

OPERATIONAL CIRCULAR

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Subject: USE OF SSRI AND SNRI ANTIDEPRESSANTS IN CHILDREN AND ADOLESCENTS - PROVISION OF INFORMATION BY THE CHIEF PSYCHIATRIST UNDER THE MENTAL HEALTH ACT 1996

Authority

The *Mental Health Act 1996* empowers the Chief Psychiatrist to give direction in respect of clinical care and treatment of mental health patients.

The Chief Psychiatrist in relation to medication used in psychiatry, is to ensure that there is an appropriate system in place for-

- (i) the maintenance of satisfactory standards, and
- (ii) the provision of information to medical practitioners about new developments including new information about adverse drug reactions.

The Chief Psychiatrist also has responsibility through the Department of Health for consistency of clinical practice within the requirements of the *Mental Health Act 1996*. The Department of Health, Operational Circular is the instrument by which the Chief Psychiatrist subsequently directs clinicians and mental health services.

Issue

The Chief Psychiatrist recommends caution when considering the use of antidepressant drugs for therapy of children and adolescents. The possible clinical benefit resulting from antidepressant use may be outweighed by the associated risks of harm, and the use of antidepressants in children and adolescents is generally contra-indicated.

Recent reviews of the safety and efficacy of selective serotonin and serotonin noradrenergic reuptake inhibitor (SSRI and SNRI) antidepressant drugs in Australia and other countries have shown an increased risk of suicide and self-harm associated with the treatment of depression and other psychiatric disorders in children and adolescents. SSRI drugs associated with this increased risk include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline, as well as related drugs venlafaxine and mirtazapine.

None of the SSRIs, and indeed no antidepressant drug, is currently approved in Australia for the treatment of depression in children and adolescents (persons aged less than 18 years). 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 less scrutiny, may be therapeutically inappropriate or may also be associated with suicidality, as well as having other undesirable effects such as toxicity in overdose.

Increases in suicidal ideation and behaviour during the early stages of antidepressant treatment are well-known clinical phenomena in adults (see FDA Warning in box below). These events can occur in children and adolescents as well. Current literature supports an association between both paroxetine and venlafaxine with an increased rate of self-harm and suicidality. Sertraline, citalopram and fluoxetine have also been implicated. There is

insufficient information for the risk/benefit for fluvoxamine and escitalopram to be assessed. The Australian Adverse Drug Reaction Advisory Committee (ADRAC) has reviewed available information and recommends that:

- Any use of SSRIs and related drugs in children and adolescents with depression 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 is irregular because of poor compliance. Cognitive Behaviour Therapy, if it is available, may enhance the outcome or represent an alternative approach.
- The choice of antidepressant for a child or adolescent should be made only after taking into account the recent evaluations of clinical trial data and the Australian Product Information. Prescribers should be aware that the manufacturers of fluvoxamine and sertraline (indicated for obsessive compulsive disorder, OCD) advise against use in children and adolescents. The Product Information documents for citalopram, escitalopram, paroxetine, venlafaxine and fluoxetine warn or caution against use in patients aged less than 18 years **for any indication**.
- Children and adolescents being treated with an SSRI should not have their medication ceased abruptly.

Close supervision should accompany initial drug therapy especially in high-risk patients. Prescribers and other health care professionals are asked to report to ADRAC any case of emergent or worsening suicidal ideation or behaviour and self-harm in children or adolescents treated with an SSRI. This information is required to aid in the understanding of the frequency of these reactions and their possible causal relationships to the drugs.

Precautionary statements within Product Information inserts and Consumer Medicine Information documents are being updated for all the SSRI antidepressants in Australia to ensure that they convey appropriate information to prescribers, patients and carers. In addition, ADRAC has requested that the Royal Australian and New Zealand College of Psychiatrists and the Royal Australian College of Physicians conjointly coordinate the preparation of clinical guidelines.

For further information, see

http://www.tga.gov.au/adr/adrac_ssri.htm

http://www.tga.gov.au/adr/ssri_tga.htm

The Office of the Chief Psychiatrist is available to advise in the delivery and implementation of the work of this Operational Circular. Telephone Contact : 9222 4462

Dr Rowan Davidson
CHIEF PSYCHIATRIST

FDA Product Information Warning

Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Although there has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. Nevertheless, patients being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.