

Medical Cannabis as Adjunctive Treatment to Mitigate Adverse Events in Patients Using High-dose Opioids for Chronic Non-cancer Pain (CNCP)

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Background

- Chronic non-cancer pain (CNCP) affects 20% of the adult population.¹
- CNCP is commonly treated with opioids despite the limited evidence for efficacy and the potential for serious adverse events including addiction, respiratory depression, and death.
- US & Canadian guidelines advise clinicians to reassess opioid doses ≥50 mg morphine milligram equivalents (MME) & avoid doses ≥ 90 mg MME due to the exponential increase in risk of opioidrelated harm.^{2,3}
- Data has emerged indicating cannabis opioid synergy, suggesting cannabis as an adjunctive therapy to optimize pain control.^{4,5}
- We propose this clinical tool to facilitate a safe trial of medical cannabis therapy in patients with CNCP who are receiving ≥ 90mg MME daily.
- This tool was developed based on clinical experience, available data and guidelines.

1) Pre-Cannabis Initiation

Step 1: Assessment

- Consider cannabis in CNCP patients prescribed an opioid dose ≥ 90 mg MME (weaker recommendation for 50-90 mg MME)
- Use validated measures to assess baseline pain
 - Brief Pain Inventory (BPI)
- Assess individual risk initiating cannabis therapy⁶:
 - Drug Interactions
 - Personal/family history of psychiatric illness
 - Risk factors for cannabis use disorder
 - Pregnant, planning to become pregnant, breastfeeding
 - Unstable cardiovascular disease
 - Respiratory disease (if smoking cannabis)
- If concerns arise refer to a clinician with expertise in medical cannabis

2) Initiation & Titration

Step 2: Start cannabis at low dose

- Oral ingestion > smoked cannabis
 - Allows for precise dosing & reduces potential respiratory harms
- For inflammatory pain
 - Start with CBD-dominant chemovar (strain) for daytime use
 - Start 5-10 mg of CBD, 1-2 times/day
- For CNCP patients with **difficulty sleeping** and/or night pain:
 - Start with 2.5 mg THC in the evening (minimizes side effects)
 - Elderly, polypharmacy, comorbidities start 1-1.25 mg THC

Step 3: Slow titration until optimal dosing

- To reduce side effects:
 - Choose orally ingested oils
 - Use CBD-dominant chemovars during daytime
 - Reserve THC strains to evening use
- If using THC-based or 1:1 THC:CBD products:
 - Increase dose by 1-2.5 mg every 2-3 days
 - Begin titration with evening dose
- For CBD-dominant products:
 - Increase dose by 5-10 mg every 1-2 days
 - Titrate until 50 mg/day of CBD
- Evaluate for daytime THC use
- Titrate daily THC to the lowest effective dose where:
 - Therapeutic effect is reached
 - Side effects are tolerated
- Therapeutic effect:
 - ≥30% reduction in pain intensity using a validated tool and/or
 - An improvement in overall function

*CNCP: Chronic non-cancer pain Step 1 *MME: morphine milligram *CUD: cannabis use disorder *Special population: elderly polypharmacy, comorbidities CNCP* patient **CNCP** patient 50-90 mg MME/day **Assess pain Brief pain inventory (BPI)** Assess risk to benefit ratio: **Assess Risk** Drug interactions Contraindications History of psychiatric illness Risk factors for CUD* Cardiovascular disease Step 2 Pregnant or breasfeeding Start cannabis at low dose Respiratory disease (if smoking) Daytime: Special population* CBD 5-10 mg 1-2 x/day THC 1-1.25 mg in evening **Evening: THC 2.5 mg** Step 3 Slow titration to optimal dosing Titrate to lowest effective dose* Increase CBD by 5-10 mg every 1-2 days • ≥ 50mg CBD consider THC Increase evening THC dose by 1-2.5 mg every 2-3 days Titrate to lowest effective dose* OR daily maximum 30 mg THC **Evaluate for daytime THC use Lowest Effective Dose** Step 4 Therapeutic effect achieved with Frequent monitoring minimal to no side effects **Assess response & side effects** every 2-4 weeks Therapeutic effect Therapeutic effect achieved: • ≥ 30% reduction in pain intensity using validated tool **Assess every 3-6 months** improvement in overall function Step 5 **Optimizing the titration** Add 2.5 mg THC at night & Non responder at CBD titrate (see step 3) without 50 mg/day? changing CBD dose Focal symptoms? **Topical cannabis** Breakthrough pain? Vaporized cannabis Step 6 **Assess Response** Decrease THC by 2.5-5 mg every Non-responder at THC 2-3 days until discontinuation 30 mg/day? Re-assess CBD 50 mg/day.

3) Monitoring & Optimization

Step 4: Frequent monitoring

- During initial titration, re-assess response & every 2-4-weeks
- Re-assess every 3-6 months once therapeutic effect is reached:

Step 5: Optimizing the titration

- If using CBD-dominant oil at 50 mg daily and NOT reaching therapeutic effect:
 - Add 1-2.5 mg THC at night +/- day & titrate without increasing CBD dose
- **Additional Options**
 - Topical cannabis for focal symptoms
 - Vaporized cannabis for breakthrough pain (rapid onset of action)

Step 6: Assess response

- If a patient receives ≥30 mg/ of THC without therapeutic effect = "non-responder":
- Decrease THC dose by 2.5-5 mg every 2-3 days until discontinuation
 - Slow titration if patient experiences rebound pain, insomnia or anxiety
 - If on CBD, stop CBD after THC discontinuation (no taper)
- Reassess CBD response
 - Non responder? >> Stop CBD (no taper)

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Flowchart to facilitate medical cannabis use in

CNCP patients prescribed high doses of opioids

Non-responder?

Stop CBD (no taper)