MMA position statement on the compassionate use of psilocybin and MDMA in Australia

November 2022

MMA recommends that at this time psilocybin and MDMA should be allowed for treatment-resistant patients – psilocybin for depression and MDMA for PTSD – on a compassionate need basis. In the case of depression, this would be defined as patients who have failed at least two previous antidepressant treatment regimes. In the case of PTSD, at least one medicine treatment course and one psychotherapy course.

These recommendations are based on the following factors:

1. New high quality clinical data on psilocybin and MDMA including papers in the very top medical journals such as NEJM JAMA Psychiatry Lancet Psychiatry and Nature Medicine plus earlier papers [refs 1-5]
2. Comparative efficacy data that reveal
    a. a short course of two or three treatments with MDMA in PTSD massively out-performs current therapies of both SSRIs and CBT therapy. [4,5]
    b. Psilocybin at a dose of 25mg has been shown to work in two trials of treatment-resistant depression [1,2]. In one [ref 2] a dose-response relationship was confirmed demonstrating efficacy is due to biological factors rather than just the experience of being in a trial.
3. Safety and tolerability data.
    a. Historical data with psilocybin [which was used as a medicine in the late 1950s and 1960s] [ref 6] show a very good safety and tolerability profile. This has been confirmed in the many recent trials – see Appendix 1 and ref 6].
    b. With MDMA concerns were raised about potential health harms from its recreational use as ecstasy. In the current registration trials conducted by MAPS there have been no reports of any serious adverse effects enduring beyond the treatment dosing day [4,5].
    c. Note - with both medicines there are acute effects which can be challenging. These should not be considered adverse effects for they are likely a necessary part of the therapeutic process. With correct preparation, patients cope with these well and they do not exhibit residual complications
    d. Both MDMA and psilocybin have advantages over other medicines and physical treatments for mental illness [e.g. ECT] in that their therapeutic effects are produced by just one [psilocybin] or 2-3 [MDMA] administrations. This reduces any risk of tolerance, dependence and abuse to virtually zero.
    e. Added to this, three independent expert groups [Refs 7 8 9], including one from Australia [9] have concluded that the dependence liability of both psilocybin and MDMA is very low EVEN WHEN USED RECREATIONALLY.

To facilitate the compassionate use of psilocybin and MDMA in Australia, MMA has made a series of development as below.

1. Set up a world-leading training course that has trained several hundred potential therapists
2. Engaged Ambassadors and an Advisory Panel of top international experts and patients and relatives with lived experience

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3. Arranged for the import into Australia of medicinal grade psilocybin and MDMA for compassionate use to be provided at affordable cost to the patients
4. Developed a protocol for treatment resistant patients that requires for each patient
    a. approval of diagnosis and treatment plan
        i. by the TGA
        ii. and by two independent psychiatrists
    b. The administering psychiatrist has been trained in whichever medicine is to be used
    c. Drug treatment is given to standard protocols including preparation and integration sessions
    d. For the whole period of the drug treatment session there are two health care professionals present
    e. The drug treatment session is filmed for safety reasons
5. A Register of Patients who are given this therapy will be set up at Monash University:
    a. Entering this register will be a requirement for treatment [though patients will be anonymised] –
    b. Patients will give informed consent as the treatment is off-licence
    c. The register will contain pre-and post-treatment data including standard measures of illness severity
    d. Data collection on any adverse effects
    e. Patient-reported outcomes especially quality of life and other relevant outcomes e.g. sleep and wellness scores
    f. Provide an independent report in a regular fashion on outcomes and safety data distributed to all stakeholders on a regular basis
    g. Clinical efficacy could be evaluated using Bayesian methods that have been shown within another compassionate-use clinical-register programme to provide most optimal statistical evidence of efficacy [10]

We believe that with the above in place, psilocybin and MDMA can be administered safely to patients who have been failed by current treatments.

This compassionate use programme for treatment-resistant depression and PTSD with a Register which is constantly updated will be the first of its kind in the world. As well as helping many hundreds of patients who are currently failed by psychiatric medicines and/or conventional therapy, it will provide critical Real World Evidence (RWE) of the value of these treatments that will make a significant contribution to the growing clinical knowledge derived from commercial and other RCTs on these medicines. RWE is now being acknowledged as a vital part of the overall evidential base for new medicines development and roll out [ref 11, 12]. The former head of the UK NICE and MHRA Sir Michael Rawlins said this in his RCP Harvey Lecture in 2008:
"Randomised controlled trials, long regarded at the 'gold standard' of evidence, have been put on an undeserved pedestal. Their appearance at the top of 'hierarchies' of evidence is inappropriate; and hierarchies, themselves, are illusory tools for assessing evidence. They should be replaced by a diversity of approaches that involve analysing the totality of the evidence base." [11]. As a result, the UK NICE and MHRA are now asking for RWE as part of decision-making [12]. It seems likely other national regulatory authorities will follow suit.

This MMA initiative will put Australian psychiatry in a unique place to optimise the use of these medicines when they eventually get full TGA registration.

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Appendix 1

- **Psilocybin treatment Adverse effects in recent trials** Note one patient in the recent COMPASSPathways trial [ref 2 Goodwin et al 2022] required tranquilisation with a benzodiazepine during their acute treatment with psilocybin

Toxicity and overdose risk	NONE REPORTED
Neurotoxicity	NONE REPORTED
Cardiovascular harms	MILD ELEVATIONS IN BLOOD PRESSURE NOT REQUIRING INTERVENTIONS
Emergency medical assistance	NONE REPORTED

Hallucinogen use disorder (addiction)	NONE REPORTED
Abuse liability and dependence	NONE REPORTED
Harms to self or others	NONE REPORTED
Challenging experiences	PART OF THERAPY
HPPD Hallucinogen persistent perceptual disorder	NONE REPORTED
Psychosis	NONE REPORTED, CASES ARE EXCLUDED