General guidance regarding medicinal cannabis use:

- The mantra for medicinal cannabis use: Start low, go slow!

- Optimal dosage will vary greatly among patients, even for the same condition

- Delta-9- tetrahydrocannabinol (THC): the primary psychoactive component of cannabis. A weak partial agonist of CB1 and CB2 receptors; anecdotal and some clinical evidence to:
  - Reduce pain
  - Increase appetite
  - Relax, sedate
  - Reduce nausea
  - Reduces spasticity/spasms
  - Reduce anxiety and depression
  - Improve sleep

  Potential short-term side effects of THC (dose-dependent):
  - Dizziness
  - Anxiety
  - Confusion
  - Sedation
  - Hypotension
  - Tachycardia
  - Short-term memory impairment
  - Euphoria
  - Attention deficit
  - Immune system suppression
  - Impaired motor skills
  - Paranoia
  - Psychotic symptoms
  - Apathy
  - Depression
  - Restlessness

- Cannabidiol (CBD): a negative allosteric modulator of CB1, has low direct affinity for CB receptors; modulates other receptor systems (e.g. TRPV1, adenosine A2A, 5-HT1A). CBD is not intoxicating, may temper the side effects of THC when used in combination and adds synergistic benefit to THC. CBD has effects that are:
  - Anticonvulsant
  - Anti-psychotic
  - Anti-inflammatory
  - Neuroprotective

- What is your patient’s history of cannabis use? Experienced users vs. naïve users will have different understanding and expectations of both risks and benefits. High THC products may be too psychoactive for patients, especially in the older population and are likely not as beneficial as products that combine THC and CBD. Whole plant products include additional terpenes and flavonoids that may add to the beneficial “entourage” effect.
Possible cannabinoid-drug interactions

- CBD and other plant cannabinoids can potentially interact with many pharmaceuticals by inhibiting the activity of cytochrome P450.\textsuperscript{1,2}
- THC and CBD are metabolized by CYP3A4 and CYP2C9.\textsuperscript{3} CYP3A4 inhibitors increase THC levels. CYP3A4 inducers decrease THC levels. CBD, but not THC, is metabolized by CYP2C193.
- inhibitors of CYP2C9 (amiodarone, cimetidine, cotrimoxazole, metronidazole, fluoxetine, fluvoxamine, fluconazole, and voriconazole) would be expected to increase the plasma concentration of THC.
- CYP3A4 inhibitors, including clarithromycin, erythromycin, cyclosporine, verapamil, itraconazole, voriconazole, and boceprevir, would be expected to produce increases in THC concentrations. Rifampin, a CYP3A4 inducer, has been reported to reduce THC levels by 20% to 40%.\textsuperscript{4}
- CBD is an inhibitor of CYP3A4 and CYP2D6. CYP3A4 metabolizes about a quarter of all drugs, therefore CBD may increase serum concentrations of macrolides, calcium channel blockers, benzodiazepines, cyclosporine, sildenafil, antihistamines, haloperidol, antiretrovirals, and some statins (atorvastatin and simvastatin, but not pravastatin or rosuvastatin).\textsuperscript{5}
- THC is a CYP1A2 inducer, thus it may decrease serum concentrations of clozapine, duloxetine, naproxen, cyclobenzaprine, olanzapine, haloperidol, and chlorpromazine.\textsuperscript{2,6}

Contraindications, per the Handbook on Cannabis (Oxford: Oxford University Press; 2015):

- acute psychosis and other unstable psychiatric conditions
- severe cardiovascular, immunological, liver, or kidney disease, especially in acute illness

Patient cannabis diary

Consider having your patient maintain a diary to help both of you keep track of usage and side effects. This is particularly important if a Dispensary, not you, is making the recommendation of a particular strain, ratio of THC:CBD, route of administration, and frequency of dosing.

You could ask patients to collect the following data:

- Date/time of dose
- Amount taken (grams or other measurement)
- Strain (name of product)
- Ratio of THC:CBD
- Formulation (gelcap, tincture, vaped product, etc.)
- + effects
- - effects
References


Resources for literature on dosing:
