

DRUG UPDATE

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MODIFIED-RELEASE METHYLPHENIDATE FOR ADHD

Modified-release methylphenidate is licensed as one component of a treatment programme for children with Attention Deficit Hyperactivity Disorder (ADHD). Taken once daily, it is as effective as immediate-release formulation taken three times daily in improving behaviour in children with ADHD and is associated with similar adverse effects. There is no evidence that modified-release methylphenidate improves concordance or self-esteem by avoiding a midday dose taken during school hours. It is expensive compared with immediate-release formulation and should not be prescribed routinely in preference to standard formulations.

What is it?

ADHD is described by three main features; inattention, hyperactivity and impulsiveness of at least 6 months' duration. It impairs social or academic functioning and is usually present before the age of seven.¹ NICE guidance endorses the use of methylphenidate as part of a comprehensive treatment programme for children with severe ADHD, though it appraised only immediate release (i/r) formulations¹. Three i/r formulations of methylphenidate are available; they are administered in two to three daily doses.

It is suggested that the need to take the midday dose at school may adversely affect the child's self-esteem and risk low concordance.^{2,3} Several modified-release (m/r) formulations of methylphenidate have been developed that avoid the midday dose; only Concerta XL[®], an osmotic pump formulation that is taken once daily, is currently licensed in the UK.^{4,5}

How effective is it?

Two fully published placebo-controlled trials have compared m/r and i/r formulations of methylphenidate, both in children aged 6 – 12 years.^{2,3} In a crossover study², 68 children received a week's treatment with placebo, m/r methylphenidate (mean dose 35 mg/day) or i/r methylphenidate (mean dose 29 mg/day). Both formulations were superior to placebo, but not significantly different from each other, in teachers' assessments of children's behaviour and in classroom

performance. The m/r formulation improved behavioural scores for up to 12 hours after morning administration. Parent's rated the m/r preparation higher in two assessments, though the difference was small, they were still significant; parental preferences were 47% for the m/r formulation, 31% for the i/r formulation, 15% for their previous methylphenidate therapy and the remainder chose placebo or no preference. There was no significant difference between the formulations in patterns of behaviour during the day and early evening.

In a parallel group study,³ 282 children were randomised to 28 days' treatment with m/r (mean dose 29.5 mg/day) or i/r methylphenidate (mean dose 34.3 mg/day) or placebo. Both formulations were superior to placebo but there was no significant differences between for the treatment of core ADHD symptoms.

How safe is it?

In clinical trials, there was no significant difference between m/r and i/r formulations in the frequency or nature of adverse effects^{2,3}. In data pooled from clinical trials involving a total of 469 children, 62% reported at least one adverse event associated with m/r methylphenidate; the most frequent were headache (26%), loss of appetite (14%), insomnia (14%) and abdominal pain (14%)⁶. Both m/r and i/r formulations significantly increase blood pressure (by 1 - 4 mmHg) and pulse (by 2 - 6 bpm)⁶. Little is known about the effects of long-term use of methylphenidate.

When should it be used?

Concerta XL® is licensed as part of a comprehensive treatment programme for children over 6 years old and adolescents with ADHD, when remedial measures alone prove insufficient. When methylphenidate is indicated, a modified-release formulation may be useful when daytime dosing is difficult due to the school routine or peer pressure, though the possible benefit to the child of avoiding the midday dose has not been evaluated in a clinical trial. In the last 12 calendar months 2,160

items of m/r methylphenidate and 18,128 items of i/r methylphenidate at a cost £92,158 and £303,191 were dispensed in the four local Strategic Health Authorities (Northumberland Tyne and Wear, County Durham and Tees Valley, North East Yorkshire and North Lincolnshire and West Yorkshire). There is no evidence that m/r methylphenidate offers superior improvement in symptoms at any time of the day, nor does it reduce the risk of adverse effects, compared with the i/r formulation. It should not be therefore be routinely prescribed in preference to standard formulations.

How much does it cost?

Cost for 30 days treatment (prices from MIMS May 2003)



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

REFERENCES

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KEY RCT - randomised controlled trial, CT-controlled trial, O-open study, MA-meta analysis, R-review, U-unpublished, A- abstract, E-editorial

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