22nd March 2004

MEDSAFE
NEW ZEALAND MEDICINES
AND MEDICAL DEVICES
SAFETY AUTHORITY
A BUSINESS UNIT OF
THE MINISTRY OF HEALTH
www.medsafe.govt.nz

Dear Health Professional,

Re: The use of SSRI antidepressants in children and adolescents

The Medicines Adverse Reactions Committee (MARC) has reviewed the efficacy and safety of SSRI antidepressants* when used to treat Major Depressive Disorder (MDD) in children under 18 years old, and considers the data to be inconclusive. While the MARC is awaiting further data, the following is advised –

- **Initiating treatment:** Pharmacological treatment is second-line therapy in the treatment of MDD in children. For children and adolescents, specialist advice should be sought before prescribing any antidepressant.
- **Continuing treatment:** Children and adolescents who are responding well to SSRI therapy should complete the usual course of treatment. If the response is inadequate, specialist advice should be sought.
- **Stopping treatment:** SSRIs should not be stopped abruptly. Doses should be tapered off gradually, and specialist advice sought about further management.
- **Monitoring:** All patients with depression should be monitored for the emergence or worsening of suicidal thoughts and behaviours. Patients should be encouraged to discuss any concerns with their doctor.

The Medicines Adverse Reactions Committee (MARC) has considered the safety and efficacy of the Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants* for use in treating major depressive disorder (MDD) in people under 18 years of age. There has been recent concern regarding a possible lack of efficacy, and possible increased risk of suicidal ideation and self-harm behaviour, when these medicines are prescribed as therapy for children and adolescents with MDD.

In New Zealand, none of the SSRIs have been approved for use in treating MDD in children or adolescents Please refer to the Medsafe web site for full prescribing information about these medicines (www.medsafe.govt.nz).

On March 10th 2004, the MARC reviewed reports from the UK Committee on Safety of Medicines (CSM), the American College of Neuropsychopharmacology, US Food and Drug Administration (FDA) advisory committees, and the Royal Australian and New Zealand College of Psychiatrists.

* Fluoxetine, Paroxetine, Citalopram, Sertraline (and Venlafaxine, a Selective Serotonin Noradrenaline Reuptake Inhibitor (SNRI) with similar properties to the SSRIs) are the only SSRIs currently marketed in New Zealand.

The CSM and FDA evaluations of data from clinical trials in children and adolescents with MDD are in broad agreement. They conclude that there is evidence for efficacy of fluoxetine and possibly citalopram, but not for paroxetine, sertraline, or venlafaxine. The evaluations also conclude that there is evidence for increased suicidal ideation and/or behaviour for citalopram, paroxetine, sertraline, and venlafaxine. The CSM concluded that the risk:benefit ratio was adverse for all SSRIs except fluoxetine, and the FDA issued strong warnings about a possible increased risk of suicidality with these medicines.

In the opinion of the MARC, the above studies are small in size and confounded by inconsistencies in how safety and efficacy are defined. It is, therefore, not possible to accurately determine the risk:benefit ratio for SSRIs in child and adolescent MDD without additional information. In order to resolve this issue, the FDA has commissioned a further analysis of the raw data from the reported trials. In the interim, the MARC does not consider it necessary to amend the New Zealand prescribing information.

The MARC notes that tricyclic antidepressants have marginal efficacy and poor safety within this age group,[1] and acknowledges that, with the support of specialist advice, SSRIs may have a role in the management of MDD in children under 18 years of age. The MARC has placed a high priority on reviewing the safety of SSRIs as more data become available.

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For further information see:

www.mhra.gov.uk/news/2003.htm#ssri (UK summary of SSRI MDD studies)
www.fda.gov/cder/drug/advisory/mdd.htm (US FDA)
www.acnp.org (American College of Neuropsychopharmacology report)

Cited reference:

1. Hazell P, O'Connell D, Heathcote D, Henry D. Tricyclic drugs for depression in children and adolescents. *Cochrane Database Systematic Review* 2003; (4):CD002317