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Medicinal Cannabis Education and Authorized Prescriber Course

Cancer Pain and Symptoms

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Presented By Dr Gull Herzberg

- There are over 200 different types of cancer
- It is estimated that 40% of people will be diagnosed with cancer at some point
- In the period 2012–2016, people diagnosed with cancer were 69% as likely to survive for at least 5 years after being diagnosed compared to the overall population.
- **5-year relative survival ranged from 11% to 95%**
  - Highest: prostate (95%), melanoma (92%) and female breast (91%)
  - Lowest: pancreas (11%), unknown primary site (13%), lung (19%), liver (20%), oesophagus (22%) and brain (22%).

Symptoms can be due to

Cancer

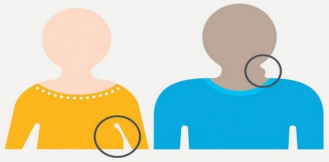
Treatment

Cancer Symptoms

Unexplained, such as

A lump or swelling

Make sure to check your whole body, not just your testicles or breasts.

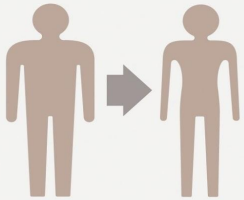


Bleeding that is not normal for you

Coughing up blood or noticing it in your urine or bowel motion is not normal. Neither is bleeding from your vagina between periods, after sex or after the menopause.

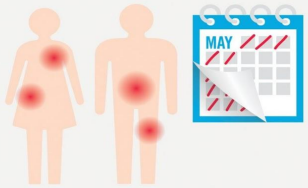
Weight loss

It is normal to see small weight changes over time. But a big weight loss, not related to dieting, may be a sign of something more serious.



Pain that does not go away

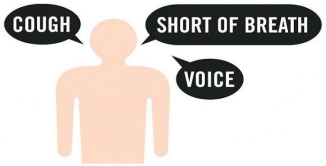
If you feel pain for more than four weeks that you cannot explain, talk to your doctor about it.



Persistent, such as

A cough, changes in your voice or feeling short of breath

Speak to your doctor if you have any of these problems for more than three weeks, especially if you are a smoker or ex-smoker.



A sore that does not heal

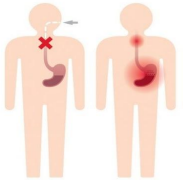
If a spot, wart or sore does not heal in a few weeks, get it checked by your doctor, even if it is painless.

Bloating

If bloating does not go away within a few weeks talk to your doctor about it.

Difficulty swallowing, indigestion or heartburn

It is not normal to have indigestion or heartburn that happens a lot or is very painful. Difficulty swallowing is not normal either. Get it checked by your doctor.



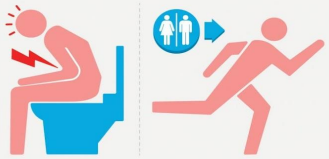
Mouth or tongue ulcer

Having a mouth or tongue ulcer for three weeks or more is not normal and needs to be checked by your doctor or dentist.

Unusual, such as

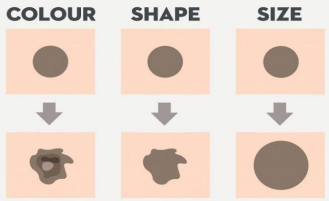
A change in your bowel or bladder habits

If you have constipation, diarrhoea or problems passing urine for more than a few weeks, talk to your doctor.



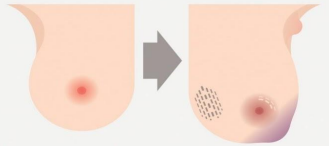
A new mole or change to an existing mole

Get into the habit of checking your skin every month for new moles. Also watch for changes in colour, shape and size of existing moles.



Any change in your breast

Get into the habit of looking at and feeling your breasts for changes in the shape, size, nipples and skin. Also watch for pain in one breast.



Cancer Focus NORTHERN IRELAND

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Cancer Symptoms

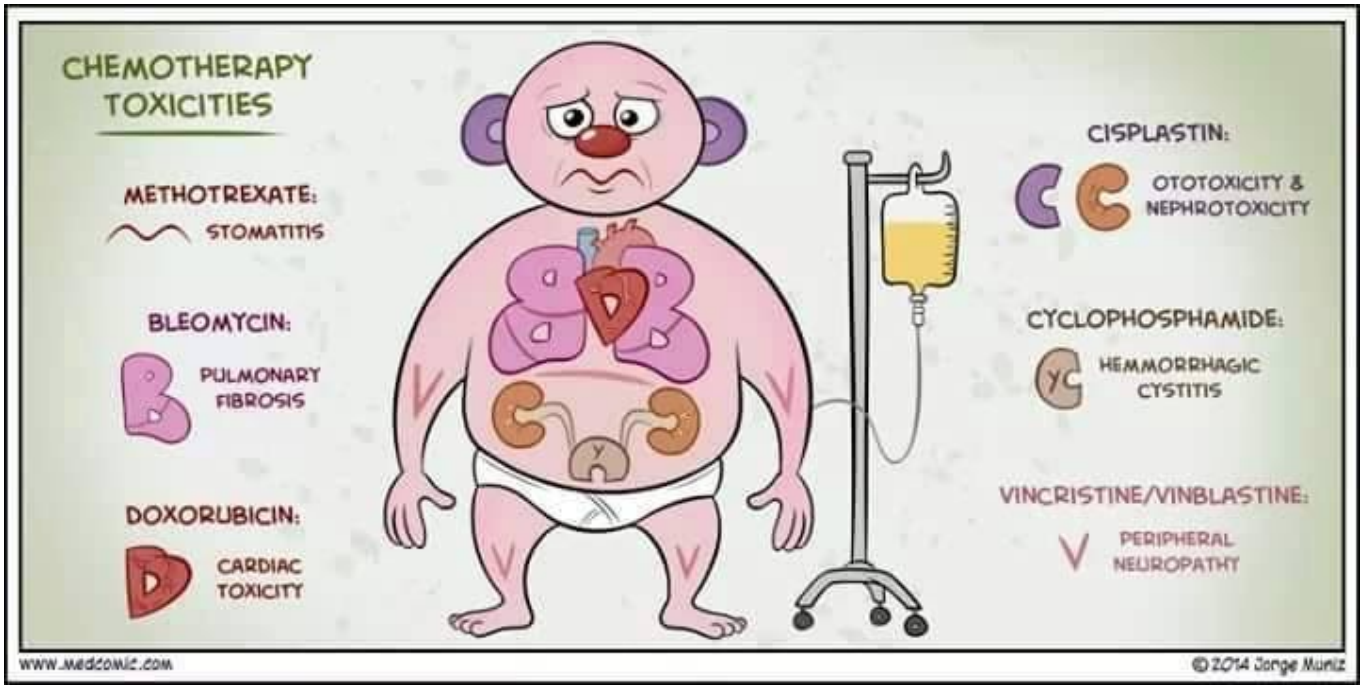
- Unexplained ache or pain
- Persistent headache or blurred vision
- Weakness in limbs and dizziness
- Abnormal sweating, especially at night
- Unexplained weight loss
- Unusual lump or swelling
- Unusual breast changes
- Seizures
- Unexplained bleeding or blood
- Fatigue
- Sore that won't heal
- New mole or changes to a mole
- Other skin changes
- Difficulty swallowing
- Loss of appetite
- Heartburn or indigestion
- Persistent cough
- Persistent sore throat
- Croaky voice or hoarseness
- Shortness of breath
- Mouth ulcer that won't heal
- Changes in bowel habits
- Blood in stool
- Change in bladder habits
- Blood in urine
- Persistent bloating

- Cancer - Common General Systemic Symptoms
  - Pain
  - Fatigue
  - Heavy Night Sweats
  - Weight Loss

Cancer – Psychological Effects

- Loss of autonomy
- Anxiety
- Depression
- Strain on personal relationships
- Impact on quality of life
- Can manifest in myriad ways

Side Effects of Cancer Treatment



Side Effects of Cancer Treatment

- Anaemia
- Appetite Loss
- Bleeding and Bruising (Thrombocytopenia)
- Constipation
- Delirium
- Diarrhea
- Oedema
- Fatigue
- Fertility Issues
- Flu-Like Symptoms
- Hair Loss (Alopecia)
- Infection and Neutropaenia
- Lymphoedema
- Memory or Concentration Problems
- Mouth and Throat Problems
- Nausea and Vomiting
- Nerve Problems (Peripheral Neuropathy)
- Immunotherapy and Organ-Related Inflammation
- Pain
- Sexual Health Issues
- Skin and Nail Changes
- Sleep Problems
- Urinary and Bladder Problems

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- Anaemia
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- Sleep Problems
- Urinary and Bladder Problems

Possible Role for Medical cannabis for these symptoms

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Review > Cureus. 2021 Sep 30;13(9):e18396. doi: 10.7759/cureus.18396.
eCollection 2021 Sep.

Medical Cannabis as Adjunctive Therapy for Head and Neck Cancer Patients

Mathew P Caputo [1], Carmen S Rodriguez [2], Tapan A Padhya [1], Matthew J Mifsud [1]

Affiliations – collapse

Affiliations

1 Otolaryngology - Head and Neck Surgery, University of South Florida Morsani College of Medicine, Tampa, USA.
2 College of Nursing, University of South Florida, Tampa, USA.

"The literature regarding the effect of cannabis/cannabinoids on head & neck cancer patients is limited. However, the current lack of evidence does not definitively disprove the efficacy of cannabis. "

Review > Can Urol Assoc J. 2021 Dec;15(12):413-419. doi: 10.5489/cuaj.7198.

Use of cannabis in urological cancer patients: A review to evaluate risk for cancer development, therapeutic use, and symptom management

Shipra Taneja [1 2 3], Jen Hoogenes [1 2 3], Marissa Slaven [4 5], Anil Kapoor [1 2 3 4]

Affiliations – collapse

Affiliations

1 Department of Surgery, Division of Urology, McMaster University, Hamilton, ON, Canada.
2 McMaster Institute of Urology, St. Joseph's Healthcare Hamilton, Hamilton, ON, Canada.
3 Urologic Cancer Centre for Research & Innovation, St. Joseph's Healthcare, Hamilton, ON Canada.
4 Juravinski Cancer Centre, Juravinski Hospital, Hamilton, ON, Canada.
5 Department of Family Medicine, McMaster University, Hamilton, ON, Canada.

"Some support existed for using cannabis for cancer pain and chemotherapy-induced nausea. There was inadequate evidence to substantiate cannabis use as a therapeutic agent for management of UCs. A lack of high-level evidence and robust methodology of the studies limited evaluation of the findings."

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Meta-Analysis > BMJ. 2021 Sep 8;374:n1034. doi: 10.1136/bmj.n1034.

Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials

Li Wang [1 2 3], Patrick J Hong [4], Curtis May [5], Yasir Rehman [2 3], Yvgeniy Oparin [6], Chris J Hong [7], Brian Y Hong [8], Mahmood AminiLari [2 3], Lucas Gallo [9], Alka Kaushal [10], Samantha Craigie [2], Rachel J Couban [2], Elena Kum [3], Harsha Shanthanna [6], Ira Price [11], Suneel Upadhye [3 12], Mark A Ware [13], Fiona Campbell [14], Rachelle Buchbinder [15], Thomas Agoritsas [3 16], Jason W Busse [6 2 3 17 18]

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Affiliations

1 Department of Anesthesia, McMaster University, Hamilton, Ontario, Canada wangli1@mcmaster.ca.
2 The Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada.
3 Department of Health Research Methods, Evidence & Impact, McMaster University, Hamilton, Ontario, Canada.
4 Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada.
5 School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada.

"Moderate to high certainty evidence shows that non-inhaled medical cannabis or cannabinoids results in a small to very small improvement in pain relief, physical functioning, and sleep quality among patients with chronic pain, along with several transient adverse side effects, compared with placebo"

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> Folia Med (Plovdiv). 2020 Dec 31;62(4):668-678. doi: 10.3897/folmed.62.e51478.

Pharmacotherapeutic Considerations for Use of Cannabinoids to Relieve Symptoms of Nausea and Vomiting Induced by Chemotherapy

Tijana Serafimovska [1], Marija Darkovska-Serafimovska [2], Gjoshe Stefkov [1], Zorica Arsova-Sarafinovska [2], Trajan Balkanov [1]

Affiliations – collapse

Affiliations

1 Ss Cyril and Methodius University, Skopje, Republic of North Macedonia.
2 Goce Delcev University, Shtip, Republic of North Macedonia.

"Across all trials, cannabinoids were more effective in relieving the symptoms of nausea and vomiting induced by cytotoxic therapy than placebo was and slightly better than conventional antiemetics."

Review > Neurooncol Pract. 2020 Jul;7(4):376-383. doi: 10.1093/nop/npaa013.
Epub 2020 Apr 3.

A systematic review and meta-analysis examining the effects of cannabis and its derivatives in adults with malignant CNS tumors

Jesus-Eduardo Rodriguez-Almaraz [1], Susan Chang [1], Jennifer Clarke [1], Nancy Ann Oberheim-Bush [1], Jennie Taylor [1], Robin Buerki [1], Mitchel Berger [1], Lydia Zablotska [2], Iryna Lobach [2], Nicholas Butowski [1]

Affiliations – collapse

Affiliations

1 University of California, San Francisco, Neuro-Oncology Division.
2 University of California, San Francisco, Department of Epidemiology and Biostatistics.

" There was limited moderate-quality evidence that supports the use of cannabinoids as adjuvant to the standard of care in the treatment of brain and CNS tumors."

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> Sleep. 2021 Sep 21;zsab234. doi: 10.1093/sleep/zsab234. Online ahead of print.

Medical Cannabis and Cannabinoids for Impaired Sleep: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Mahmood AminiLari [1 2], Li Wang [2], Samuel Neumark [3], Taranah Adli [3 4], Rachel J Couban [2], Aidan Giangregorio [1 5], Colleen E Carney [6], Jason W Busse [1 2 5 7 8]

Affiliations – collapse

Affiliations

1 Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada.
2 The Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada.
3 Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada.

"Among patients with chronic pain, moderate certainty evidence found that medical cannabis probably results in a small improvement in sleep quality"...

...Moderate to high certainty evidence shows that medical cannabis vs. placebo results in a small improvement in sleep disturbance for chronic non-cancer pain … and a very small improvement in sleep disturbance for chronic cancer pain...

Conclusion: Medical cannabis and cannabinoids may improve impaired sleep among people living with chronic pain, but the magnitude of benefit is likely small."

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Entourage Effect?

Cannabinoids and Terpenes known* or suspected* to be helpful for Pain

Cannabinoid

- THC
- CBD
- CBG
- Beta- Caryophyllene
- Myrcene
- Linalool
- Alpha-pinene
- Beta-pinene
- Limonene
- ? others

Products containing these molecules in some combination are possibly a good place to start.

- *Very Limited Published evidence
- *Anecdotal evidence
- Trial in your patients

CINV – Chemotherapy induced nausea and vomiting

Entourage Effect?

Cannabinoids and Terpenes known* or suspected* to be helpful for nausea and vomiting

Cannabinoid

- THC
- CBD
- Limonene
- Caryophyllene
- Humulene
- Myrcene
- Alpha-pinene
- Beta-pinene
- ? others

Products containing these molecules alone or in some combination are possibly a good place to start.

- *Very Limited Published evidence
- *Anecdotal evidence
- Trial in your patients

CINV – Chemotherapy induced nausea and vomiting

- **Regular use oral THC and CBD** in balanced ratio- titrated to patient symptom relief
  - Should be administered 2hrs prior to worst nausea periods and maintained throughout cycle of chemotherapy
  - THC/ CBD 1:1 ratio - combined THC and CBD / "Split Protocol"
  - 2-30mg THC and CBD BD or TDS
- **Inhaled THC high / balanced chemovars cannabis flower**
  - Indica dominant varieties may be more effective at increasing appetite and relieving anorexia
  - Fast onset and increased plasma levels – dose as required/ immediately prior to meals
  - Dose: vaporized cannabis flower 0.1-0.5g QID prn

With thanks to Dr John Teh

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- **Option 1-** mild/ moderate pain
- balanced 1:1 (THC:CBD) oral/ sublingual cannabis preparation
- Titrate accordingly- 1mg to 15mg CBD/ THC BD or TDS
- **Option 2-** moderate to severe pain
- Titrate accordingly-- "Split Protocol"- CBD and THC oral/ sublingual cannabis preparation (2 separate bottles)
- BD dosing – 30-50mg CBD BD / 5-30mg THC BD
- TDS dosing – 20-35mg CBD TDS / 5-30mg THC TDS
- **Option 3-** Add inhaled/ vaporized cannabis for BREAKTHROUGH Pain
- Titrate accordingly- 0.1-0.5g BD/ TDS PRN vaporized cannabis

With thanks to Dr John Teh

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Review > J Cancer Res Clin Oncol. 2021 Sep;147(9):2507-2534.
doi: 10.1007/s00432-021-03710-7. Epub 2021 Jul 14.

Cannabinoids in the landscape of cancer

Nagina Mangal [1 2], Simon Erridge [1], Nagy Habib [1], Anguraj Sadanandam [2], Vikash Reebye [1], Mikael Hans Sodergren [3]

Method: A database search of peer reviewed articles published in English as full texts between January 1970 and April 2021 in Google Scholar, MEDLINE, PubMed and Web of Science was undertaken. References of relevant literature were searched to identify additional studies to

"Plant-based, endogenous and synthetic cannabinoid compounds have shown merits in not only alleviating the unwanted side effects of antineoplastic drug regimens, but have also shown promising evidence in decreasing tumour burden, and one in vivo study so far concludes increasing survival rates in mice"

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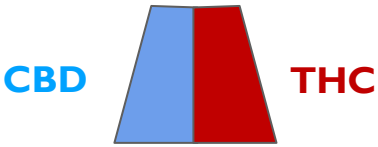
Dosing



- **Option 1-** mild/ moderate symptoms
- balanced 1:1 (THC:CBD) oral/ sublingual cannabis preparation
- **Titrate accordingly- 1mg to 15mg CBD/ THC BD or TDS**
- **Option 2-** moderate to severe symptoms
- Titrate accordingly-- "Split Protocol"- CBD and THC oral/ sublingual cannabis preparation (2 separate bottles)
- **BD dosing – 30-50mg CBD BD / 5-30mg THC BD**
- **TDS dosing – 20-35mg CBD TDS / 5-30mg THC TDS**
- **Option 3-** Add inhaled/ vaporized cannabis for BREAKTHROUGH symptoms
- Titrate accordingly- **0.1-0.5g BD/ TDS PRN vaporized cannabis**

With thanks to Dr John Teh

- **Start Slow, Go Slow**
  - Especially with THC

- If, after up-titrating, there is limited or no benefit, or the negative aspects outweigh any positive, consider changing product.
- If possible, change to one with a significantly different entourage of cannabinoids & terpenes.
- If a number of different products have been trialled, using reasonably high, or intolerable doses, then it may be concluded that medical cannabis is not a relevant management strategy for this symptom in this patient.

THC and Driving

NSW (? and the rest of Australia EXCEPT Tasmania)

Please check the laws in your state

Legal issues for patients

Roadside drug testing in Australia tests for THC in saliva. In NSW, it is an offence to drive

(a) with the presence of THC in oral fluid, blood or urine; or

(b) under the influence of THC.

There is no medical defence to these offences specified in the *Road Transport Act 2013 (NSW)* for using a prescribed cannabis medicine. There may also be insurance implications for patients who are convicted of these offences.

https://www.medicinalcannabis.nsw.gov.au/__data/assets/pdf_file/0025/2869/Cannabis-and-Driving-Fact-Sheet-Health-Professionals-FINAL.pdf

THC and Driving

TASMANIA ONLY

Medicinal cannabis and driving

- Medicinal cannabis can cause impairment and affect fitness to drive.
- It is recommended that patients do not drive whilst being treated with medicinal cannabis.
- A person who drives a vehicle while under the influence of a drug to the extent that the person is incapable of having proper control of the vehicle is guilty of an offence (even if the drug is prescribed).
- THC is the main psychoactive substance in cannabis and is present in some medicinal cannabis products.
- Driving with any detectable amount of THC in your system is an offence in Tasmania unless the product was obtained and administered in accordance with the Poisons Act 1971.

https://www.health.tas.gov.au/health-topics/pharmaceutical-services/medicinal-cannabis/medicinal-cannabis-information-patients-and-general-public

Entourage Effect

- Each product has a different entourage of cannabinoids and terpenes.
- To some extent, the same product may have similar effects in different people.
- There may be a wide range of doses needed
- There may be quite different effects and tolerability in different patients

Possible sources of data on product entourage effects:

- Published medical literature
- Colleagues
- How other patients have responded
- Clinician Forum
- Supplier Medical Liaison / Reps
- Internet

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Australian Government
Department of Health
Therapeutic Goods Administration

Medicinal cannabis products by active ingredients

Proportion of cannabidiol (CBD) content compared with the total cannabinoid content

- Category 1: CBD medicinal cannabis product (CBD ≥ 98%)
- Category 2: CBD dominant medicinal cannabis product (CBD ≥ 60% and < 98%)
- Category 3: Balanced medicinal cannabis product (CBD <60% and ≥ 40%)
- Category 4: THC dominant medicinal cannabis product (THC 60% - 98%)
- Category 5: THC medicinal cannabis product (THC >98%)

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Australian Government
Department of Health
Therapeutic Goods Administration

Within each category there are a range of dosage forms:

1. Capsule
2. Herb, dried for vaporisation
3. Oral Liquid
4. Inhalation
5. Inhalation, pressurised (Metered Dose Preparation)
6. Spray, solution
7. Tablet
8. Pastille
9. Wafer
10. Topical

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1. Capsule
2. Herb, dried for vaporisation
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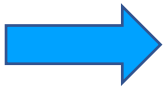
6. Spray, solution
7. Tablet
8. Pastille
9. Wafer
10. Topical

Product prescription

- The range of medical cannabis products and their entourage effects is potentially vast

- Product choice will depend on"
  - Content
    - THC
    - CBD
    - Other cannabinoids
    - Terpenes
  - Dosage form
    - Which will affect delivery method
  - Concentration
  - Cost



Product prescription

- The specific choice of products and starting doses is beyond the scope of this presentation.

- As with any therapeutic intervention, medical cannabis or otherwise, the clinicians knowledge, understanding and confidence in the products, their possible effects, positive or negative and communication with the patient are key to clinical effectiveness.

- In terms of the products used, there is no clinical difference in prescribing medical cannabis as an Authorised Prescriber compared with using SAS B approval process.

- Suffice to say that the option to use a reasonably wide range of dosage forms and cannabinoid concentrations, with a sense of the entourage effects of each, as far as possible, will likely enhance effectiveness and ease of prescribing, depending on the clinical indications adapted for the patient in question.

Dear Dr Herzberg,

Notice of decision to grant an authority under subsection 19(5) of the Therapeutic Goods Act 1989 (Authorised Prescriber Scheme) in relation to:

Product - AP Estab. Hx-Category 1-CBD medicinal cannabis product (CBD≥98%) - - Capsule

Dear Dr Herzberg,

Notice of decision to grant an authority under subsection 19(5) of the *Therapeutic Goods Act 1989* (Authorised Prescriber Scheme) in relation to:

Product: Category 5-THC medicinal cannabis product (THC greater than 98%) - - Herb, dried (for vaporisation)

Cancer Pain and Symptoms - Reference

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2. https://www.cancer.org.au/cancer-information/what-is-cancer/cancer-symptoms
3. https://ncci.canceraustralia.gov.au/outcomes/relative-survival-rate/5-year-relative-survival
4. https://cancerfocusni.org/cancer-info/signs-symptoms/signs-symptoms-of-cancer-infographic/
5. Caputo MP, Rodriguez CS, Padhya TA, Mifsud MJ. Medical Cannabis as Adjunctive Therapy for Head and Neck Cancer Patients. Cureus. 2021 Sep 30;13(9):e18396. doi: 10.7759/cureus.18396. PMID: 34729274; PMCID: PMC8555939.
6. Taneja S, Hoogenes J, Slaven M, Kapoor A. Use of cannabis in urological cancer patients: A review to evaluate risk for cancer development, therapeutic use, and symptom management. Can Urol Assoc J. 2021 Dec;15(12):413-419. doi: 10.5489/cuaj.7198. PMID: 34171211; PMCID: PMC8631835.
7. Wang L, Hong PJ, May C, Rehman Y, Oparin Y, Hong CJ, Hong BY, AminiLari M, Gallo L, Kaushal A, Craigie S, Couban RJ, Kum E, Shanthanna H, Price I, Upadhye S, Ware MA, Campbell F, Buchbinder R, Agoritsas T, Busse JW. Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. BMJ. 2021 Sep 8;374:n1034. doi: 10.1136/bmj.n1034. PMID: 34497047.
8. Serafimovska T, Darkovska-Serafimovska M, Stefkov G, Arsova-Sarafinovska Z, Balkanov T. Pharmacotherapeutic Considerations for Use of Cannabinoids to Relieve Symptoms of Nausea and Vomiting Induced by Chemotherapy. Folia Med (Plovdiv). 2020 Dec 31;62(4):668-678. doi: 10.3897/folmed.62.e51478. PMID: 33415919.
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11. https://www.tga.gov.au/medicinal-cannabis-products-active-ingredients
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