PROPOSED AMENDMENTS TO POISONS STANDARD

ACMS and Joint ACMS/ACCS Meeting June 2020

Comments by The Pharmacy Guild of Australia to the proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS) and the Joint ACMS/ACCS

1. **Cannabidiol 2.2**
2. **Cannabidiol 2.5**

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Contact [redacted]

National Secretariat
Level 2, 15 National Circuit, Barton ACT 2600
PO Box 310, Fyshwick ACT 2609
P: +61 2 6270 1888 • F: +61 2 6270 1800 • E: guild nat@guild org au
www.guild.org.au

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CANNABIDOL 2.2

It has been proposed to amend the Poisons Standard as follows:

Schedule 8

CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use, when:

a) cultivated or produced, or in products manufactured74, in accordance with the *Narcotic Drugs Act 1967*; and/or
b) for use in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or
c) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act* 1989; and/or
d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act* 1989, **except** when:

i. it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations* 1990 applies; or
ii. separately specified in the NABIXIMOLS entry in this Schedule; or
iii. captured by the CANNABIDIOL entry in Schedule 4; or
iv. it is a whole plant cannabis product or distillate or isolate which contains at least 98 per cent cannabidiol and less than or equal to 0.2 per cent tetrahydrocannabinol (THC).

Schedule 4

CANNABIDIOL in preparations for therapeutic use where:

a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation and any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation; or

b) ~~any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation~~. cannabidiol is a synthetic or semi-synthetic copy of the molecule and comprises 98 per cent or more of the total cannabinoid content of the preparation and any other synthetic or semi-synthetic cannabinoids, other than cannabidiol, must comprise 2 per cent or less of the total cannabinoid content of the preparation.

except when cannabidiol comprises 98 per cent or more of the total cannabidiol content and the tetrahydrocannabinol (THC) content is less than or equal to 0.2 per cent of the total cannabidiol content of the preparation.

Overview

While the Guild is supportive of greater patient access to medicinal cannabis products, we do not support the proposed scheduling changes. There are significant risks to public safety associated with this proposal. The Guild supports the regulation of all cannabidiol containing formulations, derived both naturally and through synthetic manufacture, through the existing Poisons Standard under the oversight of the Therapeutic Goods Administration (TGA).

The risks and benefits of the use of a substance

While the purported risk of cannabidiol (CBD) containing products is low, there is a clear lack of quality evidence for its clinical safety or efficacy. The medication has not been used widely in clinical practice in

Australia. The recent review[1] into the published evidence for the safety of CBD by the TGA recommended that '*Given that CBD has not been widely used in clinical practice and the evidence for which effects conditions it is effective has not thoroughly been identified, it remains important that…the appropriate regulatory controls are maintained to ensure both safety and quality of products containing CBD*'. Therefore, supply with a direct involvement of a pharmacist will ensure some clinical oversight and a chance to support QUM in relation to the use of these products.

The purposes for which a substance is to be used and the extent of use of a substance

CBD has been reported to be effective in the treatment of many conditions including anxiety, depression, epilepsy, chronic pain, insomnia. There is a lot of anecdotal evidence from people who have used CBD containing products but not any high-quality level trials data that supports its effectiveness in the treatment of any of these indications. It is also unclear what the therapeutic dose or the concentration of CBD and other components such as TCH, was in these consumed products. Hence, it is difficult to draw conclusions about the efficacy or the dose response curve of CBD for any of the suggested conditions.

The toxicity of a substance

There are reports of significant drug interactions through the cytochrome P450 (CYP450) metabolism pathways, which are also the metabolism pathways for many of the prescription medicines that are often used for the same indications. This poses a significant risk of drug interactions and adverse events if CBD is used concurrently. Self-selection of CBD containing substances could lead to harm in patients who may be taking prescribed medicines for the treatment of these conditions, which would be more common than exceptional in the management of these conditions. Hence, self-selection without the input of a health professional could lead to unintentional harm, despite written warning labels.

The dosage, formulation, labelling, packaging and presentation of a substance

Clear labelling in line with the requirements according to the Schedule should be expected of all CBD containing products. There are currently no commercially available products in this Schedule.

The potential for abuse of a substance

Although products containing 98% CBD are known not to exhibit euphoric effects of cannabis, which is not likely to be common knowledge, the general public may be tempted to try it, driven by curiosity or a genuine misapprehension that it might produce a euphoric effect. There is high propensity for this to occur, especially if the products are marketed as complementary medicines, as consumers often assume that herbal products are safe or safer than medicines.

The applicant has not addressed the issue of overuse and misuse or how they propose to place any limit on sales of these products. The applicant has not made any suggestion of including the CBD containing preparations to a drug monitoring register, such as any of the real time prescription monitoring systems that are in operation in different jurisdictions across the country.

[1] Therapeutic Goods Administration 2020, Safety of low dose cannabidiol, *Commonwealth Department of Health*. < https://www.tga.gov.au/alert/review-safety-low-dose-cannabidiol >. Last accessed 28 April 2020.

Given the high potential for misuse of these substances, the Guild believes that all sales of CBD containing products should be recorded and monitored.

Summary

The Guild does not support the proposal. Given the significant risk of drug interactions, misuse of the products and uncertainty around clinical effectiveness, cannabidiol containing products should not be exempt from the oversight by the TGA, as a substance listed in the Poisons Standards.

CANNABIDIOL 2.5

Proposal

It has been proposed to amend the Poisons Standard as follows:

Schedule 8

CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use, when:

e) cultivated or produced, or in products manufactured74, in accordance with the *Narcotic Drugs Act 1967*; and/or
f) for use in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or
g) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act* 1989; and/or
h) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act* 1989, **except** when:

i. it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations* 1990 applies; or
ii. separately specified in the NABIXIMOLS entry in this Schedule; or
iii. captured by the CANNABIDIOL entry in Schedule 4; or Schedule 3

Appendix D, Item 1 (Poisons available only from or on the prescription or order of an authorised medical practitioner)

CANNABIS for human use.

Appendix K

CANNABIS **except** cannabidiol when included in Schedule 4

Schedule 4

CANNABIDIOL in preparations for therapeutic use where:

c) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and
d) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation;

except when included in Schedule 3.

Schedule 3- New Entry

CANNABIDIOL in preparations for therapeutic use when:

a. the cannabidiol is either plant derived, or when synthetic only contains the (-) CBD enantiomer; and
b. the maximum recommended daily dose is 60 mg or less of cannabidiol; and
c. in packs containing not more than 30 days' supply; and
d. cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and
e. any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation; and
f. for adults aged 18 years and over.

Overview

The Guild is supportive of the proposed scheduling change that would see improved patient access to medicinal cannabis products. Specifically, those products containing 98% or more cannabidiol (CBD) in low doses. However, we propose that additional safeguards are added to the schedule, in the form of Appendix M, to minimise the risk of patient harm and the potential for misuse. Without the addition of these safeguards, we would recommend that the existing scheduling (S4) is maintained, so as to balance the benefit of improved access to treatment and the interest of patient safety.

We note that this proposal follows a review of the safety of low dose CBD containing products that was undertaken by the Therapeutic Goods Administration (TGA). It aligns with the recommendations of the findings of the inquiry by the Senate Community Affairs References Committee into the current barriers to patient access of medicinal cannabis in Australia.

The risks and benefits of the use of a substance

The Guild supports evidence-based use of medicines. Although CBD has been used for a long time and there is a large amount of purported evidence of efficacy, the Guild believes that medicinal cannabis products should be held to the same standard of quality, safety and efficacy as other therapeutic substances, in line with the Quality Use of Medicines and the National Medicines Policy. There is currently a clear lack of high-quality clinical evidence to support the purported clinical indications of CBD containing products. TGA's recent review[2] of safety of CBD containing products indicates that CBD appears to be relatively safe when used as prescribed, in low doses, but it does not address the question of efficacy. Given the clear lack of evidence for the purported clinical indications, the Guild would be supportive of ongoing high quality clinical trials to build the body of evidence for the effectiveness and therapeutic use of CBD.

The purposes for which a substance is to be used and the extent of use of a substance

CBD has been reported to be effective in the treatment of a broad range of health conditions including anxiety, depression, epilepsy, chronic pain, insomnia, muscle spasticity. The recent TGA literature review highlights that there is a clear lack of high quality clinical evidence regarding the effectiveness of CBD and these claims remain largely anecdotal and unsupported by high quality clinical trials data.

[2] Therapeutic Goods Administration 2020, Safety of low dose cannabidiol, *Commonwealth Department of Health*. < https://www.tga.gov.au/alert/review-safety-low-dose-cannabidiol >. Last accessed 28 April 2020.

The toxicity of a substance

The recently completed TGA report into safety of low dose cannabidiol, and which has informed this scheduling proposal, has demonstrated some evidence of safety of CBD when used in low-doses. The review also recommends that CBD containing products should be supplied under the oversight of a health professional, including vigilance around concurrent use of a range of prescription medicines with potential for drug interactions.

The dosage, formulation, labelling, packaging and presentation of a substance

There are currently no commercially available products containing CBD that are listed on Schedule 3. The Guild expects that when commercial products become available, they will comply with existing standards. In addition, the following should be considered in the interest of public safety:

Labelling

a) Ingredients

The TGA safety review makes a distinction between the different mechanism of action and the physiological effects of enantiomers of CBD. This is particularly applicable to synthetically derived CBD, which contains both the (-) and the (+) enantiomers of CBD. All future commercial products should be clearly labelled with the source of CBD, its purity of the active CBD (-) enantiomer, as well as an analysis of the other components contained in the product. This will enable pharmacists to check for drug interactions more easily and to help ensure safe use of medicines. CBD containing products should continue to be regulated under the Poisons Standard, to ensure that any products that are available in the Australian market comply with the quality and safety standards that apply to other therapeutic products.

The Guild recommends recording of the supply of CBD containing products, including in the pharmacy's dispensing software. In order to monitor compliance with the recommended maximum monthly supplies, the supplies should also be recorded in the real time prescription monitoring system in use in the different jurisdictions across Australia. Real time prescription monitoring (RTPM) systems are currently used to monitor supplies of prescription opioids and include SafeScript, in Victoria and DORA which is in use in the ACT and Tasmania. A system is currently in development for use in Queensland, while South Australian and Western Australian state health regulators are also undertaking a development of RTPM technologies.

b) Dosage and indications

The Guild recommends that the manufacturers clearly specify the indications and the dose range for their products. This should be included both on the pack/ product label and in any product information, including the Consumer Medicines Information leaflets (CMIs). As there is a clear lack of high-quality evidence for the purported indications, the manufacturers should support pharmacists to supply these products safely. Pharmacists should not be placed in a position where they are supplying or recommending these products in an 'off label' manner.

The potential for abuse of a substance

There is potential for CBD containing products to be misused. The proposal has recommended maximum monthly supplies and a maximum daily dose but has not proposed a method to monitor the sales of the substance. Monitoring of CBD supplies should be instituted to minimise the risk of overuse or intentional misuse.

Any other matters necessary to protect public health

Addition of Appendix M criteria

In the interest of public health, the Guild recommends that additional criteria should apply to the Schedule 3 supply of CBD containing products.

The Appendix M criteria should include:

- Completion of an accredited training course by pharmacists that meets the requirements of a competency-based framework for the supply of CBD
- Mandatory recording and labelling of all supplies in the pharmacy's dispense system
- The availability of real time monitoring infrastructure to monitor the supply of CBD containing products, such as via the real time prescription monitoring systems in use in States and Territories.

Without the addition of these safeguards, we would recommend that the existing scheduling (S4 listing) is maintained, and that the benefit of improved access to treatment is foregone in the interest of consumer safety.

Exclusion of Appendix H listing for CBD

While supportive of greater consumer access to CBD containing products, the Guild believes that advertising of these products is not in the public interest. It may induce demand and potential for misuse, and place community pharmacies under undue pressure from the public seeking the substance.

Summary

The Guild is supportive of this scheduling proposal. We call for more research to inform therapeutic indications in line with the principles of quality use of medicines. In the interest of public safety, we recommend an addition of Appendix M criteria to ensure all supply are recorded and monitored via a real time prescription monitoring systems in use in States and Territories.