

14 April 2025

## WHO Expert Committee on Selection and Use of Essential Medicines

emlsecretariat@who.int

RE: Application reference: A.19 Methylphenidate – attention deficit hyperactivity disorder

Dear Members of the Essential Medicines for Children Committee,

The Australasian ADHD Professionals Association (AADPA) is a binational multidisciplinary association with over 800 members. AADPA represents the broad group of healthcare professionals from Australian and New Zealand who work with and support people with ADHD in our communities. Membership includes Paediatricians, Psychiatrists, General Practitioners, Psychologists, Nurses, Allied health professionals and ADHD Coaches. AADPA developed the national ADHD Evidence-Based Guideline for ADHD assessment and treatment for Australia. The Guideline is endorsed by the National Health and Medical Research Council and all main medical colleges and psychology associations. AADPA has also produced a national Prescribing Guide that provides detailed support for safe and effective prescribing of ADHD medications.

AADPA would like to express our strong support for the inclusion of methylphenidate in the WHO Model List of Essential Medicines for the treatment of children and adolescents between the ages of 6 to 17 years with Attention Deficit/Hyperactivity Disorder (ADHD), and the corresponding application "A.19 Methylphenidate – attention deficit hyperactivity disorder".

## Our support is based on:

1. The urgent need to prioritise the best interests of children and young people around the world living with ADHD and those supporting them.

While there remain problems accessing medications in high income countries like ours, these are largely internal or related to supply issues and require local action and advocacy for resolution. Once a diagnosis of ADHD is made it is possible for most Australians with ADHD to access medications at a reasonable cost. For many children and young people living in low- and middle-income countries (LMIC) ADHD medications in general, and methylphenidate specifically, are either not licensed, or if they are, are not affordable for most people. Ninety percent of the world's children and adolescents live in LMIC (15). In these countries, government decisions on which medications are available for the population without cost are heavily based on the WHO Model List of Essential Medicines. Until methylphenidate is included in the Model List children and young people in LMIC will continue to face inequity with regards access to evidence based care for their ADHD. Since 2023 the WHO has acknowledged that methylphenidate should be considered a treatment option for ADHD. The mhGAP guideline for treatment of ADHD clearly indicates that methylphenidate should be a treatment option for those with ADHD. Quite correctly this is couched in the context of a management plan that also addresses psychosocial risks

and vulnerabilities and environmental factors that have an impact on symptoms and functioning. AADPA fully supports this recommendation. Our own guidelines are very clear that while medications should not be considered a standalone treatment for ADHD they should be considered as a part of a multimodal package of treatment that includes both psychoeducation and non-medication supports. The rationale, based on the best available evidence, is that while ADHD medications are the only treatments with evidence of efficacy for core ADHD symptoms, the other non-medication treatments including parent training programs and cognitive behavioural therapy help people manage the impacts that these core ADHD symptoms have on their day to day lives. AADPA strongly support the WHO mhGAP program. We are using it as a framework for designing care pathways that improve access to care for the many remote communities within Australia that are not currently able to access good enough care for ADHD. While we will be able to implement the medication recommendations within mhGAP relatively easily once we are able to put the services and people with ADHD together, those living in LMIC they will require improved access to methylphenidate as well as innovative services to implement the mhGAP program. The application, A.19 Methylphenidate – attention deficit hyperactivity disorder, would help allow this recommendation to be realized across low-middle income countries (LMICs)

## 2. Improved confidence in the longer-term safety of methylphenidate.

The committee has previously raised concerns about the quality of evidence around the safety of methylphenidate. We believe that evidence published in the last few years has provide much stronger support for safety.

While there have been several important publication we would highlight the findings of the Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) program conducted a series of systematic reviews into the long term safety of methylphenidate<sup>1-3</sup>, several big-data studies of cohorts from the UK, Germany and Hong-Kong<sup>4-6</sup> and a primary naturalistic, longitudinal trans-European study<sup>7</sup>. This study compared three cohorts of children and adolescents: 1) ADHD treated with methylphenidate; 2) ADHD no-medication treatment and 3) typically developing children and adolescents. All participants were followed up for 2 years with detailed assessments at baseline and then 6 monthly. A total of 1,410 children and youth aged 6-17 years were included with 756 treated with methylphenidate for 2 years. ADDUCE reported on a wide range of outcomes including growth and puberty, cardiovascular health, and psychiatric and neurological adverse events.

**Growth and puberty:** there were no differences in height velocity at any time point between those with ADHD taking and not taking methylphenidate<sup>7</sup>. While weight velocity showed an initial slowing at 6 months in the methylphenidate group, there were no differences were seen after this point. There were also no group differences with respect to body mass index (BMI) at any time point. Methylphenidate use had no impact on the timing of puberty<sup>8</sup>.

**Cardiovascular health:** there were some effects on pulse and blood pressure with a greater increase in systolic and diastolic blood pressure in the methylphenidate group compared with the no- methylphenidate group at 6, 12, and 24 (but not 18) months from baseline and increase pulse rate at 12 and 24 months, but not at 6 or 18 months. Another ADDUCE study conducted as part of the ADDUCE program



looked in more detail at the cardiovascular effects of long term (>3years) on cardiac function in young adults using 24-hour blood pressure monitoring and echocardiograms<sup>9</sup>. They identified that increases in blood pressure were restricted to daytime when medications were active and were not seen at night. There was also no evidence of left ventricular hypertrophy in the medicated group.

Psychiatric/neurological safety: Key findings from ADDUCE include that methylphenidate use was not associated with suicidal ideation or behaviours but was associated with improvements in mood after 24 months of treatment<sup>7</sup>. Psychotic-like symptoms also improved over the course of the study with no differences seen between the medicated and unmedicated ADHD group.

Taken together we believe that these data highlight the importance of monitoring for potential adverse effects associated with methylphenidate treatment while at the same time highlighting the safety of long-term treatment with methylphenidate

3. The importance of ensuring that children and young people, especially in LMIC are not inappropriately treated with alternative more accessible but less effective and more harmful medications.

We are aware that children and young people of all ages around the world, including preschoolers, are increasingly being prescribed antipsychotic medications to help manage 'behavioural' problems10-13. Many of these children have ADHD which if appropriately treated with ADHD medications will also significantly reduce the challenging behaviours. While many of the data come from HIC we are aware that is also a pressing problem in LMIC where methylphenidate is not available. These antipsychotic medications such as risperidone, olanzapine and aripiprazole have serious short- and long-term adverse effects including weight gain, metabolic syndrome and movement disorders all of which have a significant negative impact on children's functioning and physical health. We understand that including methylphenidate in the WHO Model List of Essential Medicines will not eradicate this practice it will provide us with an alternative narrative and options to work with our colleagues in LMIC to improve outcomes and reduce harm.

Sincerely

**Professor David Coghill** 

President, Australasian ADHD Professionals Association (AADPA) On behalf of the AADPA Board

- 1. Carucci S, Balia C, Gagliano A, et al. Long term methylphenidate exposure and growth in children and adolescents with ADHD. A systematic review and meta-analysis. *Neurosci Biobehav Rev.* 2021;120:509-525.
- 2. Hennissen L, Bakker MJ, Banaschewski T, et al. Cardiovascular Effects of Stimulant and Non-Stimulant Medication for Children and Adolescents with ADHD: A Systematic Review and Meta-Analysis of Trials of Methylphenidate, Amphetamines and Atomoxetine. *CNS Drugs.* 2017;31(3):199-215.
- 3. Krinzinger H, Hall CL, Groom MJ, et al. Neurological and psychiatric adverse effects of long-term methylphenidate treatment in ADHD: A map of the current evidence. *Neurosci Biobehav Rev.* 2019;107:945-968.
- 4. Man KK, Coghill D, Chan EW, et al. Methylphenidate and the risk of psychotic disorders and hallucinations in children and adolescents in a large health system. *Transl Psychiatry*. 2016;6(11):e956.
- 5. Man KKC, Coghill D, Chan EW, et al. Association of Risk of Suicide Attempts With Methylphenidate Treatment. *JAMA Psychiatry*. 2017;74(10):1048-1055.
- 6. McCarthy S, Neubert A, Man KKC, et al. Effects of long-term methylphenidate use on growth and blood pressure: results of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). *BMC Psychiatry*. 2018;18(1):327.
- 7. Man KKC, Hage A, Banaschewski T, et al. Long-term safety of methylphenidate in children and adolescents with ADHD: 2-year outcomes of the Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) study. *Lancet Psychiatry*. 2023;10(5):323-333.
- 8. Carucci S, Zuddas A, Lampis A, et al. The Impact of Methylphenidate on Pubertal Maturation and Bone Age in ADHD Children and Adolescents: Results from the ADHD Drugs Use Chronic Effects (ADDUCE) Project. *J Atten Disord.* 2024:10870547241226726.
- 9. Buitelaar JK, van de Loo-Neus GHH, Hennissen L, et al. Long-term methylphenidate exposure and 24-hours blood pressure and left ventricular mass in adolescents and young adults with attention deficit hyperactivity disorder. *Eur Neuropsychopharmacol.* 2022;64:63-71.
- 10. Harrison JN, Cluxton-Keller F, Gross D. Antipsychotic medication prescribing trends in children and adolescents. *J Pediatr Health Care*. 2012;26(2):139-145.
- 11. Nakane S, Tanaka-Mizuno S, Nishiyama C, et al. Trends in Prescribing Antipsychotics for Children and Adolescents in Japan: A Descriptive Epidemiological Study Using a Large-Scale Pharmacy Dataset. *Child Psychiatry Hum Dev.* 2023;54(5):1250-1257.
- 12. Pringsheim T, Lam D, Patten SB. The pharmacoepidemiology of antipsychotic medications for Canadian children and adolescents: 2005-2009. *J Child Adolesc Psychopharmacol.* 2011;21(6):537-543.
- 13. Gomez-Lumbreras A, Garcia Sangenis A, Prat Vallverdu O, et al. Psychotropic use in children and adolescents in Scandinavia and Catalonia: a 10-year population-based study. *Psychopharmacology* (*Berl*). 2021;238(7):1805-1815.