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Cannabidiol as an Adjunct for the Treatment of Anorexia Nervosa (CAFTAN): An Open Label Pilot Trial with Extension in Young People

Information Sheet – Parent

(1) Introduction

This is an invitation for your child to take part in a research project testing a new treatment for anorexia nervosa. The young person has been invited to take part because they have anorexia nervosa, are aged between 12-17 years old, are currently receiving a psychological intervention and are in the care of a medical practitioner.

This Information Sheet provides you with information about the research project. It explains the treatments involved and what will be required of you and your child if you choose to participate. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. If you have any questions or would like more information, you can speak to the trial coordinator, Sarah-Catherine Rodan, on **+61403224986**. Feel free to discuss the information in this sheet with a relative, friend or your child's medical practitioner before making your decision.

Participation in this research is voluntary. If you do not wish your child to take part, they do not have to. This will not impact the quality of their care or access to care in any way.

The research is being sponsored by the University of Sydney and conducted by the Lambert Initiative for Cannabinoid Therapeutics and the InsideOut Institute for Eating Disorders. The results of this research will be used by the study investigator Sarah-Catherine Rodan to obtain a doctorate (PhD) degree.

If you decide you would like your child to take part in the research project, you will be asked to sign a consent form, which you will find at the end of this Participant Information Sheet (and which is yours to keep).

(2) What is the purpose of this research?

This study aims to determine the safety and preliminary efficacy of a new pharmacological treatment, cannabidiol (CBD) – the non-intoxicating component of the cannabis plant – that has been demonstrated to be effective for treatment of anxiety in young people (12-25 years old). Anorexia nervosa is characterised by high levels of anxiety and frequently co-exists with other anxiety disorders. This study will pilot this treatment in people with anorexia nervosa.

Eating disorder-driven resistance to re-feeding and weight gain is often a result of the extreme anxiety the young person is experiencing. Therefore, an intervention that aims to reduce this anxiety **may make treatment easier to deliver, reduce the stress on families and the young person, subsequently improving weight gain and eating disorder recovery.**

Your child's participation in this study will benefit the eating disorder research community and may benefit your child as well as future patients by helping us to develop, implement and improve current treatment programs for problematic eating behaviours and long-term recovery.

We cannot guarantee that your child will receive benefit from this trial however, we have new evidence of the effectiveness of CBD from a study we completed in young people aged 12-25 with severe treatment-resistant anxiety, who had not responded to other medication/therapies. CBD was administered over 12 weeks with the same dose in this study (200-800 mg/day) which produced a higher than anticipated reduction in anxiety. Two-thirds of participants had a >33% reduction and 40% of participants had a >50% reduction in anxiety by end of treatment. Please refer to the Lambert Initiative website for further details about this study (<https://www.sydney.edu.au/lambert/our-research/anxiety.html>). This provides a strong incentive to explore this treatment in young people with anorexia nervosa.

(3) What is CBD?

The new treatment, cannabidiol (CBD), is a non-intoxicating compound known as a 'cannabinoid' extracted from the cannabis plant. The cannabis plant contains hundreds of different cannabinoids with the two most studied being cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). Unlike THC, CBD is non-intoxicating and will not get your child 'high' or 'stoned'. CBD will be administered in the form of a capsule.

CBD is widely prescribed in Australia to treat a variety of conditions including anxiety, chronic pain (including cancer pain and symptoms), epilepsy, and insomnia. CBD is known to have a good safety profile and side effects are typically mild and tolerable.

Cannabidiol (CBD) is considered an experimental drug and has not been approved in Australia for the treatment of anorexia nervosa. This study will be conducted under the Therapeutic Goods Administration (TGA) Clinical Trials Notification (CTN) Scheme and has been approved by a Human

Research Ethics Committee (HREC). This allows the investigators to use this product for medical research purposes.

(4) What does the young person's participation in this research involve?

(4.1) Psychological intervention

Your child will need to be already engaged in an ongoing psychological intervention in the community. For example, but not limited to, family based therapy (FBT).

(4.2) CBD investigational drug

Your child will be prescribed CBD capsules. As the parent, you will be responsible for administering CBD to your child. You will be sent the medication via post to the address you provide free of charge. The treatment with CBD will continue every day for 12 weeks. Dosing will start at 200mg/day, with the option to increase to 800mg/day if this is appropriate for your child. You and your child will meet with the trial doctor throughout the study to determine a dose that is best suited for your child. Your child will have the option to increase the dose to 400mg per day by week 2, 600mg per day by week 4 and 800mg by week.

Dosing:

- 200 mg/day (1 capsule at night)
- 400 mg/day (1 capsule in the morning + 1 capsule at night).
- 600mg/day (1 capsule in the morning + 2 capsules at night).
- 800mg/day (2 capsules in the morning + 2 capsules at night).

You will be provided with a medication card and contact details of the trial coordinator and trial doctor. A medication diary will also be provided to help. If a dose is missed, you will need to give the missed dose as soon as possible and inform the trial doctor immediately.

Throughout the trial you **must keep all the bottles (including any unused CBD capsules)**. After the trial has concluded you must return the bottles (including any unused CBD capsules) and the medication diary to the research team. We will organise a courier to collect this.

Please be aware that further access to CBD will not be made available to you after this trial has been concluded.

(4.3) Medical Management with your Medical Practitioner

Upon entering the trial, your medical practitioner will be given a form to complete. Information from your child's medical records will be collected as part of clinical care during the intake assessment and referral process. The medical practitioner is then asked to confirm that your child is medically stable,

not pregnant (if applicable) and that there has been no use of illicit drugs in the past 4 weeks, as confirmed with urine test. Your medical practitioner will be required to inform the research staff if there is any deterioration in your child's medical or mental health as this may impact their eligibility to continue taking the CBD. This information will be kept strictly confidential. **The safety of your child is our priority.**

Regular medical review is an important component of treatment for anorexia nervosa. To ensure the safety of your child, it is a requirement of this trial that your child is monitored regularly by their medical practitioner throughout the duration of the trial. Your child will need to meet with their medical practitioner at week 4, 8 and 12 of the trial. You will also need to meet with your medical practitioner at 3-months post the end of the study.

(4.4) Trial doctor

The trial doctor will complete telehealth sessions with you and your child at intervals specified at their discretion and a phone call at week 2, week 4 and week 8.

(4.5) Questionnaires, assessments, and forms

In agreeing to participate in the trial, your child will be required to complete a series of questionnaires which will gather information about their eating disorder symptoms, anxiety levels, and general mental health. The parent will also be required to complete one questionnaire throughout the trial.

If your child is aged 12-15 years, you will be sent a link via email for your child to complete online. If your child is aged 16-18 years, an email will be sent to them directly to complete. Email reminders will be sent to you / your child as needed. Each questionnaire will take between 5-25 minutes to complete. The questionnaires will include the following:

- *Eating Disorder Examination Questionnaire (EDE-Q)*: A 28-item questionnaire to measure eating disorder symptoms.
- *Yale-Brown-Cornell Eating Disorder Scale Self Report Questionnaire (YBC-EDS-SRQ)*: A 19-item questionnaire to measure obsessive and compulsive symptoms.
- *Overall Anxiety Severity and Impairment Scale (OASIS)*: A 5-item questionnaire to measure anxiety symptoms.
- *Beck Depression Inventory (BDI-II)*: A 21-item questionnaire to measure depression.
- *Fear of Food Measure – Adolescent Version (FOFM-A)*: A 10-item measure to assess anxiety about eating, food avoidance behaviours and food avoidance.
- *Quality of life (EQ-5D-Y or EQ-5D-5L)*: A 6-item questionnaire to assess quality of life.
- *OASIS-Youth*: A 7-item care-giver report of the young person's anxiety (**completed by the parent**).

The questionnaires will be administered at baseline, week 4, week 8, week 12, and 3-month follow-up (a total of 5 times).

Once the trial has been concluded, you will be invited to complete a short survey to share your experience with the CBD treatment. As mentioned previously, weight and height will be measured routinely throughout the treatment by your child's medical practitioner. Your medical practitioner will be required to confirm the weight and height of your child at three-month follow-up.

(4.6) Urine Samples

Collection of urine is a mandatory component of the research. Prior to the commencement of the study, a urine sample will be collected by the medical practitioner from your child to confirm absence of illicit drugs.

Your child will need to provide a sample of urine every month using specimen containers provided to you at the start of the trial. We will organise for a courier to collect the urine sample from your home address and ship it to our laboratory at the Brain and Mind Centre at the University of Sydney. **Please store the urine sample in the fridge until the courier arrives to pick it up.** The urine sample will be analysed for CBD to ensure medication adherence.

(5) What does the parent have to do?

As the parent you will be required to ensure the CBD treatment is taken regularly in accordance with the instructions provided. You will be responsible for handling the study medication and dispensing it daily to your child. If a dose is missed, you will need to administer the missed dose and inform the trial doctor immediately.

(6) Other relevant information about the research project

This is a small open-label trial. We aim to recruit 30 participants in the community. 'Open label' means that everyone will be receiving the same treatment and will know which treatment they are receiving.

(7) Does your child have to take part in this research project?

Participation in any research project is entirely voluntary. If you do not wish for your child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw them from the project at any stage.

Your decision to take part or to withdraw from the trial **will not affect** your child's treatment or you/your child's relationship with their treatment team, or with the researchers at the University of Sydney, Lambert Initiative for Cannabinoid Therapeutics, or InsideOut Institute for Eating Disorders.

(8) What are the alternatives to participation?

Your child does not have to take part in this research project to receive treatment. Other options are available; these include continuing with treatment as usual with no drug intervention. You can also discuss other treatment options with your child's medical practitioner.

(9) What are the possible benefits of taking part?

We cannot guarantee or promise that your child will receive any benefits from this research. This study will contribute to important research into the effects of CBD treatment on anorexia nervosa. This evidence may assist in improving pharmacological treatment for eating disorders in the future, even if this does not benefit you and your child directly.

(10) What are the possible risks of taking part?

(10.1) Cannabidiol

Overall, CBD is generally well-tolerated and has a good safety profile. It is non-intoxicating and does not cause addiction, dependence, or tolerance. The most common side effects include nausea, headaches, gastrointestinal upset and sometimes changes to liver function (raised liver enzymes) which may be accompanied by symptoms below:

Tell the study doctor if you notice any of the following side effects:

- Nausea, vomiting and/or diarrhea
- Fever or feeling unwell
- Unusual tiredness or sleepiness
- Pain or discomfort in the right upper stomach area
- Chest pain

Other side effects observed in a recent 12-week trial of 800mg/day CBD treatment in young people with treatment-resistant anxiety included fatigue, low mood, insomnia, changes in appetite, headache, and gastrointestinal upset. Side effects were mild-to-moderate in severity and transient (resolved).

Medical treatments often cause side effects. Your child may have none, some or all of the effects listed above, and they may be mild, moderate or (very rarely) severe. If your child has any of these side effects, **please contact the trial doctor immediately**. Their contact details will be listed on the medication card given to you.

Note that changes to liver function are common in anorexia nervosa. This may be due to malnutrition and/or re-feeding. To closely monitor your child's liver function, your medical practitioner will **conduct blood tests monthly for the duration of the study**. If your child has elevated liver function enzymes fortnightly tests may be necessary for ongoing monitoring.

The effects of CBD on the liver can be exacerbated by the use of other medications. This is known as a 'drug-drug interaction'. **It is important that you inform your medical practitioner and trial doctor of the use of any new medications (prescription, over-the-counter, complementary and supplements) throughout your child's participation in the trial.** Should any signs of potential drug-drug interactions develop, the trial doctor and GP will review their treatment plan and may discontinue the drug intervention.

There may be other side effects that the researchers do not expect or do not know about, and that may be serious. Please note that this would be highly unlikely. You should tell the trial doctor **immediately** about any new or unusual symptoms. Most side effects are temporary and go away shortly after treatment ends.

(10.2) Pregnancy and risks to unborn child

It is important that your child is not pregnant and does not become pregnant (or impregnate a sexual partner if male) during the course of the trial. The young person will not be eligible to participate in the trial if pregnant or trying to become pregnant. This will be confirmed by the medical practitioner using a urinary pregnancy test.

If your child is female and of child-bearing potential (i.e., menstruating), the medical practitioner will discuss appropriate and reliable contraception if deemed appropriate (e.g., oral contraceptive, or long-acting reversible contraception such as a hormonal implant, injection, or IUD). Anorexia nervosa can cause amenorrhea (the absence of menstruation); however, ovulation can still occur without menstruation. Therefore if your child is sexually active, they must use appropriate contraception.

If your child is male, they are strongly advised to use effective contraception (e.g., condoms) and to not donate sperm during the course of the trial and for at least 7 days after the last dose of study medication. The medical practitioner will provide sexual health counselling to support their participation in the trial.

If at any time you think your child (or your child's sexual partner, if male) may have become pregnant, it is important to let the trial doctor know immediately.

(11) What will happen to my child's urine samples?

Urine samples will be stored at the Brain and Mind Centre Freezer Bank at the University of Sydney, Camperdown until analysis is completed to check for medication adherence. Any remaining samples will be destroyed after analysis.

(12) What if new information arises during this research project?

Sometimes during a research project, new information becomes available about the treatment that is being studied. If this happens, the trial doctor will tell you about it and discuss with you whether you want your child to continue in the research project. If you decide to withdraw your child from the study, they will continue with their other treatment as usual.

(13) Can the child have other medicines during this research project?

No, you must notify the researchers of any planned changes to current medications or procedures while your child is participating in this study.

You must tell us about any medicines your child may be using. This is in your child's interest as well as being important for the study because they may interact or interfere with the study drug. You must tell us about any prescription (antidepressants or mood stabilisers) or over-the-counter medications, including vitamins, herbal remedies, or other supplements your child is taking.

You should also tell the trial doctor about any changes to these during the young person's participation in the research project. The trial doctor will explain to you, which treatments or medications need to be stopped for the time the child is involved in the research project.

(14) What if I withdraw the child from this research project?

If you decide to withdraw your child from the project, please notify the trial doctor or a member of the research team before you cease taking the CBD medication. This notice will allow the trial doctor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your child during the research project, the trial doctor and relevant study staff will ask if you and your child if you are willing to complete a brief exit questionnaire (XX mins to complete) and will ask about reasons for withdrawing.

Following this, no further personal information will be collected. Personal information already collected will be retained to ensure that the results of the research project can be measured properly. You should be aware that data collected up to the time of withdrawal will form part of the research project results. If you do not want this to happen, you must inform a member of the research team before the participant enrolls in the research project.

(15) Could this research project be stopped unexpectedly?

This research project may be changed or stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects in multiple participants or
- If the trial doctor decides it is in the best interest of your health and welfare to stop.

(16) Are there any reimbursements?

The cost of the medication and medical oversight by the trial doctor will be provided free of charge. This does not include costs associated with visits to your child's medical practitioner (i.e., GP or paediatrician) or any tests ordered by your medical practitioner. There are no additional costs associated with participating in this research project. No additional reimbursements will be provided to you or child for your participation in the research project.

(17) What happens when the research project ends?

You will receive (via email) a summary of the major research findings once the trial has concluded and data analysis activities are complete. The results of this research will also be used for manuscript preparation and submission for publication as well as presentation to conferences. No participants will be identified in any report or publication of this study or its results.

We will share the study results by publishing them in relevant journal articles and / or presenting them at national and international scientific conferences. We will make sure that information is published / presented in such a way that neither you nor your child are identifiable.

Your child's data will be securely stored for a minimum of 15 years after the study finishes or until the youngest participant turns 25 years.

(18) What will happen to information about your child?

By signing the consent form you consent to the trial doctor and relevant research staff collecting and using personal information about your child for the research project. Any information obtained in connection with this research project that can identify your child will remain confidential and secure, except when:

- It is subpoenaed by a court,
- Failure to disclose information would in the reasonable belief of the clinicians place you, your child or another person at serious risk,
- Your prior approval has been obtained to discuss material with another person (e.g., a parent, employer or health provider).

All data and participant information collected for the purposes of this study will be entered electronically and stored on a research database named REDCap (Research Electronic Data Capture). This is a secure, web-based, non-commercial, data management tool designed for research purposes, hosted, and backed up on the University of Sydney servers on a daily basis. The data will be analysed by the researchers at the University of Sydney. Your child will be identified with a unique participant code, assigned at enrolment. The key linking your child with their unique trial code will be stored in a password encrypted file, accessible only to the research staff. Your child will not be identified in any report or publication of this study or its results.

Information about participation in this research project may be recorded in your child's health records when they visit their local GP only with your permission.

In accordance with relevant Australian NSW privacy and other relevant laws, you have the right to request access to the young person's information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your child's information.

(19) Complaints and Compensation

If the participant suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment for the participant. If the participant is eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In addition, you may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if the participant's injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). You and the participant do not give up any legal rights to compensation by participating in this study.

Research involving Humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the Sydney Local Health District – RPAH Zone (Protocol No. X21-0440). As part of this process, we have agreed to carry out the study according to the National Statement on Ethical Conduct in Human Research (2007). If you have any complaints about the ethical nature of this research project, please contact the Sydney Local Health District using the details outlined below. Please quote the study title and protocol number.

- **Telephone:** (02) 9515 7035
- **Email:** SLHD-RPAEthics@health.nsw.gov.au

(20) Who is organising and funding the research?

The research is being organised and funded by the InsideOut Institute for Eating Disorders and Lambert Initiative for Cannabinoid Therapeutics from the University of Sydney.

(21) Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Sydney Local Health District.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

(22) Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project you can contact any of the following people:

Clinical contact person:

Name	Sarah-Catherine Rodan
Telephone	0403224986
Email	sarah-catherine.rodan@sydney.edu.au

For matters relating to the interventional drug, the CBD capsules:

Trial doctor:

Name	Dr Karen Spielman
Email	drkarenspielman@gmail.com

Appendix A

List of Investigators

Principal Investigator (Trial Oversight)

Name: Professor Iain McGregor
Address: Brain and Mind Centre, 94 Mallet Street, Camperdown NSW 2050
Telephone: +61 2 9351 3571
Email: iain.mcgregor@sydney.edu.au

Principal Clinical Investigator (Medical/Supervision of Trial doctor)

Name: Professor Janice Russell
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Co-investigator (Trial doctor/GP specialist)

Name: Dr. Karen Spielman
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Co-investigator (Trial Oversight)

Name: A/Prof Sarah Maguire
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Co-investigator (Clinical trial coordinator/PhD Student)

Name: Ms Sarah-Catherine Rodan
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Co-investigator (Trial management)

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