# Medicinal cannabis:

## Epilepsy in paediatric and young adult patients

This fact sheet summarises the evidence and clinical guidance in the Therapeutic Goods Administration's (TGA) Guidance for the use of medicinal cannabis in the treatment of epilepsy in paediatric and young adult patients in Australia.

There has been increasing interest in recent years regarding medicinal cannabis*. However, there is a limited body of evidence to support its efficacy and safety in clinical practice.[1-3]

While anecdotal reports, animal data and some research on human subjects have suggested some therapeutic potential, there is insufficient evidence from high quality studies, such as randomised controlled trials (RCTs), for most conditions.[2]

In response the TGA has published guidance documents to assist health professionals and patients in the use of medicinal cannabis, including for epilepsy in paediatric and young adult patients.

Note that medicinal cannabis is not recommended as a first line treatment in any condition. Prescribing should always be considered on a case-by-case basis and once all other standard approved treatments have been unsuccessful.

## Evidence[4]

About the TGA Guidance for the use of medicinal cannabis in the treatment of epilepsy in paediatric and young adult patients in Australia:

- a systematic review and meta-analysis of 36 individual studies, including randomised controlled trials (RCTs) and observational studies.
- GRADE (grading of recommendations, assessment, development and evaluation) approach to evaluate evidence quality found the large majority of studies were moderate to very low quality.
- Most studies have been on the medicinal cannabis product, cannabidiol (CBD), which is the active ingredient of the cannabis plant that doesn't have psychoactive effects,[5] as an adjunctive treatment to other anti-epileptic drugs (AEDs).

### Efficacy

For the primary endpoint of 'proportion of patients experiencing ≥50% reduction in seizure frequency', meta-analysis of two RCTs of CBD (low GRADE) found the number needed to treat (NNT) was 8.0 (95% CI 6 to 17).

For secondary endpoints, two RCTs of CBD (low GRADE) had a NNT for 'Quality of life outcomes' of 5.0 (CI 95% 4 to 9) and three RCTs (low GRADE) found the NNT for 'complete seizure freedom' was 171 (CI 95% 155 to 339).

There is no evidence on medicinal cannabis as 'rescue' therapy for status epilepticus.

### Adverse events

Adverse events for CBD include: diarrhoea (20%), somnolence (18%), decreased appetite (17%), increased appetite (17%), worsening of seizures (15%), pyrexia (13%), convulsion (12%), fatigue (11%), status epilepticus (10%), gastrointestinal problems (9%), irritability (8%), weight gain (7%), weight loss (7%), nausea (7%), behavioural difficulties (7%) and vomiting (6%).

*NPS MedicineWise has adopted the term 'medicinal cannabis', which is used by the TGA, many health departments and affiliated organisations. Variations include cannabis medicines, cannabinoids, cannabis-based products (CBP).

The number needed to harm (NNH) for CBD for any adverse event was 3.0 (CI 95% 3 to 6). For a serious adverse event such as status epilepticus or elevated aminotransferase enzymes levels, the NNH was 23.0 (CI 95% 18 to 40).

Studies of other products such as CBD:THC (delta-9 tetrahydrocannabinol) combinations had a very low quality of evidence and were not included for meta-analysis for NNT and NNH.

### Drug-drug interactions

A recent open-label safety study of CBD found significantly changed serum levels of AEDs including clobazam, rufinamide, topiramate, zonisamide, and eslicarbazepine; and abnormal liver function test (LFT) results for valproate. This study emphasised the importance of monitoring both serum AED and liver function during treatment with CBD. More research is needed on drug-drug interactions in epilepsy.

## Clinical guidance[4]

- Medicinal cannabis is not recommended as a first-line treatment for epilepsy in children and young adults aged up to 25 years old.
- The place in therapy for medicinal cannabis is as an adjunctive treatment to drug-resistant epilepsy, where four or five other AEDs have not controlled the epilepsy.
- Commencing medicinal cannabis needs the involvement of a paediatric neurologist due to the complexity of these patients.
- If deciding to prescribe medicinal cannabis, CBD is the most studied product. It comes in various preparations (pharmaceutical-grade and non-standardised), none of which are TGA-registered.[6]
- The therapeutic aim of prescribing CBD is to decrease seizure frequency and improve overall quality of life. Achieving full seizure remission is likely to be rare.
- Be aware of the adverse events of CBD. If treatment is likely to be long-term, it is important that any side-effects from CBD are not greater than side effects of AEDs.
- Be aware of the potential for drug-drug interactions and monitor both serum AED and liver function during treatment with CBD.
- In the absence of strong evidence for dosing and specific preparations, patients should be re-evaluated 12 weeks after commencement for response to treatment.

## Prescribing guidance

The NSW Cannabis Medicines Prescribing Guidance is a suite of resources intended to assist medical practitioners in their prescribing and management of cannabis medicines (for NSW patients within current regulatory frameworks and clinical practice).

Visit the Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE) to download the documents.

## Further information

Studies included in the TGA guidance document, as well as the latest results from RCTs and other studies are found here.

### National sources:

NPS MedicineWise

Office of Drug Control

TGA

### State and territory health departments:

ACT

Northern Territory

NSW

Queensland

South Australia

Tasmania

Victoria

Western Australia

## References

1. Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in Australia – Overview. Canberra: Government of Australia, Department of Health, 2017. https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-australia-overview (accessed 10 May 2020).
2. Queensland Health. Clinical Guidance: for the use of medicinal cannabis products in Queensland. 2016. https://www.health.qld.gov.au/__data/assets/pdf_file/0023/634163/med-cannabis-clinical-guide.pdf (accessed 10 May 2020).
3. Martin JH, Bonomo Y, Reynolds AD. Compassion and evidence in prescribing cannabinoids: a perspective from the Royal Australasian College of Physicians. Med J Aust 2018;208:107–9. https://www.ncbi.nlm.nih.gov/pubmed/29438641.
4. Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in the treatment of epilepsy in paediatric and young adult patients in Australia. Canberra: Government of Australia, Department of Health, 2017. https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-epilepsy-paediatric-and-young-adult-patients-australia.pdf (accessed 10 May 2020).
5. Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in the treatment of chronic non-cancer pain in Australia. Canberra: Government of Australia, Department of Health, 2017. https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-chronic-non-cancer-pain-australia.pdf (accessed 10 May 2020).
6. Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in Australia – Patient information. Canberra: Government of Australia, 2017. https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-australia-patient-information.pdf (accessed 10 May 2020).





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