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A/Prof **Sarah Maguire**
*Director of InsideOut Institute for Eating Disorders*
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**CAnnabidiol for the Treatment of Anorexia Nervosa (CAFTAN)**

**Medical Clearance Form**

**Date:**

Dear _____ [*GP name*],

RE: [*Patient name]*

Ms/Mr [*Patient name]*, has advised us that you are her/his/their treating medical practitioner (general practitioner or pediatrician). He/she has agreed to participate in an open-label trial conducted by the University of Sydney for cannabidiol (CBD) treatment for anorexia nervosa. This study will examine safety and feasibility of adjunctive CBD and examine preliminary efficacy at reducing anxiety. CBD has recently been shown to be safe in young people and adults and highly effective in managing treatment-resistant anxiety. As you know, medical practitioners play a very important role for patients and their families undergoing treatment for anorexia nervosa, and as such we would like to provide you with information about the trial and ask for your help in collecting important data.

To confirm the person's eligibility for the trial, they require a complete medical assessment confirming they are medically stable. As you may be aware, anorexia nervosa comes with a risk of medical complications and, at times, instability. As such, medical clearance and regular monitoring is required. We would be grateful if you would agree to be involved by providing medical support and monitoring for the duration of the trial.

As part of the study, and for ethical and safety considerations, the participants are asked to have a general medical check-up to ensure their current medical stability. This will include a urine screen to check for illicit drug use and urine/serum screen for pregnancy. It is important in the urine referral

that it is clearly indicated that the urine screening required is a clinical screen and does not need to be conducted as a supervised drug screen.

If you agree to be involved, you must acknowledge that:

- You consent to be the participant's nominated medical practitioner for the duration of the study,
- You have medically checked the participant and will share the test results with the research team,
- Confirm that they are medically stable,
- Will hold responsibility for medical assessment and escalation (when required),
- Will continue to medically monitor the participant, at least monthly for the duration of the study,
- Will collect weight and liver function tests at least monthly for the duration of the study and share these results with the research team
- Will collect weight and liver function tests at 3-months post end of the study and share results with research team
- Will agree to a phone call with the trial doctor to review suitability and establish communication pathways prior to initiating the trial medication
- Will be available to speak to the trial doctor for the duration of the study.

We would be grateful if you could share a copy of the ED Plan used to refer this patient to their psychological provider. To ensure that the data included is complete, please refer to this document – GP Quick Tools – for more information or access to a template form.

In addition, we ask specifically if you could complete the following:

- A urine test to confirm absence of illicit drugs,
- A urine or serum/blood test (if female) confirming they are not pregnant,
- A discussion with the participant about effective and reliable use of contraception during the trial, with or without the presence of parents where appropriate. It is important that the participant does not fall pregnant (or impregnate a sexual partner if male participant) while taking the investigational drug. This will be reiterated to the participant as they enter the trial by the research staff.

Clinical responsibility for management of the patient remains, at all times, with the treating team in the community (i.e., you, medical practitioner) as per usual practice. Please let the research staff know if at any time you believe the participant's medical status changes otherwise or if you believe that they may no longer be suitable for the trial.

The research team will notify you if there is any evidence of rapid weight loss for the participant (as per the trial criteria) or other indicators that the parent/participant shares with the research team that could potentially change their medical status. In this case, you will be contacted by the research staff and asked to monitor the participant's medical parameters. If you have any concerns or questions at any time, you can reach out and discuss with trial doctor or research team.

We are very interested in the perception of health professionals of new treatments, so you will also be asked to complete a brief survey at the end of the trial to share your thoughts on the efficacy of CBD.

An appendix has been included detailing further information about the trial and guidelines for how to monitor the participant through the trial.

For support from your local Eating Disorder Coordinator, such as to discuss local service pathways, treatment providers and training opportunities, please visit: https://www.slhd.nsw.gov.au/mentalhealth/pdf/NSW_Eating_Disorder_Coordinators.pdf

If you have any questions, please contact myself, trial specialist GP [Karen Spielman via the trial email], or the research staff at the University using the contact details provided below.

I _____ [*medical practitioner name*] agree that patient [*patient name; DOB*] is safe to participate in the trial.

I can confirm that:

1. I have medically checked the patient
2. I agree that he/she is medically stable to participate in the trial with the interventional drug, cannabidiol.
3. I understand that I must medically monitor the participant as frequently as clinically indicated (monthly)
4. I understand that I hold responsibility for the medical assessment and escalation (if required) of the young person
5. I consent to be the participant's nominated medical practitioner for the duration of the study.

Name: _____

Provider Number : _____

Phone : _____

Email : _____

Signature : _____

Date : _____

## Appendix A

Information for Medical Monitoring of Patients

As part of the study, and for ethical and safety considerations, the participants are asked to have a general medical check-up to ensure their current medical stability. As per the ED plan we advise a general medical examination with specific attention to weight (body mass index), ECG, pulse, blood pressure, and blood tests as per attached guidelines, random blood sugar, electrolytes (especially potassium and phosphate, also zinc and magnesium levels), renal function, liver function, albumin, haematology and baseline thyroid function, and iron status, $B_{12}$ and folate.

We also ask you to discuss if there are any risks of pregnancy with the patient without the presence of parents and to order a urine screen to check for illicit drug use and urine/serum screen for pregnancy. It is important in the urine referral that it is clearly indicated that the urine screening required is a clinical screen and does not need to be conducted as a supervised drug screen. If you are unsure regarding participant's risk of pregnancy please contact the trial doctor to discuss.

Thank you for assessing and taking medical care of the person throughout the trial and community treatment.

**Monitoring Medical Signs**

If the person reports symptoms of possible medical instability, they must see their medical practitioner immediately. If the person cannot see their medical practitioner, they are *advised to* present to their nearest Emergency Department for an assessment. Possible symptoms could include:

- Feeling like fainting or passing out when going from sitting to standing
- Constipation
- Nausea
- Shakiness
- Headaches
- Weakness

If the person describes or the family reports the person experiencing any of the following symptoms, they are *required to* present to their nearest Emergency Department or call 000 immediately:

- Shortness of breath
- Chest pains
- Rapid or low heart rate
- Fainting
- Dizziness
- Loss of consciousness
- Confusion
- Weakness
- Oedema/ swollen ankles
- Palpitations
- Vomiting of blood
- Abdominal distension
- Abdominal pain
- Muscle pain
- Tingling around mouth and/or fingers and toes

**Monitoring Liver Function**

Elevated liver serum enzymes are common in anorexia nervosa, due to malnutrition and/ or re-feeding. While elevated liver function enzymes have not been reported in trials investigating CBD outside of paediatric epilepsy in young persons, this has been reported in healthy adults. It is imperative that liver serum enzymes are monitored **monthly for the duration of the study** and at **3-month follow-up from the end of the study**. It is important that you share these results with the research team.

If a patient being considered for eligibility has elevated LFTs up to 2xULN, the research team will consider the patient for eligibility if you agree that the patient is medically stable. In this instance LFTs will need to be monitored **at least on a fortnightly basis**. In addition, if patients are on other medications that are known to elevate liver enzymes, such as:

- Roaccutane (Isotretinoin)
- Valdoxan (Agomelatine)
- Tetracyclines (e.g. minocycline, doxycycline)
- Griseofulvin
- Antifungal triazoles (e.g. ketoconazole, fluconazole, clotrimazole)
- Antifungal echinocandins (e.g. caspofungin, micafungin)

LFTs will also need to be monitored on a fortnightly basis.

If at any point **LFTs become elevated to 3xULN** they will need to be **discontinued** from the trial.

**Weight Monitoring**

We would appreciate if you could weigh the participant monthly for the duration of the trial and at 3-month follow-up from the end of the study. It is important that you share the weight with the research team and use the same scales throughout.

**Weight Loss Management Plan**

Given the risks associated with weight loss, the following weight loss management strategy will be used for all participants.

*Response to Rapid Weight Loss:*
If there is evidence of rapid or consistent weight loss*, the following actions are put in place:

- The study coordinator is alerted by the medical practitioner,
- The participant will be discontinued from the trial if there is any observable deterioration in participant's medical or psychiatric parameters as noted by medical practitioner. In this instance, the discontinuation protocol would be activated. The study coordinator would advise the participant, their family (if young person) and their medical practitioner in writing that they were discontinued from the study.

*Rapid weight loss is indexed by > 1kg a week for two weeks. Note that this is different definition to the NSW Eating Disorders Toolkit (2018). This ensures that the IOI site holds a lower risk threshold.

If you observe any of the following at any time please ensure the patient has assessment at an emergency department as needed. Further, if the below indicators are reported by the young person, family or medical practitioner to the therapist, the therapist will encourage the family to attend their local hospital for an urgent assessment:

**Indications for Hospitalisation**

**A hospital admission may be indicated for any of the following criteria:**

- Heart Rate <50 bpm,
- Cardia arrhythmia including a prolonged QTc interval (>450 msec)
- Postural tachycardia >20bpm increase heart rate
- Blood pressure <80/40 mm/Hg or postural drop >30 mm/Hg
- Temperature < 35.5°C
- Low serum potassium ≤3.0 mmol/L
- BSL <3.0mmol/L
- Other significant electrolyte imbalances
- BMI ≤ 14
- Rapid or consistent weight loss (e.g., > 1kg each week for six or more weeks)
- Acute dehydration or patient has ceased fluid intake
- Intensive community-based treatment has proven ineffective
- Comorbid or pre-existing psychiatric conditions that require hospitalisation
- Suicidality with an active intent and plan
- Other special considerations such as diabetes or pregnancy

*Figure 1. Indications for hospitalisation according to the NSW Eating Disorders Toolkit (2018)*

We advise that participants attend ongoing medical monitoring appointments with you for the duration of the trial at intervals you determine for adequate medical monitoring or otherwise.

It is not anticipated that there should be any serious side effects from this treatment. However, if you become concerned regarding the participant's medical stability throughout the trial or consider him/her to be unsafe to participate in the trial, please notify us and refer the participant for additional care appropriately according to the National Eating Disorder Collaboration's Professional Resource for General Practitioners. You can access the guidelines using the following link: https://insideoutinstitute.org.au/resource-library/eating-disorders-a-professional-resource-for-general-practitioners. Additionally, if you are unsure about how to detect and respond to high-risk symptoms or behaviours please refer to the guide created by the Victorian Centre of Excellence in Eating Disorders (CEED) titled, 'Physical Risk in Suspected Eating Disorders Mental Health Clinician Response Guide', which can be accessed using the following link. http://www.ceed.org.au/sites/default/files/resources/documents/CEED_Handout_ED%20Physical%20Risk%20Management%20-%20Mental%20Health%20Clinician%20Response%20Guide_May2017_ES_Colour.pdf.

You may also contact the trial GP specialist for guidance.

## Appendix B – Participant Information Sheet

## Appendix C

List of Investigators

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**Principal Clinical Investigator (Medical/Supervision of Trial doctor)**

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**Co-investigator (Trial doctor/GP specialist)**

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