



Advisory Committee on Medicines

Meeting statement

Meeting 22, Thursday 6 and Friday 7 August 2020

Section A: Pre-market registration applications referred for advice

At this meeting, the committee's advice was sought on 8 applications under evaluation by the TGA. The applications included:

- three for the registration of a new chemical entity
- one for the registration of a new combination of active ingredients
- two seeking extension of indications
- two seeking major variations to the dose or form of a product

Further details of the ACM discussion and advice associated with these items are released within the Australian Public Assessment Reports (AusPARs). Please note that there is a delay from when an application was considered at ACM and the publication of the AusPAR. To browse all AusPARs see: <<https://www.tga.gov.au/ws-auspar-index>>

Section B: Post-market item referred for advice

The ACM considered information on whether there is a causal association between increasing rates of antidepressant dispensing on the Pharmaceutical Benefits Scheme and rates of youth suicide in Australia.

Numerous selective serotonin reuptake inhibitor (SSRI) and serotonin and noradrenaline reuptake inhibitor (SNRI) antidepressants are supplied in Australia. The active ingredients in SSRIs are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline. The active ingredients in SNRIs are desvenlafaxine, duloxetine and venlafaxine. The medicines are supplied under various brand names, including generic brands.

In Australia, these medicines are approved for use in major depression in adults (some also have additional approved uses in adults, including anxiety, social phobia and obsessive compulsive disorder). Product Information (PI) documents state that use for

depression in children and adolescents under the age of 18 is advised against or not recommended as efficacy and safety in young people has not been established. The SSRIs fluvoxamine and sertraline are approved for children and adolescents with obsessive compulsive disorder (OCD). In the United States and Europe, fluoxetine (an SSRI) is approved for use in major depressive disorder in children aged 8 years and older.

Clinical worsening of depression and suicidal thoughts is a recognised and well-known risk observed in clinical trials of antidepressant medicines. This can occur in a small number of patients during the early phases of treatment. The TGA approved PI documents for antidepressants include warnings about these risks and specifically mention children, adolescents and young adults. This information is also conveyed in the Consumer Medicines Information (CMI) for these products. It should be noted that there were no deaths from suicide in the clinical trials that prompted the inclusion of these warnings in the PI and CMI.

Antidepressants can be prescribed off-label to children and adolescents for psychiatric indications in Australia. Guidelines produced by the [Royal Australian and New Zealand College of Psychiatrists](#) recommend psychological therapies, such as cognitive behavioural therapy (CBT) and interpersonal therapy (IPT), as the first line treatment for major depressive disorder of all levels of severity in young people. Fluoxetine is recommended by the [Royal Australian and New Zealand College of Psychiatrists](#) as second line treatment for moderate to severe major depressive disorder in children and adolescents.

A [recent article by Whitely, Raven and Jureidini](#) identified a signal from ecological evidence correlating an estimated 66% increase in dispensing of antidepressants to young Australians aged less than 28 years between 2008-09 to 2017-18 and a 49% increase in suicide rates in young Australians aged less than 25 years from 2009 to 2018.

The ACM discussed the information presented in this paper and highlighted that:

- Confounding by the condition being treated (known as confounding by indication) remains an unresolved issue when interpreting data of this type.
- Correlation does not prove causation.
- Suicide is a complex outcome with many factors affecting the mental health of children and adolescents, including family dynamics, school and social dynamics, drug and alcohol use, social media and gaming use.

The ACM did not support Whitely et al's interpretation of a possible causal relationship between the dispensing of antidepressants on the PBS and rates of youth suicide in Australia.

The ACM advised that there is a valid and important role for SSRIs and SNRIs in current clinical practice in treating moderate-to-severe depression in children and adolescents, supported by professional guidelines.

The ACM noted that current clinical guidelines place a strong emphasis on psychosocial therapies as the preferred mode of treatment for depressive disorders in children and adolescents, with the use of SSRIs reserved for moderate-to-severe depression when other treatments have failed. However, in practice, access to publicly funded psychological therapies is often extremely limited, general practitioners face great difficulty in having their patients seen by a child and adolescent psychiatrist in a timely manner, referral pathways are complex and there are significant equity issues in accessing private psychiatric services.

The ACM supported prescriber and consumer education on what to expect when they start treatment with an antidepressant.

The Committee advised that current warnings and precautions in PI documents were adequate. Possible emergence of suicidal thoughts during the initial few months of antidepressant treatment or at times of dose adjustment is addressed in PI documents. The risk is minimised by starting with a low dose and increasing slowly.

The Committee did not support additional restriction on the availability of antidepressants as it would further disadvantage young people, especially in regional, rural and remote areas. However, the Committee did express concern around the increasing use of antidepressants in young people.

The Committee suggested that improving access to information and care, in particular improved access to psychological therapies, will assist young people and represents an opportunity to minimise risk in this population. The Committee also highlighted the need for additional clinical guidance for general practitioners around the management of depression and prescribing of antidepressants to young people.

Further information

For further information on the Advisory Committee on Medicines, please visit: <https://www.tga.gov.au/committee/advisory-committee-medicines-acm>.

or contact the ACM Secretary by email: ACM@health.gov.au.