

## **Cannabis-based products for medicinal use (CBPMs) in humans**

An assessment of the impact of rescheduling CBPMs to Schedule 2 under the Misuse of Drugs Regulations 2001 (MDR) and recommendations to mitigate the issues identified

**November 2020**

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# 1. Introduction

## (i) Definitions used in this report

1.1. For the purposes of this report:

- **'CBPMs'** refers to those products that meet the following definition of a “*cannabis-based product for medicinal use in humans*” as per Regulation 2(1) of the Misuse of Drugs Regulations 2001 (MDR) (as amended):

*“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, or paragraph 10 of Schedule 5, applies, which:*

*(a) is or contains cannabis, cannabis resin, cannabinal or a cannabinal 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;”.*

- **'unlicensed CBPMs'** refers to those products that fall under the definition of a CBPM and that have not been assessed by the medicines regulator (the Medicines and Healthcare products Regulatory Agency [MHRA] or the European Medicines Agency [EMA]) for safety, quality or efficacy.

There are a range of products that have been prescribed in the UK that would fall under this definition including, for example, Tilray (2:100 cannabidiol [CBD] oil), Bedrolite, Bedica.

- **'licensed CBPMs'** refers to products that have been granted marketing authorisation by the medicines regulator (the MHRA or the EMA) but that continue to fall under the definition of a CBPM as per Regulation 2(1) of the MDR.

The term has not been used extensively in this report, as there are no such products currently available in the UK.

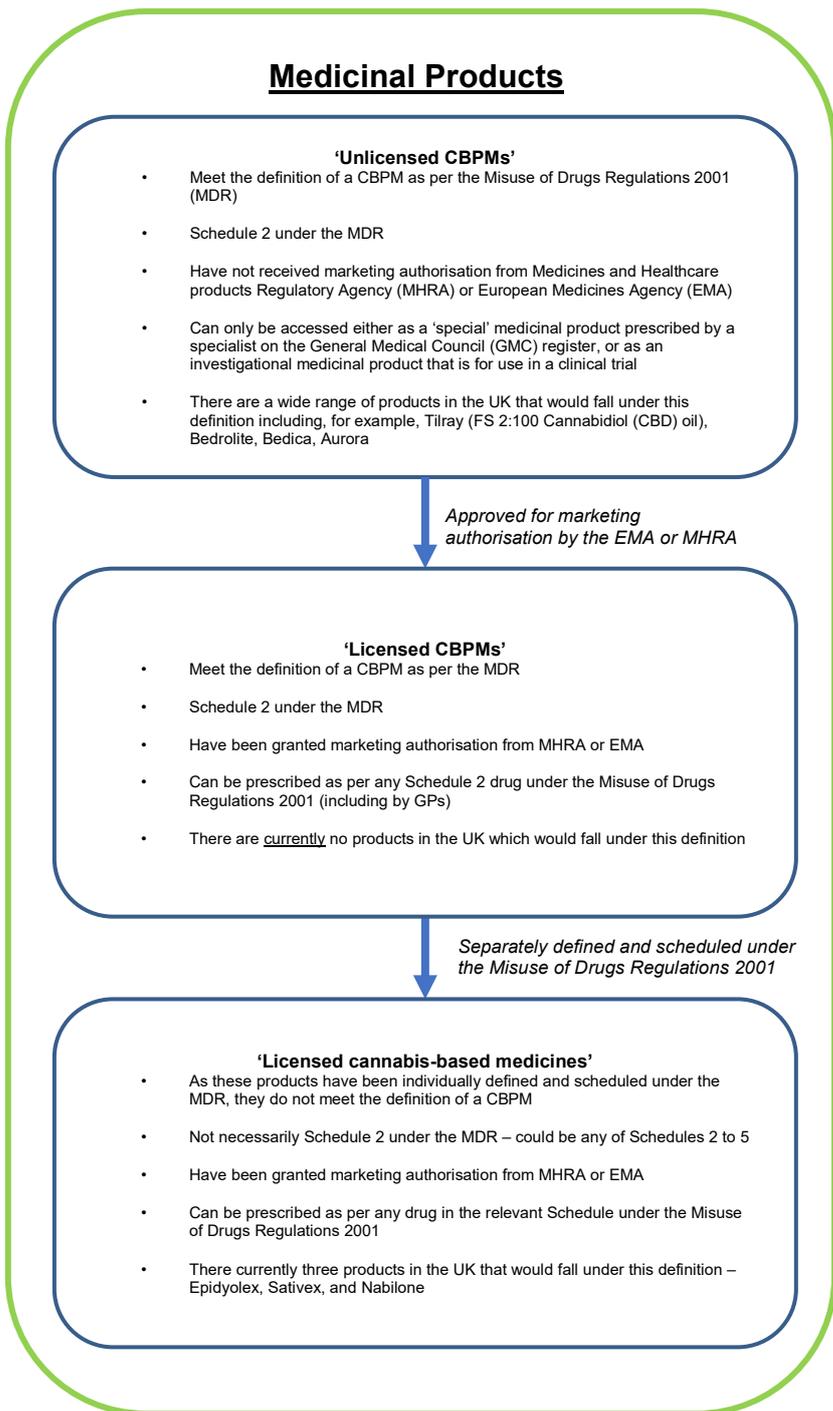
- **'licensed cannabis-based medicines'** refers to products that have been granted marketing authorisation by the medicines regulator (the MHRA or the EMA) and

have been defined and scheduled separately under the MDR such that they do not fall under the definition of a 'CBPM'.

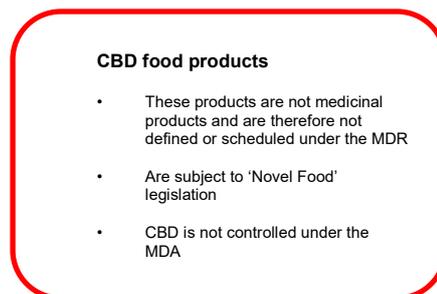
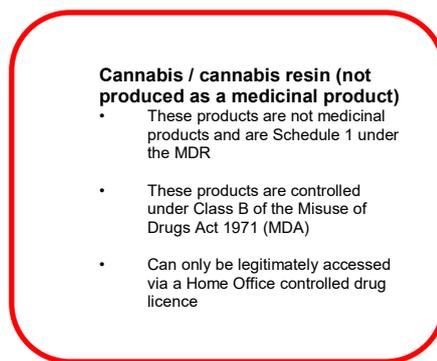
Unlike the term 'CBPM', the term 'licensed cannabis-based medicines' is not defined in legislation and has been used for simplicity for the purposes of this report.

There are currently three products in the UK that fall under this definition: Epidyolex, Nabilone and Sativex.

Epidyolex received its marketing authorisation in September 2019 and was rescheduled with a bespoke entry under the MDR in June 2020. For the purposes of this report, for the period between Epidyolex receiving its marketing authorisation and the rescheduling, Epidyolex has been included as a 'licensed cannabis-based medicine' (to reflect its current status).



Situation in November 2020



**Note:** Cannabidiol (CBD) food products, and illicit cannabis, are referred to throughout this report – but neither are medicinal products.

**Figure 1: The different categories of medicinal products referred to in this report are enclosed within the green boundary**

## (ii) Background

- 1.2. In June 2018 the then-Home Secretary announced the Government's intention to commission a two-part review of cannabis and cannabis-related products. The first part of the review was led by the then-Chief Medical Officer (CMO) for the UK Government, Professor Dame Sally Davies. The findings of the review provided by Professor Dame Sally Davies, recommended that "*cannabis-based medicinal products are moved out of Schedule 1 of the Misuse of Drugs Regulations 2001 (MDR)*". The Advisory Council on the Misuse of Drugs (ACMD) was then formally commissioned in July 2018 to consider the appropriate scheduling of cannabis and cannabis-related products under the MDR and whether there are further provisions that could be made to reduce the risks of harm and diversion [Home Office, 2018].
- 1.3. In the ACMD's advice in response to the then-Home Secretary's commission, the ACMD agreed with the CMO's finding that there had emerged evidence of medicinal benefit for some cannabis-based products for medicinal use (CBPMs) for certain conditions in patients. The ACMD advised that clinicians in the UK should have the option to prescribe CBPMs that meet the requirements of medicinal standards to patients with certain medical conditions. It was therefore found to be appropriate for these medications to not be subjected to the requirements of Schedule 1 of the MDR. The ACMD instead recommended that the Home Office, Department of Health and Social Care (DHSC) and the Medicines and Healthcare products Regulatory Agency (MHRA) develop a clear definition to set out what constitutes a CBPM – and that, once developed, products meeting this definition should be moved into Schedule 2 of the MDR pending further ACMD advice [ACMD, 2018a].
- 1.4. On 1 November 2018, following further short-term ACMD advice on the refinement of the proposed CBPM definition and additional recommendations intended to strengthen the proposed legislative change for CBPMs [ACMD, 2018b] – CBPMs were added to Schedule 2 of the MDR.
- 1.5. Following this legislative change, in February 2019 the ACMD was formally commissioned to conduct a longer-term review of CBPMs [Home Office, 2019]. This commission was split into three components, asking the ACMD to:
  - 1) conduct an assessment of the impact of the rescheduling of CBPMs and to report its findings and any recommendations to mitigate the issues identified;
  - 2) provide an updated harms assessment on synthetic cannabinoids, and a recommendation on the appropriate classification under the Misuse of Drugs Act 1971 (MDA) and scheduling under the MDR of synthetic cannabinoids; and

- 3) advise whether the scheduling of products that currently fall under the definition of CBPMs is appropriate, and whether any further legislative amendments regarding CBPMs are required under the MDR.
- 1.6. The ACMD will advise on the first component of this commission within this report. The first aspect of this component required the ACMD to set out how it would assess the various impacts of the rescheduling of CBPMs to Schedule 2 under the MDR, and the data sources that will be used – this impact assessment framework was provided by the ACMD in December 2019 [ACMD, 2019]. As well as considering the impacts of the rescheduling of CBPMs on various datasets relating to CBPMs themselves, the ACMD also committed to considering the impact of the rescheduling on datasets relating to licensed cannabis-based medicines.
- 1.7. Utilising this impact assessment framework, the ACMD then compiled data to populate the framework (using information currently available) with the targeted datasets. To examine change over time, where possible, datasets representing three time periods were examined:
  - one dataset relating to the year immediately preceding the rescheduling of CBPMs (i.e. 01/11/2017 – 31/10/2018);
  - another dataset relating to the year immediately following the rescheduling (i.e. 01/11/2018 – 31/10/2019); and
  - a final dataset corresponding to the period between November 2019 and summer 2020.
- 1.8. This report will attempt to assess these data to quantify the factors listed in the ACMD's 2019 impact assessment framework [*ibid.*] – and ultimately to draw conclusions regarding the impact of the rescheduling of CBPMs to Schedule 2 of the MDR.
- 1.9. This report will focus on the impact of the rescheduling of CBPMs on the following areas:
  - prescribing of CBPMs and licensed cannabis-based medicines;
  - the market, monitoring, trials and research for CBPMs and licensed cannabis-based medicines;
  - professional education, and public knowledge and attitudes towards cannabis, CBPMs, and licensed cannabis-based medicines; and
  - crime, enforcement and regulation related to CBPMs and licensed cannabis-based medicines.

## 2. Impacts on CBPM prescribing

### (i) Numbers of patients with prescriptions of licensed cannabis-based medicines and number of prescribed licensed cannabis-based medicine items

- 2.1. The legislative change that rescheduled cannabis-based products for medicinal use (CBPMs) to Schedule 2 of the Misuse of Drugs Regulations 2001 (MDR), and de-designated these products from the Misuse of Drugs (Designation) Order 2015 allowed a legal route for the prescription of CBPMs without a Home Office licence. Unlicensed CBPMs will not have been fully tested for safety, efficacy and quality and can therefore only be accessed:
- either as a ‘special’ medicinal product that is for use in accordance with a prescription or direction of a specialist medical practitioner on the specialist register of the General Medical Council (GMC); or
  - as an investigational medicinal product without marketing authorisation that is for use in a clinical trial.

Practitioners on the specialist register of the GMC who prescribe unlicensed CBPMs take on responsibility for the safety, quality and efficacy of the product – and for determining whether the prescription of these products is in the best interest of the patient. Licensed CBPMs, on the other hand, would be fully tested for safety, efficacy and quality – and could therefore be prescribed in the same ways as any other drug in Schedule 2 of the MDR (for example, they can be prescribed by general practitioners [GPs]), subject to the terms of the marketing authorisation. However, as defined at the outset of this report (in Section 1[i]), there is a difference between ‘licensed CBPMs’ and ‘licensed cannabis-based medicines’ – and there are currently no products considered ‘licensed CBPMs’ in the UK. In contrast, there are three products that are described in this report as ‘licensed cannabis-based medicines’: Epidyolex, Nabilone and Sativex. Each of these products is separately defined and scheduled under the MDR (see Table 1).

	Product	Scheduling under the MDR
<b>Licensed cannabis-based medicines</b>	Epidyolex	5
	Nabilone	2
	Sativex	4 (Part I)
<b>Non-exhaustive list of examples of unlicensed CBPMs</b>	Tilray (2:100 CBD <sup>1</sup> oil)	All products meeting the definition of a CBPM are scheduled under Schedule 2 of the MDR
	Bedrocan oil 1% CBD 2% THC <sup>2</sup>	
	Bedrolite oil 10% CBD	
	Bedica oil 2% THC	
	Capilano CBD + THC	

Notes:1 Cannabidiol.  
2 Tetrahydrocannabinol.

**Table 1: An indication of the three products referred to as ‘licensed cannabis-based medicines’ in this report – alongside a non-exhaustive list of examples of unlicensed CBPMs prescribed in the UK**

- 2.2. The Advisory Council on the Misuse of Drugs (ACMD) impact assessment framework [2019] noted that a possible impact of the rescheduling of CBPMs to Schedule 2 of the MDR could have been the facilitation of prescriptions of licensed cannabis-based medicines. This impact would be indicated by a change in the number of patients with prescriptions of licensed cannabis-based medicines, and possibly by a change in the number of prescribed licensed cannabis-based medicine items. The number of prescribed CBPM items is distinct from the number of patients with prescriptions of CBPMs – as one patient, for instance, could be prescribed multiple items of CBPMs
- 2.3. From data provided by the relevant bodies in each of the administrations of the UK (England, Wales, Scotland and Northern Ireland), the ACMD found that the level of prescribing of licensed cannabis-based medicines in the UK remained stable in the year following the rescheduling of CBPMs to Schedule 2 of the MDR. Between 1 November 2017 and 31 October 2018, at least 803 patients were reported to have been prescribed licensed cannabis-based medicines across the UK (the figure of 803 patients is made up of 359 reported in the English data, 76 in the Welsh data, 199 in the Scottish data and 169 in the Northern Irish data – but is an estimate as the English data did not include prescribing to patients privately, and the Scottish and Welsh data did not include prescription figures from both primary and secondary care). This figure appears to have fallen very slightly, with at least 782 patients reported to have been prescribed licensed cannabis-based medicines across the UK between 1 November 2018 – the date of the rescheduling of CBPMs – and 31 October 2019.
- 2.4. The licensed cannabis-based medicines being prescribed in the period reported above were largely Nabilone and Sativex. Epidyolex received marketing authorisation on 19 September 2019, so has been considered as a *licensed* cannabis-based medicine by the ACMD (see clarification in Section 1[i] ‘Definitions used in this report’) for only a small proportion of that reporting period. However, Epidyolex was available as an unlicensed product via an Early Access Programme from 12 November 2018 (these prescribing figures will therefore not have been included in *this* section, which is looking only at the prescription of licensed cannabis-based medicines).
- 2.5. In the months following 1 November 2019, the level of prescribing licensed cannabis-based medicines appeared to show a moderate increase. Table 2 below indicates that more patients were prescribed licensed cannabis-based medicines by the NHS in England between November 2019 and March 2020 (five months) than in the entire preceding year. This increasing trend in prescribing licensed cannabis-based medicines also appeared to be reflected in the data in Scotland, Wales and Northern Ireland.

<b>No. of patients prescribed licensed cannabis-based medicines by the NHS in England</b>	
<b>01/11/2017 – 31/10/2018</b>	359
<b>01/11/2018 – 31/10/2019</b>	320
<b>01/11/2019 – March 2020</b>	328 <sup>1</sup>
<b>Note 1: In addition to the 328 patients identified, an unidentified number of patients were prescribed 276 licensed cannabis-based medicines in this period – the number of patients could not be specified where a unique patient ID was not identifiable from the prescription.</b>	

**Table 2: Annual patient count for NHS prescriptions of licensed cannabis-based medicines in England**

- 2.6. Whilst this trend could, to some degree, be attributable to Epidyolex receiving marketing authorisation in autumn 2019, meaning that prescriptions of Epidyolex began to be counted as prescriptions of licensed cannabis-based medicines (rather than as unlicensed CBPMs) – this does not appear to be the major factor. Epidyolex was only available for prescription by the NHS from 6 January 2020, following an NHS agreement with the manufacturer of Epidyolex that allowed the National Institute for Health and Care Excellence (NICE) to recommend this product as an option for the treatment of seizures associated with both Dravet and Lennox-Gastaut syndromes [NICE, 2019a; 2019b]. Instead, a significant increase in the levels of prescribing of Sativex and Nabilone appear to have also contributed to this trend. For example, at least 288 patients aged 18 and over were prescribed Sativex by the NHS in England between November 2019 and March 2020 alone, in comparison with the 272 patients (all ages) who were prescribed Sativex by the NHS in England for the entire year from 1 November 2018 to 31 October 2019. The driver behind this increase is probably a result of NICE guidance on ‘cannabis-based medicinal products’ in November 2019 (which covered CBPMs, licensed cannabis-based medicines, plant-derived cannabinoids and synthetic compounds such as dronabinol) and the publication of NICE’s technology appraisal guidance for the treatment of Lennox-Gastaut and Dravet syndromes with Epidyolex [*ibid.*]. Both publications included recommendations for healthcare professionals on the appropriate prescribing of Epidyolex, Nabilone and Sativex.
- 2.7. However, the full extent of the apparent increasing trend of prescriptions of licensed cannabis-based medicines is unclear. The emergence of the COVID-19 pandemic in the UK in March 2020 had a significant impact on multiple different areas of crucial data collection for the ACMD’s assessment. For example, as a result of the pandemic, by March 2020 prioritisation had meant that the NHS Business Services Authority (NHS BSA) had temporarily suspended the central counting of private prescriptions. Similarly, in addition to the 288 patients aged 18 and over who were prescribed 628 items of Sativex in England between November 2019 and March 2020, NHS BSA reported that ‘an unidentified number’ of patients had been prescribed 233 items of Sativex in England by the NHS in the same period. Without

exact figures it is challenging to accurately judge the impact of the rescheduling of CBPMs to Schedule 2 of the MDR on the levels of prescribing of licensed cannabis-based medicines. Additionally, as noted earlier data have been collected separately from each administration of the UK, each of which caveated the data submitted in different ways – with English data submitted on the prescription of licensed cannabis-based medicines, for example, not including private prescriptions. This further complicates the assessment of the impact of the rescheduling of CBPMs on levels of prescribing for licensed cannabis-based medicines.

**Conclusion 1:** Many of the various impacts of rescheduling CBPMs in November 2018 have been gradual, and the timeframe over which this review has been conducted is too short to reach a conclusive understanding of changes over time – particularly given the emergence of the COVID-19 pandemic, which has impacted on crucial data collection since March 2020. Data collection and comparison was further complicated by differing methods of data collection across each administration of the UK, which resulted in differently caveated data.

**Conclusion 2:** Three licensed cannabis-based medicines are now available in the UK and approved by NICE for conditions where the evidence is strongest – around 800 patients a year received a licensed cannabis-based medicine from 2017 to 2019. There is evidence of an increase in the number of patients being prescribed licensed cannabis-based medicines across the UK in the four to six months following November 2019, possibly as a result of:

- the publication of NICE guidance on ‘cannabis-based medicinal products’ [NICE, 2019; 2019c];
- the publication of NICE’s technology appraisal guidance for the treatment of Lennox-Gastaut and Dravet syndromes with Epidyolex [NICE, 2019a; 2019b], and/or
- the granting of marketing authorisation for Epidyolex in the UK.

## (ii) Number of patients with prescriptions of unlicensed CBPMs and number of prescribed unlicensed CBPM items

2.8. The ACMD’s impact assessment framework suggested that an impact of the rescheduling might be seen in the level of prescribing of unlicensed CBPMs in the UK [ACMD, 2019]. This would be indicated by the number of patients with prescriptions of unlicensed CBPMs, and by the number of items of unlicensed CBPMs being prescribed.

2.9. In the year immediately prior to the rescheduling of CBPMs on 1 November 2018, fewer than 13 patients across the UK were reported to have been issued with prescriptions of unlicensed CBPMs (178 unlicensed CBPM items were dispensed). These prescriptions could have occurred, for example, under Home Office licence and/or through clinical trials. In the year following the rescheduling, more than 75

patients across the UK were reported to have been issued with prescriptions of unlicensed CBPMs (452 unlicensed CBPM items were dispensed) – see Table 3.

	01/11/2017 – 31/10/2018	01/11/2018 – 31/10/2019
<b>England</b> (Source: NHS BSA)	On NHS: <5 patients <sup>1</sup> Private: 0 patients	On NHS: <5 patients <sup>1</sup> Private: 63 patients
<b>Wales</b> (Source: Welsh Analytical Prescribing Support Unit [WAPSU])	On NHS: 0 patients Private: 0 patients	On NHS: 0 patient Private: 0 patients
<b>Scotland</b> (Source: Medicines Division – Scottish Government)	On NHS: 0 patients Private: 0 patients	On NHS: 0 patient Private: 12 patients
<b>Northern Ireland</b> (Source: Department of Health, NI)	On NHS: 8 patients Private: 0 patients	On NHS: <5 patients <sup>1</sup> Private: 0 patients
<p><b>Note:</b> 1. The number of patients is being withheld in accordance with the General Data Protection Regulation, due to the number of items attributed to fewer than five patients and the potential for patient identifiable information to be published. The given administration (England, Scotland, Wales or Northern Ireland) relates to the geographical location of the dispensing prescriber, rather than the patient.</p>		

**Table 3: A comparison between the number of patients being issued prescriptions of unlicensed CBPMs, in the year immediately preceding, and the year immediately following the date of the rescheduling of CBPMs (01/11/2018)**

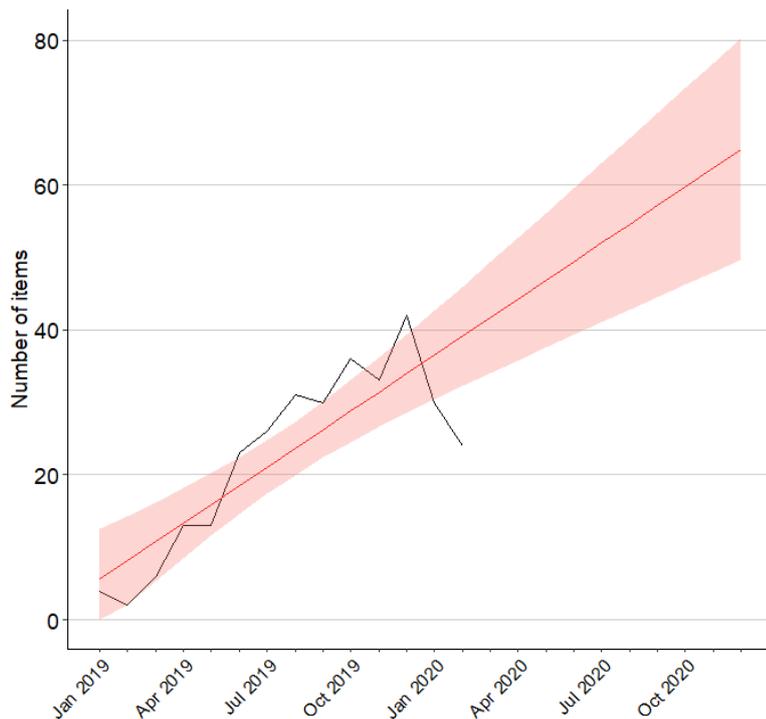
2.10. As illustrated in Table 2, the increase in the number of patients being issued prescriptions of unlicensed CBPMs in the year immediately following the rescheduling of CBPMs in November 2018 to Schedule 2 of the MDR largely resulted from an increase in the level of private prescribing.

- The vast majority of prescriptions of unlicensed CBPMs issued in the UK in the year following the rescheduling were issued privately.
- Only in Northern Ireland were all of the reported prescriptions of unlicensed CBPMs issued via the public healthcare system, Health and Social Care (HSC).
- All 12 of the patients prescribed unlicensed CBPMs in this period in Scotland received their prescriptions privately, as did 63 of the patients prescribed unlicensed CBPMs in this period in England.

2.11. The Care Quality Commission (CQC) also reported that the number of prescriptions of unlicensed CBPMs was low throughout 2019 but was increasing, with the majority of prescribing in the independent sector [CQC, 2020]. CQC reported that the amount of CBPM items prescribed privately as a percentage of the total increased steadily month-by-month from January 2019 (67%) to December 2019 (98%).

2.12. As a result of the emergence of the COVID-19 pandemic – which led to NHS BSA temporarily suspending the processing of private prescriptions of unlicensed CBPMs – there were challenges in the ACMD’s assessment of whether the increase in the

number of patients being issued private prescriptions of unlicensed CBPMs continued from 1 November 2019 into 2020. However, the DHSC was able to provide the ACMD with an estimate of actual and projected trends in prescribing to assist in this task (see Figure 2). NHS BSA had reported that, in the year following the rescheduling of CBPMs (01/11/2018 – 31/10/2019), a total of 184 private prescriptions of unlicensed CBPMs were dispensed in England. Over the four months from November 2019 to February 2020, 129 private prescriptions of unlicensed CBPMs were dispensed. Prescribing grew steadily up to December 2019 but dropped in January and February 2020. If prescribing continued to increase, and if the drop in January and February was a temporary disruption, estimated numbers of private prescriptions dispensed between November 2019 and July 2020 inclusive could be between 300 and 400 items. Over the year November 2019 to October 2020, the figure could reach between 400 and 600 items, with the embedding of new private clinics offsetting the impact of COVID-19. This would equate to an estimate of between 149 and 224 unique patients projected to have been privately prescribed unlicensed CBPMs in England over the course of that year.



**Note:** The shaded area indicates upper and lower estimate of items.

**Source:** NHS Business Services Authority.

**Figure 2: Actual and projected numbers of private prescriptions of unlicensed CBPMs dispensed in England**

- 2.13. The data suggest that the rescheduling of CBPMs did not have a significant impact on the reported level of NHS prescriptions of unlicensed CBPMs across the UK in the year immediately following the legislative change (1 November 2018 – 31 October 2019).
- In Wales and Scotland, no patients had been prescribed unlicensed CBPMs by the NHS in the year prior to the legislative change – this did not change in the year following the legislative change.
  - Similarly, in England the number of patients in receipt of prescriptions of unlicensed CBPMs by the NHS in the year prior to the rescheduling of CBPMs (fewer than 5) did not change in the year following the rescheduling – although the number of items of unlicensed CBPMs dispensed to those patients in those years did increase, from 3 to 19.
  - In Northern Ireland, the reported number of patients prescribed unlicensed CBPMs by the HSC even fell in the year following the rescheduling of CBPMs to Schedule 2 of the MDR compared with the year immediately prior to the legislative change (from eight to fewer than five patients). By May 2020 (by which point Epidyolex had received marketing authorisation in September 2019), fewer than five patients in Northern Ireland were reported to still be in receipt of prescriptions of unlicensed CBPMs from the HSC.
- 2.14. For clinicians considering whether a prescription of an unlicensed CBPM would be appropriate, the NICE guidance on CBPMs refers these clinicians to GMC guidance. This guidance notes, as with all unlicensed medications, that the decision to prescribe CBPMs should be based on an assessment of the individual patient and may be necessary where there is no suitable licensed medicine that will meet the patient's need. Without a CBPM patient registry in place (as of October 2020), it is unclear whether private clinics are prescribing licensed cannabis-based medicines prior to the initiation of unlicensed CBPMs, and for what indications. It is also unclear why the level of prescribing of unlicensed CBPMs by the NHS is not equivalent to the level in private practice. A CBPM patient registry could make this clearer.
- 2.15. As part of this assessment, the ACMD considered the barriers to physicians prescribing CBPMs that remain, despite the rescheduling to Schedule 2 of the MDR. For the treatment of epilepsy, the only product for which there are efficacy and safety data is for the licensed cannabis-based medicine Epidyolex. A NICE Technology Appraisal recommended Epidyolex for the treatment of two epilepsy syndromes: Dravet, and Lennox-Gastaut syndromes. When considering other CBPMs for the treatment of epilepsy, there are little data as to the efficacy or safety of these products, or the ratio of tetrahydrocannabinol:cannabidiol (THC:CBD) to prescribe. Whereas, for licensed cannabis-based medicines, the manufacturer will be accountable for any harm resulting from the product when used within its licence, it is the prescriber who assumes the responsibility for any harm that occurs as a result of the prescription of an unlicensed CBPM (unless the harm was a result of a defect in the product) [Nutt *et al.*, 2020]. There is also no clear route for physicians to fund

treatment with CBPMs. If physicians were to apply for funding, this would need to be an individual funding request (IFR) – an application for funding for a treatment that is not usually given by the NHS, in situations where a clinician believes their patient's clinical situation is so different to other patients with the same condition that they should have their treatment paid for where others would not. Additionally, although a children's 'Refractory Epilepsy Specialist Clinical Advisory Service' has been set up where patients can be referred for discussion by a panel of paediatric neurologists, this service has not been developed as a CBPM decision-making service.

- 2.16. The rescheduling of CBPMs to Schedule 2 also had the impact of increasing the range of unlicensed CBPMs prescribed in the UK. In the year prior to the legislative change, only four products – Bedica oil, Bedrolite oil, Epidyolex (considered an unlicensed CBPM until it received marketing authorisation in September 2019) and Tilray (2:100 CBD oil) – had been prescribed to patients in the UK. In the year following the rescheduling of CBPMs, a range of unlicensed CBPMs were prescribed (mostly prescriptions issued privately) to patients across the UK – 29 unlicensed products were privately prescribed in England alone. These unlicensed CBPMs were associated with varying CBD:THC contents and were prescribed in varying quantities, for varying lengths of treatment, and for a variety of medical conditions – including conditions that were not supported by the NICE guidance.
- 2.17. As with the data relating to the prescription of licensed cannabis-based medicines, the ACMD found that the emergence of the COVID-19 pandemic in the UK in March 2020 had a significant impact on crucial data collection relating to the levels of prescribing of unlicensed CBPMs. Prioritisation meant that NHS BSA had suspended central counting of private prescriptions of CBPMs by March 2020. NHS BSA was also unable to report to the ACMD the number of patients who had been prescribed unlicensed CBPMs on NHS prescription, as patient details were not being captured for NHS prescriptions as a result of a pause in data processing during the COVID-19 pandemic.

**Conclusion 3:** Currently, only a limited number of patients (strongly presumed to be fewer than 5) have been prescribed unlicensed CBPMs by the NHS, despite a range of unlicensed CBPMs being available. This may be expected for a number of reasons, including:

- licensed cannabis-based medicines are now available to clinicians and are recommended by NICE guidance for certain conditions – unlike unlicensed CBPMs;
- there is a lack of safety and efficacy data for many unlicensed CBPMs;
- prescription of unlicensed CBPMs is limited only to practitioners on the specialist register of the GMC; and
- lack of evidence on cost effectiveness and the relatively high costs of these unlicensed medicines.

**Conclusion 4:** Compared with the number of patients prescribed unlicensed CBPMs by the NHS, there had been a considerable increase in the number of patients privately prescribed unlicensed CBPMs in England in the year immediately following the rescheduling of CBPMs (63 patients, up from 0 in the preceding year). A continuation of this trend is expected based on DHSC projections, with between 149 and 224 unique patients estimated to have been privately prescribed unlicensed CBPMs in England over the course of 2020. It is unclear how many of the patients receiving privately prescribed unlicensed CBPMs – products that often lack robust evidence of safety, quality and efficacy data – were first prescribed licensed cannabis-based medicines before commencing treatment with unlicensed CBPMs.

### (iii) Introduction of patient registry, collection of patient outcome data for a range of conditions

- 2.18. Before the November 2018 legislative change that rescheduled CBPMs to Schedule 2 of the MDR, there had been no patient registry for CBPMs despite the availability of a limited number of products with marketing authorisation, such as Sativex. In the ACMD's impact assessment framework, it had been considered that one of the possible impacts of the legislative change would be an improvement to the evidence-base for CBPMs via the enactment of a patient registry and a uniform dataset [ACMD, 2019].
- 2.19. Following the November 2018 legislative change, NHS England and NHS Improvement (NHS-E/I) began to develop a patient registry for CBPMs. The ACMD supported this development throughout, considering it to be crucial in improving the CBPM evidence base.
- 2.20. By May 2020 the NHS Arden and Greater East Midlands Commissioning Support Unit had been commissioned to develop that registry and had developed a 'wireframe' (demo) of this registry.

**Conclusion 5:** The development of a CBPM patient registry is a very significant step in allowing for a careful analysis of the extent and pattern of prescription of CBPMs and their benefits and risks.

### 3. Impacts on the development of the CBPM market and on monitoring, trials and research

#### (i) Costs of licensed cannabis-based medicines and unlicensed CBPMs

- 3.1. In the Advisory Council on the Misuse of Drugs (ACMD) impact assessment framework, it had been suggested that a potential impact of the rescheduling of cannabis-based products for medicinal use (CBPMs) to Schedule 2 of the MDR could have been on the costs of both licensed cannabis-based medicines and unlicensed CBPMs [ACMD, 2019]. This was justified as the legislative change could have facilitated access to medicines and encouraged suppliers to enter the market – leading to an eventual fall in the cost of licensed cannabis-based medicines and unlicensed CBPMs.
- 3.2. Following the rescheduling of CBPMs, the costs of licensed cannabis-based medicines appears to have remained largely stable. By June 2020 only the drug tariff price of Sativex (270 doses) had fallen (by 20%) since the legislative change in November 2018. The drug tariff prices for Nabilone remained unchanged (see Table 4). The drug tariff prices listed will not reflect any price discounts negotiated by the National Institute for Health and Care Excellence (NICE) and the manufacturers during the development of the November 2019 NICE guidelines, which recommended these products for use on the NHS (and which are commercially sensitive). Epidyolex, which received marketing authorisation in September 2019, does not yet appear in the drug tariff.

	November 2018	June 2020
<b>Sativex</b> (27ml, 270 doses)	£375.00	£300.00
<b>Nabilone</b> (20 capsules, 1mg)	£196.00	£196.00
<b>Nabilone</b> (20 capsules, 250 micrograms)	£150.00	£150.00
<b>Epidyolex</b> (100ml)	<i>Had not yet received marketing authorisation</i>	<i>Epidyolex does not yet appear on the drug tariff</i>

**Table 4: The cost on the drug tariff of licensed cannabis-based medicines in the UK in November 2018 as compared with June 2020**

- 3.3. Comparative data are not available to contrast current UK market costs of unlicensed CBPMs to the UK market costs, prior to the legislative change in November 2018, of products that would now be considered unlicensed CBPMs.

However, from data provided by the Department of Health and Social Care (DHSC) in April 2020, it had been shown that the average price for unlicensed CBPM oils per mg of cannabidiol (CBD) was around 30p per mg, and around 55p per mg for tetrahydrocannabinol (THC). Although prices per mg or gram (flower) are useful for comparing product pricing, they do not reflect costs to patients (or the NHS) of prescriptions. These costs will vary widely depending on the strength, volume and dose prescribed, which will vary by patient and condition.

3.4. *[Paragraph 3.4 has been redacted from the published version of this report]*

**Conclusion 6:** The price of licensed cannabis-based medicines has remained largely unchanged. The price of unlicensed CBPMs is currently high in comparison to licensed cannabis-based medicines. The market for unlicensed CBPMs, licensed CBPMs and licensed cannabis-based medicines is still in its infancy.

## (ii) Number of imports of CBPMs

- 3.5. The ACMD's framework had also noted that an indicator of the impact of the rescheduling of CBPMs to Schedule 2 of the MDR on the development of a UK CBPM market could have been observed by a change in the number of imports of CBPMs into the UK [ACMD, 2019].
- 3.6. Specialist importers of CBPMs must notify the Medicines and Healthcare products Regulatory Agency (MHRA) of their intention to import unlicensed CBPMs into the UK. The date of the first notification to the MHRA of an import of a product that would have met (as of 1 November 2018 rescheduling of CBPMs) the definition of an unlicensed CBPM was reported to have been 13 June 2018. Between that date and the 1 November 2018 legislative change, 10 import notifications (representing 152 packs of such products) were notified for import.
- 3.7. In the year immediately following the rescheduling, 181 CBPM import notifications (representing 1,749 packs of unlicensed CBPMs) had been made to the MHRA (see Table 5). An increase in the rate of notifications was then observed over the next four months to February 2020 – more import notifications were issued over these four months than over the entire year immediately following the rescheduling of CBPMs. However, an even greater increase in the rate of import notifications was observed following changes to import policy announced by the Government on 2 March 2020 [DHSC, 2020]. These increases are again illustrated in Table 5. The changes enabled the import of CBPMs in anticipation of prescriptions and for licensed wholesalers to hold supplies of products to be drawn on when in receipt of a prescription or direction from a specialist doctor on the General Medical Council (GMC) specialist register – whereas previously licensed wholesalers could only apply to import the quantity specified on a prescription.

	Number of import notifications made to the MHRA	Number of packs of unlicensed CBPMs notified for import
<b>13/06/2018 (date of first import notification) – 01/11/2018<sup>1</sup></b>	10	152
<b>01/11/2018 – 31/10/2019<sup>1</sup></b>	181	1,749
<b>01/11/2019 – 29/02/2020</b>	182	1,992
<b>01/03/2020 – 01/10/2020</b>	1,043	37,543
<b>Note: 1. These figures will have included import notifications relating to Epidyolex. Prior to the date of its marketing authorisation (19 September 2019), Epidyolex met the definition of an unlicensed CBPM.</b>		

**Table 5: The number of CBPM import notifications made to the MHRA (alongside the number of packs of CBPMs notified) since the date of the first import notification made to the MHRA (13/06/2018).**

- 3.8. The number of import notifications will not equate to the number of unlicensed CBPMs that have actually been imported. The MHRA's letters of 'no objection' do not have an expiry date and allow an importer to import up to a maximum of the quantity specified on the notification – an importer may choose to import less than the amount notified, or to defer importation in instalments over time.
- 3.9. This caveat limits the merits in using levels of import notifications as an indicator of the impact of the rescheduling of CBPMs on the development of the UK CBPM market. However, the data serve as a proxy indicator for potential CBPM market interest – even if it remains unclear the extent to which a 'real' market is developing.

**Conclusion 7:** There has been a considerable increase in CBPM import notifications made to the MHRA – as well as the number of packs of CBPMs notified for import – which does not necessarily reflect an actual increase in the quantity of CBPM imports. It is currently unclear what this increase in CBPM import notifications represents, and whether it is indicative of increased CBPM usage within the UK.

### (iii) Development of the UK cannabidiol market

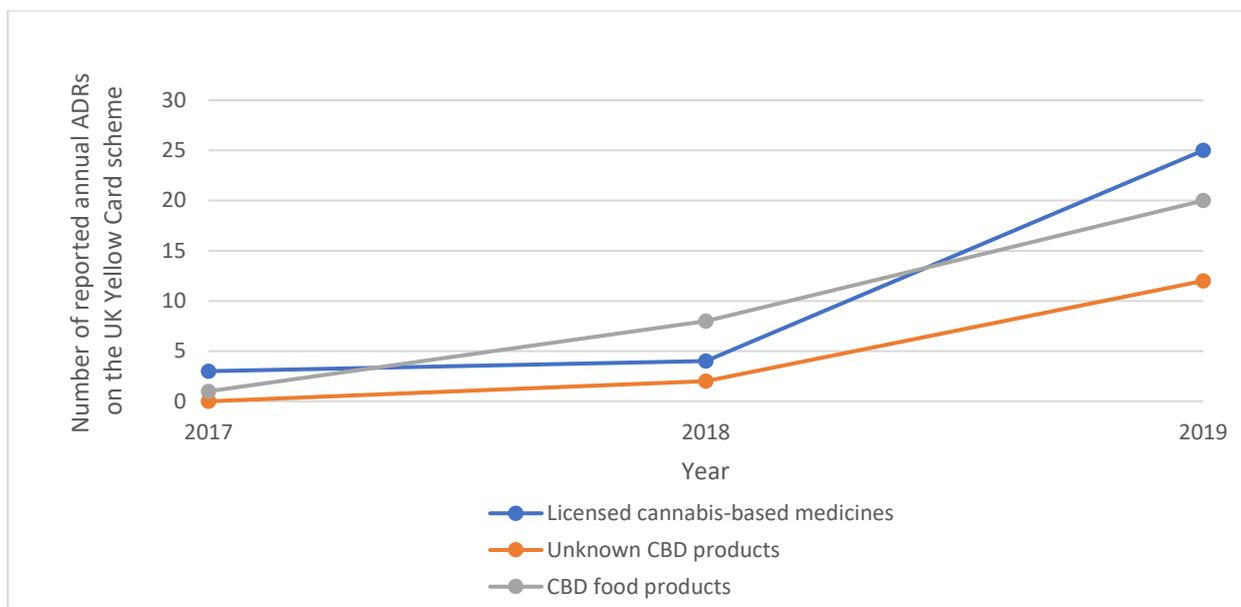
- 3.10. Over the course of this assessment, the ACMD has also considered whether the rescheduling of CBPMs has had an impact on the development of the UK CBD market.
- 3.11. In parallel with the rescheduling of CBPMs, there has been widescale commercialisation of other products, including dietary supplements and other consumables containing CBD. Particularly over the past five years, there has been a significant increase in public interest in the potential health benefits of CBD – despite there currently being little evidence to support health benefit claims for CBD food

products, and little investigation of their safety via controlled trials [Chesney *et al.*, 2020].

- 3.12. The Food Standards Agency (FSA) has classified such consumables as 'novel foods', which require adequate safety data to be available in order to allow them to be marketed. As part of the FSA's assessment, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) reviewed available data on the toxicity of CBD [COT, 2020]. As a result, the FSA has recently issued guidance to consumers, including recommended maximum limits on the quantity of CBD that should be ingested each day, and to producers, requiring them to provide the quality and safety data necessary to enable their products to remain on sale [FSA, 2020].
- 3.13. While the recommended maintenance dosage for Epidyolex for specified medical applications is 10mg of CBD/kg/day (i.e. 700mg/day for a 70 kg adult), the FSA has advised consumers to keep to a significantly lower maximum dosage of CBD from 'novel foods' of 1mg /kg/day (70mg for a 70 kg adult).

#### (iv) Number of reported adverse drug reactions on UK Yellow Card Scheme

- 3.14. In the ACMD's framework, it had been noted that some impacts of the rescheduling of CBPMs could potentially be identified through pharmacovigilance schemes, such as the UK's 'Yellow Card' scheme run by the MHRA [ACMD, 2019]. For example, it was hypothesised that updated MHRA guidance on CBPMs might facilitate access to medicines (both importations and domestic) and reduce the risk to prescribers, patients and the public. A comparison was therefore conducted of the number of reported adverse drug reactions (ADRs) related to licensed cannabis-based medicines, unlicensed CBPMs and CBD products on the Yellow Card scheme before and after the legislative change.
- 3.15. ADRs reported on the UK Yellow Card scheme related to licensed cannabis-based medicines, unlicensed CBPMs and CBD products have increased between 2017 and 2019 (see Figure 3). This increase was notable between 2018 and 2019 i.e. in the year following the rescheduling of CBPMs to Schedule 2 of the Misuse of Drugs Regulations 2001 (MDR).



**Figure 3: The number of adverse drug reactions (ADRs) related to licensed cannabis-based medicines, unlicensed CBPMs and CBD products reported annually between 2017 and 2019 on the UK Yellow Card scheme**

3.16. However, this information should be used with caution as some of the Interactive Drug Analysis Profiles (IDAPs) contain overlaps between licensed medicinal products and food substances. It is also important to note that ADR reports are not proof that the adverse drug reaction is occurring due to the medicine but only a suspicion by the reporter that a medicine may have caused the adverse drug effect. ADR reports may therefore relate to true side effects of the product, or they may be due to coincidental illnesses that would have occurred in the absence of the medicine. When interpreting these data, it was important to note that the number of reports received should not be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients using the drug, are included in these data. ADR data are therefore limited in their use as a reliable indicator of the frequency of actual ADRs to medicines. However, the ACMD chose to include these data in this assessment as a proxy indicator of the impact:

- of the rescheduling of CBPMs on the development of the CBPM market and on the availability of these products; and
- on stimulated public knowledge of CBPMs and non-medical cannabis-derived products (for example, CBD food supplements).

3.17. A number of fatal ADRs had consistently been reported between 2017 and 2019 for products listed under the ‘cannabis sativa’ heading of the UK Yellow Card scheme’s IDAPs (three in 2017; seven in 2018; and three in 2019). These fatalities all related to the use of illicit cannabis, rather than to the use of CBPMs – no fatal ADRs were reported in 2017 and 2018 for products listed under the ‘cannabidiol’ heading of the UK Yellow Card scheme’s IDAPs. One fatal case was then reported via the scheme

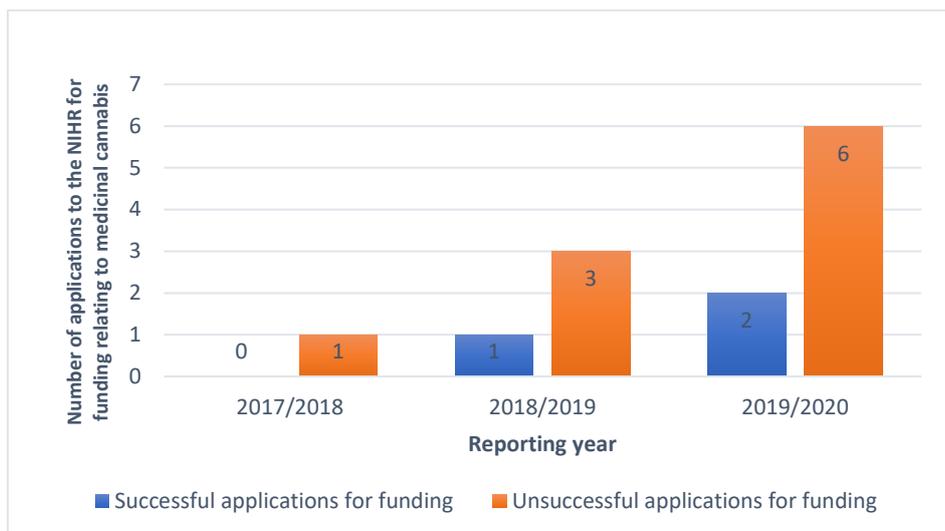
in 2019 for Epidyolex (oral use) – the reaction and outcome was reported to be seizure and vomiting, followed by death.

**Conclusion 8:** MHRA Yellow Card data on adverse drug reactions indicated a low level of reported harm for unlicensed CBPMs, CBD food products and licensed cannabis-based medicines, although some of the harms that were reported (including one fatality associated with a licensed cannabis-based medicine) were severe. The level of ADR reporting associated with these products has increased since the rescheduling of CBPMs, however, this increase was from extremely limited levels of ADR reporting in 2017. It is too soon to draw conclusions about the safety of these products from the current Yellow Card data available.

### (v) Number of trials registered, reporting and completed, and amount of funding and patients involved in trials

- 3.18. The ACMD had previously suggested that the rescheduling of CBPMs might lead to an improved evidence base for their therapeutic value as a result of an increase in clinical trials and other studies. This could, in turn, have an impact on the number of patients legitimately accessing unlicensed CBPMs or licensed cannabis-based medicines. Patients could access unlicensed CBPMs or licensed cannabis-based medicines for a specific condition by participating in a relevant clinical trial. It would not be necessary for the results of that clinical trial to emerge before admissible patients could access the relevant product.
- 3.19. However, the ACMD recognised that it was unlikely that a significant increase in the amount of relevant clinical trials would be observed over the course of this assessment. A time lag was to be expected – given the significant amount of time required to arrange and conduct clinical trials. As the National Institute for Health Research (NIHR) has reported, it can take 6 to 12 months even to design a clinical trial, produce the detailed trial protocol and secure all of the necessary permissions [NIHR, 2019]. The trials themselves would typically take place over the course of multiple years. Additionally, the emergence of the COVID-19 pandemic in the UK in March 2020 interrupted research and clinical trials relating to licensed cannabis-based medicines and unlicensed CBPMs – again, reducing the likelihood of an increasing number of clinical trials in this field being observed over the course of this assessment.
- 3.20. The total number of applications made to the NIHR on cannabinoids, licensed cannabis-based medicines and unlicensed CBPMs has increased since the legislative change in November 2018. In the financial year 2017/2018, only one such application (eventually unsuccessful) had been submitted to the NIHR. By 2018/2019, this had risen to four, and by 2019/2020 this had risen again to eight. This could be indicative of increased research interest in CBPMs, cannabinoids and

licensed cannabis-based medicines as a result of the rescheduling. Although only one of the four applications in 2018/2019 was successful and only two of the eight applications in 2019/2020 were successful (see Figure 4), the ACMD noted that this success rate was not surprising and reflected similar success rates in applications for funding in other fields. After a consideration of the aims of those studies funded through the NIHR programme, the ACMD did, however, recognise that a number of the studies related to the harms associated with illicit cannabis, rather than to the study of the therapeutic value of licensed cannabis-based medicines or unlicensed CBPMs.



**Figure 4: A breakdown of the number of successful and unsuccessful applications for funding made to the NIHR relating to the medicinal use of cannabinoids, licensed cannabis-based medicines and unlicensed CBPMs**

3.21. Since the rescheduling of CBPMs in November 2018, three studies relating to licensed cannabis-based medicines – all industry-funded – had received support from the NIHR Clinical Research Network (CRN) infrastructure. Although studies relating to cannabinoids were supported by the NIHR CRN infrastructure prior to the rescheduling of CBPMs, these studies were often related to the harms of illicit cannabis use (for example, the link to schizophrenia and other psychoses), rather than to the potential therapeutic value of unlicensed CBPMs or licensed cannabis-based medicines. The three studies relating to licensed cannabis-based medicines receiving NIHR CRN support after November 2018 were:

- an open-label extension trial to investigate the long-term safety of cannabidiol oral solution (GWP42003-P, CBD-OS) in patients with Rett syndrome;
- a randomised, double-blind, placebo-controlled trial to investigate the efficacy and safety of cannabidiol oral solution (GWP42003-P, CBD-OS) in patients with Rett syndrome, and;

- a randomised, double-blind, placebo-controlled, parallel-group trial of the efficacy and safety of nabiximols oromucosal spray as add-on therapy in patients with spasticity due to multiple sclerosis.

3.22. Grants have also been awarded by the Wellcome Trust to fund studies into cannabis since the rescheduling of CBPMs in November 2018. For example:

- £3,853,752 was granted on 30 September 2019 for a randomised controlled trial into the treatment of patients with subthreshold symptoms at clinical risk/ultra-high risk (UHR) of psychosis, with CBD; and
- £300,000 was granted on 6 November 2019 for a University College, London (UCL) study into understanding and predicting individual differences in cannabis-induced psychosis-like experiences.

However, again these studies relate to cannabis rather than unlicensed CBPMs or licensed cannabis-based medicines. Additionally, grants relating to cannabis and licensed cannabis-based medicines were also awarded by the Wellcome Trust prior to the rescheduling of CBPMs in November 2018. For example:

- a vacation scholarship was awarded on 27 April 2017 to Trinity College Dublin for a study into the targeting of innate immune receptor signalling by plant-derived cannabinoids as a potential therapeutic avenue for the treatment of multiple sclerosis;
- a £250,000 grant was awarded on 8 November 2018 to the University of Bristol for a study to explore how early life stress is associated with frequent adolescent cannabis use and to identify pathways between frequent adolescent cannabis use and adult common mental disorder.

3.23. The ACMD also sought to assess whether the rescheduling of CBPMs had an impact on the amount of research related to the medicinal use of cannabinoids, licensed cannabis-based medicines and unlicensed CBPMs being funded by the Medical Research Council (MRC). In an MRC-funded study published in *The Lancet Psychiatry* in October 2020, the first-ever randomised, placebo-controlled trial showed CBD 400mg and 800mg to be safe and more efficacious than a placebo in the treatment of cannabis use disorder [Freeman *et al.*, 2020]. Additionally, shortly after the rescheduling in November 2018, the MRC granted £2,046,740 for a study into understanding the contribution of cortical interneuron dysfunction to schizophrenia, which included a consideration of how cannabis use may impact the function of some of the cortical inhibitory circuits that are known to be particularly susceptible to pathological gene variation linked to schizophrenia. However, the MRC had also been providing significant grants into studies into cannabis and cannabinoids prior to the rescheduling of CBPMs. For example, as well as providing numerous grants for studies into the links between cannabis and psychosis, the MRC granted £1,620,857 in 2016 to a study investigating how cannabis use affects teenagers' brains, cognitive functions and psychological well-being. This study

included an exploration into whether teenagers' response to the acute effects of cannabis varied with CBD content.

- 3.24. The ACMD also considered the condition of the international evidence supporting the therapeutic use of CBPMs as part of this assessment. Specifically, with respect to the international evidence behind the treatment of epilepsy with CBPMs, clinical trials to date – including one clinical trial for the use of Epidyolex to treat Dravet syndrome [Devinsky *et al.*, 2017] and two clinical trials for the use of Epidyolex to treat Lennox-Gastaut syndrome [Devinsky *et al.*, 2018; Thiele *et al.*, 2018] – have been international, recruiting from centres in the USA, Europe and Australia. This includes the epilepsy in tuberous sclerosis study about to be reported [Thiele *et al.*, 2020; Wu *et al.*, 2020]. International trials are likely to be limited by funding if they are not commercially supported. International 'open label' studies (studies in which there is no 'blinding' of treatments i.e. both the researchers and the participants know which treatment is being administered) have been reported from Canada and Israel [Tzadok *et al.*, 2016; McCoy *et al.*, 2018]. There was one report of a randomised controlled trial of cannabinoids in epilepsy in the US (clinicaltrials.gov).
- 3.25. With respect to the status of the international evidence behind the treatment of pain with CBPMs, an International Association for the Study of Pain (IASP) presidential taskforce has been developed to review and evaluate current clinical evidence for the benefits and harms (including psychiatric risks) of cannabinoids as analgesic drugs. This review will be peer-reviewed and published in '*PAIN*' (the journal of the IASP), and is intended to inform an IASP Position Statement, expected to be published in early 2021. The work of this taskforce is expected to have a powerful influence on the practice around prescribing unlicensed CBPMs and licensed cannabis-based medicines for the treatment of pain, as well as on the direction of further research in this area.

**Conclusion 9:** There is a process in place by which the NIHR can fund research into the medicinal use of cannabinoids, licensed cannabis-based medicines and unlicensed CBPMs. The availability of peer-reviewed research will be essential in determining the benefits and harms of these products. Therefore, the extent of their therapeutic role is likely to emerge gradually and over the course of the next few years.

**Conclusion 10:** There appears to have been relatively little interest from the manufacturers of unlicensed CBPMs to apply for regulatory approval. There are only three licensed cannabis-based medicines (Epidyolex, Nabilone and Sativex) for which the respective manufacturers have successfully applied for marketing authorisation in the UK.

## 4. Impacts on public knowledge and attitudes towards cannabis and CBPMs, and on professional education

### (i) Changes in use indicated by existing measures/surveys

- 4.1. In the Advisory Council on the Misuse of Drugs (ACMD) impact assessment framework, the Council had suggested that the legislative change was, at least in part, in response to changing social norms on cannabis and an increasing public demand for access to cannabis-based products for medicinal use (CBPMs) [ACMD, 2019]. The ACMD had also considered that the rescheduling of CBPMs to Schedule 2 of the Misuse of Drugs Regulations 2001 (MDR) and the availability of CBPMs could promote positive social norms towards cannabis more generally, leading to an increase in illicit cannabis usage.
- 4.2. The Crime Survey for England and Wales (CSEW) had not indicated a statistically significant increase in last-year cannabis use and lifetime cannabis use in England and Wales between the 2017/2018 and 2018/2019 surveys. However, for both the 16–24 and the 16–59 age groups, a statistically significant increase in last-month cannabis use was shown from 2017/18 to 2018/19 – from 7.3% to 9.5% and from 3.3% to 4.0%, respectively – see Table 6 for a full summary (derived from the Crime Survey for England and Wales; data from 2017/18 and 2018/19).

	2017/2018	2018/2019		2017/2018	2018/2019
<b>Proportion of 16- to 59-year olds reporting ever having used cannabis in their lifetime</b>	30.0%	30.2%	<b>Proportion of 16- to 24-year-olds reporting ever having used cannabis in their lifetime</b>	30.8%	30.3%
<b>Proportion of 16- to 59-year-olds reporting use of cannabis within the last year</b>	7.2%	7.6%	<b>Proportion of 16- to 24-year-olds reporting use of cannabis within the last year</b>	16.7%	17.3%
<b>Proportion of 16- to 59-year-olds reporting use of cannabis within the last month</b>	3.3%	4.0%	<b>Proportion of 16- to 24-year-olds reporting use of cannabis within the last month</b>	7.3%	9.5%

Table 6: CSEW data relating to the prevalence of cannabis use in the UK in 2017/18 and 2018/19, for different age groups

- 4.3. The CSEW had previously shown a long-term decline in cannabis usage from 2002/2003 to 2012/2013. The levels of cannabis usage reported in the CSEW have since shown a slight increase, particularly in young people. For example, the

proportion of 16- to 24-year-olds reporting the use of cannabis in the last year increased incrementally from 13.5% to 17.3% from 2012/2013 to 2018/2019. However, given that the rescheduling of CBPMs was only implemented in November 2018, and that the increase over that reporting period is not unique to cannabis usage in young people (a similar rise is seen in other drugs commonly misused in the UK, such as ecstasy and powder cocaine), it is unlikely that this trend indicated by the CSEW is in any way attributable to the legislative change with respect to CBPMs in November 2018.

- 4.4. Similarly, the 'Smoking, Drinking and Drug Use among Young People in England' 2018 survey (data obtained from 13,664 pupils aged mostly 11 to 15 attending 193 mainstream schools throughout England) showed a long-term decrease in last-year cannabis use from 2001 (13.4%) to 2014 (6.7%), before rising incrementally until 2018 (8.1%), the last year recorded by the survey [NHS Digital, 2019]. However, it is again unlikely that the increase in cannabis prevalence amongst young people reported from 2014 to 2018 reported by this survey is attributable to the rescheduling of CBPMs – given that the rescheduling was only implemented in November 2018 and that the increase was not unique to cannabis.
- 4.5. Recently, surveys have been conducted that highlight interest amongst the general public in the UK in using cannabis and cannabinoids to self-treat medical conditions, or to use a CBPM if prescribed by their GP. For example, one study from the cannabis industry-funded Centre for Medicinal Cannabis (CMC) conducted in October 2019 suggested that there are a large number of people in Britain obtaining cannabis illicitly and using it to relieve the symptoms of a medically diagnosed condition [CMC, 2019]. Similarly, another industry-funded opinion poll suggested that around two thirds of respondents (67%) would consider using CBPMs or licensed cannabis medicines if they had a condition that it could be prescribed for, and 69% would talk to their doctor about cannabis medicines if they felt more informed about the topic [Opinium for Open Cannabis, 2020]. The poll also found that 5% of respondents reported already using cannabis to self-treat a self-identified medical condition. Other studies have also shown that there is public interest in the UK in the small-scale cultivation of cannabis to be used for various medical purposes [Hakkarainen *et al.*, 2015]. However, there have not yet been independent robust, peer-reviewed research conducted to estimate the prevalence of self-medication with cannabis and cannabinoids across the UK.

**Conclusion 11:** A sufficient period of time has not yet passed for evidence to have emerged to indicate whether the rescheduling of CBPMs has had an impact on the prevalence of illicit cannabis use.

## (ii) How frequently patient information pages/websites are being accessed

- 4.6. The ACMD's impact assessment framework had noted that the rescheduling of CBPMs, and actions related to this change, could have an impact on patient demand, education, and expectations relating to CBPMs [ACMD, 2019]. For example, the ACMD considered that resources would likely have to be published to inform the public on which products are likely to be prescribed, for which conditions, and the route by which they can be prescribed. The ACMD had suggested that a specific indicator of whether this impact had been realised would be the development of National Institute for Health and Care Excellence (NICE) guidelines related to CBPMs – and the amount of public interest this stimulated.
- 4.7. Prior to the legislative change in November 2018, NICE guidelines on CBPMs had not yet been published. As mentioned earlier in this report, these guidelines were published just over a year after the legislative change, on 11 November 2019 [NICE, 2019c]. Electronic viewing figures indicate the extent of public interest in these guidelines – the relevant page was viewed multiple thousands of times per day for the first few days after publication. Between the date of publication, and 5 February 2020, the relevant page was viewed over 26,000 times and downloaded over 2,200 times. This initial surge in interest appears to have waned, however, with the relevant page then only being viewed just over 800 times and downloaded just over 600 times between 6 February and 28 May 2020.
- 4.8. An NHS Digital information page on 'Medical cannabis (and cannabis oils)' was also published in January 2019 following the rescheduling of CBPMs [NHS Digital, 2019]. As of 15 September 2020, this page had been visited over 540,000 times, and had had over 490,000 unique visitors.

## (iii) Number of successful completions of accredited learning modules

- 4.9. The ACMD had also highlighted that a potential impact of the rescheduling of CBPMs could have been changes in the education of prescribers and healthcare professionals. Given that CBPMs were, at the time of the rescheduling, an unfamiliar category of drugs for most clinicians, the ACMD considered that additional training would likely be required to develop the understanding of these professionals of CBPMs, to support safe and effective prescribing. The ACMD suggested that a specific impact of the rescheduling of CBPMs on the training of healthcare professionals would be the development of accredited learning modules related to CBPMs by NHS England and NHS Improvement (NHS-E/I) – and the number of successful completions of these modules.

- 4.10. Prior to the legislative change in November 2018, NHS-E/I e-learning on CBPMs had not yet been published. By August 2019 NHS-E/I had developed an information package on cannabis and CBPMs, in collaboration with Health Education England (HEE) and the University of Birmingham. The modules developed, which included a 'medicines and surgery' and a 'paediatric' variant, are freely accessible to all healthcare professionals across the UK.
- 4.11. Between the date of the publication of this e-learning (17 July 2019) and 1 February 2020, the 'medicines and surgery' variant was completed 610 times, and the 'paediatric' variant was completed 37 times. Between 1 February 2020 and 17 June 2020, the rate of completion of these two modules had remained relatively constant with 878 and 64 completions respectively, despite the impact that the emergence of the COVID-19 pandemic in the UK will have had on the availability of healthcare professionals.
- 4.12. Following the rescheduling of CBPMs in November 2018, NHS England issued the following series of related communications to organisations and clinicians.
- Further education for prescribers and healthcare professionals was issued in the form of an NHS England letter of guidance, setting out the organisation's expectations of what this regulatory change for CBPMs would mean in practice for clinicians working in the NHS and in private practice in England [NHS England, 2018a]. The webpage containing this letter was viewed 15,903 times between the date of publication and 23 September 2020.
  - A further letter of guidance was issued by NHS England on 20 November 2018 to provide additional guidance to clinicians and organisations relating to the status of the clinical guidance issued, and to provide further clarification as to the impact of the rescheduling of CBPMs on regulations surrounding synthetic cannabinoids [NHS England, 2018b]. This webpage was viewed 3,322 times between the date of publication and 23 September 2020.
  - One additional letter of guidance was issued by NHS England on 21 December 2019 to highlight some new resources to help to clarify the process for prescribing CBPMs [NHS England, 2019]. This webpage was viewed only 348 times between the date of publication and 23 September 2020 (although this timeframe of course reflects a shorter period, greatly impacted by the COVID-19 pandemic).

## 5. Impacts on crime, enforcement and regulation related to CBPMs

### (i) Number of compounds rescheduled under the Misuse of Drugs Regulations 2001

- 5.1. The Advisory Council on the Misuse of Drugs (ACMD) impact assessment framework had noted that one feasible impact of the rescheduling of cannabis-based products for medicinal use (CBPMs) to Schedule 2 of the Misuse of Drugs Regulations 2001 (MDR) could have been the rescheduling of *other* compounds under the MDR [ACMD, 2019]. For example, if significant evidence of harms and lack of medicinal benefit had emerged for one or many of the products falling under the definition of CBPMs – those moved to Schedule 2 of the MDR – it may have been necessary to return those compounds to Schedule 1 of the MDR. Alternatively, if CBPMs had not been sufficiently broadly defined under the MDR to cover an appropriate range of products to meet clinical needs, it may have proved necessary for additional compounds/groups of compounds to be separately rescheduled to Schedule 2 of the MDR.
- 5.2. As of the date of publication of this advice [ACMD, 2018a; 2018b], the only CBPM that has been moved out of Schedule 2 of the MDR following the rescheduling of CBPMs as a whole to this schedule in November 2018 is Epidyolex.
- 5.3. Epidyolex received marketing authorisation from the European Commission on 19 September 2019. The ACMD found in January 2020 that Epidyolex, where  $\Delta^9$ -tetrahydrocannabinol (THC) is present only as an impurity and is specified within the product's approved marketing authorisation to be limited to less than 0.10% weight for weight, has a low risk of abuse potential, low risk of dependency and low risk of diversion. As a result, the ACMD recommended that Epidyolex (as defined by a suitable description of its components) should be moved to Schedule 5 of the MDR.
- 5.4. The relevant amendment to the MDR came into force on 24 June 2020. No other products defined as CBPMs under the MDR have received marketing authorisation from the European Commission since the rescheduling of CBPMs to Schedule 2 of the MDR, and the ACMD has not reviewed the scheduling of any other specific product falling under the definition of a CBPM in Schedule 2 of the MDR.

## (ii) Number of reports to the Medicines and Healthcare products Regulatory Agency (MHRA) notifying diversion, or counterfeits being seized – and number of MHRA sanctions for regulatory breaches

- 5.5. The ACMD had highlighted that a potential unintended consequence of the rescheduling of CBPMs could have been the diversion of prescribed CBPMs into the illicit market. This could have resulted from an increased number of CBPM prescriptions, poor prescription practices, and the failure of monitoring systems. The ACMD had also considered the possibility that counterfeit CBPMs might be introduced into the illicit market, under the guise of legitimate CBPMs.
- 5.6. Prior to the rescheduling of CBPMs, there had been no reports of diversion or counterfeit seizures for products that would now meet the definition of CBPMs – nor had the MHRA issued any regulatory sanctions. As of June 2020, this remained to be the case – despite the changed regulatory environment relating to CBPMs, the MHRA had received no reports of counterfeit seizures or of diversion, nor had it issued any regulatory sanctions.

## (iii) Reports of illicit cannabis being misrepresented as CBPMs

- 5.7. The ACMD's impact assessment framework had noted that a possible impact of the rescheduling of CBPMs to Schedule 2 of the MDR could have been the diversion of prescribed CBPMs into the illicit market – or the misrepresentation of illicit cannabis as 'medicinal' [ACMD, 2019]. The latter could have seen those found in possession of illicit cannabis claiming that:
- the intention was to use the illicit cannabis for self-medicating purposes (a claim that could, if supported by evidence, be a mitigating factor influencing the decision of the Crown Prosecution Service [CPS] as to whether it is in the public interest to prosecute an adult offender for an offence of possession); or
  - the item in their possession was not in fact illicit cannabis, but rather a CBPM (which can be legally possessed) [CPS, 2019].
- 5.8. In response to a request from the ACMD, the National Crime Agency (NCA) issued a request to all police forces in the UK (except the British Transport Police) to explore the prevalence of the diversion of prescribed CBPMs into the illicit market, and the misrepresentation of illicit cannabis as 'medicinal'; 14 out of 45 police forces responded to this request. The NCA provided a summary of those responses and from anecdotal intelligence from Drug Expert Witness and Valuation Association (DEWVA) meetings, noting that there had been no recorded incidents of cannabis products (including oils, sprays and 'edibles') being misrepresented as licit CBPMs. In contrast, the labelling of illicit cannabis female flowering head material as 'medicinal cannabis' was found to be widespread but not encountered everywhere. The Northumbria, Staffordshire, West Midlands, Metropolitan, Kent, and Avon and

Somerset police forces reported the practice to be prevalent within their jurisdictions. This practice was found to be encountered in the following three common formats.

- Imported cannabis female flowering head material from North America in packaging labelled as medicinal cannabis.
- Domestically produced female flowering head material being decanted into packaging and misrepresented as North American medicinal cannabis. This packaging is purchased from North American outlets.
- Domestically produced cannabis female flowering head material being decanted into packaging and labelled as produced in the UK. This cannabis purports to be medicinal cannabis permitted by UK legislation.

5.9. In October 2020 UK police forces reported incidents of harm related to sweets that were believed to have contained THC. Anecdotally, these sweets were reported to have been labelled in such a way as to suggest that they were intended for medical use [*Evening Standard*, 2020]. The Metropolitan Police Service, for example, reported that 17 children from one school were taken to hospital as a precaution following ingestion of these sweets [MPS, 2020].

5.10. The Welsh Emerging Drugs & Identification of Novel Substances (WEDINOS) project analyses samples of drug samples submitted anonymously by users from across the UK. WEDINOS had also reported to the ACMD that no samples submitted to WEDINOS between 1 April 2019 and 31 March 2020 were marked or described as CBPMs. However, 26 samples were submitted to WEDINOS (during that same period) labelled as 'cannabidiol' (CBD) products. Following analysis of those samples, using ultra-performance liquid chromatography coupled with quadruple/time-of-flight mass spectrometry, only 54% were found to contain CBD only. A further 16% were found to contain a mixture of cannabinoids including THC, CBD and cannabinol. Cannabinoids were not identified in the remaining 30% of samples.

**Conclusion 12:** There is little current evidence of the diversion of unlicensed CBPMs or licensed cannabis-based medicines into illicit markets, following the rescheduling of CBPMs. However, several police forces across the country have reported observing illicit cannabis being mislabelled as a medicinal product. The impact of this mislabelling on policing is currently unclear.

#### (iv) Number of specialist licensed importers and number of licensed domestic manufacturers

5.11. The ACMD had previously highlighted that a possible impact of the rescheduling of CBPMs could have been the development of the UK CBPM market. One suggested

indicator of this impact was the number of specialist licensed importers recognised by the MHRA.

- 5.12. While there is no MHRA register of importers specific to CBPMs, the MHRA has noted that there are over 300 registered importers that may notify for import *any* unlicensed medicines (i.e. including CBPMs) provided they have the appropriate licences – it was possible to assess the level of notifications made by importers to the MHRA for the import of unlicensed CBPMs. This was discussed earlier in the report, in Section 3(ii) ‘Number of imports of CBPMs’.
- 5.13. Similarly, the ACMD had suggested that the number of domestic manufacturers licensed by the MHRA to produce unlicensed CBPMs and licensed cannabis-based medicines might act as an indicator of the development of the UK CBPM market. The number of licensed domestic manufacturers in the UK had increased to two as of June 2020; both were manufacturers of licensed cannabis-based medicines, rather than unlicensed CBPMs.

*[Paragraphs 5.14 to 5.18 (including Figure 5 and Table 7) have been redacted from the published version of this report]*

## 6. Conclusions

### Impacts on cannabis-based products for medicinal use (CBPMs) prescribing

- 6.1. **Conclusion 1:** Many of the various impacts of rescheduling CBPMs in November 2018 have been gradual, and the timeframe over which this review has been conducted is too short to reach a conclusive understanding of changes over time – particularly given the emergence of the COVID-19 pandemic, which has impacted on crucial data collection since March 2020. Data collection and comparison were further complicated by differing methods of data collection across each administration of the UK, which resulted in differently caveated data.
- 6.2. **Conclusion 2:** Three licensed cannabis-based medicines are now available in the UK and approved by the National Institute for Health and Care Excellence (NICE) for conditions where the evidence is strongest – around 800 patients a year received a licensed cannabis-based medicine from 2017 to 2019. There is evidence of an increase in the number of patients being prescribed licensed cannabis-based medicines across the UK in the four to six months following November 2019, possibly as a result of
- the publication of NICE guidance on cannabis-based medicinal products [NICE, 2019c];
  - the publication of NICE’s technology appraisal guidance for the treatment of Lennox-Gastaut and Dravet syndromes with Epidyolex [NICE, 2019a; 2019b], and/or;
  - the granting of marketing authorisation for Epidyolex in the UK.
- 6.3. **Conclusion 3:** Currently, only a limited number of patients (strongly presumed to be fewer than five) have been prescribed unlicensed CBPMs by the NHS, despite a range of unlicensed CBPMs being available. This may be expected for a number of reasons, including:
- licensed cannabis-based medicines are now available to clinicians and are recommended by NICE guidance for certain conditions – unlike unlicensed CBPMs;
  - there is a lack of safety and efficacy data for many unlicensed CBPMs;
  - prescription of unlicensed CBPMs is limited only to practitioners on the specialist register of the GMC; and
  - lack of evidence on cost effectiveness and the relatively high costs of these unlicensed medicines.
- 6.4. **Conclusion 4:** Compared with the number of patients prescribed unlicensed CBPMs by the NHS, there had been a considerable increase in the number of patients privately prescribed unlicensed CBPMs in England in the year immediately following

the rescheduling of CBPMs (63 patients, up from 0 in the preceding year). A continuation of this trend is expected based on Department of Health and Social Care (DHSC) projections, with between 149 and 224 unique patients estimated to have been privately prescribed unlicensed CBPMs in England over the course of 2020. It is unclear how many of the patients receiving privately prescribed unlicensed CBPMs – products that often lack robust evidence of safety, quality and efficacy data – were first prescribed licensed cannabis-based medicines before commencing treatment with unlicensed CBPMs.

- 6.5. **Conclusion 5:** The development of a CBPM patient registry is a very significant step in allowing for a careful analysis of the extent and pattern of prescription of CBPMs and their benefits and risks.
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### **Impacts on the development of the CBPM market and on monitoring, trials and research**

- 6.6. **Conclusion 6:** The price of licensed cannabis-based medicines has remained largely unchanged. The price of unlicensed CBPMs is currently high in comparison to licensed cannabis-based medicines. The market for unlicensed CBPMs, licensed CBPMs and licensed cannabis-based medicines is still in its infancy.
- 6.7. **Conclusion 7:** There has been a considerable increase in CBPM import notifications made to the Medicines and Healthcare products Regulatory Agency (MHRA) – as well as the number of packs of CBPMs notified for import – which does not necessarily reflect an actual increase in the quantity of CBPM imports. It is currently unclear what this increase in CBPM import notifications represents, and whether it is indicative of increased CBPM usage within the UK.
- 6.8. **Conclusion 8:** MHRA Yellow Card data on adverse drug reactions indicated a low level of reported harm for unlicensed CBPMs, CBD food products and licensed cannabis-based medicines, although some of the harms that were reported (including one fatality associated with a licensed cannabis-based medicine) were severe. The level of adverse drug reaction (ADR) reporting associated with these products has increased since the rescheduling of CBPMs, however, this increase was from extremely limited levels of ADR reporting in 2017. It is too soon to draw conclusions about the safety of these products from the current Yellow Card data available.
- 6.9. **Conclusion 9:** There is a process in place by which the National Institute for Health Research (NIHR) can fund research into the medicinal use of cannabinoids, licensed cannabis-based medicines and unlicensed CBPMs. The availability of peer-reviewed research will be essential in determining the benefits and harms of these products.

Therefore, the extent of their therapeutic role is likely to emerge gradually and over the course of the next few years.

- 6.10. **Conclusion 10:** There appears to have been relatively little interest from the manufacturers of unlicensed CBPMs to apply for regulatory approval. There are only three licensed cannabis-based medicines for which the respective manufacturers have successfully applied for marketing authorisation in the UK.

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### **Impacts on public knowledge and attitudes towards cannabis and CBPMs, and on professional education**

- 6.11. **Conclusion 11:** A sufficient period of time has not yet passed for evidence to have emerged to indicate whether the rescheduling of CBPMs has had an impact on the prevalence of illicit cannabis use.
- 6.12. **Conclusion 12:** There is little current evidence of the diversion of unlicensed CBPMs or licensed cannabis-based medicines into illicit markets, following the rescheduling of CBPMs. However, several police forces across the country have reported observing illicit cannabis being mislabelled as a medicinal product. The impact of this mislabelling on policing is currently unclear.

## 7. Recommendations

**Recommendation 1:** The Advisory Council on the Misuse of Drugs (ACMD) should be commissioned to conduct a further assessment of the impact of the rescheduling of cannabis-based products for medicinal use (CBPMs) in the two years following the publication of this report – as there is not yet sufficient evidence available to fully assess any and all consequences of the legislative change. Much of this evidence would not be expected to fully emerge for several years.

**Lead:** Home Office.

**Measure of outcome:** Continued assessment of the impact of the rescheduling of CBPMs in November 2018 using the assessment framework developed by the ACMD; a further ACMD report to be published in November 2022.

**Recommendation 2:** The availability of a CBPM patient registry should be recognised as crucial for future assessments of the impact of the rescheduling of CBPMs in November 2018. The Government should continue to support the development of an official CBPM patient registry. Depending on whether the official CBPM patient registry is developed to be able to collect all necessary CBPM private prescription data, the Government may wish to consider how the official registry can interact with those in development outside of Government.

**Lead:** Department of Health and Social Care (DHSC); NHS England and NHS Improvement.

**Measure of outcome:** Availability of an official CBPM patient registry.

**Recommendation 3:** Research should be commissioned:

- a) to assess the impacts of the rescheduling of CBPMs in November 2018 on public knowledge and attitudes towards cannabis, unlicensed CBPMs, licensed CBPMs and licensed cannabis-based medicines; and
- b) to explore the safety, quality and efficacy of unlicensed CBPMs, licensed CBPMs and licensed cannabis-based medicines.

**Lead:** National Institute for Health Research.

**Measure of outcome:** Reports available containing information about the impact of the rescheduling of CBPMs on public perception of cannabis, unlicensed CBPMs and licensed cannabis-based medicines.

**Recommendation 4:** Government departments should conduct a full review of international approaches to legislation facilitating the medicinal usage of cannabis-based medicines.

**Leads:** Home Office; DHSC.

**Measure of outcome:** A joint report compiled by both leads to explore recommended initiatives, technologies or investments which could be beneficial in the UK.

## Annex A: List of abbreviations used in this report

<b>ACMD</b>	<b>Advisory Council on the Misuse of Drugs</b>
CBD	Cannabidiol
CBPMs	Cannabis based products for medicinal use in humans
CMO	Chief Medical Officer
CPS	Crown Prosecution Service
CQC	Care Quality Commission
DHSC	Department of Health and Social Care
GMC	General Medicinal Council
HEE	Health Education England
HSC	Health and Social Care (Northern Ireland)
MDA	Misuse of Drugs Act 1971
MDR	Misuse of Drugs Regulations 2001
MHRA	Medicines and Healthcare products Regulatory Agency
NCA	National Crime Agency
NHS BSA	National Health Service Business Services Authority
NHS-E/I	NHS England and NHS Improvement
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
THC	Tetrahydrocannabinol
WEDINOS	Welsh Emerging Drugs & Identification of Novel Substances project

## Annex B: ACMD membership at time of publication

<b>ACMD membership, at time of publication</b>	
<b>Professor Judith Aldridge</b>	Professor of Criminology, University of Manchester
<b>Dr Kostas Agath</b>	Consultant Psychiatrist (addictions), Change Grow Live Southwark
<b>Professor Owen Bowden-Jones</b>	Chair of ACMD, Consultant psychiatrist, Central North West London NHS Foundation Trust
<b>Dr Anne Campbell</b>	Lecturer in social work, Queens University Belfast
<b>Mr Mohammed Fessal</b>	Chief Pharmacist, Change Grow Live
<b>Dr Emily Finch</b>	Clinical Director of the Addictions Clinical Academic Group and a consultant psychiatrist for South London and Maudsley NHS Trust
<b>Professor Sarah Galvani</b>	Professor of Social Research and Substance Use, Manchester Metropolitan University
<b>Lawrence Gibbons</b>	Head of Drug Threat (Intelligence Directorate, Commodities), National Crime Agency
<b>Professor Graeme Henderson</b>	Professor of Pharmacology, University of Bristol
<b>Dr Hilary Hamnett</b>	Senior Lecturer in Forensic Science, University of Lincoln
<b>Dr Carole Hunter</b>	Lead pharmacist at the alcohol and drug recovery services, NHS Greater Glasgow and Clyde
<b>Professor Roger Knaggs</b>	Associate Professor in Clinical Pharmacy Practice, University of Nottingham
<b>Professor Tim Millar</b>	Professor of Substance Use and Addiction Research Strategy Lead, University of Manchester
<b>Mr Rob Phipps</b>	Former Head of Health Development Policy Branch, Department of Health, Social Services and Public Safety, Northern Ireland
<b>Harry Shapiro</b>	Director, DrugWise
<b>Dr Richard Stevenson</b>	Emergency Medicine Consultant, Glasgow Royal Infirmary
<b>Dr Paul Stokes</b>	Reader in Mood Disorders and Psychopharmacology, King's College London
<b>Dr Ann Sullivan</b>	Consultant physician in HIV and Sexual health and National co-lead for HIV Surveillance, PHE
<b>Professor Matthew Sutton</b>	Chair in Health Economics, University of Manchester
<b>Professor David Taylor</b>	Professor of Psychopharmacology, King's College, London and Director of Pharmacy and Pathology, South London and Maudsley NHS Foundation Trust

### **ACMD membership, at time of publication**

<b>Professor Simon Thomas</b>	Consultant physician and clinical pharmacologist, Newcastle Hospitals NHS Foundation Trust and Professor of Clinical Pharmacology and Therapeutics, Newcastle University
<b>Dr Derek Tracy</b>	Consultant Psychiatrist and Clinical Director, Oxleas NHS Foundation Trust
<b>Ms Rosalie Weetman</b>	Public Health Lead (Alcohol, Drugs and Tobacco), Derbyshire County Council
<b>Dr David Wood</b>	Consultant physician and clinical toxicologist, Guys and St Thomas' NHS Trust

## **Annex C: ACMD CBPM working group membership at time of publication**

Professor Owen Bowden-Jones – Chair of the ACMD CBPM working group and Chair of the ACMD

Dr Anne Campbell – ACMD Member

Dr Cathy Stannard – Consultant in Pain Medicine

Professor David Taylor – ACMD Member

Dr Derek Tracy – ACMD Member

Dr Emily Finch – ACMD Member

Gillian Arr-Jones – formerly Chief Pharmacist at the Care Quality Commission

Professor Harry Sumnall - Professor In Substance Use, Liverpool John Moores University

Professor Helen Cross - The Prince of Wales's Chair of Childhood Epilepsy and Head of the Developmental Neuroscience Programme at UCL-Great Ormond Street Institute of Child Health

Dr Mike White – Former Forensic Intelligence Adviser

Professor Raymond Hill – Professor of Pharmacology, Imperial College London

Ric Treble – retired Laboratory of the Government Chemist (LGC) Expert

Dr Richard Stevenson – ACMD Member

Professor Robin Murray - Professor of Psychiatric Research Professor of Psychiatric Research, King's College London

Professor Roger Knaggs – ACMD Member

Professor Simon Gibbons - Professor of Natural Product Chemistry, University of East Anglia

Professor Steve Alexander - Associate Professor of Molecular Pharmacology, University of Nottingham

## Annex D: Quality of evidence

### *Range of evidence*

Evidence gathered for this report was considered in line with the Advisory Council on the Misuse of Drugs (ACMD) standard operating procedure (SOP) for using evidence in ACMD reports [ACMD, 2020] and the ACMD Framework for the assessment of the impact of rescheduling cannabis-based products for medicinal use (CBPMs) [ACMD, 2019].

This report has primarily considered data requests, submissions and guidance documents from Government Departments (and their agencies), and devolved administrations. The ACMD has received contributions from:

- Department of Health (Northern Ireland)
- DHSC
- Health and Social Services, Welsh Government
- Home Office
- MHRA
- NCA
- NHS England and NHS Improvement
- NHS/HSC Business Services Authority
- NHS Scotland
- NICE
- NIHR
- Pharmacy and Medicines Division, Scottish Government

### *Quality of evidence (design, limitations, bias)*

- There is currently insufficient evidence to fully assess any and all consequences of the legislative change.
- The number of patients being issued prescriptions of unlicensed CBPMs is low and in some cases so low that GDPR regulation required numbers to be obfuscated.
- There remains a lack of safety and efficacy data for many unlicensed CBPMs and it is too soon to draw conclusions.
- The timing of the COVID-19 pandemic has impacted on crucial data collection since March 2020. Data collection and comparison was further complicated by differing methods of data collection across each administration of the UK, which resulted in differently caveated data.

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