SANTÉ CANNABIS

DETERMINING THE RIGHT TREATMENT

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DISCLOSURE

- The Prescriber Training Program is supported by an unrestricted educational grant provided by Spectrum Therapeutics
- Funding facilitates the program offered free-of-charge to all Quebec physicians
- No service fees for patients to access shared-care education service
- Santé Cannabis is identified as a Contractual Research Organization (CRO) and collaborates with select companies (pharma industry) in research consultations and clinical trials

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DISCLOSURE

Dr Alain Watier is:

- A speaker on Cannabis for Therapeutic Purposes
  (physicians, pharmacists, nurses, trainees in medicine and pharmacy)
- Member of the advisory committee for cannabis for therapeutic purposes:
  Canopy Growth Corporation, Tilray, Aurora
- Conferences subsidized by medical cannabis licensed sellers
- Author of Webinars on the subject

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DETERMINING THE RIGHT TREATMENT

OVERVIEW

- MEDICAL CANNABIS ADMINISTRATION
- THC & CBD
- TERPENES & STRAINS
- INDICATIONS FOR MEDICAL CANNABIS
- PATIENT ASSESSMENT
- DOSING MEDICAL CANNABIS
- SIDE EFFECTS

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PRESENTATION OBJECTIVES

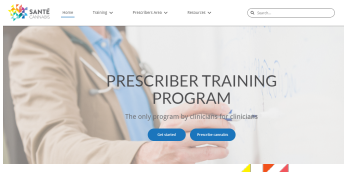
With this presentation, you will have an overview of:

- Medical cannabis formats
- Administration
- Patient assessment
- Treatment initation
- Side effects management

For more in-depth training, Santé Cannabis developed the

Prescriber Training Program

- Prescriber Guidebook
- Self-learning Modules
- Ongoing training opportunity



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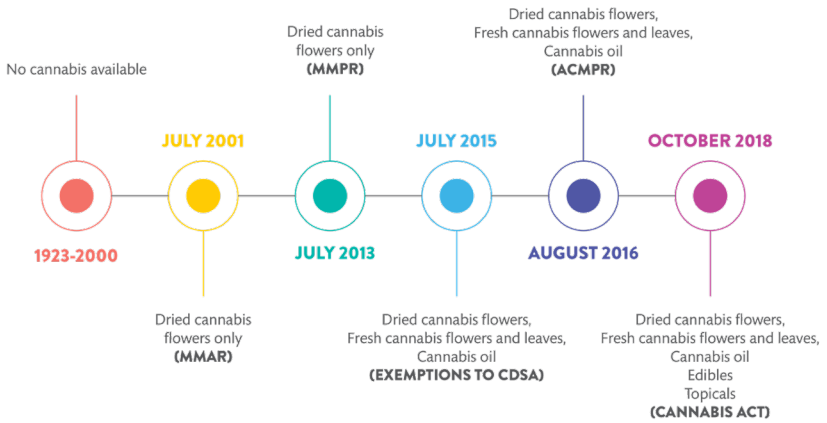
CANNABIS PRODUCTS IN CANADA



ABBREVIATIONS:
ACMPR: Access to Cannabis for Medical Purposes Regulations
CDSA: Controlled Drug and Substance Act
MMAR: Medical Marijuana Access Regulation
MMPR: Marijuana for Medical Purposes Regulations

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CANNABIS: MEDICAL VS PHARMACEUTICAL

Pharmaceutical cannabinoids	Medical cannabis
• Have a **Drug Identification Number** (DIN)	• no Drug Identification Number (DIN)

• **Synthetized** cannabinoid
  • Nabilone/Cesamet™, THC analog
• or specific **formulation** containing **purified** cannabis extracts
  • Nabiximols/Sativex™, with THC+CBD
	• **Cannabis flowers**,
	• **Whole-plant** oil extracts

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CANNABIS ADMINISTRATION

1) Oral
2) Oromucosal
3) Inhaled
4) Topical

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ADMINISTRATION METHODS – **ORAL**

Cannabis products:

- Cannabis oil
- Capsules
- Pharmaceutical cannabinoids (nabilone/Cesamet™)

Cannabinoid concentrations:

- CBD-rich: contains CBD and small amount of THC
- THC-rich: contains THC and small amount of CBD
- Balanced THC and CBD: contains both cannabinoids in a ratio of about 1:1

Onset of action: 1 to 2 hours

Duration of effects: 6 to 8 hours

Could be compared to "long action" prescription drugs

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ADMINISTRATION METHODS – **OROMUCOSAL**

Cannabis products:

- Nabiximols/Sativex™ (pharmaceutical cannabinoids formulation). Oromucosal spray directed under the tongue or inside the cheek

Cannabinoid concentrations:

- Balanced THC and CBD: contains both cannabinoids in a ratio of about 1:1 [nabiximols]

Onset of action: 30 min to 1 hour

Duration of effects: 4 to 6 hours

Faster onset of action compared to cannabis oils and capsules

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ADMINISTRATION METHODS – **INHALED**

Cannabis products:
- Dried cannabis

Inhalation method:
- With a vapourizer [strongly recommended]
- smoked

Vapourizer: device that heats dried cannabis, creating a vapour carrying cannabinoids
- Lower heat than with smoking
- Does not burn cannabis
- Reduce exposure to combustion by-products (compared to smoking)

Cannabinoid concentrations:
- CBD-rich: contains CBD and small amount of THC
- THC-rich: contains THC and small amount of CBD
- Balanced THC and CBD: contains both cannabinoids in a ratio of about 1:1

Onset of action: 5 to 15 min

Duration of effects: 2 to 4 hours

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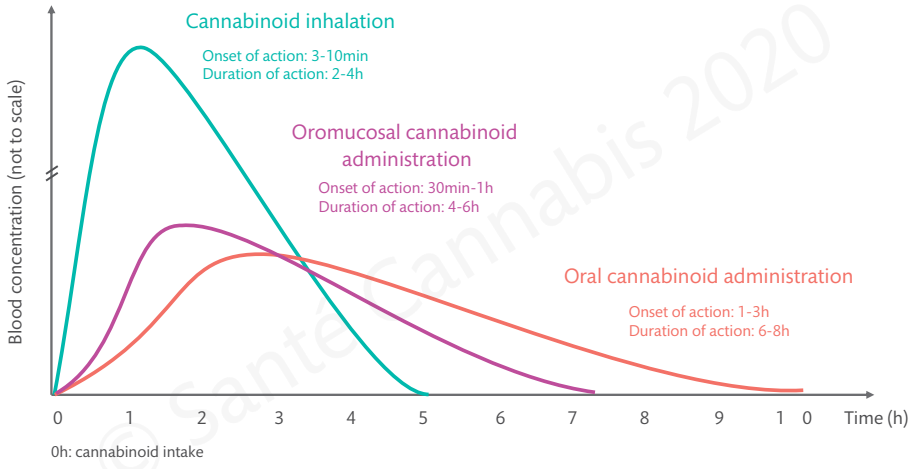
CANNABINOID ADMINISTRATION & ABSORPTION



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Qualitative representation of cannabinoid absorption

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ADMINISTRATION METHODS –**TOPICAL**

Santé Cannabis, sometimes considers topical products in addition to a baseline treatment; there are no extensive clinical results supporting topical products at the moment

More research is needed on this method of administration

Cannabis products:

- Creams and oils
- Drops
- Suppositories

Cannabinoid concentrations:

- CBD-rich: contains CBD and small amount of THC
- THC-rich: contains THC and small amount of CBD
- Balanced THC and CBD: contains both cannabinoids in a ratio of about 1:1

Onset of action: variable

Duration of effects: variable

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PHARMACEUTICAL CANNABINOIDS

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PHARMACEUTICAL CANNABINOIDS

SATIVEX™ (NABIXIMOLS):

- Oromucosal spray of THC and CBD (natural cannabis extract)
- Indicated for spasticity related to **multiple sclerosis**
- Could also help for moderate to severe **pain related to advanced cancer and multiple sclerosis**

NABILONE (CESAMET™):

- Capsule (Tablet) or syrup of synthetic THC analogue
- Indicated for **chemotherapy-related nausea/vomiting**
- Could also help relieve **pain** and improve **sleep**

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PHARMACEUTICAL CANNABINOIDS

DRONABINOL (MARINOL™):

- Synthetic THC tablet/synthetic THC syrup
- Indicated for **chemotherapy-related nausea/vomiting**
- Indicated for the treatment of **anorexia** in HIV/AIDS patients.
- May also help relieve **pain** and improve **sleep**

EPIDIOLEX™ (CBD):

- Pure CBD oral solution
- Indicated for **convulsions** in patients with Lennox-Gastaut syndrome or Dravet's syndrome.
- Indicated in children and adults

*** Epidiolex and Dronabinol are not available in Canada**

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ADMINISTRATION METHODS – SUMMARY

Depending on the administration method, a dose may last for a longer or shorter period of time :

Product	Cannabis Oil	Capsules	Oromucosal Spray	Dried Cannabis	Topical products
Administration	oral	oral	oromucosal	inhalation	topical
Example					creams, drops, suppositories
Onset of action:	Slow 1-2 hours	Slow 1-2 hours	Intermediary 30 min-1 hour	Fast 5-15 minutes	Variable
Length of action	Long 6-8 hours	Long 6-8 hours	Intermediary 4-6 hours	Short 2-4 hours	Variable

*Available in Canada

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THC AND CBD

Therapeutic properties of these cannabinoids

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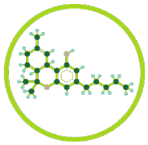
THERAPEUTIC PROPERTIES OF THC AND CBD



THC

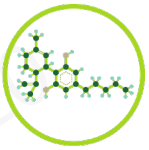
- **Psychoactive effects**

- Analgesic
- Anti-emetic
- Anti-spasmodic
- Anti-inflammatory
- Sedative
- Stimulates the appetite
- Anxiolytic *

CBD

- **May reduce THC's psychoactive effects**

- Anti-convulsant
- Anti-inflammatory
- Mild Analgesic
- Anxiolytic
- Anti-spasmodic
- Anti-psychotic



Precautions regarding psychoactive effects

Non-intoxicating cannabinoid

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MAXIMUM DOSE - DATA FROM LITERATURE

Clinical studies with oral THC:

- Doses up to **25-28 mg** THC/day in patients with multiple sclerosis (Zajicek et al. 2003, 2013)
- Doses of **20-40 mg** THC/day have been used to stimulate appetite in patients with HIV (Bedi at al. 2010)

Max 50 mg / day

Clinical studies with oral CBD:

- Doses of **75 to 600 mg** CBD/day in patients with Parkinson's disease (Crippa et al. 2019; Kluger et al. 2015)
- For anxiety, doses of **400 to 600 mg** CBD/day (Bergamaschi et al. 2011; Crippa et al. 2011)
- In healthy volunteers, doses of **1500 to 6000 mg** of CBD with no serious or severe side effects (Taylor et al. 2018)
- In children with epilepsy (Dravet, Lennox-Gastaut), doses of 20 mg/Kg/day up to 50 mg/Kg/day.

→ 2000-3000 mg / die

In a medical context, CBD doses can be much higher than THC doses;

In clinical practice at Santé Cannabis:
max 50mg THC/day
max 120mg CBD/day (for financial considerations)

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TERPENES

And entourage effect

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TERPENES AND FLAVONOIDS

Terpenes (or terpenoids) and flavonoids are a large group of plant compounds found in cannabis and many other types of plants.

- Terpenes are generally responsible for the distinct aroma and flavor associated with cannabis strains
- Flavonoids are responsible for the color
- Terpenes are pharmacologically active and well tolerated

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SOME TERPENES IN CANNABIS

Alpha-pinene	Linalol	Beta-caryophyllene	Myrcene	Limonene
Also present in pine needles	Also present in lavender	Also present in black pepper	Also present in hops	Also present in citrus fruits
Anti-inflammatory Bronchodilator Antibacterial Good for memory	Anesthetic Anti-convulsant Analgesic Anxiolytic	Anti-inflammatory Analgesic Antispasmodic Anticolitics	Anti-inflammatory Sedative Sleeping aid Muscle relaxant	Sedative Antiseptic Anxiolytic Antidepressant

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THE ENTOURAGE EFFECT

- Hypothetical synergy between cannabis compounds (including cannabinoids, terpenes, flavonoids and others)
- Supported by anecdotal evidence that whole cannabis could have magnified therapeutical benefits (hypothetical multiple compounds synergy) than isolated compounds
- Further research is needed on the subject

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CANNABIS STRAINS : SATIVA VS INDICA

Cannabis sativa:

Said to be more energizing and stimulating

Cannabis indica:

Said to be more sedative or calming

Hybrid:

As there has been a lot of cross-breeding and hybridization of cannabis over the centuries,

We mostly find **hybrid** strains on the market today

**sativa, indica* and *hybrid* terms are not scientific designations

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INDICATIONS FOR CANNABIS

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INDICATIONS FOR MEDICAL CANNABIS

Diagnosis for which scientific studies **support** the benefits of cannabis for medical purposes:

- Chronic pain, related or not to cancer and neuropathic pain
- Chemotherapy-induced nausea and vomiting
- Refractory epilepsy
- Multiple sclerosis (spasticity)

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INDICATIONS FOR MEDICAL CANNABIS

Diagnosis for which scientific studies support **favourably or to a limited extent** the benefits of cannabis for medical purposes :

- Sleep Disorders
- Headaches and migraines
- Anxiety and depression
- Post-Traumatic Stress Disorder
- Dementia
- Parkinson's disease
- Alzheimer's disease
- Post-traumatic brain injury
- Tourette's Syndrome
- Crohn's Disease and Ulcerative Colitis
- Glaucoma

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PATIENT ASSESSMENT

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PATIENT ASSESSMENT

*Before considering medical cannabis, **a patient must have unsuccessfully tried conventional treatments** [as per the 2018 directives of the Collège des Médecins du Québec]

When considering medical cannabis, it is important to check if:

1. The patient has a valid **indication** for cannabis;
2. The patient presents **no contraindication**;
3. Any special **precautions** have been identified;
4. Any **drug interactions** have been identified;

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CONTRAINDICATIONS

Current exclusions at Santé Cannabis

- Pregnancy, planned pregnancy and breastfeeding
- Unstable/uncontrolled heart diseases (arrhythmia, ischemia, hypertension)
- Current or personal history of psychosis or schizophrenia

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PRECAUTIONS

Proceed with caution (especially with THC):

- ❑ Patients under 25 years old
- ❑ Allergy or hypersensitivity to cannabinoids
- ❑ Severe hepatic or renal dysfunction
- ❑ Personal history of substance abuse
- ❑ Severe lung disease (inhaled cannabis)
- ❑ Naive patient vs patient with previous cannabis experience
- ❑ History of cannabis-related side effects
- ❑ Elderly patient
- ❑ Patient with multiple drug intolerances
- ❑ Polymedicated patient

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DRUG INTERACTIONS

- Cannabis interacts with other drugs
- Clinically significant interactions are rare

Rationale for drug interactions:

- THC and CBD are metabolized by enzymes of the CYP450 (CYP34A and CYP2C19 primarily)
- THC and CBD also inhibit enzymes of the CYP450

*Although there is only one article on the subject:

Immunotherapy could be less efficient with cannabis

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MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *European Journal of Internal Medicine*. 2018;49:12-19.

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Medication	Potential Interaction	Monitoring
Warfarin	↑ Warfarin anticoagulant activity	Monitor INR closely and ↓ the warfarin dose accordingly
Clobazam (Epilepsy)	CBD may increase the plasma concentration of active metabolites	Serum drug levels, liver function and side effects should be monitored. Clobazam doses should be decreased as CBD doses are increased.
Valproate (Epilepsy)	CBD may increase hepatic enzymes levels	Close monitoring of AST ALT is advised. Caution should be exercised with patients taking drugs known to be substrates for CYP450 enzymes: amitriptyline, fentanyl and derivatives
Clozapine, duloxetine with smoked cannabis	↓ plasma levels	↓ la dose de cannabis ou ↑ le médicament en conséquence
Cyclosporin	CBD may ↑ cyclosporine plasma levels	Monitor plasma drug levels closely and decrease/readjust the dose accordingly.
Tacrolimus (Anti-rejection)	CBD may ↑ tacrolimus plasma levels.	Monitor plasma drug levels closely and readjust the dose accordingly
Stiripentol (Epilepsy)	Plasma level of Stiripentol might ↑	Monitor for cannabinoid side effects and ↓ the dose accordingly
Ketoconazole (Antifongic)	↑ CBD and THC plasma levels	Monitor for cannabinoid side effects and ↓ the dose accordingly
Rifampicin (Antibiotic)	Decreases plasma CBD and THC levels	Higher doses of cannabinoids might be needed for symptom control

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DOSING MEDICAL CANNABIS

- Dosing frequency
- Titration
- First dose

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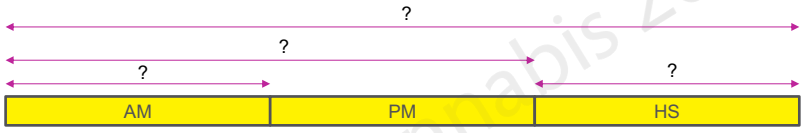
DOSING FREQUENCY

The frequency of the doses depends on the targeted symptom:

- When is the symptom present?
- How long does it last?



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DOSING FREQUENCY

Once daily (DIE) - typically at bedtime (HS)

Ex: patient with insomnia

AM	PM	Dose HS

2 doses daily (BID)

Ex: patient suffering from epilepsy; starting the treatment with 2 doses in the day

Dose AM	Dose PM	HS

3 doses daily (TID)

Ex: patient with pain 24h/24

Dose AM	Dose PM	Dose HS

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DOSING FREQUENCY

With 2 doses/day or 3 doses/day as a baseline treatment,

- If a symptom is not completely relieved and/or varies in intensity

Such as:

- Pain peak,
- Migraine/headache,
- Anxiety attack, ...

For quick relief, consider adding :

- Inhaled dried cannabis *when needed (PRN)*

or

- Oromucosal spray *when needed (PRN)*

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TITRATION

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TITRATION

Why titrate with medical cannabis?

- There is no well-known or fixed dose per application
- Dosage must be individualized and is largely based on dosage adjustment
- Need to go through trial and error on a regular basis

Titration method:

- Start with very low doses, which may be ineffective to relieve symptoms
- Slowly increase to a dose that relieve symptoms without side effects

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TITRATION

Usefulness of titration:

- The endocannabinoid system develops a certain tolerance when constantly exposed to a ligand
- Helps to reduce the side effects of cannabis-based treatment

Always remember:

- **Start low, go slow**

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TITRATION

Some concepts

- Patients don't have to feel "high" to benefit from the positive effects of medical cannabis.
- The symptomatic response precedes the euphoric experience
- Once the optimal dose has been reached, it usually remains stable
- Escalation of doses is not necessary
- During treatment initiation and the adjustment phase, no changes are made to the patient's current medication

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TITRATION

Nabilone and Sativex

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TITRATION – **Nabilone (Cesamet™)**

- Capsule (Tablet) of synthetic THC analogue
- Indicated for **chemotherapy-related nausea/vomiting**
- Can also help relieve pain and improve sleep
- Available in 0.25mg, 0.5mg and 1mg capsules or syrup (0.5mg/5mL)

- ➢ For the first few days of treatment, start with 0.25mg doses
- ➢ Gradually increase to 0.5mg doses or more as needed.
- ➢ Maximum recommended dose: 6mg in divided doses (ex: 2 mg TID)

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TITRATION – Nabiximols (Sativex™)

- Oral spray of THC and CBD (natural cannabis extract)
- Indicated for spasticity related to **multiple sclerosis**
- Can help relieve neuropathic pain related to **multiple sclerosis**
- Can help relieve moderate to severe **pain related to advanced cancer**

Bedtime dose (HS)

SATIVEX™	HS
Days 1-2-3	1 spray
Days 4-5-6	2 sprays
Days 7-8-9	3 sprays
Days 10-11-12	4 sprays
…	…

- Start with a low dose
- Lowest possible dose: 1 spray = 100ul = 2.7 mg THC + 2.5 mg CBD
- *Maximum 12 sprays/day

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*GW Pharma Ltd. Product Monograph Sativex. 2015. https://www.bayer.ca/omr/online/sativex-pm-en.pdf. Accessed March 29, 2019.

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TITRATION – Nabiximols (Sativex™)

- Start with a low dose
- Lowest possible dose: 1 spray = 2.7 mg THC + 2.5 mg CBD

2 doses per day (BID)

SATIVEX™	AM	PM
Days 1-2-3		1 spray
Days 4-5-6	1 spray	1 spray
Days 7-8-9	2 sprays	2 sprays
Days 10-11-12	3 sprays	3 sprays
Days 13-14-15	4 sprays	4 sprays
…	…	…

3 doses per day (TID)

SATIVEX™	AM	PM	HS
Days 1-2-3			1 spray
Days 4-5-6	1 spray		1 spray
Days 7-8-9	1 spray	1 spray	1 spray
Days 10-11-12	2 sprays	2 sprays	2 sprays
Days 13-14-15	3 sprays	3 sprays	3 sprays
…	…	…	…

*Maximum 12 sprays/day

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*GW Pharma Ltd. Product Monograph Sativex. 2015. https://www.bayer.ca/omr/online/sativex-pm-en.pdf. Accessed March 29, 2019.

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TITRATION

Cannabis oils and capsules

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TITRATION – OILS AND CAPSULES

For patients who have little or no experience with cannabis

- **CBD-rich oil** : Start with 5 mg of CBD and increase by 2.5 mg of CBD every 3 days.
- **Balanced THC and CBD oil** : Start with 1.25 mg of THC and 1.25 mg of CBD and increase by 1.25 mg of THC and CBD every 3 days.
- **THC-rich oil** : Start with 1.25 mg THC and increase by 1.25 mg THC every 3 days.

General advice :

- CBD-rich or THC:CBD oil during the day; THC-rich oil at night
- Start with CBD up to a 12.5mg dose, then add THC if CBD alone is not effective (if indicated)

Also, it is recommended to make only one change at a time

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TITRATION – OILS AND CAPSULES

<u>For more sensitive, elderly or fragile patients :</u>

- Slower titration, for example every 5 days
- Monitor side effects carefully
- Consider a frequency of administration only once or twice a day at the beginning

<u>For patients already using cannabis or with more experience :</u>

Consider using the same approach as with inexperienced patients, but slightly faster

- Start with greater doses and increase every 3 days
- Consider reducing THC doses or increasing CBD doses for harm reduction or to reduce cannabis use

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TITRATION TABLE - IN MILLIGRAMS

Example:

CBD-Rich						
	BID		TID			HS only
	AM	PM	AM	PM	HS	HS
Days 1-2-3	------	5.0mg	---	---	5.0 mg	5.0mg
Days 4-5-6	5.0mg	5.0mg	5.0mg	---	5.0mg	7.5mg
Days 7-8-9	7.5mg	7.5mg	5.0mg	5.0mg	5.0mg	10.0mg
Days 10-11-12	10.0mg	10.0mg	7.5mg	7.5mg	7.5mg	12.5mg
Days 13-14-15	12.5mg	12.5mg	10.0mg	10.0mg	10.0mg	15.0mg
Days 16-17-18	15.0mg	15.0mg	12.5mg	12.5mg	12.5mg	17.5mg
If elderly, frail, polypharmacy or sensitivity to medication, consider making an increase every 5 days instead of 3.						

CBD: Non-intoxicating cannabinoid, easier to dose

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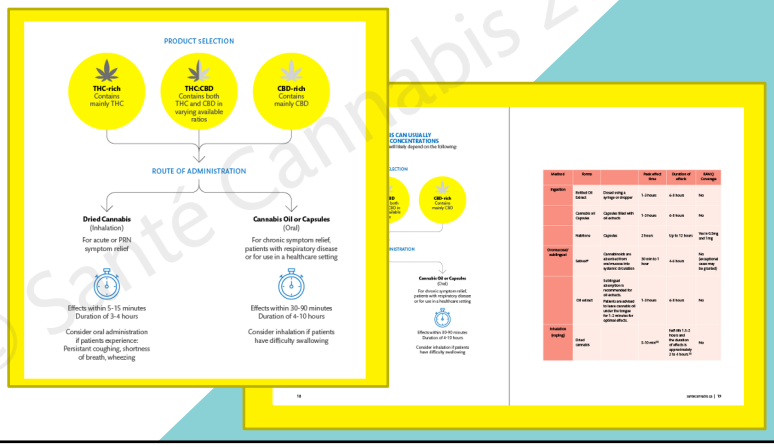
PRESCRIBER GUIDEBOOK - DOSING AND TITRATION

For more tips on how to dose and monitor your patients, our Prescriber Guidebook provides easily-to-follow titration tables, instructions for developing a treatment plan and tips for choosing the right type of treatment while mitigating side effects.



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CONVERSION MG TO MILILITRES

If you prescribe 2.5 mg of THC in the form of an oil at the concentration of 25 mg THC /ml

→ The patient should take a 0.1 ml dose with a syringe

In general, 0.05ml of THC-rich oil (that is 1.25 mg THC) is considered a safe starting dose

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TITRATION TABLE – **FOR PATIENTS** (mL)

CBD-Rich						
	BID		TID			HS only
	AM	PM	AM	PM	HS	HS
Days 1-2-3	------	0.2mL	---	---	0.2mL	0.2mL
Days 4-5-6	0.2mL	0.2mL	0.2mL	---	0.2mL	0.3mL
Days 7-8-9	0.3mL	0.3mL	0.2mL	0.2mL	0.2mL	0.4mL
Days 10-11-12	0.4mL	0.4mL	0.3mL	0.3mL	0.3mL	0.5mL
Days 13-14-15	0.5mL	0.5mL	0.4mL	0.4mL	0.4mL	0.6mL
Days 16-17-18	0.6mL	0.6mL	0.5mL	0.5mL	0.5mL	0.7mL
If elderly, frail, polypharmacy or sensitivity to medication, consider making an increase every 5 days instead of 3.						

CBD: Non-intoxicating cannabinoid, easier to dose

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TITRATION

Inhaled Dried Cannabis

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VAPORIZED DRIED CANNABIS SHOULD BE REGARDED AS COMPLEMENTARY TO CANNABIS ORALLY

IT SHOULD BE CONSIDERED AS AN IN-BETWEEN DOSE

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INHALED DRIED CANNABIS

- Vapourization is recommended
- Start with 1 inhalation

→ pause for 10-15 min, wait for the onset of effects (beneficial/undesirable)

- Gradually increase the number of inhalations, if necessary, to a dose that controls symptoms without side effects.

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INHALED DRIED CANNABIS

For inexperienced patients,

- consider a product with a balanced ratio of THC and CBD during the day
- In the evening, consider a product with a balanced ratio of THC and CBD or a product rich in THC

- If symptoms are not adequately controlled after 10 inhalations, switch to a different type of cannabis and reassess the situation

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INHALED DRIED CANNABIS

- After determining the ideal number of inhalations, vapourization periods can be repeated every 4-6 hours.

- If the patient is vapourizing every 4 hours, optimize the base treatment by readjusting the cannabis oil dosage while trying to limit vapourization episodes to an *as needed* option

To reduce side effects:

- Reduce the number of inhalations
- Do not hold breath during inhalation
- Change the type of cannabis (favoring a strain with more CBD)

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TAKING THE FIRST DOSE

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TAKING THE FIRST DOSE: CONTEXT

General advice for the patient when taking their first cannabis dose:

- Start at bedtime
  This way, the patient may not be inconvenienced by drowsiness or other possible side effects
- Or start on the weekend
  At a moment where the patient does not have any obligation to fulfil
- Take the first dose in a controlled, stress-free environment

Ideally, the patient should each day record in a diary:

- dosage time, dose, changes
- benefits experienced
- side effects experienced

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SIDE EFFECTS & INTERVENTIONS

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SIDE EFFECTS

- It's important to start at LOW DOSES and increase SLOWLY with medical cannabis.
- Side effects can be avoided with a PROGRESSIVE adjustment and close monitoring.
- Adverse effects are often associated with THC use rather than CBD.

Most common	Less common	Rare
Drowsiness	Euphoria	Panic attacks
Fatigue	Vasodilatation	Hallucinations
Dizziness	Headaches	Depression
Dry mouth	Vomiting	Cognitive impairment
Irritation of breathing passages (cough, phlegm)*	Disorientation	Ataxia/dyscoordination
Nausea	Confusion	Dysphoria, paranoia
Anxiety	Hypertension	Psychosis**
Altered judgment or decreased attention	Blurred Vision	Postural, orthostatic hypotension
Impaired motor coordination and motor performance	Change in appetite	Tachycardia
Increased appetite		Diarrhea

*With smoked cannabis
**More common in adults under 25

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MITIGATE SIDE EFFECTS

If a patient experiences a **mild** side effect, they should :

- keep the same dose; the side effect should disappear over time
- wait until the side effect has disappeared before increasing the dose

If a patient experiences a **moderate** side effect, they should :

- reduce the dose
- wait longer before increasing the dose

If a patient experiences a **severe** side effect, they should :

- Stop taking the cannabis treatment

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MITIGATE SIDE EFFECTS

Other strategies to improve treatment if the patient experiences side effects include :

- Change administration method (Capsules/Vapourization…)
- Try another cannabis variety or product with different cannabinoid concentrations.
- Discontinue treatment if these strategies do not work.

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ACTIONS TO CONSIDER DEPENDING ON SIDE EFFECTS

RECOMMENDATIONS

SIDE EFFECTS EXPERIENCED	SLOW DOWN TITRATION	REDUCE THC DOSE	INCREASE CBD DOSE	CHANGE TIMING BETWEEN DOSES	RESTART TREATMENT AFTER DISCONTINUATION PERIOD*
COGNITIVE EFFECTS	X	X	X		X
ANXIETY	X	X	X		X
EUPHORIA (OR "HIGH")			X		X
FEELING LETHARGIC, WEAK OR GENERAL BODY DISCOMFORT		X		X	X

*Restart at a lower dose

Also in our **Prescriber Guidebook**

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IN CONCLUSION

- Be careful with naive / elderly patients
- Try to avoid the euphoric effect of THC
- Promote vapourization as an "in between" dose
- Think about the timing of administration
- Start low, go slow and stay low
- Reasonable therapeutic trial: 3 months
- Think of the cost

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QUESTIONS?
COMMENTS?

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ANNEXES

- Terpene table
- Titration tables in mL
- Tolerance & dependence

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TITRATION TABLE - **FOR PATIENTS** (mL)

THC:CBD balanced						
	BID		HS	TID		
	If patient is sensitive to THC			Adults without any major contraindications		
	AM	PM	HS only	AM	PM	HS
Days 1-2-3	------	0.1mL	0.1mL	---	---	0.2mL
Days 4-5-6	0.1mL	0.1mL	0.2mL	0.2mL	---	0.2mL
Days 7-8-9	0.2mL	0.2mL	0.3mL	0.2mL	0.2mL	0.2mL
Days 10-11-12	0.3mL	0.3mL	0.4mL	0.3mL	0.3mL	0.3mL
Days 13-14-15	0.4mL	0.4mL	0.5mL	0.4mL	0.4mL	0.4mL
Days 16-17-18	0.5mL	0.5mL	0.6mL	0.5mL	0.5mL	0.5mL
Do not exceed 1mL THC per dose **If elderly, frail, polypharmacy or sensitivity to medication, consider making an increase every 5 days instead of 3.**						

CBD balances the psychoactive effects of THC

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TITRATION TABLE - **FOR PATIENTS** (mL)

THC-Rich						
	BID		TID			HS only
	AM	PM	AM	PM	HS	HS
Days 1-2-3	------	0.05mL	---	---	0.05mL	0.05mL
Days 4-5-6	0.05mL	0.05mL	0.05mL	---	0.05mL	0.1mL
Days 7-8-9	0.1mL	0.1mL	0.05mL	0.05mL	0.05mL	0.15mL
Days 10-11-12	0.15mL	0.15mL	0.1mL	0.1mL	0.1mL	0.2mL
Days 13-14-15	0.2mL	0.2mL	0.15mL	0.15mL	0.15mL	0.25mL
Days 16-17-18	0.25mL	0.25mL	0.2mL	0.2mL	0.2mL	0.3mL
Do not exceed 1mL THC per dose **If elderly, frail, polypharmacy or sensitivity to medication, consider making an increase every 5 days instead of 3.**						

THC) Precautions regarding its psychoactive effects

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TOLERANCE

- Defined as a decrease in the intensity of a substance's effects when its dosage is constant over time.
- Characterized by
  - An acceleration in the degradation of cannabinoids
  - An increase in the cannabinoid receptor stimulation threshold
  - A decrease in the number of these receptors
- During prolonged consumption of cannabinoids, the nervous system adapts to new conditions.
- At low doses and for therapeutic indications, the phenomenon of tolerance develops very little, even after several months of treatment.*

*Grotenhermen, Franjo. 2009. "Cannabis en médecine: un guide pratique des applications médicales du cannabis et du THC". Éditions Indica. Sélestat, 212p.

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DEPENDENCE

- The risk of dependence to cannabis is low even after prolonged exposure in a therapeutic context.
- Signs of withdrawal are reduced compared to alcohol, benzodiazepines, opiates.
- Patients will report excessive sweating, irritability, sleep disorders that can last for a few days to two weeks.
- It is important to assess the risk of dependence at the first assessment

→ if it is moderate to high, it is better to limit THC

- When using cannabis for **medical purposes**, the risk of dependence is low *

→ Close follow-ups can help to manage the risk of dependence

→ Cannabis is less addictive than some opioids

*Devane, W. A. et al. 1992. "Isolation and Structure of a Brain Constituent That Binds to the Cannabinoid Receptor." *Science* 258(5090): 1946–49.

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