

**Recommendations** and **Guidance** on  
Medical Cannabis under Prescription  
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# Recommendations and Guidance on Medical Cannabis under Prescription



Medical Cannabis  
Clinicians Society

Guidance on the use of cannabis-based  
products for medicinal use | 2020

Written by the  
Medical Cannabis Clinicians Society

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## 1. Background

In June 2018 the Home Secretary announced a review to look into the scheduling of cannabis under the Misuse of Drugs Regulations 2001.

The first part of the review was conducted by Professor Dame Sally Davies DBE FRS FMedSci, the Chief Medical Officer for England [1]. Her review found conclusive evidence of the therapeutic benefit of cannabis-based products for certain medical conditions and reasonable evidence of therapeutic benefit in several other medical conditions. She recommended 'that the whole class of cannabis-based medicinal products (CBPMUs) be moved out of Schedule 1 of the Misuse of Drugs Regulations.'

The Advisory Council on the Misuse of Drugs (ACMD) then published their interim findings in July 2018 [2] and agreed that cannabis products should be rescheduled, subject to certain provisos.

The Home Secretary and the Secretary of State for Health and Social Care published the details of the rescheduling on 1st November 2018 [3]. Guidance was also issued for the public [4]. **The Misuse of Drugs (Designation) (England, Wales and Scotland) Order 2015** was amended to reschedule cannabis-based products for medicinal use in humans to Schedule 2 of the Misuse of Drugs Regulations 2001. That meant that from 1st November 2018 there was a legal route for cannabis-based products for medicinal use to be prescribed by doctors on the General Medical Council (GMC) Specialist Register without the requirement for a Home Office licence.

The simultaneous letter [5] from the Department of Health and Social Care and NHS England referred to additional guidance from the Royal College of Physicians [6] and the British Paediatric Neurology Association [7]. In late 2019 the National Institute for Health and Care Excellence (NICE) also published guidelines on the clinical use of these products [8]. NICE has also produced further guidance on the use of cannabidiol and clobazam in the Lennox-Gastaut syndrome [9] and Dravet syndrome. [10] NHS England has published further guidance [11] on cannabis-based products for medicinal use following their own review of the subject in March 2019 [12].

Despite the change in the Regulations the prescription of Cannabis-Based Medicinal Products (CBMPs) in the National Health Service (NHS) has been limited to a few prescriptions of the CBD dominant anti-epilepsy product, Epidyolex and the 1:1 CBD:THC mixture, Sativex, which is prescribed for drug resistant spasticity in the context of multiple sclerosis. We believe that there have been around 50 patients prescribed CBMPs in the private sector during the course of 2019. Recently the Centre for medical cannabis has produced data to show that there about 1.4 million users of illegal cannabis in the UK for medical purposes [13]. The MCCS feels that it is important for medical practitioners to be fully aware of the range of opinion and evidence on this matter in order to reach a balanced prescribing decision in the best interests of their patients. The MCCS hopes that this guidance assists in that process. We emphasise that this is a guidance document and not a definitive review of the academic literature on the subject. It represents the expert opinion of the members of the MCCS executive committee.



## 2. UK Regulations

### 2.1 Who can prescribe?

A medical practitioner on the GMC Specialist Register of the General Medical Council or a **doctor under their direction** (para 7.13 of Explanatory Memorandum to the Misuse of Drugs (Amendments) (Cannabis and Licence Fees)(England, Wales and Scotland) Regulations 2018 No. 1055) can prescribe [14]. The recent NICE guidance stated that shared care prescribing was possible after the initial prescription by the specialist. The MCCA support this guidance and indeed recommend that in due course general practitioners be allowed to initiate prescribing. They are, after all, specialists in day to day symptom and chronic disease management and CBMPs are largely medicines that manage common but often difficult-to-treat symptoms.

### 2.2 What can they prescribe?

**The Misuse of Drugs (Amendments) (Cannabis and Licence Fees) (England, Wales And Scotland) Regulations** define a cannabis-based product for medicinal use (CBPM) as follows:

“(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;”  
If the three definitions are met, then the preparations or products are considered as a ‘cannabis-based products for medicinal use in humans’ and a Schedule 2 drug under the 2001 Regulations.

**Nabilone** and **Dronabinol** and any other synthetic cannabinoids are excluded from this definition, as is **Sativex (Nabiximols)** which already has a licence for use in resistant spasticity in multiple sclerosis under Part 1 of Schedule 4 of the Misuse of Drugs Regulations 2001. **Epidyolex** has now been approved by the European Medicines Agency as an approved controlled drug under Schedule 2 of the Regulations for the seizure treatment of Lennox-Gastaut and

Dravet syndromes.

Other, unlicensed, medicines are now available in the UK. These products need to meet stringent quality controls so that the prescriber can be satisfied about safety and consistency of the product. Generally, they need to meet EU Good Manufacturing Practice standard and their import (all so far are imported products) needs approval by the Medicines and Healthcare products Regulatory Agency (MHRA) and will need an import license from the Home Office. Usually a product is imported on a “named patient” basis which makes the product unnecessarily expensive. Some parents are now paying up to £2000 per month privately for the medicine for their epileptic children. The bulk importation of unlicensed products is an area that needs to be addressed as a matter of urgency so that the cost to the patient can be as cheap as possible under private prescription prior to wider availability on the NHS. The MHRA has produced advice on the importation of appropriate products [15,16]. The product should be properly and clearly labelled so the prescriber can readily determine the dose in milligrams of the two most well-known and major cannabinoids, THC and CBD. For example, labelled as ‘each capsule (or millilitre in the case of oil) contains 1mg THC and 20mg CBD, etc’.

The MCCA feel that, as a minimum, the proportion and dosage of CBD (cannabidiol) and THC (tetrahydrocannabinol) should be clearly labelled. Preferably the products should also list any other minor cannabinoids and terpenes and a Certificate of Analysis (COA) should be available. Advertising of unlicensed products (to both doctors and patients) is not allowed and producers can make no medical claims.

It should be noted the hemp-derived CBD products (which are either ‘THC free’ or contain less than 0.2% THC) are legal[16] and readily available from retail outlets (OTC) (see Definitions section) under the category of a nutritional supplement not as a prescribable medicine.



### 2.3 The mechanism for prescription

The CBMP will be prescribed under the “Specials” system on a “named patient” basis. The prescribing doctor will need to be familiar with the regulations around a “Specials” prescription. They will be expected to prescribe within the boundaries of their knowledge and generally not prescribe if licenced or “off label” products are available and have not been used. It is not mandated that all such products be tried first and CBMPs are not necessarily medicines of last resort. It is up to the prescriber to determine the reasonable use of CBMPs for an individual patient, having regard for the evidence for cannabis use in similar cases and the evidence in general for that indication and clearly having regard to the circumstances of the individual patient.

**It is up to the doctor to make that final decision and not up to any external body to do so.** The doctor should be fully aware of the GMC Guidance on prescribing unlicensed medicines [18] and of the clinical governance procedures in their own Trust. It is good practice to seek confirmation from the Trust Medical Director or similar individual (the responsible person may vary from Trust to Trust) and seek confirmation from a peer colleague. Doctors in the private sector may also prescribe but similar clinical governance arrangements will be expected by the Care Quality Commission who approves relevant private licensed premises.

### 2.4 What conditions can be prescribed for?

There are **no restrictions** with regard to specific conditions. It is not just those conditions for which some guidance has been produced (nausea and vomiting during chemotherapy, chronic pain and childhood epilepsies).

### 2.5 Who pays for the prescription?

The prescription will be paid for by the NHS Hospital Trust if it is a valid NHS prescription. Private prescription (with similar governance arrangements and Good Practice Guidelines) is also possible.

### 2.6 How is the CBPM administered?

The Regulations exclude the use of smoking. Other forms of ingestion or application are thus presumably allowed (for example: vaporising, edibles, creams, tinctures, capsules, oils, sprays, suppositories, pessaries). However, it is likely that **capsules and oils for under-the-tongue (sublingual) and oral use** will be the commonest form of prescription.

### 2.7 General Medical Council (GMC) advice

The GMC has made it clear that a doctor must follow the law and the GMC professional guidance to take account of clinical guidelines and must work in partnership with patients to make a decision about their care. Ultimately they must act in the Best Interests of their patient. Some doctors have expressed concern on this point but can be reassured.

## 3. Definitions

The MCCS is aware of some confusion surrounding terminology.

This section should provide clarification.

### 3.1 Full extract cannabis oils (FECO)

These are oils extracted from the cannabis plant (usually the unfertilised female flower) using various extraction techniques (such as alcohol or super-critical CO2 extraction). The oils contain a mixture of cannabinoids and terpenes (and other components such as flavonoids) in proportions according to the strain of plant and the type of extraction technique.

### 3.2 Pure isolates

Some manufacturers produce pure cannabinoid isolates as a finished product.

### 3.3 Hemp products / CBD-only products

Hemp-based CBD products that contain minimal or no THC are legal in the UK and can be purchased online or over-the-counter in health food stores. They cannot be marketed with any medical claims. The Regulations are very complex<sup>[19]</sup> and indeed might be changed in the coming months due to further guidance regarding the EU Novel Food Regulations (EU 2015/2283).

Hemp is a cannabis plant that has been bred to produce CBD at the expense of THC, producing very low THC plant material and flowers. It is often used for non-medical products such as animal feed, rope and building material and, in many countries, governed under different regulations as 'hemp'. If individuals buy such products for medical use they will need to be aware that they do so without any medical guidance on efficacy or dosage as the supplier is not allowed to make medical claims. Doctors should be aware that some patients may be using CBD-only products for their medical condition. It seems unlikely that doctors can prescribe such products as they would need to meet the basic criteria as being produced for medicinal use in humans (see para 2.2 above) The MCCS is aware that many thousands of people are using these products for medical purposes in the absence of prescribed products being available. As a minimum, we encourage producers to supply proper labelling so that consumers can be aware of the constituents of the product and dose of the cannabinoids contained in the product as well as a detailed COA for product safety. This area is in urgent need of better regulation.

### 3.4 Illegal cannabis

Illegal cannabis products obtained on the black market are generally high in THC and low in CBD. These products are designed for the recreational "high" and such products have an increased incidence of side effects, particularly mental health problems (see side effects section). Generally, medical cannabis products are lower in THC and also combined with CBD, which counteracts the effects of THC. There is overlap between street cannabis and medical cannabis but the side effects of medical cannabis are generally much less than those of illegal cannabis and the two should not be confused.

### 3.5 Cannabis plant

Traditionally, before modern interbreeding produced thousands of hybrid strains, there were two main types of cannabis plants – Cannabis sativa and Cannabis indica and a third subspecies called ruderalis. They were said to have somewhat different recreational effects, sativas being thought of as more 'energizing' and indicas being thought of in popular culture to be more 'sedating.' But in medical terms, and certainly even more so because most medical cannabis strains are hybrids, it is best to focus on the proportion of the different cannabinoids. This is a more accurate system of classification known as chemovar (i.e. the mix of cannabinoids) classification. The cannabinoids are most concentrated and produced in highest amount in the unfertilised female flower. The cannabinoids in the plant are in their acidic form (such as THCA (tetrahydrocannabinolic acid) and CBDA (cannabidiolic acid)). Whilst the acidic cannabinoids have some medical properties, they are less studied and understood clinically. Therefore, currently for medical use the plant material is usually heated to decarboxylate the acid forms into 'active' forms in most capsules and oils (e.g. from THCA to THC and CBDA to CBD). If dried flower is prescribed (as in Canada and Germany, for example) then it is important to remind the patient that decarboxylation by heating is usually required before use, as is using a vape, for example. Acidic cannabinoids are not psychoactive.

### 3.6 Cannabinoids

The plant contains about 120 cannabinoids. The

best known are THC (tetrahydrocannabinol) and CBD (cannabidiol). The former is the main psychotomimetic/psychotropic cannabinoid and the latter is anxiolytic and counteracts the THC psychotomimetic/intoxicating effects. Most medical studies have been conducted focusing on these two cannabinoids. The other cannabinoids studied also have medical properties. THCV, for example, (tetrahydrocannabivarin) is known to have marked anti-obesity effects in animal models. Some are psychomimetic/psychotropic and some are not. The content label of the product should indicate the amount of the other "minor" cannabinoids but at the moment most emphasis will be on the proportions of THC and CBD. In the future, this may evolve to include more specifics about the other cannabinoids as more research in humans emerges.

### 3.7 Terpenes and flavonoids

Terpenes give cannabis its characteristic smell and flavonoids give colour. They also have medicinal properties although the published research in humans elucidating the details is still very preliminary in the cannabis plant. Some patients are aware that they prefer a particular strain with a certain mixture of terpenes and minor cannabinoids, which matches with anecdotal clinical observations from prescribing in other jurisdictions where medical cannabis has been more widely prescribed, such as in Canada. The MCCS recommend that labelling of products includes at least the terpene profile so that our understanding of the value of these components can develop over time, and possibly included in any clinical data collection.

### 3.8 Endocannabinoid system (ECS)

This is the neurotransmitter system contained throughout the human body. There are natural endocannabinoid receptors (CB1 and CB2) found in the nervous and immune systems and elsewhere. There are natural ligands to these receptors (anandamide and 2-AG). The ECS is known to have a wide range of effects. The phytocannabinoids found in the plant are thought to work through the ECS (and other neurotransmitter systems). There is now a wide range of information available about the science of the ECS. The MCCS recommends that doctors familiarise themselves with at least the basics of this system in order to better understand the plant / human interaction.

## 4. Evidence



It is not the purpose of this document to provide a definitive scientific review of the evidence for cannabis use in different medical conditions. The reader can refer to a number of review publications on the subject (see References) as well more detailed research evidence on individual symptoms and diseases. The MCCS is now working on an evidence database. The MCCS recommend that a prescribing physician is fully familiar with the evidence relating to their particular area of expertise. This document makes general comments and broad recommendations, but the prescribing decision is for the doctor. The MCCS recommend that given that there are few doctors familiar with cannabis medicine, a specialist does not refuse prescription based on their own lack of understanding but seeks to work with or consult an expert cannabis physician. There are many examples of joint working / shared care arrangements in many branches of medicine and medical cannabis should not be an exception. The recent NICE guideline supports this approach.

### 4.1 Cannabis evidence

The MCCS is aware, and agrees, that the “gold standard” of pharmaceutical evidence is the double blind placebo-controlled study. This is not easy to conduct for the complex cannabis plant which has many tens of cannabinoids as well medically active terpenes and flavonoids. There are over 2000 different strains of the plant and thus it is really a family of medicines and not a single pharmaceutical entity. Double blind trials are possible and indeed GW Pharmaceuticals have paved the way in establishing that standard of evidence for their cannabis medicines Epidyolex and Sativex. We strongly encourage other cannabis producers to follow this route. However, developing these studies and awaiting results will take many years and we are concerned that many tens of thousands of people will be disadvantaged if this is deemed the only route of approval.

We note that the early clinical data from medical cannabis patients in other jurisdictions suggests that medical cannabis products may work better for some patients vs isolated pharma cannabinoid-derived drugs that only contain THC (in the case

of dronabinol and nabilone) or CBD. One possible explanation may be that the many bioactive cannabinoids and other plant chemicals have a synergistic effect on symptoms related to pain regulation and inflammation pathways. More research to elucidate this phenomenon is needed to fully understand it.

We encourage bodies, such as NICE and the MHRA, to give serious consideration to “real world” data which encompasses observational trials, case series and other valid entities. Many indications for cannabis medicine have a plethora of data from such sources but are lacking, for the moment, in double blind trial data. We agree with the statement by Sir Michael Rawlins (ex-Chair of Nice and current Chair of MHRA) when he stated in his Harveian Oration in 2008 – “Randomised controlled trials, long regarded as the “gold standard” of evidence, have been put on an undeserved pedestal. Their appearance at the top of “hierarchies” of evidence is inappropriate; and hierarchies, themselves, are illusory tools for assessing evidence. They should be replaced by a diversity of approaches that involve analysing the totality of the evidence-base”.

Many countries which have now allowed prescription of cannabis for medical purposes have introduced a parallel licensing and approval system for the plant to recognise the real problems around a purely pharmaceutical approach. We note, for example, the Office of Medicinal Cannabis in Holland which oversees production and approval processes and education in this space

We also wish to point to the favourable risk:benefit profile of cannabis medicine. There is a generally mild side effect profile, particularly of the high CBD products. (See side effect section below). The side effects of alternative medications also need to be considered. This includes, for example, the worrying crisis in opioid medication deaths. For further example, the serious side effects of multiple anti-convulsants in drug-resistant epilepsy need to be considered as well the effects of otherwise continuing seizures and the risk of Sudden Expected Death in Epilepsy (SUDEP) if seizures remain uncontrolled. A doctor must always balance the risks of one medication against the potential benefits of other medications and the risks of the alternatives and the risks of taking no action.

### 4.2 Cannabis as personalised medicine

It is clear that there are many strains of cannabis with varying proportions of THC and CBD and other components. **Cannabis is not a single medicine but a whole family of medicines and compounds existing in a single plant.** There is much trial and re-trial to cannabis medicine and there is no single strain that suits any particular condition. It can take some weeks for the physician and the patient to find the right medicine and the right dose.

### 4.3 Cannabis and quality of life

The MCCS wish to point out that cannabis can help many symptoms but rarely is a cure for any condition. Thus, prescribing doctors need to bear in mind that cannabis can be used for improvement in quality of life and they need to avoid a disease-oriented approach or advising a patient that cannabis is a curative approach. Take cancer as an example. There is certainly some early evidence that many cannabinoids have anti-cancer properties. There are many case studies showing that cannabis may reduce tumour load in specific tumours in single cases. However, the MCCS accept that the overall evidence for a “cure” of some cancers is thin, and due to the varied nature of tumour receptors expressed on cancer

cells, even within the same organ cancer (e.g. breast cancer) can have very different responses to different cannabinoids, possibly tumour promoting in some cases and in others, tumour reducing. We are likely many years away from having a full understanding of how we can safely and effectively recommend cannabis as a cancer treatment for the primary disease itself. Nevertheless, cannabis can help many problems associated with cancer, including anti-nausea effects during chemotherapy, reduction of pain, reduction of spasticity in nervous system tumours, reduction of anxiety, improved sleep and improved appetite. Thus a prescription of cannabis for a patient with cancer may be a very reasonable consideration for an improved quality of life.

### 4.4 Conclusive or substantial evidence of effectiveness

The MCCS now consider the evidence in specific conditions. These comments are based upon the conclusions of the National Academies of Sciences, Engineering and Medicine[20]. There is broad (but not complete) consensus on the evidence from the influential and thorough reports listed in the reference section [21,22,23,24,25].

#### 4.4.1 Spasticity –

Most studies have been conducted

with Sativex which is licenced for treatment resistant, moderate or severe spasticity in multiple sclerosis. It is a Schedule 4 product and can be prescribed as a licensed medication. The MCCS recommend Sativex (Nabiximols) is tried in the first instance for spasticity management if more standard medication has not produced the desired improvement. If a reasonable trial of Sativex fails to show improvement, it is still reasonable to conduct a trial of unlicensed medical cannabis using the ‘start low go slow’ approach.

#### 4.4.2 Pain –

The MCCS consider that cannabis should not be first line treatment for chronic pain management as there are acceptable licensed products available. However, the MCCS has doubts about the wisdom of using opioid medication before cannabis for chronic pain. The side effects of opioids and the risk of death from overdose are well known. The MCCS are aware of the “opioid sparing” effect of cannabis, whereby the dose of opioids can often be reduced or even stopped after the introduction of cannabis. The MCCS consider that serious consideration should be given to using cannabis medicine when otherwise opioids may have been considered. The MCCS suggest trying a balanced THC:CBD product first for pain as high CBD / low THC products are probably less efficacious as analgesics then products with a higher THC content. However, if anxiety or sleep are particular issues in a given patient then a high CBD product could be used first in an attempt to alleviate those symptoms. It would

be reasonable to use Sativex as the initial balanced product (being broadly 50:50 THC:CBD and delivering about 2.7mgs of THC and 2.5mgs CBD per spray) as it is licensed, although in the UK use for pain would be 'off-label'. We consider use of a licensed product is preferable to an unlicensed product in the first instance. If this approach fails then thought should be given to introducing a different full extract, unlicensed, product to see if a different strain or a higher proportion of THC may have a better effect. Vaping a balanced or higher THC product for breakthrough pain should also be considered.

#### 4.4.3 Nausea and Vomiting in Chemotherapy –

The MCCC recommend that standard licenced therapy is first choice but feel that, given the side effect profile and associated benefits (such as appetite stimulation), that cannabis products should be given consideration fairly early in the treatment plan. We note the NICE recommendation that Nabilone be used. We do not agree with this recommendation as we consider that a full extract cannabis product is likely to have better efficacy and less side effects. We recommend using an oral or sublingual product due the possible fungal/bio contaminants existing in dried cannabis that may be dangerous to persons with an impaired immune response such as patients undergoing cancer therapy. We consider further trials should be carried but in the meantime consideration should be given to a licensed cannabis product used in the first instance after failure of standard therapy and before an unlicensed product.

#### 4.4.4 Epilepsy –

Epidyolex (a full extract product but containing mainly (99%+) CBD) has now been licenced in the USA for Dravet and Lennox Gastaut syndromes following positive trials [26,27]. It has recently been approved in Europe. Whilst specific studies are lacking there is no logical reason why cannabis medicine should not be used for any epilepsy in childhood or adulthood which is resistant to standard drugs and not just for the licensed indications – Dravet and Lennox Gastaut. The relatively safe side effect profile of cannabis and the significant side effects of standard medication needs to be borne in mind as well as the effects of continuing seizures. The MCCC do not recommend cannabis as first line medication but equally do not consider it should be a drug of last resort. The MCCC recommends that Epidyolex is used first. If this is not successful or if tolerance develops then Sativex spray could be added to give a small dose of THC (plus more CBD). If this is not successful then a full extract unlicensed product should be considered which may contain a small amount of THC [28]. It would be a matter for the prescribing physician to use the best product for the individual.

The following paragraphs indicate those conditions for which there is less evidence of efficacy. We firmly encourage research into these conditions and symptoms. We recommend that standard licensed medications for these conditions are used first then 'off-label' licensed cannabis products may be tried (Epidyolex and Sativex) and if there is still room for improvement then unlicensed CBMPs could be initiated if it is considered in the Best Interest of the patient.

### 4.5 Moderate evidence of effectiveness

#### 4.5.1 Sleep –

There is improvement of short-term outcomes in those with obstructive sleep apnoea syndromes, fibromyalgia, chronic pain and multiple sclerosis. These are the diagnoses in which studies have been undertaken but there is no reason why sleep disturbance in other conditions should be not be helped. Preparations containing at least some THC seem to be most effective in most people for sleep, based on the evidence so far.

### 4.6 Limited evidence of efficacy

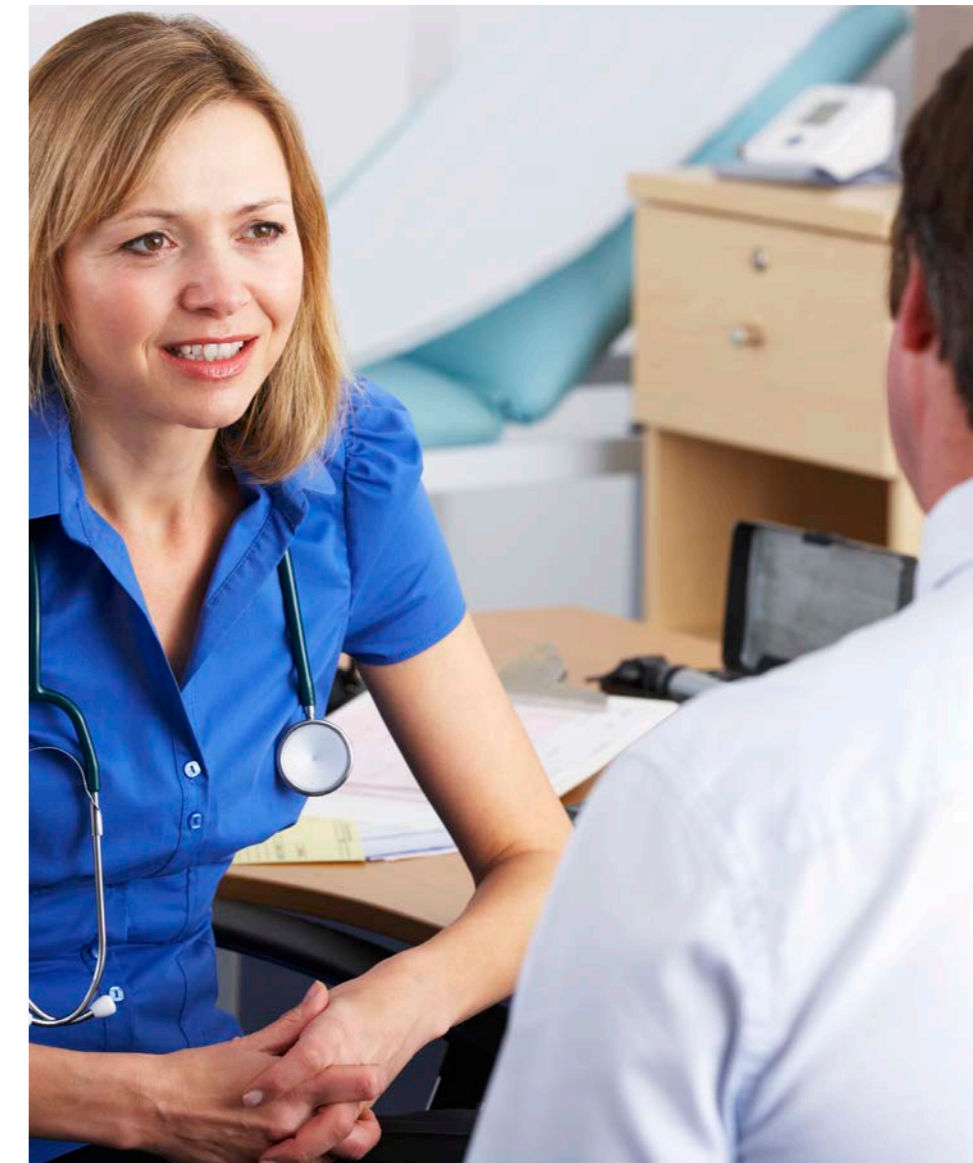
- **Increasing appetite** and decreasing weight loss, particularly in HIV/AIDS.
- **Anxiety** – the MCCC consider there is some evidence for the use of a CBD product for anxiety states. The MCCC recommend that such prescription is considered before every licenced anti-anxiety medication has been tried although clearly licenced product categories should be prescribed first – just not every drug in each category. CBD products for anxiety are extremely well-tolerated and have a good safety profile as long as it has been made under EU GMP practices and the product is validated with an independent COA.
- **Post-traumatic stress disorder**-There are multiple preliminary positive studies for the use of medical cannabis in the treatment of PTSD and should therefore be considered on a patient to patient basis with a psychiatrist with knowledge of this area
- **Symptoms of Tourette's syndrome**
- Better outcome after **traumatic brain injury** and intracranial haemorrhage

### 4.7 No conclusive evidence of efficacy

Cannabis is used in many other conditions and indeed some jurisdictions have allowed use in a large number of other disorders [29]. However, the evidence base for these conditions is lacking. This does not mean that cannabis is not effective in some circumstances but means that the studies have not allowed a firm conclusion to be drawn or have not been conducted. The MCCC note again that cannabis can be used as a product to enhance quality of life, regardless of condition, given its effectiveness for relief of pain, nausea, spasticity, sleep disturbance, poor appetite, anxiety, etc.

These conditions (not a definitive list) are:

- Motor control in Parkinson's disease
- Dystonia
- Huntington's disease
- Behavioural control in dementia
- Gastrointestinal disorders including IBS, Crohn's and ulcerative colitis
- Depression
- Obsessive compulsive disorder
- Autism spectrum disorder
- Cancer





## 5. Side effects

Prescribers need to be aware of the short-term side effects of cannabis. The MCCS note that it is mainly the higher THC products that produce more troublesome short-term effects such as drowsiness, dry mouth, disorientation, euphoria and confusion. These problems are more prevalent in high THC street cannabis and generally are less of an issue in lower THC medical cannabis, especially when counteracted by CBD. Patients, on higher THC products especially, should be warned **not to drive or operate heavy machinery** whilst under the influence of side effects of a cannabis product.

There appears to be a small increased risk of psychosis from higher THC cannabis although that risk is not entirely clear from the available literature. Nevertheless, the MCCS consider a **contraindication would be a history of schizophrenia or psychosis or a family history** of these conditions in a first degree relative - for THC containing products. This is especially the case in younger males and those under 25 years of age.

The MCCS is not convinced of the evidence of risk of **lung cancer** from smoking cannabis but nevertheless **smoking is not an allowable mode of administration**.

There is disputed and conflicting evidence of longer term **cognitive damage or adverse effects** from street cannabis which will tend to be high in THC and very low in CBD, which seems to be protective. These damaging effects with properly prescribed medical cannabis have not been found so far.

Cannabis (usually high THC products) can cause high pulse rate and a relative contraindication would be a **heart condition that could be exacerbated by a high pulse**. There is limited evidence that cannabis can trigger myocardial infarction or stroke in a high risk individual. That evidence is weak and disputed but caution is wise in people with risk factors for cardiovascular disease. Unstable cardiac disease such as unstable angina is a contraindication, especially with THC products, in general until the patient is haemodynamically stable.

There is substantial evidence of worsened respiratory symptoms and increased chronic bronchitis episodes with long term cannabis smoking but smoking is not legally allowed or desirable. Vaporizing medical cannabis has not been shown to have this side effect thus far, and because THC is a bronchodilator, some patients who use vaporized cannabis for another indication such as chronic pain who also have co-morbid asthma may find they find their breathing

symptoms improve with cannabis.

**Cannabis use disorder** (cannabis dependency syndrome) can occur in about 9% of chronic users (recreational use primarily) but these studies have largely been carried out on 'street' cannabis users with higher THC (and much less CBD) than is generally the case with medical cannabis. Cannabis use disorder developing from appropriately prescribed and monitored medical cannabis is very rare, based on the available clinical experience (expert opinion) but large data sets are lacking in the published literature for this subset.

**Cannabis hyperemesis syndrome** is rare complication, mainly occurring in high THC street product users. It is characterised by severe vomiting that may become chronic and cyclical that can require hospitalisation. Rehydration may be needed. The only 'cure' is discontinuation of cannabis.

Other **contraindications** would be:

A prior **history of allergy** to cannabis or carrier oils;

**Hepatitis C** infection as there is limited and controversial evidence of worsening with cannabis medication.

Patients on cancer immunotherapy medications which may have a reduced efficacy due to the immunomodulatory effects of cannabis (preliminary evidence, must weigh against patient quality of life and overall prognosis on a case-to-case basis).

**Drug interactions** need to be considered, particularly clobazam prescription in epilepsy as cannabis can increase circulating levels. Other drug interactions would need to be considered by the prescriber [30].

Cannabis should not be used, like any other medicine, in **pregnancy** or while breastfeeding unless absolutely essential.

There has been no reported death from **cannabis overdose**. High dose THC in overdose can cause extreme anxiety, increased pulse and paranoia and rarely psychosis, amongst other symptoms. THC in overdose in a cardiac patient with unstable angina may result in a cardiovascular event, including fatal ones. Treatment is to wait for the effects to settle, although hospitalisation is needed occasionally for acute anxiety, panic attacks or psychosis.

This is not a definitive statement of side effects and contraindications.



## 6. Dosage recommendations

These guidelines cannot provide definitive advice on dosage for particular products but some general points may be useful.

### 6.1 Start with high CBD / low THC product

There are few medical conditions that definitely need a high THC product for all patients with that indication. Thus it is best to start with a high CBD / low THC product at first to reduce incidence of possible side effects. The dose should slowly be increased. If the desired effect is not achieved, then changing to a more balanced THC/CBD product is the next step. Most producers make a range of products with a mix of THC and CBD in varying but broadly balanced proportions. Only if these products do not help sufficiently should a high THC / low CBD product be prescribed. In this way the side effects should be minimised. In any condition there will be some people who need a high THC / low CBD product (pain is usually a symptom which generally requires higher THC) but in most cases a high CBD / low THC or a balanced product will suffice.

In cannabis naive patients if a higher THC is to be used after a trial of a low THC / high CBD product is not adequate, many clinicians recommend starting the THC in the evening to minimize psychomimetic side effects especially in the initial 4-6 weeks of therapy and using a strain high in myrcene, which seems to be calming and/or mildly sedating in addition to the THC itself.

### 6.2 Start low and go slow

A basic principle is to start at a low dose and gradually increase at, say, weekly intervals. As a rough guide most people will need around 100 mg CBD per day for the desired effect but some will need a much lower dose (see below) and a few a much higher dose.

The licensed CBD product Epidyolex seems to need a higher dose – around 10-20mg/kg is more usual, especially for treating seizure disorders. The dose of pure isolates is generally around 5 times higher than FECO products.

The dose of THC is much lower. In cannabis naive patients, the THC starting dose should be 2mg at night or 1mg at night for geriatric patients or patients with a cardiac history. The dose could be escalated by about 1 to 2.5mg increments at weekly intervals until the desired effect is reached, although sometimes much slower increments are needed (see Delayed effect below). The average efficacious THC dose is around 10 to 15mg per day but can be higher. The average required dose varies considerably from person to person.

### 6.3 Sensitive individuals

A few people (maybe around 10%) seem to need much smaller doses. These people may have issues with metabolism of cannabinoids, possibly a variant of the CYP2c9 enzyme and other enzymes. Hence an initial low dose is the best course of action.

### 6.4 Biphasic response

Sometimes cannabinoids act biphasically. An effect at a particular dose is not necessarily improved by a dose increase and indeed the opposite may be true. A higher dose may worsen the response whereas a lower dose may improve the response.

### 6.5 Delayed effect

Sometimes the positive effect of cannabinoids may be delayed. Some children, for example, can take up to 6 weeks or so to respond to a specific dose and thus caution needs to be exercised about escalating the dose too quickly. Cannabinoids are lipophilic so they do tend to be stored in fatty tissues.



## 7. Research

The MCCS encourages research on the medicinal effects of cannabis. There is much to be learnt about the effects of different strains on different conditions, different modes of administration and dosages. The MCCS supports the themed call [31] by the National Institute for Health Research (NIHR) on “cannabis-based products for medicinal use”.

## 8. Education

The MCCS considers that a top priority is education for medical practitioners. Doctors have not been trained in cannabis medicine and many are, quite rightly, reluctant to prescribe due to their lack of knowledge. The MCCS encourages the establishment of training programmes and hope that Health Education England (and the counterparts in Scotland, Wales and Northern Ireland) will work with others to establish educational programmes in this field.

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