



# AUSTRALIAN DRUG EVALUATION COMMITTEE ADVERSE DRUG REACTIONS ADVISORY COMMITTEE

## Use of SSRI antidepressants in children and adolescents

(Dated 15 October 2004. Replaces statement of 17 June 2004)

The Australian Adverse Drug Reactions Advisory Committee (ADRAC) has reviewed data on the safety and efficacy of SSRIs\* in the treatment of major depressive disorder (MDD) and other psychiatric disorders in children and adolescents. The data reviewed has included the US FDA analysis in collaboration with a group at Columbia University.<sup>†</sup> ADRAC has also consulted again with the Royal Australian and New Zealand College of Psychiatrists and the Royal Australasian College of Physicians.

None of the SSRIs, and indeed no antidepressant, is currently approved in Australia for the treatment of MDD in children and adolescents (persons aged less than 18 years). Fluoxetine, but none of the other SSRIs, is approved in the US for MDD in young people without a specified lower age limit. Two of the SSRIs, fluvoxamine and sertraline, are approved in Australia for children and adolescents with obsessive compulsive disorder (OCD).

Assessment of the published and unpublished data available for SSRI use in children and adolescents indicates that there is evidence of an increased risk of suicidality, including suicidal ideation, suicide attempts and self-harm events, associated with each of the SSRIs.<sup>1</sup> The strongest association has been found with paroxetine and venlafaxine, but sertraline, citalopram and fluoxetine have also been implicated, with fluoxetine possibly having the smallest risk.<sup>1,2</sup> There are very few data for fluvoxamine.

Increases in suicidal ideation and behaviour during the early stages of antidepressant treatment are well-known clinical phenomena in adults. It is clear that these events can occur in children and adolescents as well. While the size of the increase compared to placebo is small, around 2 to 3 patients per 100, the effect is stronger with some SSRIs than others in young people.

In a recent study,<sup>2</sup> at the completion of therapy fluoxetine was beneficial for the treatment of depression in adolescents with moderate to severe symptoms of MDD. Treatment with fluoxetine plus cognitive behaviour therapy was more beneficial and decreased suicidal ideation compared with placebo by the end of the treatment period. *During therapy* with fluoxetine there was, however, an increase in some psychiatric adverse events (acts and ideation of suicide, self-harm, aggression, violence).

In general clinical trials of SSRIs in children and adolescents have excluded severely depressed patients and have not adequately monitored participants for self-harm or suicide-related events. Other non-SSRI antidepressants have been subjected to even less scrutiny, and may be ineffective and also associated with suicidality, as well as having other undesirable effects such as the toxicity in overdose of the tricyclics.

ADRAC recommends:

1. Any use of SSRIs in children and adolescents with MDD and other psychiatric conditions should be undertaken only within the context of comprehensive management of the patient. Management should include careful monitoring for the emergence of suicidal ideation and

behaviour which may particularly develop early in therapy, or if therapy is interrupted or irregular because of poor compliance. Cognitive behaviour therapy, if it is available, may enhance the outcome in MDD.

2. The choice of an SSRI for a child or adolescent with MDD or other psychiatric condition should be made only after taking into account the recent evaluations of clinical trial data and the Australian product information (PI). Prescribers should be aware that the marketers of fluvoxamine and sertraline (indicated for OCD) advise against use in children and adolescents with MDD, and of citalopram, escitalopram, paroxetine, venlafaxine and fluoxetine warn or caution against use in patients aged less than 18 years for any indication.
3. Children and adolescents being treated for MDD with an SSRI should not have their medication ceased abruptly.

In addition, ADRAC asks that cases of emergent or worsening suicidal ideation or behaviour and self-harm in children or adolescents treated with an SSRI be reported to aid understanding of what might be an idiosyncratic response to the medication.

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\* The SSRI antidepressants included are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline, and the related medicine, venlafaxine.

† The FDA review also included mirtazapine which is not approved for use in children, bupropion which is not indicated as an antidepressant, and nefazodone which is no longer available in Australia.

1. Mosholder AD. Suicidality in pediatric clinical trials of antidepressant drugs: comparison between previous analyses and Columbia University classification. Centre for Drug Evaluation and Research, Food and Drug Administration, 16 August 2004. <http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1-11-TAB09a-Mosholder-review.pdf>
2. Treatment for Adolescents with Depression Study (TADS) Team. Fluoxetine, cognitive-behaviour therapy and their combination for adolescents with depression. *JAMA* 2004;292:807-20.