usually be given once daily and no more than twice daily
- Modified-release preparations may be preferred to increase adherence and in circumstances where there are concerns about substance misuse or diversion
Immediate-release preparations should be given up to four times daily.
Due to the differing release mechanisms and the duration of action, modified release methylphenidate preparations must always be prescribed by their brand name.

2. Either lisdexamfetamine or atomoxetine can be prescribed second-line after trials of at least two forms of modified release methylphenidate if methylphenidate has been shown to work but side-effects and/or duration of action are an issue. Switching from one M/R formulation of methylphenidate to another can provide in some patients more effective symptom control due to the differing release parameters of the M/R forms of methylphenidate or minimise side-effects related to sleep disturbance or appetite suppression. Lisdexamfetamine has the benefit that it can be taken just on the days when the drug is needed and may therefore be significantly less expensive than atomoxetine.

**Dosing:**

**Lisdexamfetamine**

- The starting dose is 30mg once daily taken in the morning.
- The dose should be titrated against symptoms and side-effects over 4 – 6 weeks.
- The treatment should be given once daily in the morning.
- The dose should be increased according to response in 20mg increments at minimum intervals of one week up to a maximum of 70mg once daily.
- Discontinue if response insufficient after one month.

Note: lisdexamfetamine is a pro-drug formulation of dexamfetamine, which is converted to free dexamfetamine by enzymes present on red blood cells.

**Atomoxetine**

- For people with ADHD weighing up to 70 kg, the initial total daily dose should be approximately 0.5 mg/kg; the dose should be increased after 7 days to approximately 1.2 mg/kg/day
- For people with ADHD weighing more than 70 kg, the initial total daily dose should be 40 mg; the dose should be increased after 7 days up to a maintenance dose of 100 mg/day
- The usual maintenance dose is either 80 or 100 mg. a trial of 6 weeks on a maintenance dose should be allowed to evaluate the full effectiveness of atomoxetine.
- Atomoxetine should be administered as a single daily dose in the morning with or without food.

3. Dexamfetamine should be reserved for third-line use due to its greater risk of diversion and it very high cost (see below)

- Initial treatment should begin with low doses (5 mg twice daily)
- The dose should be titrated against symptoms and side effects over 4–6 weeks
- Treatment should be given in divided doses
- The dose should be increased according to response up to a maximum of 60 mg per day
- The dose should usually be given between two and four times daily.
Cost comparisons – maximum licensed doses – prices from Drug Tariff (October 2015)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cost for 30 days</th>
</tr>
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<tbody>
<tr>
<td>Methylphenidate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate release generic</td>
<td>20mg TDS</td>
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</tr>
<tr>
<td>Equasym XL® (8 hours)</td>
<td>60mg OD</td>
<td>£70.00</td>
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<tr>
<td>Medikinet XL® (8 hours)</td>
<td>60mg OD</td>
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<tr>
<td>Concerta XL® (12 hours)</td>
<td>72mg OD*</td>
<td>£82.90</td>
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<td>Xenidate XL® (12 hours)</td>
<td>72mg OD*</td>
<td>£55.18</td>
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<td>Atomoxetine</td>
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<tr>
<td>Lisdexamfetamine</td>
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<tr>
<td>Dexamfetamine</td>
<td>60mg OD</td>
<td>£318.21</td>
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</tbody>
</table>

* Note: Total daily dose of 30mg of immediate release methylphenidate is considered equivalent to Concerta XL®, Xenidate XL® and Matoride XL® 36mg once daily due to residual drug in the XL matrix.

Monitoring

To be undertaken in line with agreed shared care guidelines by the specialist team.

References

2. UKMI Medicines Q&As. Can methylphenidate be used for adults with attention deficit hyperactivity disorder (ADHD)? Prepared August 2015.

These guidelines were approved by the Trust’s Drugs & Therapeutics Group on 26th October 2015

Ray Lyon – Chief Pharmacist – Strategy

October 2015           Review October 2017