Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Notice of final decisions to amend (or not amend) the current Poisons Standard in relation to psilocybine and MDMA

3 February 2023

TGA Health Safety Regulation

Contents

1 Notice of final decisions to amend (or not amend) the current Poisons Standard

This web publication constitutes a notice for the purposes of regulation 42ZCZS of the *Therapeutic Goods Regulations 1990* (the **Regulations**). In accordance with regulations 42ZCZS, this notice publishes:

- the decisions made by a delegate[1] of the Secretary of the Department of Health and Aged Care (the **Delegate**) pursuant to regulations 42ZCZR;
- the reasons for those final decisions; and
- the date of effect of those decisions.

2 Final decisions on proposed amendments referred to the Advisory Committee on Medicines Scheduling (ACMS #38, June 2022)

2.1 Final decision in relation to psilocybine and MDMA

This section contains two independent final decisions in relation to (i) psilocybine and (ii) MDMA (the **Substances**). Given the current scheduling and amendments to the Poisons Standard in relation to the Substances are similar, the reasons for making the final decision for each substance are substantially the same. As such, the reasons have been consolidated to assist the reader.

Proposals

Psilocybine

The applicant proposed the creation of a Schedule 8 entry for the use of psilocybine in combination with psychotherapy for treatment-resistant mental illness in medically controlled environments in certain circumstances (the **current psilocybine proposal**). Psilocybine is currently included in Schedule 9, which limits its use to authorised research and analytical purposes only.

MDMA

The applicant proposed the creation of a Schedule 8 entry for the use of MDMA in combination with psychotherapy for treatment-resistant mental illness in medically controlled environments in certain circumstances (the **current MDMA proposal**). MDMA is currently included in Schedule 9, which limits use to authorised research and analytical purposes only.

Final decisions

Pursuant to regulation 42ZCZR of the Regulations, the Delegate has made final decisions to vary the interim decisions and amend the current Poisons Standard in relation to both psilocybine and MDMA.

[1] For the purposes of s 52D of the *Therapeutic Goods Act 1989* (Cth).

The final decision in relation to psilocybine is as follows:[2]

Schedule 9 – Amend entries

PSILOCYBINE **except** when included in Schedule 8.

Schedule 8 – New entries

PSILOCYBINE in preparations for human therapeutic use for the treatment of treatment-resistant depression.

Appendix D – New entries

5. Poisons for which possession without authority is illegal (e.g. possession other than in accordance with a legal prescription):

26A PSILOCYBINE.

10. Poison available only when prescribed or authorised in certain circumstances

PSILOCYBINE in preparations for human use may be supplied only for the treatment of treatment-resistant depression:

(a) if psilocybine is prescribed, or its supply is authorised, by a medical practitioner:

(i) registered under State or Territory legislation that forms part of the Health Practitioner Regulation National Law as a specialist psychiatrist; and

(ii) for whom an authority under subsection 19(5) of the Act that covers psilocybine is in force; or

(b) for use in a clinical trial that is approved by, or notified to, the Secretary under the Act.

The final decision in relation to MDMA is as follows:

Schedule 9 – Amend entries

N,α-DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA) **except** when included in Schedule 8.

Schedule 8 – New entries

N,α-DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA) in preparations for human therapeutic use for the treatment of post-traumatic stress disorder.

Appendix D – New entries

5. Poisons for which possession without authority is illegal (e.g. possession other than in accordance with a legal prescription):

22A N,α-DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA).

[2] Proposed additions are shown in green underlined font, proposed deletions are shown in red strikethrough font, and text without this formatting represents the current text in the Poisons Standard.

10. Poison available only when prescribed or authorised in certain circumstances

N,α-DIMETHYL-3,4-(METHYLENEDIOXY)PHENYLETHYLAMINE *(MDMA) in preparations for human use may be supplied only for the treatment of post-traumatic stress disorder:

(a) if MDMA is prescribed, or its supply is authorised, by a medical practitioner:

(i) registered under State or Territory legislation that forms part of the Health Practitioner Regulation National Law as a specialist psychiatrist; and

(ii) for whom an authority under subsection 19(5) of the Act that covers MDMA is in force; or

(b) for use in a clinical trial that is approved by, or notified to, the Secretary under the Act.

Materials considered

In making these final decisions, the Delegate considered the following material:

In relation to psilocybine

- The application to amend the current Poisons Standard with respect to psilocybine (the **psilocybine application**);
- The 6,650 public submissions on the current psilocybine proposal, including 2,332 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice concerning the Psilocybine Application received from the 38th meeting of the Advisory Committee on Medicines Scheduling (the **Committee**)[3];
- The Delegate's final decision to not amend the Poisons Standard in relation to psilocybine on 15 December 2021 and the materials considered in making that decision;
- The Delegate's interim decision to not amend the Poisons Standard in relation to the psilocybine application on 21 October 2022 and the materials considered in making that decision;
- The 3,442 public submissions on the current psilocybine proposal, including 1,758 with a written component, received in response to the interim decision consultation under regulation 42ZCZP of the Regulations (the **psilocybine interim submissions**); and
- The published study titled *Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression*,[4] published in the New England Journal of Medicine on 3 November 2022.

In relation to MDMA

- The application to amend the current Poisons Standard with respect to MDMA (the **MDMA application**);

[3] Established under sections 52B and 52C of the *Therapeutic Goods Act 1989* (Cth).

[4] Goodwin et al, N Engl J Med 2022; 387:1637-1648 https://www.nejm.org/doi/full/10.1056/NEJMoa2206443

- The 6,505 public submissions on the current MDMA proposal, including 2,068 with a written component, received in response to the pre-meeting consultation under regulation 42ZCZK of the Regulations;
- The advice concerning the MDMA Application received from the 38th meeting of the Committee;
- The Delegate's final decision to not amend the Poisons Standard in relation to MDMA on 15 December 2021 and the materials considered in making those decisions;
- The Delegate's interim decision to not amend the Poisons Standard in relation to the MDMA application on 21 October 2022 and the materials considered in making that decision; and
- The 3,403 public submissions on the current MDMA proposal, including 1,658 with a written component, received in response to the interim decision consultation under regulation 42ZCZP of the Regulations (the **MDMA interim submissions**).

In relation to both Substances

- The Independent expert panel report titled *"An evaluation of the therapeutic value, benefits and risks of methylenedioxymethamphetamine (MDMA) and psilocybin for the treatment of mental, behavioural or developmental disorders"* (the **Expert Report**);
- The Royal Australian and New Zealand College of Psychiatrists' (RANZCP) clinical memorandum on the therapeutic use of psychedelic substances published in July 2022;
- A presentation to the Therapeutic Goods Administration (TGA) by Professor David Nutt on 21 November 2022;
- The international regulatory status of the Substances and access pathways;
- Subsection 52E(1) of *the Therapeutic Goods Act 1989* (Cth) (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health.
- The Scheduling Policy Framework 2018 (the **SPF**), pursuant to paragraph 52E(2)(a) of the Act; and
- The Scheduling handbook: Guidance for amending the Poisons Standard (the **Handbook**)

Reasons for the final decisions (including findings on material questions of fact)

I have made two independent final decisions to vary my psilocybine interim decision and my MDMA interim decision, and amend the current Poisons Standard in relation to psilocybine and MDMA for treatment-resistant depression (TRD) and post-traumatic stress disorder (PTSD), respectively, as set out above.

The amendments allow expanded access to the Substances outside of clinical trials as Schedule 8 medicines subject to controls over prescribing rights and treatment protocols, thereby sufficiently mitigating the risks expressed in my interim decisions. The benefits to patients and public health of my final decisions will therefore outweigh the risks.

In making my final decisions, I have taken into account the material detailed in the interim decisions and the responses received after the second call for public submissions, published on 21 October 2022 under regulation 42ZCZP of the Regulations.

I have decided to place several controls over access to psilocybine and MDMA as Schedule 8 medicines through amendment of Appendix D of the Poisons Standard, the first of which are to limit access to the Substances only if prescribed by psychiatrists who have been authorised to do so under the Authorised Prescriber Scheme (the **AP scheme**) under section 19(5) of the Act.

The applicant proposed that medical practitioners prescribe the Substances only on the authorisation of psychiatrists. I consider that registered psychiatrists have the training and expertise to diagnose and appropriately treat those conditions for which there is emerging evidence for the use of the Substances. As such, they are suitably placed to prescribe the Substances and monitor the outcome of therapy. This extends to any adjunct therapies that are deemed appropriate by the physician for each patient. In particular, in addressing the issues previously identified in the interim decisions under paragraph 52E(1)(f) of the Act, clinical decisions best reside with a specialist psychiatrist for: therapies for which there is only emerging evidence of therapeutic benefit; where the treatment protocols are not yet established, and the justification for treatment with the Substances is strongest for those resistant to existing treatments and thereby already under the management of a specialist. All of these circumstances are pertinent to the intended therapeutic uses of the Substances. I would like to emphasise that psychiatrists who have been authorised to prescribe the Substances under the AP scheme will still be required to comply with the relevant legislation of the State or Territory in which they practice.

The AP scheme allows authorised medical practitioners to supply therapeutic goods that are not included in the Australian Register of Therapeutic Goods (ARTG) to specified patients under their immediate care with a particular medical condition subject to certain conditions. In particular, approval must be granted by both a Human Research Ethics Committee (HREC) that is registered with the National Health and Medical Research Council (NHMRC) and, only once that approval has been granted, a senior medical officer at the TGA in their capacity as a delegate of the Secretary of the Department of Health and Aged Care. The TGA delegate will also expect that psychiatrists will have considered all clinically appropriate treatment options that are included in the ARTG before applying to access a psilocybine- or MDMA-containing product for their patient under the AP scheme.

The AP scheme is an established, proven and robust pathway for permitting therapeutic use of unapproved medicines, with sufficient oversight and monitoring, to ensure safe use of the Substances and address many of the concerns articulated in the interim decisions. While the Special Access Scheme (SAS) permits access to the Substances on a patient-by-patient basis, the standard pathway of approval for the AP scheme entails a rigorous application process for a qualified medical professional through both the TGA and an HREC. Under the AP approval process, I am confident that the TGA decision maker and HREC will ensure they are satisfied of matters including the applicant prescriber's clinical justification for their treatment regimen, governance over the treatment process, and the use of suitable measures to protect patients, such as records of informed consent. Consistent with the terms of the AP scheme, authorised prescribers will be required to submit regular reports on the numbers of patients treated and any associated adverse events.

I am of the view that consideration of these factors should alleviate concerns raised in the RANZCP clinical memorandum.[5] The memorandum urged caution on permitting access to the Substances for therapeutic use due, in part, to the lack of established treatment protocols. However, under the AP scheme, an HREC and authorising officer at the TGA will be able to require that a prospective prescribing psychiatrist provides evidence and justification that a suitably robust treatment protocol has been developed. I agree with the RANZCP that there does not currently appear to be any established treatment protocols. However, my decision recognises that the evidence landscape is rapidly evolving toward establishing such protocols, and so places the onus and opportunity with a prospective prescriber of the Substances to devise and provide evidence of a suitable treatment protocol to the HREC and authorising TGA officer.

I have also considered the concerns of all stakeholders, including relevant peak bodies and state and territory health authorities, regarding the various controls included in the applicant's original proposal for new Schedule 8 entries. This related to use of the Substances in conjunction with psychotherapy in medically controlled environments, specific training for prescribers, and the requirement for two independent psychiatrists to review each patient's diagnosis and proposed treatment plan. The interim decisions identified the potential difficulties in the implementation of these conditions as proposed by the applicant.

However, it is through the suite of all the above mentioned elements of the AP scheme and other controls set out below that I am satisfied that the risks of prescribing the Substances to vulnerable patients will be sufficiently mitigated. In balancing these mitigated risks against the potential benefits with reference to paragraph 52E(1)(a) of the Act, I am satisfied to amend the scheduling for the Substances under these conditions.

To further address my concerns from the interim decisions regarding paragraph 52E(1)(e) of the Act, specifically the risks of improper access to the Substances throughout the supply chain, I have also decided to include an entry for each of the Substances in item 5 of Appendix D. This provides that possession of the Substances without a valid prescription is illegal and is consistent with the applicant's original proposal.

The new Schedule 8 entries limit the therapeutic use of the Substances to TRD for psilocybine, and PTSD for MDMA. This provides for narrower access than originally proposed by the applicant, but in view of paragraphs 52E(1)(a) and (b) of the Act, is aligned with the current body of clinical evidence supporting the therapeutic use of the Substances that pertains primarily to these mental health conditions. The use of psilocybine and MDMA to treat all indications other than TRD and PTSD, respectively, will remain captured by the existing Schedule 9 entries for the Substances, limiting their use to medical and scientific research, including clinical trials. I consider that the body of evidence demonstrating the efficacy of the Substances for the treatment of other indications is insufficient at this time to justify increased access for therapeutic use.

In addition to the evidence previously considered, I have noted the recently completed study published in the New England Journal of Medicine[4] on the use of psilocybine for the treatment of TRD, which indicated that a single dose of 25 mg reduced depression scores significantly more than a 1 mg dose over a period of 3 weeks. The results of this study further strengthen the already promising body of evidence for the efficacy of psilocybine in the treatment of TRD and support my decision to increase the accessibility of this substance for this purpose.

[5] RANZCP clinical memorandum of the therapeutic use of psychedelic substances, July 2022 http://www.ranzcp.org/files/resources/college_statements/clinical_memoranda/cm-therapeutic-use-of-psychedelics.aspx

I have considered the Schedule 8 scheduling factors in the SPF in relation to the degree to the available evidence for the therapeutic value of the Substances. I acknowledge, as stated in my interim decisions, and even for the narrow indications included in this decision, the therapeutic value of each of the Substances is not established at this time. However, taking into account all the factors I am required to consider under section 52E of the Act, and in particular the benefits and risks of the access to these substances under a Schedule 8 classification, I am satisfied that the amendment I have decided to make is appropriate and consistent with the intent of the framework.

I have considered the written public submissions received in response to the interim decisions on the Substances. Many of these were opposed to the interim decisions to not amend the Poisons Standard in relation to psilocybine and MDMA and followed a similar pattern to the pre-meeting submissions. The majority of the submissions relating to the Substances were brief, related to personal circumstances, and did not attempt to address the issues raised in the interim decisions, particularly the lack of established therapeutic value for the Substances for the treatment of mental health conditions. However, I am of the view that the number of such submissions is a reasonable indicator of the scope and gravity of the issues for individual and public health addressed in the application. In consideration of paragraph 52E(1)(a) of the Act, the submissions confirm the need for greater access to alternative treatments for patients with persistent mental health conditions where currently available treatments have not been effective. In balancing this clinical need against the current level of evidence of safety and efficacy, I consider that it is justified to increase access to the Substances under the controls explained above.

Contrary to the claims made in a significant number of submissions, I note that the therapeutic use of the Substances remains largely prohibited outside of clinical trials in many countries, including Canada, New Zealand, the United Kingdom and most of the European Union. However, I recognise that the status of the Substances is under review in many of these countries, such as the USA where the Food and Drugs Administration (FDA) has designated MDMA as a "breakthrough therapy" for TRD. While it is important to note that this status is designed to expedite the development and review of particular medicines and is not an endorsement or approval for the therapeutic use of MDMA outside of a clinical trial environment, with reference to paragraph 52E(1)(f) of the Act, it is indicative of the FDA's standpoint on the potential of MDMA for the treatment of TRD.

In response to many comments in the public submissions, I would like to clarify that the both the existing Schedule 9 entries, and the entries as amended according to my final decisions, relating to the Substances do not prohibit their use in research and clinical trials. While my decisions restrict therapeutic use of the Substances to the indications specified in each of the new Schedule 8 entries, it should be noted that the Schedule 9 entry has no such restrictions on the indications that can be investigated for the Substances in clinical research. I note with interest that at the time of writing this decision there are three Phase II clinical trials in Australia that are recruiting patients to investigate the use of psilocybine in the treatment of depression and/or anxiety disorders, and one mixed Phase I/II trial investigating the use of MDMA-assisted psychotherapy for the treatment of PTSD. These trials are in addition to the second MAPS-sponsored Phase III trial of MDMA-assisted therapy for PTSD,[6] which was recently completed and is expected to have results publicly available later in 2023[7], and the Swinburne University trial investigating psilocybine for the treatment of TRD, which will commence in 2023.[8] The

[6] https://maps.org/2022/11/17/mapp2-second-maps-sponsored-phase-3-trial-of-mdma-assisted-therapy-for-ptsd-completed/
[7] https://maps.org/2023/01/05/prior-positive-results-confirmed/
[8] https://www.swinburne.edu.au/news/2023/01/Australias-biggest-research-trial-using-psychedelics-to-treat-depression-to-commence-in-2023/

evidence arising from current and future trials investigating the therapeutic benefits of the Substances will continue to be monitored and considered in the context of any future applications to further amend the scheduling for the Substances.

To address a point raised in many of the public submissions, I would like to reiterate that the term "psilocybine" is included in the Poisons Standard, as this is the International Nonproprietary Name (INN) and British Approved Name (BAN) for the substance, and is the spelling used in the United Nations Convention on Psychotropic Substances 1971. The substance is also commonly known by its synonym, "psilocybin".

Implementation date

1 July 2023