

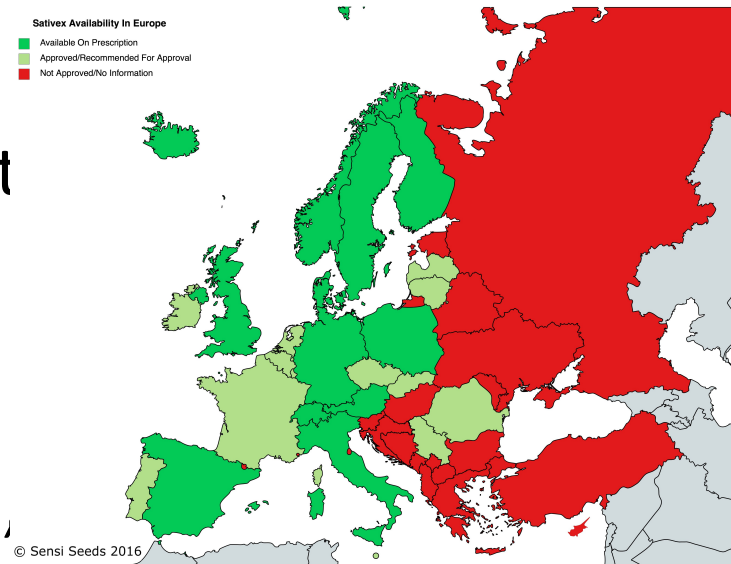
Cannabinoids and Health

Module 4

Lecture 6: General Guidelines To Reduce Harm and Maximize Benefits

Risks in medical patients?

- Most research on risks has been done with recreational users
- Medical users represent a different population who view being “high” a side effect
- Plant derived medication (“Sativex”, has been approved for use in Canada (since 2005), the U.K, and many other countries



Adverse Effects of Sativex

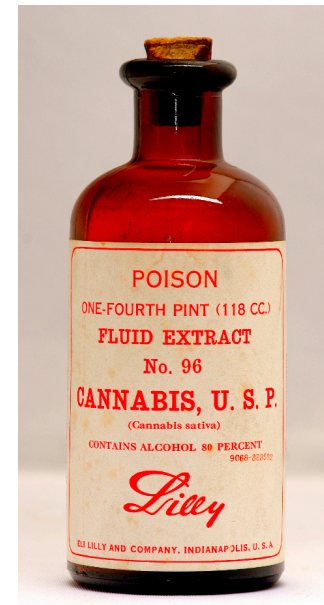
- Data from phase III clinical trials and post marketing registries (Etges, 2016; Fernandez, 2016)
 - 941 patients, mean of 954 days of use, mean dose 14.6 mg THC/ 13.5 mg CBD
- Most common side effects were dizziness, fatigue which dissipated
- Importantly, no evidence of abuse liability or diversion and no evidence of short or long term cognitive effects

Back to the future?

GW 2009



Lilly 1909



General guidelines to reduce risk and maximize benefits

- Surprisingly (or not), very few clinical scientists have addressed this in published papers (but see MacCallum & Russo, 2018)
- General recommendation is “Start low, go slow, stay low” (sound advice!)
- Recommendations for inhalation
 - 1 inhalation every 15 minutes until desired effect (or until start to feel effects you don’t like)
- Oral/edible admin better for chronic condition because effects last longer
 - Start with product that has 2.5 mg of THC or less
 - **WAIT** 2 hours or longer before taking more or you may take too much because the effects are delayed
- Can supplement edible with inhalation if need fast acting effect to address breakthrough symptoms
- CBD can mitigate THC side effects

More from MacCallam & Russo

- Best to start using at bedtime to mitigate adverse events
- Days 1–2:
 - 2.5 mg THC oral (or 1 small inhalation) at bedtime
- Days 3–4:
 - if previous dose tolerated, increase by 1.25–2.5 mg THC at bedtime
- Days 5–6:
 - increase by 1.25–2.5 mg THC at bedtime every 2 days until desired effect or side effects emerge

If also using during the day, consider the following:

- Days 1–2:
 - 2.5 mg THC-equivalent once a day
- Days 3–4:
 - 2.5 mg THC twice a day
- Increase as needed and as tolerated to 15 mg divided into 2-3 doses per day
- Doses exceeding 20–30 mg/day may increase adverse events without increasing efficacy

CBD Dosing and THC contraindications

- CBD predominant product dosing
 - Dosing effects not clear for most indications though some studies suggest very high doses (> 500 mg) are necessary
 - For products in state-regulated markets, dose will be limited by THC (e.g., a 20 to 1 CBD to THC preparation would have 100 mg of CBD and 5 mg of THC)
- Contraindications include
 - Pregnancy and lactation
 - Cardiac disease (talk to HCP)
 - Lung disease (for inhaled forms)
 - History of psychosis or addiction (CBD only is the exception)
- Over time, most patients develop tolerance to side effects and negative effects (e.g., motor control, cognitive) without loss of positive effects

Possible Side Effects

Table 4

Adverse events associated with cannabis-based medicines.

Side effect	Most common	Common	Rare
Drowsiness/fatigue	✓		
Dizziness	✓		
Dry mouth	✓		
Cough, phlegm, bronchitis (Smoking only)	✓		
Anxiety	✓		
Nausea	✓		
Cognitive effects	✓		
Euphoria		✓	
Blurred vision		✓	
Headache		✓	
Orthostatic hypotension			✓
Toxic psychosis/paranoia			✓
Depression			✓
Ataxia/dyscoordination			✓
Tachycardia (after titration)			✓
Cannabis hyperemesis			✓
Diarrhea			✓

More from MacCallum & Russo

- HCPs should be clear about the potential risks like any psychoactive medication (See <https://www.drcarolinemaccallum.com/cannabis-resources/>)
- Recommend patients keep 'symptom inventory' chart recording effects (See <https://www.drcarolinemaccallum.com/cannabis-resources/>)

Conclusions

- Many of the harms discussed in last module may be mitigated by using appropriate products and dosing
- Use of flower through inhalation is faster acting and easier to titrate but may irritate lungs and may not be desirable for many
- Oral/edible preparations offer some advantages in terms of longer acting
- CBD combined with THC has potential advantages (may mitigate some undesirable effect, may add some therapeutic effects) and no disadvantages
 - Look for products 1:1 or greater ratio of CBD to THC

Additional Thoughts

- Public health messages like “start low, go slow” are important
- Need to educate (health care providers, dispensary workers, and consumers)
 - Risks, side effects, dosing – keep out of the reach of children and pets
 - Know where the cannabis product comes from, what is used to produce it, how was it tested (avoid contaminants, heavy metals, mold, etc)
 - Are you confident that the labeled dose accurate?
- Need to communicate (health care providers to patients and vice versa)
- Dose carefully
 - Even small doses of THC can have very strong effects in naïve users
- Risk/benefit profile may change dramatically with age