

WELSH HEALTH CIRCULAR



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For Action by:
*NHS Wales Chief Executives, Medical Directors,
and Chief Pharmacists*

Action required by: Immediate action required

Sender: Welsh Government

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Enclosure(s): Joint letter from the Chief Medical Officer & Chief Pharmaceutical Officer

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Llywodraeth Cymru
Welsh Government

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Chief Pharmaceutical Officer

To: Chief Executives, Medical Directors, and Chief Pharmacists

Cc: Health Inspectorate Wales

30 October 2018

Dear Colleagues,

Cannabis-based products for medicinal use

The UK Government on the 11 October laid The Misuse of Drugs (Amendments) (Cannabis and License Fees) (England, Wales and Scotland) Regulations 2018 which amend the Misuse of Drugs Regulations 2001 to reschedule certain cannabis-based products for medicinal use. The 2018 amendment regulations will come into force on 1st November 2018. This letter provides guidance to clinicians working in the NHS and independent health sector in Wales, following the regulatory change.

Background

In June 2018 the Home Office launched a review into the scheduling of cannabis for medicinal purposes. Part one of the [review](#), undertaken by Professor Dame Sally Davies, Chief Medical Advisor to the UK Government, considered the therapeutic and medicinal benefits of prescribing cannabis-based products in humans, and concluded there to be good evidence of therapeutic benefit for certain medical conditions, and reasonable evidence in several other medical conditions. The review recommended cannabis-based products be moved out of Schedule 1 of the Misuse of Drugs Regulations.

The Advisory Council on the Misuse of Drugs (ACMD) conducted part two of the review. Following the first part of its [review](#),¹ The ACMD recommended that “*cannabis-derived medicinal products of the appropriate standard*” be moved out of Schedule 1 and, subject to agreeing a suitable definition of *cannabis product for medicinal use*, listed in Schedule 2 of the Misuse of Drugs Regulations. Rescheduling cannabis-based products for medicinal use as Schedule 2 controlled drugs would mean some cannabis-based products could be used medicinally where there is an unmet clinical need.

The UK Government has laid an amendment to the Misuse of Drugs Regulations which will reschedule cannabis-based products for medicinal use, with the exception of synthetic

¹ The second part of the ACMD review is expected to be concluded during summer 2019.

cannabinoids². Subject to Parliamentary process, these regulations will come into force on 1st November 2018.

Prescribing cannabis-based medicinal products

Definition of cannabis-based medicinal products

In the 2018 amendment regulations the UK Government has defined a cannabis-based product for medicinal use in humans as:

“A preparation or other product, other than one to which paragraph 5 of part 1 of Schedule 4 applies³ which—

(a) is or contains cannabis, cannabis resin, cannabinal or a cannabinal derivative (not being dronabinol⁴ 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 preparation or manufacture of an ingredient of, a medicinal product.”

Who can prescribe cannabis-based medicinal products?

Due to the limited evidence base and their unlicensed nature, the UK Government has restricted prescribing of cannabis-based products to only those clinicians listed on the Specialist Register of the General Medical Council (GMC). This restriction is set out the 2018 amendment regulations.

Relevance of existing procedures when prescribing and supplying cannabis-based medicinal products

In the UK, all cannabis-based products for medicinal use apart from Sativex (which is currently listed in Schedule 4 of the Misuse of Drugs Regulations) will be **unlicensed medicines**. Further information on licensing is provided in an annex to this letter. In addition, it is expected doctors should only prescribe within their specialist area of practice.

As with any unlicensed medicines, the prescribing of cannabis-based products must be on a named patient basis. Organisational procedures regarding the prescribing of unlicensed medicines must be followed; arrangements must be in place to ensure all prescribing of cannabis-based products is auditable. As schedule 2 controlled drugs, the prescribing of unlicensed cannabis-based products must also follow organisational procedures for prescribing controlled drugs.

² Rescheduling applies only to cannabis and cannabis preparations (such as extracts from cannabis as well as cannabinoids isolated from cannabis). It does not include synthetic versions of naturally occurring cannabinoids (e.g. marinol/dronabinol) or any non-natural cannabinoids obtained by chemical synthesis (e.g. nabilone).

³ i.e. Sativex

⁴ In the United Kingdom, “dronabinol” does not refer to a tetrahydro derivative of a plant based cannabinal derivative, or to 3-alkyl homologues of such cannabinal derivatives or their tetrahydro derivatives, but instead to a synthetic product that is not plant based.

Relevant professional guidance

Any decision to prescribe a cannabis-based product must take account of the [GMC](#) and [Medicines and Healthcare Product Regulatory Agency](#) (MHRA) guidance regarding the prescribing of unlicensed medicines, as well as the relevant procedures for prescribing controlled drugs and unlicensed medicines in place within the health board, NHS trust or independent healthcare provider.

Organisational oversight

As a matter of good practice, we would expect any decision to prescribe a cannabis-based product will have been made only following discussion of the relevant case, between the prescribing doctor and a peer whose name is included in the same specialist register maintained by the GMC. Within NHS organisations, appropriate arrangements should be put in place to ensure each decision to prescribe is approved by the organisation's Medical Director or Senior Clinician(s) nominated by the Medical Director. Peer discussions and Medical Director approval should be appropriately documented.

Therapeutic indications for cannabis-based products

Cannabis-based products for medicinal use should only be prescribed for indications where:

1. There is clear evidence of benefit;
2. A patient's clinical need cannot be met by a licensed medicine; and
3. Established treatment options have been exhausted.

Where cannabis-based products are prescribed for medicinal purposes clear treatment goals should be agreed prior to initiation of treatment. Arrangements for regular review of prescribing against treatment goals should be in place with treatment discontinued where these goals are inadequately achieved.

Selection of cannabis-based products for prescribing

Doctors are expected to only prescribe cannabis-based products where they can be certain of their content and quality. For example, products should not be prescribed where the content of cannabinoid constituents in the product is either not known, uncertain or not declared on the product label. Products would be expected to meet the requirements set out in [MHRA Specials Guidance](#).

Before prescribing a cannabis-based product, the prescriber should discuss sourcing a suitable product, which meets the requirements set out by the MHRA, with the organisation's pharmacy department, this discussion should involve the organisation's Chief Pharmacist or a senior pharmacist nominated by the Chief Pharmacist. Pharmacy departments should follow professional best practice in sourcing, procurement and supply of unlicensed cannabis-based products in accordance with the Royal Pharmaceutical Society (RPS) Professional [Guidance](#) for the Procurement and Supply of Specials.

Clinicians and pharmacists working in the independent sector are similarly expected to follow processes for prescribing and supplying unlicensed special medicines, which take account of the GMC, RPS and MHRA guidance.

Clinical Guidelines

To support specialist clinicians' prescribing decisions, the National Institute for Health and Care Excellence (NICE) will produce a clinical guideline on the prescribing of cannabis-based products for medicinal use. This guidance is expected to be available by October 2019.

In the interim, the British Paediatric Neurology Association ([BPNA](#)) will develop clinical advice on the use of cannabis based products in paediatric epilepsy. The Royal College of Physicians ([RCP](#)) will develop additional advice regarding prescribing for intractable chemotherapy induced nausea and vomiting and chronic pain.

Pharmacovigilance

In all situations where cannabis-based products for medicinal use are prescribed, treating clinicians should maintain a detailed assessment of clinical and patient outcome measures to support patient safety and longer term understanding of the effectiveness of cannabis-based products. This will include reporting **all** suspected adverse reactions to the product (whether licensed or unlicensed) to the MHRA's Yellow Card Scheme.

Responsibilities of Controlled Drug Accountable Officers

Cannabis-based products will be schedule 2 controlled drugs. Controlled Drug Accountable Officers (CDAOs) have a statutory responsibility to secure the safe management and use of controlled drugs within their organisation and, in the case of local health board CDAOs, within organisations and by professionals for which their health board is responsible. CDAOs must ensure (and be assured) that procedures are in place to demonstrate this. This includes a duty to monitor the prescribing, supply and administration of all controlled drugs. It is expected CDAOs will consider whether additional governance arrangements will be required to ensure the safe introduction of cannabis-based products for medicinal use in clinical practice.

Yours sincerely



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Prif Swyddog Meddygol/Cyfarwyddwr Meddygol,
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Chief Medical Officer/Medical Director NHS Wales



Andrew Evans

Prif Swyddog Fferyllol
Chief Pharmaceutical Officer

Annex I - Types of Products

Cannabis has many active chemical constituents and two of these constituents, tetrahydrocannabinol (THC) and cannabidiol (CBD) have been investigated the most in respect of their medicinal value. THC is the major psychoactive constituent of cannabis and is considered responsible for giving so called “highs” to users of cannabis. CBD on the other hand, is not psychoactive.

Products falling within Schedule 2 will contain varying quantities and ratios of THC and CBD and may be available in a range of pharmaceutical forms, including as the herbal material or as extracts formulated for example as oils and capsules. Manufacturers should adhere to Good Manufacturing Practice. "Pure CBD" is not a controlled drug for the purposes of the 1971 Misuse of Drugs Act.

There is also a wide range of other cannabis products available on the internet and in some commercial outlets such as health food outlets and from cannabis ‘dispensaries’ internationally. These products are of unknown quality and contain CBD and THC in varying quantities and proportions. In the opinion of the Home Office (see its guidance note [here](#)), any CBD product that contains any amount of THC will be a controlled drug within the meaning of the 1971 Misuse of Drugs Act, except under very specific circumstances. Therefore using cannabis-based products that do not meet the official definition of a cannabis-based product for medicinal use (such as home-grown or street cannabis) for therapeutic benefit is illegal and potentially dangerous and patients should be reminded of this. The evidence that cannabis and some of its constituents can be addictive and harmful is well known and is not disputed by recent science.

The health harms of smoking are clear, therefore the regulations prohibit the self-administration of a cannabis-based product for medicinal use in humans by way of smoking other than for research purposes, and patients should be informed of the health risks associated with such use.

Current Licensing

Sativex® - (cannabis extracts containing THC and CBD) is the only licensed cannabis based medicinal product that is available in the UK. It has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) as a treatment for spasticity in multiple sclerosis since 2010. Sativex is listed under Schedule 4 of the Misuse of Drugs Regulations 2001 at present. However Sativex® is currently subject to a NICE ‘do not do’ recommendation: *Do not offer Sativex to treat spasticity in people with MS because it is not a cost effective treatment.*

To date, the MHRA has licensed **no** other cannabis products as medicines. However, nabilone, a synthetic, non-natural cannabinoid, is licenced in the UK for use in treatment resistant nausea and vomiting caused by chemotherapy; dronabinol, a synthetic nature-identical, version of THC is listed under Schedule 2 of the Misuse of Drugs Regulations 2001, but it does not have a Market Authorisation from the MHRA in the UK, although it is available internationally.

Manufacture, importation, distribution and supply

[MHRA guidance](#) sets out the requirements for the manufacture, import, distribution and supply of cannabis-based products for medicinal use. This applies the same principles that apply to other unlicensed medicines, and manufacturers and importers of these products will require the necessary licences issued by the MHRA.



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An Roinn Sláinte
Máinnystrie O Poustie



Llywodraeth Cymru
Welsh Government

Tuesday 20th November 2018
Gateway Publications clearance: 08652

Dear Colleagues

Supplementary information on cannabis-based products for medicinal use

Following the letter issued on the 31st of October 2018, this supplementary letter provides further guidance to clinicians and organisations following the re-scheduling of cannabis-based products for medicinal use on November 1st 2018.

Clinical Guidance

We have been asked to clarify the status of the clinical guidance issued.

As highlighted previously, the National Institute for Health and Care Excellence (NICE) has been asked by the Department of Health and Social Care to produce a clinical guideline on the prescribing of cannabis-based products for medicinal use in humans. This guideline is expected by October 2019 at the latest.

The interim clinical guidance published by the British Paediatric Neurology Association (BPNA) on the use of cannabis-based products for medicinal use in children and young people with epilepsy and the Royal College of Physicians (RCP) guidance around prescribing of cannabis-based products for medicinal use in chemotherapy induced nausea and vomiting, chronic pain and pain in palliative care patients is based on the best available clinical evidence. NHS England have also asked the Association of British Neurologists (ABN) to provide interim guidance on the use of cannabis-based products for medicinal use in adult neurological conditions, including Multiple Sclerosis (MS).

Whilst this interim guidance is available to support specialist doctors on the Specialist Register of the General Medical Council (GMC) in deciding whether to prescribe cannabis-based products for medicinal use in a limited number of conditions, this does not remove or replace the clinical

discretion of the prescriber in accordance with their professional duties. We expect clinicians to work with their individual patients or their carers (where appropriate) to agree the best treatment, taking into account the clinical evidence base, GMC prescribing guidance on licensed, off label and unlicensed medicines, and local medicines governance systems. This is in line with normal clinical practice.

A set of clinical frequently asked questions (FAQs) is currently being prepared to provide further support to prescribers; once available these will be published [here](#). In the meantime, clinicians should discuss any queries around prescriptions with their local hospital Chief Pharmacist/Director of Pharmacy in the first instance.

Synthetic Cannabinoids

Cannabis-based products for medicinal use can be divided into those that are naturally occurring in the cannabis plant and those that are synthetic. A summary of naturally occurring products are provided in annex 1.

We would also like to provide further clarification in relation to synthetic cannabinoids for medicinal use. This clarification is intended to help clinicians understand the distinctions between the different types of synthetic cannabinoids and to raise awareness that two synthetic cannabinoids (Dronabinol and Nabilone) remain available for prescribing and have not been affected by the recent legislative change.

There are three main groups of chemical compounds that fall within the broad category of 'synthetic cannabinoids'.

1. Synthetic compounds which are identical in structure to naturally occurring cannabinoids such as delta-9-tetrahydrocannabinol (THC) e.g. Dronabinol.
2. Synthetic compounds structurally *related* to naturally occurring cannabinoids that have been developed to mimic naturally occurring cannabinoids such as THC e.g. Nabilone.
3. Synthetic compounds not structurally related to naturally occurring cannabinoids but which bind to cannabinoid receptors in the body.

With respect to group 1 compounds, Dronabinol has been developed as a medicinal product. In addition, in group 2, Nabilone has also been developed for medicinal use and is available as a licensed medicinal product. See Annex 2 for further details.

Group 3 synthetic compounds not structurally related to naturally- occurring cannabinoids but which bind to cannabinoid receptors in the body are not available as licensed medicinal products. Many of the compounds in group 3 have frequently been found in illicit street products referred to by the street names of Spice and Black Mamba, and are predominantly new psychoactive substances (NPS). There is clear evidence of significant harm and several deaths associated with their illicit use.

The Advisory Council on the Misuse of Drugs (ACMD) has particular concerns with compounds falling within group 3 and others within group 2, with the exception of Nabilone, and is of the view that further research into this complex group of diverse substances is important, given the associated potency and harms. The ACMD stated that they needed further time to consider and

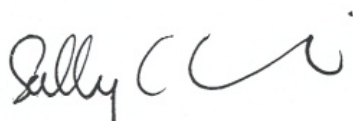
consult on the unintended consequences of the potential rescheduling of these products. Therefore, all synthetic cannabinoid compounds, unless authorised for medicinal use, will remain in Schedule 1 of the Misuse of Drugs Regulations 2001 (and Misuse of Drugs (Northern Ireland) Regulations 2002) at least until the full ACMD review is concluded; this is due to be published by July 2019. Consideration may then be given as to whether to re-schedule any further synthetic cannabinoid compounds for medicinal use.

As it currently stands: Compounds in group 1, such as Dronabinol, can lawfully be prescribed. Only compounds in group 2 that have been rescheduled individually under the Misuse of Drugs Regulations 2001 can be prescribed e.g. Nabilone. None of the synthetic compounds in group 3 are available for prescribing.

Further information can be found [here](#)¹ and on the current classifications of cannabis products for medicinal use in the annexes to this letter.

This letter has been agreed by Chief Medical Officers and Chief Pharmaceutical Officers across the United Kingdom.

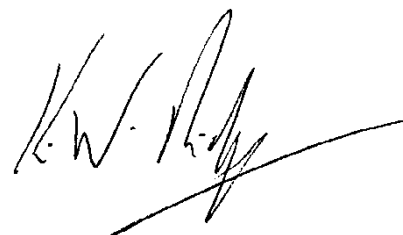
Yours sincerely,



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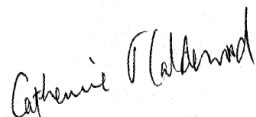
¹ <https://www.england.nhs.uk/medicines/support-for-prescribers/cannabis-based-products-for-medicinal-use/>
<https://gov.wales/docs/dhss/publications/whc2018-039en.pdf>
<https://www.health-ni.gov.uk/sites/default/files/publications/health/hss-md-28-2018.pdf>
[https://www.sehd.scot.nhs.uk/cmo/CMO\(2018\)15.pdf](https://www.sehd.scot.nhs.uk/cmo/CMO(2018)15.pdf)



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Annex 1

Summary of Naturally Occurring Cannabis-Based Products for Medicinal Use

Product	Constituents	Licensing	Indication	Controlled Drug Status	Which clinicians can prescribe?	Commissioning arrangements in England only ²
Cannabis-based products for medicinal use as defined by the change in regulations on 1st November 2018						
Cannabis-based products for medicinal use³ e.g. Tilray and Bedrocan products that were supplied under a Home Office (HO) licence.	A range of preparations containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) with differing percentages of the active constituents. The product to be specified by brand/supplier; cannabis strain and content of THC/CBD (and ratio of THC/CBD where relevant), as appropriate.	Unlicensed specials Suppliers should comply with MHRA guidance and Good Manufacturing Practice standards.	Available on a named patient basis for indications where there is clear published evidence of benefit or UK Guidelines and in patients where there is a clinical need which cannot be met by a licensed medicine and where established treatment options have been exhausted.	Schedule 2	Specialist doctors on the GMC specialist register only can take the decision to prescribe.	Commissioning will depend on the indication that these products are prescribed for. Trusts will need to pick up the costs for named patients until normal commissioning processes can be defined.
Cannabis-based products already available for medicinal use in the UK prior to 1st November 2018						
Epidiolex® oral solution	Cannabidiol (CBD) isolated in pure form from Cannabis.	Unlicensed in the UK.	Approved by the US Food and Drug Administration (FDA) for Lennox-Gastaut Syndrome or Dravet Syndrome in patients 2 years of age and older.	Not a controlled drug	No restrictions on prescribing however likely to be specialist prescribing due to the nature of the proposed indications.	Lennox-Gastaut Syndrome and Dravet Syndrome is commissioned by NHS England Specialised Commissioning. Not routinely commissioned currently but this will be tariff excluded from April 2019 subject to a consultation.

² Arrangements for the routine availability of medicines will differ in Scotland, Wales and Northern Ireland and clinicians should confirm specific arrangements in line with local protocols.

³ Note: Other cannabis-based products are on the market, often sold as food supplements. There is no assurance they have been manufactured to Good Manufacturing Practice standards using pharmaceutical grade ingredients or that they have consistent levels of ingredients between batches. These products should not be prescribed.

			Currently going through licensing in Europe. The marketing authorisation for the UK may further define who should prescribe.		Currently unlicensed so accessed on a named patient basis.	Currently going through normal commissioning processes and a NICE Technology Appraisal due for publication in November 2019. Early Access Programme available – speak to your local hospital Chief Pharmacist.
Sativex® (nabiximols) oromucosal spray	Extracts from two strains of cannabis with standardised content of the active constituents delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).	Licensed	Symptom improvement in adult patients with moderate to severe spasticity due to Multiple Sclerosis (MS) who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy.	Schedule 4	Must be initiated and supervised by a doctor with specialist expertise in treating MS patients as defined by the Marketing Authorisation.	Sativex® falls under the commissioning responsibility of Clinical Commissioning Groups (CCGs). However, it is currently not recommended by NICE.

Annex 2

Summary of Synthetic Cannabis-Based Products for Medicinal Use

Product	Constituents	Licensing	Indication	Controlled Drug Status	Which clinicians can prescribe?	Commissioning arrangements in England only ⁴
Synthetic cannabis-based products already available for medicinal use in the UK prior to 1st November 2018						
Dronabinol capsule	Synthetic structurally-identical form of delta-9-tetrahydrocannabinol (THC) (Group 1).	Unlicensed in the UK.	It has been approved by the US Food and Drug Administration (FDA) to treat loss of appetite in people with AIDS, and to treat severe nausea and vomiting caused by cancer chemotherapy in patients with inadequate response to conventional antiemetic treatments.	Schedule 2	No restrictions on prescribing. Unlicensed so accessed on a named patient basis.	Chemotherapy and HIV services are commissioned by NHS England. This would be in tariff but as an unlicensed medicine it would not be routinely commissioned. Trusts would pick up costs.
Nabilone capsule	Synthetic non-natural cannabinoid that mimics delta-9-tetrahydrocannabinol (THC) (Group 2).	Licensed	Nausea and vomiting caused by chemotherapy, unresponsive to conventional antiemetics.	Schedule 2	No restrictions on prescribing. Summary of product characteristics states: Preferably administered in a Hospital setting, under close supervision. GP's may prescribe once initiated.	NHS England is responsible for commissioning chemotherapy and associated supportive drugs if given as part of a chemotherapy regimen. If used outside an agreed regimen it is considered in tariff.

⁴ Arrangements for the routine availability of medicines will differ in Scotland, Wales and Northern Ireland and clinicians should confirm specific arrangements in line with local protocols.