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Legal and ethical implications of cannabis based medicines

9th April 2019

Pharmacy Law and Ethics Association

Time for legal change?

https://www.bbc.co.uk/news/health-44968386

Cannabis based medicinal products

Cannabis sativa

- Contains over 700 chemicals
- At least 100 cannabinoids have been isolated
- As cannabis is a natural product the composition depends on variety and growing conditions

- Cannabis has become much more potent
  - genetic (selected seed varieties and cultivation of female plants)
  - variation in cannabinoids and concentration of THC, CBD, etc
  - environmental (hydroponic cultivation techniques, prevention of fertilisation and seed production)
  - freshness (the risk of storage degradation of THC is less likely t

Cannabis: major components

THC

- principal psychoactive constituent of cannabis
- partial agonist activity at the CB1 receptor
- Associated with euphoria and psychosis

CBD

- very low affinity for the CB1 and CB2 receptor
- May be indirect antagonist at CB1 and CB2 receptors
- May reverse some of central effects of THC

Cannabis and common mental health conditions

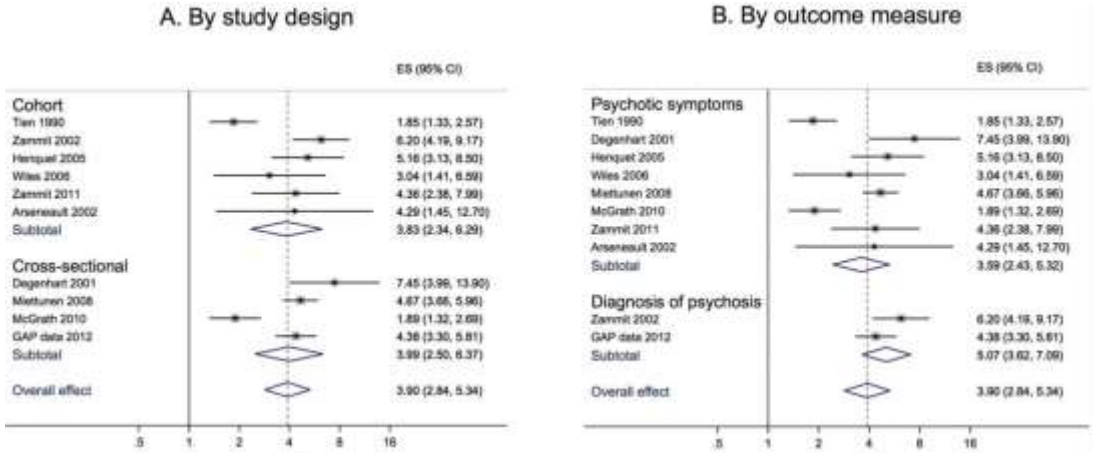
- Anxiety
  - Anxiety is one of the most common negative reactions to cannabis
  - Cannabis may exacerbate longer lasting forms of anxiety disorders such as panic disorder

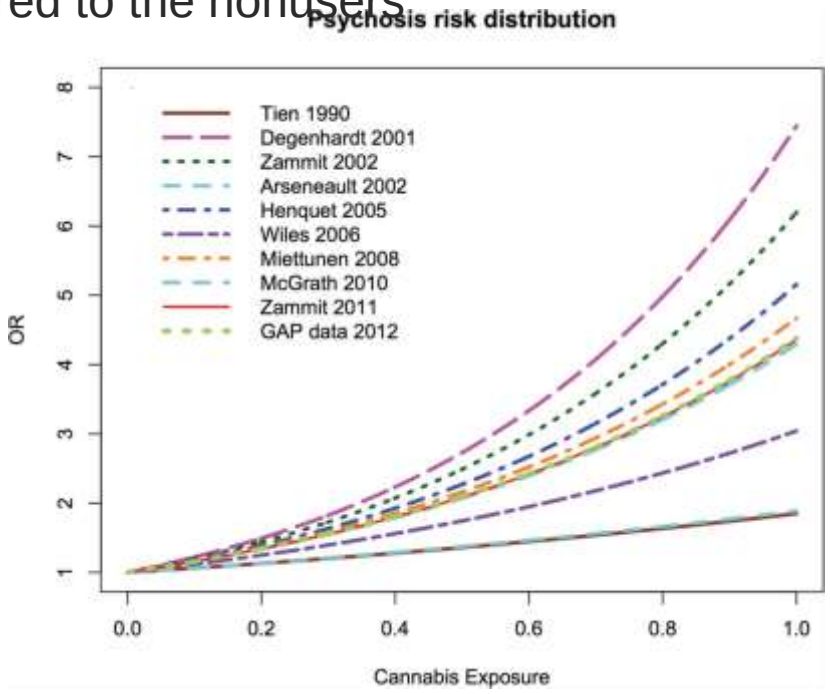
- Depression
  - Early, regular and heavy users are more likely to develop depression

- Many longer term users report that they continue to use cannabis because it relieves unpleasant feeling states such as anxiety and depression

Cannabis and psychosis

- Higher levels of cannabis use were associated with increased risk for psychosis
- A logistic regression model gave an OR of 3.90 (95% CI 2.84 to 5.34) for the risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to the nonusers





Marconi A et al. Schizophrenia Bulletin 2016; 42: 1262–1269.

Oral statement to Parliament

Home Secretary statement on medical use of cannabis

Sajid Javid announces review of the scheduling of cannabis

- Commissions review in 2 parts
  - Part one of the commission will consider the evidence available for the medicinal and therapeutic benefits of cannabis-based medicines
  - Part 2 but will provide an assessment, based on the balance of harms and public health needs, of what, if anything, should be rescheduled

‘Let me be absolutely clear that this step is in no way a first step to the legalisation of cannabis for recreational use’

https://www.gov.uk/government/speeches/home-secretary-statement-on-medical-use-of-cannabis

Controlled drug schedules

- Misuse of Drugs Regulations 2001

- Schedule 1
  - by definition have little or no therapeutic potential

- Moving these drugs out of Schedule 1 would allow them to be prescribed under controlled conditions by registered practitioners for medical benefit
- Will allow the evidence base on the therapeutic benefits associated with using this class of drugs to be improved through research, maximising benefits to patients.

Davies S. Cannabis scheduling review part 1: the therapeutic and medicinal benefits of cannabis-based products. July 2018.

Cannabinoid uses

- **Epilepsy** - limited but high quality evidence for the use of medicinal cannabis products in epilepsy
- **Multiple sclerosis** - low to moderate quality evidence for treating symptoms of pain (pharmaceutical grade THC) and some evidence for treating spasticity
- **Nausea and vomiting** – some evidence of effective treatment but likely inferior to other treatment options
- **Chronic pain** – some moderate evidence that patients using cannabinoids for MS related pain and for non-MS neuropathic pain experienced a decrease in their pain scores
- **Palliative care** - some limited evidence but from a low number of generally poor quality studies

Davies S. Cannabis scheduling review part 1: the therapeutic and medicinal benefits of cannabis-based products. July 2018.

Cannabis-derived medicinal products recommended to be available on prescription

The ACMD has recommended that cannabis-derived medicinal products should be placed in Schedule 2 of the Misuse of Drugs Regulations 2001.

Published 24 July 2018

- *Cannabis*-derived medicinal products [*Cannabis* (excluding Sativex), *Cannabis* resin, cannabinol and cannabinol derivatives (not being Dronabinol or its stereoisomers)] of the appropriate medicinal standard should not be subjected to Schedule 1 requirements
- The DHSC and MHRA to promptly develop a clear definition of a *Cannabis*-derived medicinal product
- Once the definition of a *Cannabis*-derived medicinal product has been developed, the ACMD advises that only products meeting this definition be moved into Schedule 2 of the MDR pending our further advice
- In addition to the provisions of Schedule 2 of the MDR, the ACMD recommends that the DHSC, MHRA and Home Office should develop additional frameworks and clinical guidance for 'checks and balances' to maintain safe prescribing of *Cannabis*-derived medicinal products
- Clinical trials to establish the effectiveness and safety of *Cannabis*-derived medicinal products ae urgently required

1 November 2018 : Medicinal cannabis becomes legal

https://www.nhs.uk/conditions/medical-cannabis/

Definition:
Cannabis based medicinal products

"cannabis-based product for medicinal use in humans" means a preparation or other product, other than one to which paragraph 5 of part 1 of Schedule 4 applies, which—

(a) is or contains cannabis, cannabis resin, cannabinol or a cannabinol derivative (not being dronabinol or its stereoisomers);

(b) is produced for medicinal use in humans; and—

(c) is—

(i) a medicinal product, or

(ii) a substance or preparation for use as an ingredient of, or in the production of an ingredient of, a medicinal product;"

Any other substance or product (which is or contains cannabis, cannabis resin, cannabinol or cannabinol derivatives) will remain a Schedule 1 drug

Cannabis based medicinal products

- Only products meeting definition will be rescheduled to Schedule 2 of the 2001 Regulations
- The definition does not impact on the offence of cultivation of the cannabis plant which would still require a Home Office licence or wider offences relating to recreational use of cannabis
- The Regulations continue to prohibit smoking of cannabis and cannabis-based products for medicinal use
- Cannabis remains controlled as a class B drug under the Misuse of Drugs Act 1971 (“the 1971 Act”) and the penalties for unauthorised supply, possession and cultivation of cannabis will remain unchanged

Cannabis based medicinal products

Cannabis based medicinal products

Which medicine?
What dose?
Interactions with other medicines?

CBD containing preparations

- Not a controlled drug

- Medicines containing CBD regulated by MHRA but many products considered food supplements

- Epidiolex
  Indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and old

CBD preparations

- As food supplements, THC or psychoactive content is legally controlled not to exceed 0.2% in the EU
- As with other herbal remedies, the declared contents of non-medicinal CBD preparations is variable, and often inaccurate, and these products sometimes exceed the legal limit of THC
- Amount of CBD in these products is typically far lower than in clinical trials (eg, 25 mg in a non-medicinal product versus 150-1500 mg/day in clinical trials)

- Should pharmacies be selling CBD preparations?

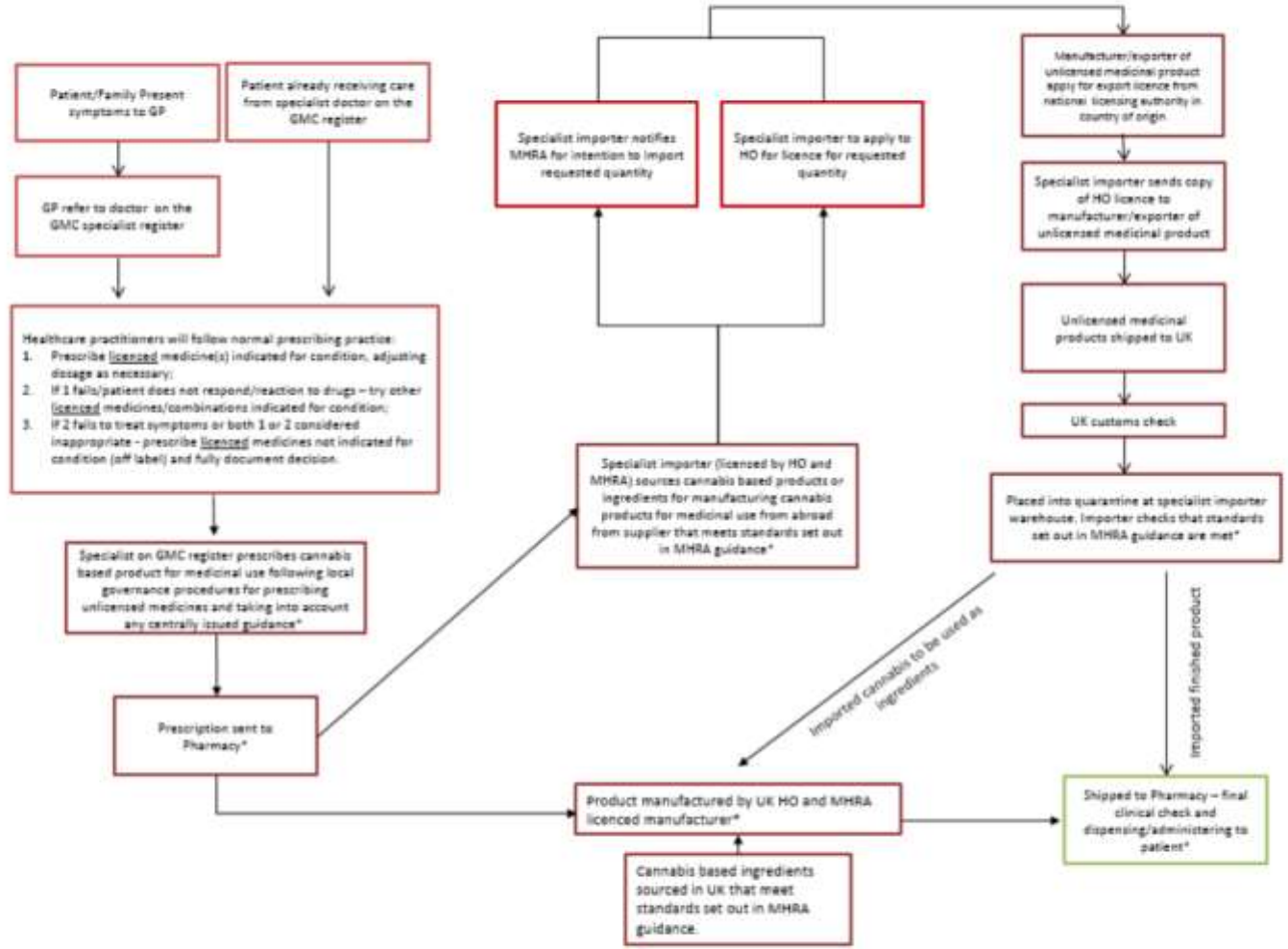
Access to cannabis based medicinal products

- May only be supplied in order to meet the special needs of an individual patient. This product should not be supplied where a licensed medicinal product can meet the special needs of the patient

Supply routes :-

- A special medicinal product for use in accordance with a prescription or direction of a doctor (who has made the decision to prescribe) on the Specialist Register of the General Medical Council;
- An investigational medicinal product without marketing authorisation for use in a clinical trial or;
- A medicinal product with a marketing authorisation

Process for prescribing, supplying & importing unlicensed cannabis-based medicinal products



Notes:

* Refer to the Quality Checklist in this guidance which details what checks should be made at each stage to ensure that the prescription/direction of the specialist doctor is fulfilled.

This is a summary only and in no way seeks to supersede the legal effect of The Misuse of Drugs Act 1971; Misuse of Drugs Regulations 2001 or Misuse of Drugs (Licence Fees) Regulations 2010.

Access to cannabis based medicinal products

- Pharmacopoeial standards
  - Specifications applied to CBPMs and their active substances should take account of all relevant pharmacopoeial monographs and current guidelines on herbal drugs, herbal drug preparations and herbal medicinal products. Suitable validated analytical methods should be applied in line with current guidelines; major cannabinoids, in particular, THC/CBD should be quantitatively determined, as appropriate
  - Label to include content of THC/CBD and additional information regarding driving

- Relevant licenses and permissions
  - Manufacture and assembly in UK
  - Importation
  - Distribution

Professional guidance

- Chemotherapy-induced nausea and vomiting
  - There is good evidence that cannabinoids are effective in preventing CINV but they have a high side effect profile and there are more efficacious agents available. Cannabinoids should remain an option for those who have failed standard therapies but not used as a first-line treatment

- Pain
  - There is limited research available from which to create guidance on the effect of CBPM on pain in palliative care patients, including those with cancer. Studies show mixed results or statistically significant results of uncertain clinical significance. In view of this and the adverse effects associated with CBPM, their place in the treatment of pain in palliative care patients is unclear and not recommended in routine clinical practice.
  - There is no robust evidence for the use of CBPM in chronic pain and their use is not recommended

Cannabinoids in paediatric epilepsy

- Prescription of a non-licensed cannabis-based product for medicinal use should be used as a treatment of last resort for children who meet the following three criteria:
  - Have an epilepsy that has proven intractable to treatment with conventional licensed anti-epileptic drugs given at therapeutic doses
  - Have not responded to the ketogenic diet or for whom the diet is inappropriate
  - Are not candidates for epilepsy surgery

Guidance on the use of cannabis-based products for medicinal use in children and young people with epilepsy

Cannabis-based products for medicinal use

In development [GID-NG10124] Expected publication date: 21 October 2019 Register as a stakeholder

Project information

Status	In progress
Developed As	CG

Provisional Schedule

Draft scope consultation	13 November 2018 - 04 December 2018
Draft guidance consultation	30 July 2019 - 28 August 2019
Expected publication	21 October 2019

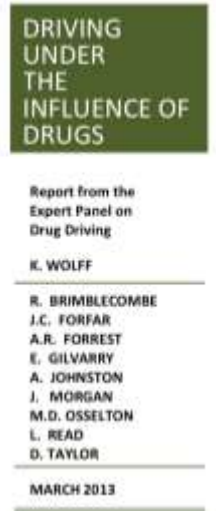
Project Team

Developer	NICE Clinical Guideline Updates Team

Email enquiries

If you have any queries please email CannabisMedUse@nice.org.uk

Cannabis and driving



- Psychomotor performance
  - Moderate to high doses results in impaired cognitive function
  - Low doses produce few effects

  - THC shows a significant dose effect for cannabis and driving performance
  - The risk of serious or fatal injury from a RTA whilst driving under the influence of cannabis ranges from OR: 1.22 to 9.50

  - Significant increased accident risk was apparent when the concentration of THC in the blood was ≥5 µg/L, whether or not ingestion had occurred recently

  - The effects of drug-use setting (e.g. polydrug use, concomitant alcohol use and sleep deprivation) are intertwined and significantly contribute to unsafe driving
  - The risk of RTA was significantly increased following combined of use of alcohol (<80 mg/100ml blood) and cannabis (≥ 1 µg/L): the risk is multiplied (alcohol use alone OR: 8.39, cannabis use alone OR: 1.89 but combined use OR: 15.86)

Academy that teaches doctors how to use medicinal cannabis that claims 'smoking joints soothes pains' is owned by tycoons set to make millions out of the drug

- **Neurologist Professor Mike Barnes, could make millions from selling shares**
- **AMC is owned by European Cannabis Holdings that invested to make a profit**

Academy for Medical Cannabis part of 'portfolio' of interests owned by European Cannabis Holdings (ECH), a company which seeks to 'invest' in the cannabis industry to create 'significant value for our shareholders'

One section titled 'How to ingest' suggests methods including vaping the drug, taking capsules and oils, applying creams or patches containing cannabis, smoking joints and eating cannabis 'edibles', illustrated with an image of gummy bears.

https://www.dailymail.co.uk/news/article-6561831/Academy-Medical-Cannabis-owned-European-tycoons-make-millions-drug.html

Cannabis

Britain's first medicinal cannabis clinic opens in Greater Manchester

The Beeches, a private centre in Cheadle, will charge £600-£700 for monthly prescriptions

A new private clinic in Greater Manchester has become the UK's first specialist medicinal cannabis centre
There are plans for further clinics in Birmingham and London

Patients at The Beeches, in Cheadle, will pay £200 for appointments with doctors and between £600 and £700 a month for a prescription

Decisions to prescribe cannabis will be taken on a case-by-case basis, and will only be considered when staff are satisfied that licensed products cannot treat the condition

https://www.theguardian.com/society/2019/mar/09/britains-first-medicinal-cannabis-clinic-opens

NIHR | National Institute for Health Research

Search

19/23 Cannabis-based products for medicinal use

Application dates: 20 March 2019 to 31 July 2019

The EME Programme are participating in the Themed Call: cannabis-based products for medicinal use.

- **19/23 Cannabis-based products for medicinal use**

In order to apply you will need to carefully review the:

- Specification document
- Guidance notes
- Supporting information

Click here to apply

Medical cannabis industry should be told to provide evidence if it wants products prescribed, MPs hear

The Pharmaceutical Journal | 28 MAR 2019

Keith Ridge told the House of Commons Health and Social Care Select Committee hearing on medical cannabis policy that he saw the primary purpose of rescheduling medical cannabis as supporting development of good evidence.

He told MPs that it was important to “consider the needs of seriously ill patients” and to ensure that “when a patient needs a medicine urgently, there are systems in place” to allow that to happen. But he emphasised that commissioning systems are “based on evidence … at the moment we find ourselves in a situation where evidence is lacking”.

https://www.pharmaceutical-journal.com/news-and-analysis/news/medical-cannabis-industry-should-be-told-to-provide-evidence-if-it-wants-products-prescribed-mps-hear/20206346.article?firstPass=false

What's happening in other countries

- Cannabis available for medicinal use in many countries
  - Australia, Canada, Colombia, Croatia, Cyrpus, Czech Republic, Finland, Germany, Greece, Israel, Italy, Jamaica, Luxembourg, Macedonia, Malta, Mexico, the Netherlands, Peru, Portugal,Switzerland, Uruguay, some US states
- Some countries do not require prescription – (e.g. Canada, Uraguay, the Netherlands, Spain)
- Some countries (Mexico and Switzerland) restrict THC content of medical cannabis (1%)
- Other countries have more restrictive laws allowing for the use of specific cannabinoids only, such as Brazil, France (e.g. Sativex)

- Recreational use decriminalised in Canada (17 October 2018)

Summary

- Cannabis has been used for euphoric effects for centuries
- Greater focus on medical use in recent years, however quality of evidence rather poor
- Few licensed medicines in any country and quality of products variable

- Changes to law have only allowed a limited number of people to access CBMPs so far

- Need for much more research to understand benefit and harms in order for more widespread use