PRODUCT INFORMATION
ARUMA FLOWER 'SOLARIS'
Dried Cannabis Flower

1. NAME AND DESCRIPTION OF THE MEDICINE

ARUMA FLOWER 'SOLARIS' (Tetrahydrocannabinol 22% w/w and Cannabidiol <1% w/w)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ARUMA FLOWER 'SOLARIS' is a THC-dominant medicinal cannabis flower with high concentrations of THC (Tetrahyrdocannabinol) and low levels of CBD (Cannabidol).

Each bottle of ARUMA FLOWER 'SOLARIS' contains 10g of *Cannabis sativa* L. dried flower with the following active ingredients:

- Tetrahydrocannabinol (THC) 22%
- Cannabidiol (CBD) <1%
- Other lesser amounts of cannabinoids and terpenes

3. PHARMACEUTICAL FORM

Dried cannabis flower

ARUMA FLOWER 'SOLARIS' is a light to dark green dried cannabis flower product produced from the dried floral heads of the cannabis sativa plant. The product is supplied in a medical-grade plastic tub, with an induction-foil seal and a tamper-evident cap.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

ARUMA FLOWER 'SOLARIS' does not have approved indications. Use is at the discretion of the prescribing practitioner based on the individual needs of the patient and the evidence for the use of dried cannabis flower with a THC-dominant ratio.

There is a growing body of evidence that medicinal cannabis products may have a role in medical conditions including but not limited to:

- Appetite Stimulation[1],[2]
- Cachexia[3],[4]
- Epilepsy[5],[6],[7],[8],[9],[10],[11]
- Chemotherapy-induced Nausea and Vomiting[12]
- Gastro-intestinal inflammation due to IBS, Ulcerative colitis, Crohn's Disease[13],[14],[15],[16],[17],[18],[19],[20]
- Multiple Sclerosis[21],[22],[23]
- Chronic Non-Cancer Pain[24]

- Palliation[25],[26]
- Parkinsonian Tremor[27],[28],[29]

Limited clinical trial evidence is available on the safety and efficacy of medicinal cannabis products.

4.2 DOSE AND METHOD OF ADMINISTRATION

DOSAGE

Consistent with TGA recommendations and international guidelines, the general approach to dosing should be to "start low, go slow".[30] Individual response to ARUMA FLOWER 'SOLARIS' may vary and it is important to slowly titrate.

Pharmacokinetic and pharmacodynamic properties in cannabis-naïve patients or those in a palliative care scenario will vary compared to average health adults. Such patients may only require 10-20% of the starting dose of a regular cannabis user to note effects (both positive and negative)[31].

In populations who are not naïve to cannabis, dosing advice is to consider tolerance in these patients. In patients undergoing weight loss treatment, dosing advice should consider the potential release of accumulated THC in fat stores.

Information on pharmacovigilance should be collected by the prescribing doctor or pharmacist.

METHOD OF ADMINISTRATION

ARUMA FLOWER 'SOLARIS' is designed to be administered via inhalation using TGA-approved vapuriser, according to the prescribing doctor's instructions.

Titration period:

A titration period may be required to reach the optimal dose. The dosage and timing of dosing will vary between patients.

To minimise the risk of adverse events, the dosage should be increased gradually. Morning doses should be taken at any time between waking and midday. Afternoon/evening doses should be taken at any time between 4 pm and bedtime.

Patients should be advised that it may take several weeks to find the optimal dose and that temporary undesirable effects can occur during this time. Physicians should consider maintaining the current dose, reducing the dose or interrupting, at least temporarily, the treatment depending on the seriousness and intensity of adverse events.

Consider the following example regimen[32]: Vapourise 0.1g according to a metered dosage schedule or as needed (PNS) according to doctor's recommendation (up to a maximum of 1g per day).

DOSE	DAY 1-2	DAY 3-4	DAY 5-6	DAY 7-8	DAY 9-10	DAY 11-12	DAY 13-14
1 (AM)	0	0.1	0.1	0.1	0.1	0.1	0.1
2 (PM)	0	0	0	0	0	0.1	0.15
3	0.1	0.1	0.1	0.1	0.1	0.15	0.15

Higher doses of ARUMA FLOWER 'SOLARIS' (exceeding 2-3g/day) may increase the risk of adverse events or induce tolerance without improving efficacy.

DOSAGE INSTRUCTIONS

1. Commence dosing at any time of day as recommended by doctor.
2. Remove the tamper evident cap from the container.
3. Remove a small dried cannabis flower from the container.
4. Break off 0.1g of the dried cannabis flower.
5. Grind or chop the material to an even, fine consistency.
6. Heat vapouriser to desired temperature (typically around 180 – 190° C).
7. Lightly pack ground cannabis material into vapouriser, allowing room for airflow to pass through the material.
8. Take 1-2 inhalations. Wait 15 minutes to assess effects.
9. Repeat as needed.

Maintenance period:

Following the titration period, patients are advised to maintain the optimum dose achieved.

Review by the physician:

All patients receiving treatment with ARUMA FLOWER 'SOLARIS' should be closely monitored by their physician.

Further titration of dosage either up or down, may be appropriate if there are any changes in the severity of the patient's condition, changes to concomitant medications or if adverse reactions develop.

Stopping rules

Pharmaceutical grade cannabinoids should be ceased where:

- the desired effect is not apparent after 4–12 weeks; and
- psychoactive or other side-effects are prohibitive.

Sample Treatment Plan

It is suggested that an initial treatment plan indicate that the medicinal cannabis product be used for a one-month trial to determine the effectiveness of the medication for the patient's condition/symptoms.

The initial treatment plan should clearly indicate:

- the treatment goals for medicinal cannabis use as well as the starting and stopping guidelines. It is recommended that these be clearly documented and discussed with the patient, related to the symptoms for which the patient is prescribed the medicinal cannabis product and, if possible, should be measurable. Examples include weight gain in patients with cachexia, cessation or minimisation of nausea and vomiting, and improved function and quality of life in patients with chronic non-cancer pain;
- the monitoring arrangements – including communication with the patient weekly, fortnightly, or monthly to establish perceptions of efficacy in symptom management, or perform any blood

tests, specialist reviews, or other investigations (as needed) for the particular medical condition and/or symptoms being treated;
- an exit strategy for situations where the medicinal cannabis product is not helping to manage the symptoms, the goals of treatment are not reached, or the patient is dissatisfied; and
- that informed consent has been obtained and the patient provided with information about the medicinal cannabis product, possible side effects and treatment goals, and that treatment will be discontinued if benefit has not been demonstrated.

4.3 CONTRAINDICATIONS[34]

ARUMA FLOWER 'SOLARIS' is contraindicated in patients who:
- have hypersensitivity to cannabinoids or to any of the excipients
- have a personal or family history of serious psychiatric disorders (particularly schizophrenia)
- have unstable or severe cardio-pulmonary disease
- are pregnant, planning on becoming pregnant or are breastfeeding. See Use in Lactation under section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Clinical trials have not yet been undertaken with ARUMA FLOWER 'SOLARIS' . However, use of other medicinal cannabis products have resulted in mild or moderate dizziness or other intoxication-like reactions being commonly reported. This is most frequent in the first few weeks of treatment.

Abuse potential

Patients who have a history of substance abuse may be more prone to abuse of THC containing medicinal cannabis products such as ARUMA FLOWER 'SOLARIS' (see Clinical Trials under section 5.1 PHARMACODYNAMIC PROPERTIES). In patients with a history of addictions or drug seeking behaviour, a risk management strategy such as management of the frequency of dispensing may be advised.

Use in hepatic impairment

No specific studies have been carried out in patients with significant hepatic impairment, therefore if ARUMA FLOWER 'SOLARIS' is used by such patients, frequent review by a physician is recommended.

Use in renal impairment

No specific studies have been carried out in patients with significant renal impairment, therefore if ARUMA FLOWER 'SOLARIS' is used by such patients, frequent review by a physician is recommended.

Use in the elderly

Elderly patients (> 65 years) may be more prone to develop some adverse reactions, such as dizziness and drowsiness, and/or fatigue.

In a clinical trials of 184 CBD/THC patients aged over 65 years, the most common side effects experienced were dizziness and drowsiness (12.1%), and fatigue (11.2%)[37].

Effects on laboratory tests

Patients should be informed that measurable concentrations of THC can be detected in saliva for many hours after administration and in urine for several days after use[38].

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

General

Care should be taken with hypnotics, sedatives and drugs with potential sedating effects as there may be an additive effect on sedation and muscle relaxing effects.

ARUMA FLOWER 'SOLARIS' may interact with alcohol, affecting co-ordination, concentration, and reaction-time. In general, alcoholic beverages should be avoided whilst using ARUMA FLOWER 'SOLARIS', particularly at the commencement of treatment or when changing the dose.

THC/CBD has been observed to induce drug metabolizing enzymes and transporters in vitro[39]

Hormonal contraceptives

ARUMA FLOWER 'SOLARIS' may affect hormones and their receptors in women and men. Therefore, it is recommended that women using systemically acting hormonal contraceptives should exercise caution and consider adding an additional method of contraception for the duration of therapy and for three months after discontinuation of therapy.[40]

UGT enzymes

In an in vitro study THC/CBD was found to inhibit the UGT enzymes, UGT1A9 and UGT2B7 at concentrations that could be achieved in the clinic[41].

Care should be taken when prescribing ARUMA FLOWER 'SOLARIS' with concomitant medications which are solely metabolised by both or either of these UGTs (e.g. Propofol and certain antivirals). Patients with genetic glucuronidation disorders (e.g. Gilbert's disease) may exhibit increased serum concentrations of bilirubin and must be treated with caution when ARUMA FLOWER 'SOLARIS' are co-administered[42].

CYP Enzymes

Most cannabinoid metabolism occurs in the liver and involves the CYP450 pathway. THC accumulates in fatty tissue and is released slowly from this storage site. It is not clear if THC also persists in the brain.

Concomitant administration of cannabis with other drugs that influence the hepatic CYP family enzymes may greatly alter the metabolism of the cannabinoids (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE - HEPATIC IMPAIRMENT)[43],[44]

Co-administration of ARUMA FLOWER 'SOLARIS' with other drugs that are metabolised through these cytochrome P-450 enzymes may accelerate the metabolism and reduce the activity of these other drugs such as coumarins, statins, beta-blockers and corticosteroids. When sensitive CYP substrates are co-administered with ARUMA FLOWER 'SOLARIS', review of their dosing regimen is advised.

The two main components of ARUMA FLOWER 'SOLARIS', tetrahydrocannabinol (THC) and cannabidiol (CBD) are metabolised by the cytochrome P_{450} enzyme system.

Concomitant treatment with CBD/THC and the CYP3A4 inhibitor ketoconazole, has been shown to produce an increase in C_{max} and AUC of THC (1.2- and 1.8-fold, respectively), its primary metabolite 11-OH-THC (3- and 3.6- fold, respectively) and of CBD (2- and 2-fold, respectively).[45].

Therefore, if concomitant drug treatment with CYP3A4 inhibitors (e.g. itraconazole, ritonavir, clarithromycin) is started or stopped during treatment with ARUMA FLOWER 'SOLARIS', a new titration of the dosage may be required (see section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Following treatment with CBD/THC and the CYP3A4 inducer rifampicin, reductions in Cmax and AUC of THC (40% and 20% reduction, respectively), its primary metabolite 11- OH-THC (85% and 87% reduction, respectively), and CBD (50% and 60% reduction, respectively), were observed.[46].

Therefore, if concomitant drug treatment with strong enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St John's Wort) is started or stopped during treatment with ARUMA FLOWER 'SOLARIS', a new titration of the dosage may be required.

Concomitant treatment with a CBD/THC containing product together with the CYP2C19 inhibitor omeprazole resulted in no notable change in any of the pharmacokinetic parameters[47].

In vitro, the components of a CBD/THC mixture did not have any effect on a range of human ABC transporters, uptake transporters or P-gp inhibition at clinically relevant plasma concentrations[48].

Based on in vitro data an inhibition of p-glycoprotein at the intestinal level by CBD cannot be excluded. Therefore, caution is recommended upon concomitant treatment with digoxin and other drugs being substrates for p-glycoprotein.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

There is limited research on the effects of THC and CBD on fertility in human populations. Fertility in rats was unaffected by oral treatment with a 1:1 mixture of THC BDS and CBD BDS, at doses up to 12.5 mg/kg/day or each active component which is in excess of clinically relevant dosage.[49]

Effects on various male reproductive parameters have been reported with cannabinoids in some animal studies, but findings were inconsistent or observed at high/toxic doses and their clinical significance is uncertain.[50]

Use in Pregnancy

Category B2.

Medicinal Cannabis use during pregnancy is contraindicated.

Use in Lactation

In view of the considerable levels of cannabinoids likely in maternal breast milk and the potential adverse developmental effects in infants, ARUMA FLOWER 'SOLARIS' are contraindicated in breast feeding mothers (see section 4.3 CONTRAINDICATIONS).

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

ARUMA FLOWER 'SOLARIS' may produce undesirable effects such as dizziness and somnolence which may impair judgement and performance of skilled tasks.

Patients should be advised that they are not able to drive while taking medicinal cannabis, including ARUMA FLOWER 'SOLARIS', as it may cause drowsiness and sedation.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most commonly reported side effect when taking medicinal cannabis products is mild or moderate dizziness and disorientation. For most patients, this is most frequent in the first few weeks of treatment.[51]

In clinical trials for medicinal cannabis extracts, psychiatric adverse events including disorientation, depression, euphoric mood and dissociation have been reported to occur more frequently in patients given THC/CBD than in those given placebo.[52],[53]

Clinical trials have not been undertaken with ARUMA FLOWER 'SOLARIS'. Reported side effects of THC/CBD containing products from published literature by indication are presented in Table 1.

Table 1 Reported side effects of THC/CBD containing products from published literature by indication

Indication	Most Commonly Reported Adverse Events	Percentage
Multiple Sclerosis[54]	• dizziness • somnolence dysphoria • euphoria • feeling 'high' • diarrhoea • vertigo • cognitive impairment	Percentages not reported
Palliation[55]	• somnolence • nausea • dizziness • confusion • vomiting • tiredness/fatigue • anaemia • pain • asthenia • diarrhoea	20% 21% 16% 10% 11% 12% 11% 10% 13% 8% 8%

Indication	Most Commonly Reported Adverse Events	Percentage
	• headache • dyspnea • hallucinations • in a small (15 patient) study, 11 had anxiety symptoms.	8% 5% 15%
Paediatric Epilepsy[56]	• Diarrhoea • Somnolence • Decreased appetite • Increased appetite • Worsening of seizures • Pyrexia • Convulsion • Fatigue • Status epilepticus • Gastrointestinal problems • Irritability • Weight gain • Weight loss • Nausea • Behavioural difficulties • Vomiting	20% 18% 17% 17% 15% 13% 12% 11% 10% 9% 8% 7% 7% 7% 7% 6%
Nausea and Vomiting[57]	• dysphoria and or depression • hallucinations • paranoid delusions • drowsiness • dry mouth	13% 6% 5% Unknown Unknown
Chronic non-cancer pain[58]	• Dizziness or vertigo (n=23) • Depressed mood (n=6) • Cognitive or attention disturbance (n=12) • Thought disturbance (n=6) • Nausea (n=14) • Drowsiness (n=19)	Percentages not reported

Serious Adverse Events

Acute toxicity of THC/CBD[59]

Medicinal cannabis products are generally regarded as having low acute toxicity. In mammals the median lethal dose of THC has been estimated to be >800mg/kg. CBD appears to be of very low toxicity. Doses of 1000mg/kg CBD appear to have been tolerated safely in humans.[60]

Reporting suspected adverse effects

Reporting suspected adverse reactions is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

There is no experience of overdose with ARUMA FLOWER 'SOLARIS' in patients.

Signs and symptoms of acute cannabinoid intoxication reactions including dizziness, hallucinations, delusions, paranoia, tachycardia or bradycardia with hypotension.

In the case of overdose, treatment should be symptomatic and supportive. For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Other Analgesics and Antipyretics ATC
Code: N02BG10

Mechanism of Action

There are at least two types of cannabinoid (CB) receptors as part of the human endocannabinoid system. CB_1 is found mainly in nerve terminals in the CNS where it modulates neurotransmitter release and CB_2 is found primarily in cells of the immune system. THC, the main psychotropic constituent of cannabis, acts as a partial agonist at both CB_1 and CB_2 receptors[61]

Clinical trials

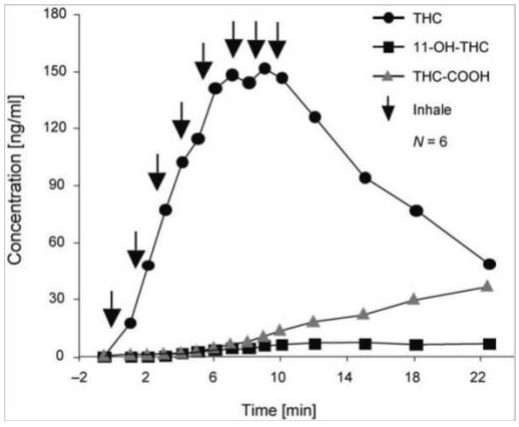
Australian clinical trials supporting the efficacy and safety of the use of medicinal cannabis are limited. Clinical trials with ARUMA FLOWER 'SOLARIS' have not yet been undertaken.

5.2 PHARMACOKINETIC PROPERTIES[62]

Absorption

Medicinal cannabis dried flower products consumed via inhalation are more rapidly absorbed than orally ingested medicinal cannabis products. Onset is rapid, with effects generally being felt within 1-15 minutes. Bioavailability of vapourised cannabinoids is high (up to 30-60 per cent). Peak effects generally occur 20-30 minutes after consumption. Effects typically last between 2-4 hours - see Figure 1.

Figure 1 Concentration of THC and its metabolites after inhalation[63].



Distribution

As cannabinoids are highly lipophilic, they are quickly absorbed and distributed into body fat. The resultant concentrations in the blood following inhalation administration are higher than those obtained by orally administering the same dose of THC because absorption is higher and redistribution into fatty tissues is rapid.

THC and CBD may be stored for as long as four weeks in the fatty tissues from which they are slowly released at sub-therapeutic levels back into the blood stream, then metabolised and excreted via the urine and faeces.

Metabolism

THC and CBD are metabolised in the liver, and approximately one third of the parent drugs and their metabolites are excreted in the urine (the remainder via the faeces). Several THC metabolites may be psychoactive. Additionally, some of the THC undergoes hepatic first pass metabolism to 11-OH-THC, the primary metabolite of THC, and CBD similarly to 7-OH-CBD. Human hepatic P_{450} 2C9 isozyme catalyses the formation of 11-OH-THC, the primary metabolite, which is further metabolised by the liver to other compounds including 11-nor-carboxy-Δ9-THC (THC-COOH), the most abundant metabolite in human plasma and urine. The P450-3A subfamily catalyses the formation of other hydroxylated minor metabolites. CBD is extensively metabolised and more than 33 metabolites have been identified in urine. The major metabolic route is hydroxylation and oxidation at C-7 followed by further hydroxylation in the pentyl and propenyl groups. The major oxidised metabolite identified is CBD-7-oic acid containing a hydroxyethyl side chain[64].

See section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS for information on drug interaction and metabolism by the cytochrome P_{450} enzyme system.

Excretion

From the literature, elimination of inhaled cannabinoids from plasma is bi-phasic with an initial half-life of approximately four hours and the terminal elimination half-lives are of the order of 24 to 36 hours or longer.

THC and its metabolites are excreted through faeces and urine. It may take up to five days for 80 to 90 per cent of the total dose to be excreted. THC may be detectable in the urine many days after ceasing use. See Section 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

N/A

6.2 SHELF LIFE

The shelf life of ARUMA FLOWER ‘SOLARIS’ is 12 months.

6.3 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C, away from heat, light and moisture. **KEEP OUT OF REACH OF CHILDREN**

6.4 NATURE AND CONTENTS OF CONTAINER

Medical-grade, plastic tub with a foil-induction seal and a tamper evident cap.

Each unit contains 10g of ARUMA FLOWER 'SOLARIS'.

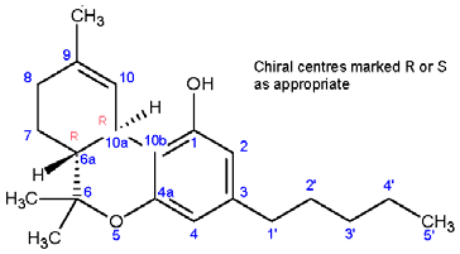
6.5 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to any pharmacy.

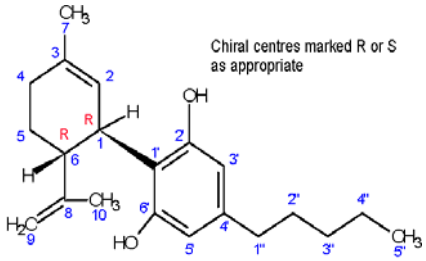
6.6 PHYSICOCHEMICAL PROPERTIES

Chemical Structure

The chemical structures of THC and CBD are shown below:



delta-9-Tetrahydrocannabinol



Cannabidiol

CAS number and molecular formula

THC is trans-delta[9]-tetrahydrocannabinol. The molecular formula of THC is $C_{21}H_{30}O_2$, its molecular weight is 314.47, and it is assigned CAS Number 1972-08-3.

CBD is cannabidiol. The molecular formula of CBD is $C_{21}H_{30}O_2$, its molecular weight is 314.47 and it is assigned CAS Number 13956-29-1.

7. MEDICINE SCHEDULE (POISONS STANDARD)

Poison schedule: Controlled Drug - Schedule 8

8. SPONSOR

Aruma Labs Pty Ltd
Level 24, Tower Three
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Barangaroo NSW 2000
Phone: 1 300 30 10 10
Email: info@arumalabs.com.au

This product is an unapproved product in Australia that is available only through the Special Access Scheme – Category B and by Authorised Prescribers of medicinal cannabis products.

ARUMA FLOWER 'SOLARIS' is a trademark of Aruma Labs Pty Ltd.

9. DATE OF REVISION

This Product Monograph was prepared in June 2022.

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