

# DRUG UPDATE

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## ADHD IN ADULTS

No drugs are licensed for the treatment of newly diagnosed adult ADHD and clinical evidence of efficacy is limited. ADHD or some of its symptoms will persist for the majority of childhood sufferers and some patients will benefit from continued drug treatment. Treatment programmes should include psychological, educational, and social measures and not medication alone. Appropriate withdrawal strategies are required for patients not continuing with drug therapy.

### What is it?

Attention-deficit-hyperactivity disorder (ADHD) is a chronic condition characterised by persistent and non-episodic symptoms of inattention, hyperactivity and impulsive behaviour.<sup>1</sup> ADHD is a relatively common childhood condition estimated to affect 3 - 4% of children, and about 1% of adults.<sup>2</sup> ADHD frequently persists into adolescence and adulthood and at 25 years old an estimated 15% of childhood sufferers still display the full condition with around 65% displaying some symptoms resulting in significant impairment.<sup>3</sup> The consequences of untreated ADHD in adults are poor social adjustment, personality problems and a predilection for other psychiatric problems.<sup>1,2</sup>

The management of children and adolescents with ADHD is well-defined and structured. NICE has issued guidance concerning the main licensed therapies<sup>4</sup> and is developing clinical guidance (due for publication in 2008) on pharmacological and psychological treatment of ADHD in child and adult populations.<sup>5</sup> Currently, care for adolescent sufferers once they reach adulthood is not well defined and existing adult mental health services may not be prepared to treat such patients.<sup>1,2</sup> Effective handover between child and adult services is necessary for care to be continued where appropriate. The adult ADHD population consists of patients diagnosed in childhood and in adulthood.<sup>1,2</sup>

Evidence-based guidelines covering all treatment aspects of adult ADHD have recently been published by the British Association for Psychopharmacology.<sup>6</sup>

Three drugs are licensed in the UK for the treatment of ADHD: atomoxetine, dexamfetamine, and methylphenidate.<sup>7</sup> None is specifically licensed for use in adults.

### Atomoxetine

Atomoxetine is a non-stimulant non-amphetamine inhibitor of noradrenaline reuptake licensed for the treatment of ADHD in children and adolescents, and adults where treatment is a continuation of adolescent therapy.<sup>7</sup> Two 10-week randomised trials in adult patients (n = 536) found that atomoxetine at a median daily dose of 90 mg significantly reduced symptom scores compared to placebo (investigator-rated score reduction of about 29% vs. 19% with placebo, and patient-rated score reductions of about 20% vs. 13% with placebo).<sup>8</sup>

A cohort of these patients entered a 3-year open-label extension study (n = 384): interim results with an average follow-up of 40 weeks demonstrated significant continued improvement in symptom scores.<sup>9</sup> A six-week study using the same outcome measure of efficacy (n = 218) also found significant symptom score reductions for atomoxetine (80 mg OD or 40 mg BD) and additionally demonstrated that a twice daily dose regimen was more effective than once daily (mean reduction of 17 vs. 13 points, p < 0.001).<sup>10</sup>

### Dexamfetamine

Dexamfetamine is a sympathomimetic stimulant licensed for the treatment of refractory hyperkinetic states in children.<sup>7</sup> In a 20-week study, 98 adult ADHD patients were randomised to treatment with dexamfetamine (n = 23), paroxetine (n = 24), both (n = 25) or placebo (n = 26).<sup>11</sup> The primary outcome was change in ADHD symptom score (range 0 to 54). Mean symptom score decreased by 11.4 with dexamfetamine, 7.5 with paroxetine, 12.7 with both and 8.7 with placebo. No significant treatment effects were observed for dexamfetamine versus non-dexamfetamine treated groups (p = 0.064). In a six-week placebo-controlled study of 45 newly diagnosed adult ADHD sufferers, treatment with dexamfetamine was associated with greater reductions in total symptom score compared to placebo (baseline 10.6, mean reduction 5.8 vs. 2.6, p = 0.045).<sup>12</sup>

### Methylphenidate

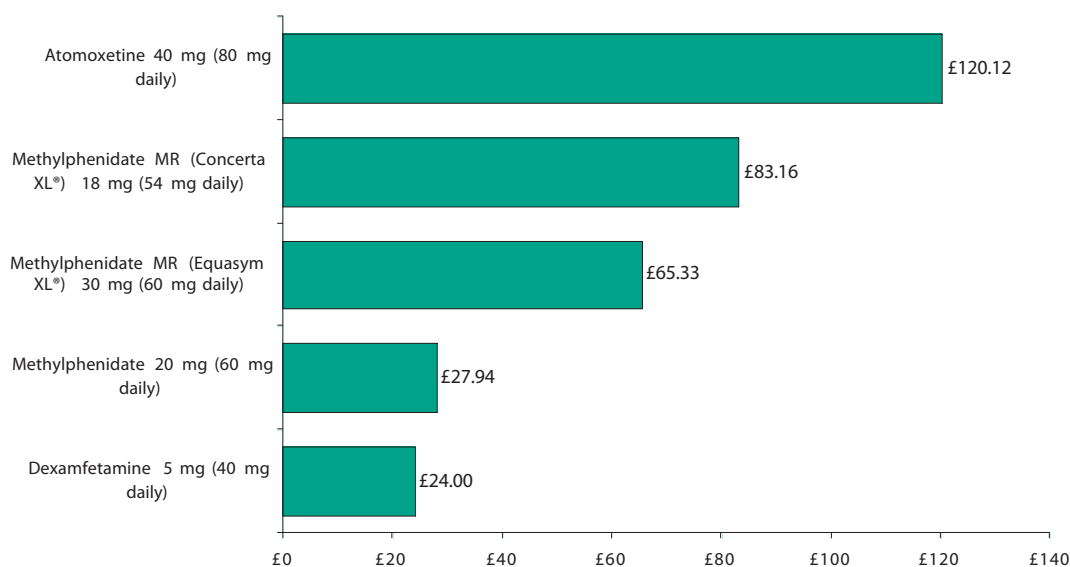
Methylphenidate is a centrally acting sympathomimetic licensed for the treatment of ADHD in children and adolescents, available in standard and modified-release presentations.<sup>7</sup> In two six-week randomised studies in adult ADHD populations, mean symptom score (range 0 to 54) reductions were greater with methylphenidate than placebo.<sup>13,14</sup> With methylphenidate three times daily (n = 104) compared to placebo (n = 42) the effect was 20.7 vs. 7.9 points (p < 0.001)<sup>13</sup> and with modified-release methylphenidate once daily (n = 67) compared to placebo (n = 74) the effect was approximately 19 vs. 13 points (p < 0.001) respectively.<sup>14</sup> A meta-analysis including 140 methylphenidate-treated and 113 placebo patients concluded that higher dose regimens (mean daily dose  $\geq$  0.9 mg/kg) were associated with a greater treatment effect.<sup>15</sup>

## How safe are they?

Dexamphetamine and methylphenidate exhibit similar adverse effects due to their shared pharmacology: small increases in blood pressure and heart rate, loss of appetite with consequent weight loss, insomnia, dry mouth, and altered mood.<sup>2,13,14</sup> Patients on methylphenidate long-term should have regular blood tests due to a small risk of blood dyscrasias.<sup>7</sup> The most frequently reported adverse effects with atomoxetine are dry mouth, slightly raised blood pressure and pulse, insomnia, nausea, dizziness, sweating, painful urination, palpitations and sexual problems.<sup>16</sup> Adverse effects resulted in a combined withdrawal rate of 9% vs. 3% in placebo-treated patients in two 10-week studies.<sup>8</sup>

## How much does it cost?

Cost for 28 days treatment (Drug Tariff March 2007)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence

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Key: G- guidelines, E-editorial, MA-meta analysis, RCT - randomised controlled trial, R-review

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