

Title: Rescheduling of cannabis-based products for medicinal use under the Misuse of Drugs Regulations 2001 IA No: HO0323 RPC Reference No: N/A Lead department or agency: Home Office Other departments or agencies: The Dept of Health & Social Care, Medicines and Healthcare Products Regulatory Agency	Impact Assessment (IA)			
	Date: October 2018			
	Stage: Final			
	Source of intervention: Domestic			
	Type of measure: Secondary legislation			
Contact for enquiries: Drugs and Alcohol Unit, Home Office				
Summary: Intervention and Options				RPC Opinion: Not applicable

Cost of Preferred (or more likely) Option				
Total Net Present Value	Business Net Present Value	Net cost to business per year (EANDCB in 2014 prices)	One-In, Three-Out	Business Impact Target Status
-£2m	£0m	£0m	Not applicable	Not a regulatory provision

What is the problem under consideration? Why is government intervention necessary?

A number of high profile cases have highlighted that where other treatments have not been effective and cannabis-based products for medicinal use (CBPM) had the potential to help, their access was restricted. This is because cannabis is classified as a Schedule 1 drug under the Misuse of Drugs Regulations 2001 (2001 Regulations). Schedule 1 substances are considered to have no therapeutic value and cannot be lawfully possessed or prescribed without a Home Office (or Department of Health Northern Ireland (DH NI)) licence. Intervention is necessary because advice from the Chief Medical Officer for England and Chief Medical Advisor to the UK Government (CMO) and the Advisory Council on the Misuse of Drugs (ACMD) indicates that there is evidence of the therapeutic value of CBPM for some medical conditions.

What are the policy objectives and the intended effects?

The policy objective is to permit the use of CBPM in healthcare, while continuing to prevent the illegal misuse of cannabis. CBPM could then be prescribed, ensuring those with a clinical need can access appropriate cost-effective medicines, while maintaining existing controls on the illegal use of cannabis.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

Option 1: Do nothing. This would leave CBPM in Schedule 1 of the 2001 Regulations. Access would rely on a successful application to the Expert Panel on cannabis -based medicines by a specialist clinician, and the issuing of a Home Office (or DH NI) licence.

Option 2: Reschedule CBPM into Schedule 2 of the 2001 Regulations. This is the **Government's preferred option**, as it permits the use of CBPM in healthcare, while continuing to prevent the illegal misuse of cannabis.

The specific circumstances in which use would be recommended will be defined in guidance.

Will the policy be reviewed? Yes. If applicable, set review date: Within two years following implementation					
Does implementation go beyond minimum EU requirements?			N/A		
Are any of these organisations in scope?		Micro Yes/No	Small Yes/No	Medium Yes/No	Large Yes/No
What is the CO ₂ equivalent change in greenhouse gas emissions? (Million tonnes CO ₂ equivalent)			Traded: N/A		Non-traded: N/A

I have read the Impact Assessment and I am satisfied that, given the available evidence, it represents a reasonable view of the likely costs, benefits and impact of the leading options.

Signed by the responsible Minister: _____ **Nick Hurd** _____ Date: 9th October 2018

Summary: Analysis & Evidence

Policy Option 2

Description: Reschedule cannabis-based products for medicinal use into Schedule 2 of the 2001 Regulations.

FULL ECONOMIC ASSESSMENT

Price Base Year 2017	PV Base Year 2017	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: -2	High: -2	Best: -2

COSTS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	2	Not quantified	2
High	2	Not quantified	2
Best Estimate	2	Not quantified	2

Description and scale of key monetised costs by 'main affected groups'

There are familiarisation costs for consultants, GPs and law enforcement bodies, estimated at £2 million. Prices are quoted in 2017 terms, reflecting the data available.

Other key non-monetised costs by 'main affected groups'

Any NHS treatment will be funded from existing NHS resources, meaning that the costs will not be financial, but rather an opportunity cost in terms of foregone health benefits elsewhere in the healthcare system. Because CBPM will only be prescribed where cost-effective to do so, the expected benefits are likely to outweigh those opportunity costs. While total funding will remain the same, overall expenditure on drugs specifically may rise, although the size of this is very uncertain. There is likely to be increased licensing activity by the Home Office, to process additional high-THC cannabis cultivation licence applications. Some patients may experience side effects from CBPM in either the short or longer-term and require additional care accordingly. There may be a cost to enforcement agencies from additional time spent trying to distinguish between CBPM and illegal cannabis.

BENEFITS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low			
High			
Best Estimate	Not quantified	Not quantified	Not quantified

Description and scale of key monetised benefits by 'main affected groups'

None.

Other key non-monetised benefits by 'main affected groups'

There may be an improvement in health and wellbeing outcomes for those receiving CBPM, and consequential benefits for their carers. There may be health-related cost savings if CBPM replaces existing medicines, or if the health improvement leads to lower treatment costs. There may be a growth in UK-based companies cultivating and producing CBPM.

Key assumptions/sensitivities/risks

Discount rate

3.5

The analysis is based on five illustrative medical conditions only. This list may differ from the final scope, and is presented without prejudice to that decision. Placing CBPM into Schedule 2 may create a risk of diversion, and of greater misuse of cannabis. There is also the risk of unknown long-term health problems to patients associated with the use of CBPM products.

BUSINESS ASSESSMENT (Option 2)

Direct impact on business (Equivalent Annual) £m:			Score for Business Impact Target (qualifying provisions only) £m:
Costs: 0.0	Benefits: 0.0	Net: 0.0	
			N/A

Evidence Base (for summary sheets)

A. Strategic Overview

A.1 Background

1. Raw cannabis and Tetrahydrocannabinol (THC) are currently listed as Schedule 1 drugs under the Misuse of Drugs Regulations 2001 (2001 Regulations). Home Office policy has typically been to permit the production, supply and possession of raw cannabis solely for research purposes under a Home Office licence.
2. The scheduling of cannabis has been brought to the forefront in several cases involving children with severe epilepsy who sought access to cannabis-based products for medicinal use (CBPM)¹, imported from abroad, that were unlawful to import, supply, possess or prescribe in the UK without a Home Office (or Department of Health Northern Ireland (DH NI)) licence.
3. The Home Secretary issued licences for these cases, and subsequently announced on 19 June 2018 that there would be a two-part review into the scheduling of CBPM.²
4. Part 1, led by Professor Dame Sally Davies, the Chief Medical Officer for England (CMO) and the Chief Medical Advisor to the UK Government, considered the evidence available on the medicinal and therapeutic benefits of cannabis-based products. This review summarised that there is conclusive evidence of the therapeutic benefit of cannabis-based medicinal products for certain medical conditions, and reasonable evidence of the therapeutic benefit in several other medical conditions. The CMO therefore recommended that the whole class of cannabis-based medicinal products be moved out of Schedule 1 of the 2001 Regulations.³
5. The evidence reviewed by the CMO included material provided by:
 1. National Academies of Sciences, Engineering, and Medicine (NASEM).
 2. Health Products Regulatory Authority (Irish equivalent of the Medicines and Healthcare Products Regulatory Agency (MHRA)).
 3. World Health Organisation Expert Committee on Drug Dependence.
 4. Australian Government Department of Health.
6. Part 2 of the review, led by the Advisory Council on the Misuse of Drugs (ACMD), provided an assessment of whether CBPM should be rescheduled, based on the balance of harms and public health needs. The ACMD agreed with the CMO, stating that '*there is now evidence of medicinal benefit for some Cannabis-derived products in certain medical conditions for some patients.*'⁴ The ACMD advised that clinicians in the UK should have the option to prescribe cannabis-derived medicinal products that meet the requirements for medicinal standards to patients with certain medical conditions, and that it is therefore appropriate for these medications to not be subjected to the requirements of Schedule 1 of the 2001 Regulations. The ACMD did make an exception with synthetic cannabinoids, and recommended they remain within Schedule 1 pending longer-term review.
7. Following on from this initial advice, the ACMD have been asked to conduct a more detailed review of CBPM. As part of this review, the ACMD have been asked to (a) assess whether a more refined listing of cannabis and cannabis-based products under the Schedules to the 2001 Regulations

¹ "Cannabis-based products for medicinal use" is the official legal term, and the abbreviation CBPM is used from now on for convenience. A detailed definition of exactly which products may be licensed or prescribed is not yet available, hence CBPM is used generically.

² <https://hansard.parliament.uk/Commons/2018-06-19/debates/6889E197-AF00-4F77-99C8-25ADC469528F/Cannabis-BasedMedicines?highlight=cannabis#contribution-6B48A3FA-3895-4980-839F-81DB32957494>

³ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/722010/CMO_Report_Cannabis_Products_Web_Accessible.pdf

⁴ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/727333/ACMD_advice_on_scheduling_of_cannabis_derived_medicinal_products.pdf

should take place; (b) undertake the assessment; (c) advise on any potential mitigation for harms and risks of diversion of rescheduling to a different schedule of the 2001 Regulations. This advice is to be provided by July 2019. Detailed guidance on CBPM prescription from NICE is expected to be ready by October 2019. An interim guidance letter will be published by NHS England in the meantime with interim clinical guidance from the Royal College of Physicians and the British Paediatric Neurology Association and guidance on the prescribing and supply of 'special' medicines by the Medicines and Healthcare Products Regulatory Agency.

Purpose of this Impact Assessment and associated limitations

8. The two-part CMO and ACMD review considered whether there was evidence of medicinal benefit of CBPM for some patients with certain medical conditions. On the basis that such evidence was conclusive, and balancing the potential harms with public health gains, the ACMD review recommended that CBPM, except for synthetic cannabinoids, should be moved out of Schedule 1. The ACMD also recommended that clinical trials be carried out to better improve understanding of these products, and to further establish the safety and effectiveness of different products.
9. While the review assessed whether there was evidence of medical benefit, it did not seek to quantify that benefit or determine the specific impacts were prescription to be permitted. Although the evidence of medical benefit in certain situations is conclusive, research is limited and varies in quality. Assessing the potential impact, especially quantitatively, requires time, further clinical research and detailed appraisal of individual products. The timescale for initial NICE guidance being provided by October 2019 reflects this.
10. In the meantime, this Impact Assessment (IA) attempts to assess the costs and benefits that might result from rescheduling. This cannot be done robustly at this stage because the evidence is limited and there is a great deal of uncertainty. Precise definitions of which medical conditions, which patients and which CBPM might be in scope for prescription are not yet available.
11. However, it is still important to provide a provisional view on possible impacts, even though such a view is very uncertain and will need to be reviewed and refined over time. Consequently, the IA aims to outline the costs and benefits by:
 - Identifying several example medical conditions which might be considered for CBPM prescription (without prejudice to any final decision).
 - Estimating the potential numbers of patients who might be given prescriptions.
 - Estimating the costs of treatment with CBPM.
 - Estimating the potential health gains arising from such treatment.
 - Considering and emphasising the importance of cost-effectiveness in deciding when treatment is appropriate.
 - Assessing possible impacts in both the short and longer (ten years) terms.
12. The evidence is not yet sufficient to address these issues robustly. The IA draws on evidence where possible, but supplements it with scenario modelling and, in some cases, illustrative assumptions. Following advice from the Expert Panel⁵, the health benefits and many of the costs are left unquantified, pending evidence improvements. However, the scenario analysis helps set out an early view to inform decision-making prior to formal analysis and guidance being produced. The range of possible outcomes also highlights the need for, and effect of, appropriate controls being in place.

A.2 Groups Affected

- Criminal justice agencies: Crown Prosecution Service; courts, HM Prison and Probation Service, the Crown Office and Procurator Fiscal Service and the Scottish Prison Service.

⁵ <https://www.gov.uk/government/publications/cannabis-based-medicines-expert-review-panel>

- Healthcare providers: NHS England (NHSE), NHS Wales, NHS Scotland.
- Law enforcement agencies: police forces; National Crime Agency and Border Force.
- Medical regulators: MHRA.
- Drugs and Firearms Licensing Unit, Home Office.
- Patients.
- Pharmacies.
- Pharmaceutical manufacturers and wholesalers.
- Professional body regulators: General Medical Council, Care Quality Commission (CQC).
- The power to make regulations under misuse of drugs legislation has been devolved to the Department of Health in Northern Ireland. The analysis in this IA provides estimates at UK level, on the assumption that similar rules are adopted. The estimates will be slightly lower if Northern Ireland is excluded.

A.3 Consultation

13. The CMO and the ACMD have both been consulted as part of the two-part review, which in turn built on previous work and existing recommendations.
14. The DHSC and the MHRA have worked with the Home Office in the development of the definition of what constitutes a CBPM.
15. Law enforcement agencies such as the National Police Chiefs' Council have been consulted to ensure enforcement of illegal cannabis use continues.
16. Healthcare providers have been consulted, and have been engaged during the process of developing clinical guidance. Guidance and advice is being provided by the Royal College of Physicians (RCP) and the British Paediatric Neurology Association.
17. A range of manufacturers and stakeholders were informally consulted to ensure the proposed policy and definition of cannabis based products for medicinal use was workable in practice and to explore possible supply chains for cannabis-based products prescribed as unlicensed medicines.
18. The devolved administrations have also been engaged on these proposals.
19. DHSC have contributed the health-related analysis to support this IA, and that in turn has been informed by discussion with a range of stakeholders including the Expert Panel on Medicinal Cannabis⁶ and the Government of the Republic of Ireland.
20. DHSC and MHRA have also had discussions with manufacturers of licensed and unlicensed CBPM, the Office of Cannabis in the Netherlands, the Cannabis Trades Association and CLEAR, the lobby group for law reform.

B. Rationale

21. Government intervention is necessary because there is now evidence of medicinal benefit for some CBPM, and access to these products is restricted under the current scheduling regulations.
22. Government intervention is therefore necessary to reschedule CBPM into Schedule 2 of the 2001 Regulations, so that they are available to patients with an unmet clinical need, while maintaining controls on the diversion and misuse of cannabis. Decisions around use, particularly within the NHS, will be driven primarily by the availability over time of licensed medicines which are assessed to be cost-effective by NICE.

⁶ <https://www.gov.uk/government/publications/cannabis-based-medicines-expert-review-panel>

C. Objectives

23. The policy objective is to permit the use of CBPM in healthcare in the UK where such treatment is judged to be clinically beneficial and, for NHS treatment, cost-effective. This will enable clinicians to be able to prescribe these products, where they meet proper safety and quality assurance standards, and when they are the most appropriate treatment for their patients. There will be three routes available for patients who require access to CBPM:
- 1) a special medicinal product supplied under the direction of a registered medical practitioner on the Specialist Register of the General Medical Council;
 - 2) an investigational medicinal product without a marketing authorisation that is for use in a clinical trial; or
 - 3) a medicinal product with a marketing authorisation.
24. A further objective is to prevent the harmful effects of drug misuse by maintaining controls on the illegal use of cannabis and preventing the diversion of CBPM. This is to be achieved by maintaining the current legal status of illegal cannabis, as a Class B substance under the Misuse of Drugs Act 1971).
25. The proposed Regulations will only permit the supply of a CBPM if it is made in accordance with a prescription or direction from a 'specialist medical practitioner', namely a practitioner on the Specialist Register of the General Medical Council. This ensures standards of patient protection are not lowered. Other doctors will not be able to prescribe these products unless under the direction of a 'specialist medical practitioner'.
26. Until these products have received marketing authorisation from the MHRA, they will not have been tested for quality, safety and efficacy. As a result, they would fall under the existing 'specials' regime in medicines legislation. In line with other unlicensed medicinal products, practitioners will take on the responsibility for the quality and safety of the product. This is an established process that is already in place within the health system for prescribing unlicensed drugs. Subject to local governance arrangements for prescribing unlicensed medicines, it will be for prescribers to decide whether prescribing these products is in the best interest of the patient, taking into account a variety of factors, including consideration of licensed products first.
27. Patients will not be able to get CBPM direct from their general practitioner and will require referral to a specialist on the basis of a clinical need.

D. Options

28. **Option 1:** Do nothing, leaving CBPM in Schedule 1 of the 2001 Regulations. Access to these products would rely on a successful application made to the Expert Panel and the issuing of a Home Office (or DH NI) licence.
29. **Option 2:** Reschedule CBPM into Schedule 2 of the 2001 Regulations.
30. Option 1 would not address the problem because the current scheduling arrangements restrict the legal supply of CBPM to a small pool of patients. Option 2 would enable CBPM to be prescribed more widely to patients with clinical need, while maintaining controls on the illegal use of cannabis. It may also facilitate further research, improving the health potential of CBPM.

E. Appraisal (Costs and Benefits)

31. Costs and benefits will be driven primarily by the volume of patients prescribed CBPM, and the impact of that treatment in each case. Other additional costs (such as familiarisation costs) will depend on how the process is structured.
32. The expectation is that within the NHS, CBPM will be provided in line with NICE recommendations on cost-effectiveness, as soon as that guidance becomes available. The guidance will also cover private prescription, although private prescribers may be less constrained than those operating within the financial constraints of the NHS.
33. There is considerable uncertainty at this stage, particularly on patient volumes and health benefits, because:
- The evidence base is limited generally.
 - Detailed guidance is not expected to be ready until October 2019. Interim assumptions about prescribing criteria need to be made in the meantime.
 - The medical benefits may vary considerably from individual to individual.⁷
 - There is currently only one licensed CBPM, Sativex, and although used in Wales, it is not currently recommended in England on cost-effectiveness grounds. In the short-term, products may remain unlicensed and prescribing would only occur in exceptional circumstances. Large scale use of CBPM will only emerge where there are new licensed products which are deemed likely to be cost-effective by NICE. It will take time to license new medications, assess cost-effectiveness, introduce any new rules or guidance and assess potential patients.
34. The following analysis sets out the evidence as currently known.

GENERAL ASSUMPTIONS & DATA

35. The analysis in this IA is limited to five medical conditions, owing to the complexity and resource implications of analysing all possible conditions where CBPM might be used. The conditions have been selected to provide a varied but representative picture of the various medical conditions where CBPM may potentially be used. They include a mix of conditions identified in the recent CMO review as having conclusive or substantial evidence of potential medical benefit, conditions where the evidence of benefit is more limited, and conditions where CBPM are available overseas. The list of five is illustrative, not definitive and may vary from final guidance when produced. The list is presented without prejudice to any final decision.
36. The five conditions⁸ are:
- Multiple sclerosis (MS) – pain or muscle spasticity.
 - Chemotherapy-induced nausea and vomiting (CINV).
 - Severe treatment-resistant epilepsy in children - specifically Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS) only.
 - Chronic pain in adults.
 - Appetite and weight loss associated with HIV/AIDS.
37. Although there is some evidence of medical benefit for each of these conditions, the quality of evidence varies. Even where the evidence is strong, CBPM may not be cost-effective, or may be cost-effective only if certain additional criteria are met. The list is used without prejudice to any final decisions on the scope of CBPM prescription. Interim guidance is being developed for some, but not all, of these conditions. Further guidance will be produced and refined as evidence improves.

⁷ Advice received from the Expert Panel.

⁸ Descriptions of each condition may be abbreviated for convenience in some tables and discussion, but the meaning remains as listed here.

38. In the specific case of MS, existing guidance from NICE advises that treatment with Sativex (the one currently licensed CBPM) is not cost-effective. This IA does not alter that advice, but nonetheless recognises that additional medical products may be licensed in the future, costs and benefits may change and the evidence may improve. The IA's timeframe (10 years) means it is appropriate to include a range of possible scenarios.

39. The main assumptions used in this IA are listed below, and are explained further in the costs and benefits sections:

- There will be 5,000 NHS and 350 private consultants in directly-affected specialties (see fuller definition below) will need to familiarise themselves with the guidance on CBPM⁹.
- It will take each consultant approximately two hours to familiarise themselves with the guidance.
- Consultants earn £51 per hour (the hourly wage for a consultant with 19 or more years of experience¹⁰).
- A further 50,000 consultants from other specialties will need some familiarisation with the guidance on CBPM.¹¹
- About 50,000 GPs will need to familiarise themselves with the guidance on CBPM¹².
- That GPs earn on average £41 per hour¹³.
- That 120,000 frontline police officers and immigration enforcement officers will need to familiarise themselves with the guidance on CBPM¹⁴.
- Frontline police officers and immigration enforcement officers earn on average £19 per hour¹⁵
- Non-wage labour costs are assumed to be equivalent to an additional 23 per cent of wage costs¹⁶ on average.
- The average reading speed is 200 words per minute - see Table 1 below. This assumes that a highly qualified audience reading specialist technical material would have an average reading speed.

Table 1, Typical reading speeds; words per minute (wpm), comprehension (%), 2018.¹⁷

Screen, wpm	Paper, wpm	Comprehension, %	Reader profile
100	110	50	Insufficient
200	240	60	Average reader
300	400	80	Good reader
700	1,000	85	Excellent, accomplished reader

⁹ Consultant numbers for England are reported here: <https://digital.nhs.uk/data-and-information/publications/statistical/nhs-workforce-statistics/june-2018>. Illustrative numbers for specialties related to the medical conditions discussed in this IA include 727 clinical oncology, 776 neurology, 603 rheumatology and 326 palliative care. Broader categories such as paediatrics, psychiatry and emergency medicine have larger numbers but may be less likely to encounter CBPM cases. Allowing for some additions for the rest of the UK, a total figure of up to 5,000 is assumed, while acknowledging uncertainty around the figure. The estimate of 350 private consultants is explained in the next section, under "Businesses".

¹⁰ <https://www.bma.org.uk/advice/employment/pay/consultants-pay-england>. Assumes £105,042 annual salary, 2,080 hours a year. Pay rates as from 1-Oct-18.

¹¹ There are around 46,600 consultants in England <https://digital.nhs.uk/data-and-information/publications/statistical/nhs-workforce-statistics/june-2018>. 5,000 have already been considered, but an adjustment is required to include the rest of the UK. A rounded 50,000, in addition to the original 5,000 is assumed.

¹² The number of GPs in England as at March 2018 was 41,848, adjusted to an estimate of 50,000 to reflect the rest of the UK <https://files.digital.nhs.uk/D0/35A78B/GPMS%20Mar%20Final%20Jun%20Prov%202018.pdf>

¹³ <https://www.bma.org.uk/advice/employment/pay/consultants-pay-england>

¹⁴ There are 103,837 frontline police officers in England and Wales and 5,213 immigration enforcement officers. A total of 120,000 is therefore assumed across the UK. <https://www.gov.uk/government/publications/border-and-immigration-cross-cutting-data-august-2018>

¹⁵ <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/datasets/occupation4digitsoc2010ashtable14>

¹⁶ Eurostat

¹⁷ <http://readingsoft.com/>

Option 2: Reschedule cannabis into Schedule 2 of the 2001 Regulations

COSTS

Set-up costs

Businesses

40. There are likely to be familiarisation costs for doctors on the Specialist Register working in the private sector who are permitted to prescribe CBPM, as they familiarise themselves with the available guidance on prescribing, and with the evidence on the effectiveness of these products. Additional doctors may require familiarisation if prescribing under the direction of such a specialist, however the degree to which this may occur is unquantified at this time. A number of consultants undertake both NHS and private sector treatment, so in these cases it is not clear whether the familiarisation costs would be borne by the NHS or their private sector employers. In the absence of information and for simplicity, it has been assumed that these familiarisation costs fall on the NHS, and only familiarisation costs for consultants working exclusively in the private sector have been included in this section.
41. It is estimated that there are 3,000 consultants working exclusively in the private sector¹⁸, which is equivalent to 7 per cent of those employed in the NHS¹⁹. As explained below, it is assumed that 5,000 NHS consultants will need to familiarise themselves with the rescheduling of CBPM. Assuming that the number of private-only consultants is equivalent to 7 per cent of 5,000, this provides an estimate of 350 private-only consultants who will need to familiarise themselves.
42. Based on input from DHSC, it is assumed that it takes each specialist practitioner approximately two hours to familiarise themselves with the guidance, and with the evidence on the effectiveness of CBPM relevant to their specialty. The average hourly labour cost of a specialist practitioner is assumed to be £62, after taking the hourly wage for a consultant with 19 or more years of experience (£51) and uplifting it by 23 per cent to account for non-wage labour costs. It is therefore estimated that the familiarisation cost for each specialist practitioner is £124 (2 x £62), and the total familiarisation cost across all private-only doctors on the Specialist Register is approximately £43,000 (350 x £124).
43. Pharmacies will be responsible for storing CBPM and dispensing them to patients. It is assumed that any familiarisation costs for pharmacies would be negligible, as they would already be familiar with the protocol for storing and dispensing Schedule 2 drugs and unlicensed medicines.

NHS

44. There are likely to be familiarisation costs for doctors on the Specialist Register of the General Medical Council (that is, those practitioners who are permitted to prescribe CBPM), as they familiarise themselves with the available guidance on prescribing, and with the evidence on the effectiveness of these products.
45. Precise rules on how decisions to prescribe should be taken, and who should be involved, will be included in guidance. It is possible that both initial and repeat prescriptions may involve direction, delegation or supervision between different clinicians, although the degree to which additional doctors may prescribe under the direction of a specialist is unquantified at this time. Based only on the five illustrative conditions covered in this IA, consultants from several specialties may potentially be involved: neurology, oncology and rheumatology are examples. The proportion of consultants within such specialties who are likely to be involved with CBPM is unknown. This IA assumes that around 5,000 NHS consultants will need familiarisation.

¹⁸ <https://www.kingsfund.org.uk/sites/default/files/media/commission-appendix-uk-private-health-market.pdf>

¹⁹ There were 42,527 consultants working in the NHS at the time of the above research (January 2014). The 7 per cent proportion is assumed to have remained unchanged. https://files.digital.nhs.uk/excel/g/p/nhs_workforce_statistics_december_2017_national_and_hes_tables1.xlsx

46. It is assumed that all of these consultants will need to familiarise themselves to some degree with the rescheduling of cannabis. Not all will be treating conditions amenable to CBPM, but equally the list of five conditions is not definitive and other medical personnel may also be involved.
47. It is assumed that it takes each doctor on the Specialist Register approximately two hours to familiarise themselves with the guidance, and with the evidence on the effectiveness of CBPM relevant to their specialty. As described previously, the average hourly labour cost of a specialist practitioner is assumed to be £62. It is therefore estimated that the familiarisation cost for each doctor is £124 (2 x £62), and the total familiarisation cost across all NHS doctors on the Specialist Register is approximately £0.6 million (5,000 x £124) in year 1 only.²⁰
48. GPs and consultants from other specialties may need to familiarise themselves with the guidance on cannabis rescheduling, as they may need to provide patients with advice or to refer them to a doctor on the Specialist Register. The guidance for healthcare professionals is likely to be approximately 1,500 words, so it is estimated that it takes eight minutes on average to read the guidance, assuming an average reading speed of 200 words per minute.
49. The cost of eight minutes of a consultant's time is £8 (£62 / 60 x 8), which results in a total familiarisation cost of £0.4 million across all 50,000 consultants from other specialties. After uprating the hourly GP wage (£41 per hour) by 23 per cent to an hourly labour cost of £50, the cost of eight minutes of a GP's time is £7 (£50 / 60 x 8), which results in a total familiarisation cost of £0.3 million across all 50,000 GPs.
50. If doctors below consultant level prescribe CBPM under direction, they too would need to familiarise themselves with the new guidance. The degree to which this might happen is unquantified at this time, but may increase the one-off costs accordingly.

Enforcement agencies

51. There are likely to be familiarisation costs for police forces and Border Force, as they familiarise themselves with the guidance on enforcing CBPM. The guidance for enforcement agencies is likely to be approximately 1,500 words, so it is estimated that it takes eight minutes on average to read the guidance, assuming an average reading speed of 200 words per minute²¹.
52. The cost of eight minutes of a police officer or immigration officer's time is £3, based on an average wage of £19 and scaling it up to an hourly wage cost of £23 after adding 23 per cent to account for non-wage labour costs. The total familiarisation cost across all 120,000 frontline police officers and immigration enforcement officers is therefore estimated at £0.4 million.

Ongoing costs

53. It is likely that access to CBPM will develop over several years rather than overnight, as it will take time to develop guidance and assess potential patients. As such, the ongoing costs may be lower in the early years, before reaching an eventual steady state.

Businesses

54. As in the public sector, private healthcare providers will be able to prescribe CBPM through doctors on the Specialist Register or through others working under direction. They receive payment for the healthcare services they provide, so any additional costs associated with prescribing CBPM would be met with increased revenue, so there will be no overall increase in costs. Similarly, any pharmacies receive payments from the NHS for each prescription dispensed, so any increase in costs to pharmacies from dispensing CBPM will be compensated. The policy may lead to increased demand for private-sector prescription of CBPM, and increased spending on drugs accordingly, although the size of this possible impact is unknown.

²⁰ For simplicity, the IA assumes all familiarisation will occur in the first year. In practice, CBPM may be introduced over time, delaying set-up costs in some cases.

²¹ <http://readingsoft.com/>

NHS

55. There will not be any net additional financial cost to the NHS from providing CBPM to patients, because time and funding will be reallocated from within existing resources. Such reallocation will only be made where CBPM is cost-effective, such that the net impact on health should be positive. There may be an increase in spending on drugs specifically, within the overall fixed budget. This section provides estimates of potential gross NHS spending on CBPM, to provide an illustration of how much expenditure might be displaced.
56. The expected policy is that unlicensed CBPM should only be used where other treatment options have not worked, so the volumes are likely to be low unless and until there are licensed products available, and where the treatment is recommended by NICE as cost-effective.
57. The gross costs of CBPM have been estimated by DHSC, using the following steps:
 1. Estimating the volume of patients who may be prescribed CBPM for five illustrative medical conditions.
 2. Estimating the average gross cost of treatment per patient for each medical condition.
 3. Multiplying the estimated volume of patients by the estimated average gross cost of treatment, to produce the total estimated gross cost of treatment for all five medical conditions.

Patient volumes

58. The number of patients likely to be prescribed CBPM depends on the number of patients with relevant medical conditions, but also on CBPM being judged cost-effective in the patients' particular circumstances. Neither of these is known with certainty.
59. Volumes have been estimated by identifying the number of patients with each of the five medical conditions, and using assumptions (see the bullet points below) to narrow the number down to a sub-population of patients for whom CBPM might be prescribed. This figure assumes that treatment will be recommended as cost-effective in 100 per cent of cases (which is unlikely) and is effectively an upper bound (notwithstanding wider uncertainties). In practice a proportion only of these is likely to meet cost-effectiveness criteria and a number of scenarios are presented to illustrate the potential effect of this. Further detail on the methodology, assumptions and limitations of the volume estimates are described in detail in Annex 1, and should be considered alongside the brief summary provided here, due to the considerable uncertainty associated with these estimates.
 - How many patients have the underlying condition (such as multiple sclerosis)?
 - Of those, what proportion have symptoms which could be mitigated by CBPM?
 - Of those, what proportion have severe and chronic symptoms?
 - Of those, what proportion have intractable symptoms where other treatments had been tried without success?
 - Of those, what proportion might be prescribed CBPM, once individual circumstances and risks have been considered?
 - Finally, a judgement is required on the proportion of cases likely to meet cost-effectiveness criteria.
60. The estimated volumes prior to considering cost-effectiveness are presented in Table 2. Low and high assumptions have been used in order to provide ranges, to reflect the level of uncertainty associated with these estimates. Actual volumes depend heavily on prescribing policies and cost-effectiveness recommendations which have not yet been established. That means there is a risk that volumes may fall outside the suggested ranges in some cases. The figure for chronic pain is particularly uncertain, given the wide range of conditions potentially covered within this category. All figures should be treated as indicative.

Table 2 - Estimated volumes of patients potentially receiving CBPM before cost-effectiveness is considered, by selected medical conditions.

Condition	Prevalence (relative to the total number with the underlying condition)	Volume (after ten years) (number of cases per year potentially receiving CBPM in the UK)	
	Central estimate	Central estimate	Indicative Range
MS pain / spasticity	1 in 75	1,700	150 to 8,000
CINV	1 in 150	600	100 to 2,000
DS / LGS	1 in 3	500	200 to 750
HIV/AIDS appetite / weight loss	1 in 500	180	13 to 900
Chronic pain adults	1 in 90	300,000	60,000 to 1 million

Source: DHSC, 2018.

61. A further adjustment is then required to isolate those cases judged to be cost-effective. This proportion is not known, and will be informed by NICE guidance in due course. In principle, cost-effectiveness recommendations may refer to any combination of particular:

- CBPM.
- Doses or delivery mechanisms.
- Medical conditions.
- Symptoms or severity of symptoms within those conditions.
- Patient history with other treatments and their effect.
- Patient characteristics, such as age or risk factors.

62. It is not as simple as saying (for example) that treating chronic pain would be judged cost-effective, or treating CINV would not. Nor is it possible to rank the different medical conditions in a robust objective way. Instead, the analysis considers a range of illustrative scenarios, corresponding to the proportion of cases judged cost-effective being 0, 10, 25, 50, 75 and 100 per cent of the central estimate shown in Table 2 above. Actual volumes may be different, see Table 3.

Table 3 - Central estimates of potential patient volumes, adjusted for cost-effectiveness (CE)

Scenario →	Estimated volume of cases where CBPM are recommended as cost-effective					
	0%	10%	25%	50%	75%	100%
MS pain	0	170	425	850	1,275	1,700
CINV	0	60	150	300	450	600
DS / LGS	0	50	125	250	375	500
HIV/AIDS appetite / weight loss	0	18	45	90	135	180
Chronic pain	0	30,000	75,000	150,000	225,000	300,000

Source: DHSC, 2018.

63. All these numbers are subject to the additional uncertainty margins listed in Table 2. The zero scenario is not intended to imply that no cases at all will be deemed to be cost-effective, but simply that certain conditions or circumstances may be. In the specific case of MS, NICE currently advises that treatment with Sativex is not currently cost-effective. In such a situation, treatment with CBPM on the NHS would be exceptional, and likely based on unique individual circumstances.

64. These volumes represent an eventual “steady state” once all potential patients have been assessed. This is unlikely to be achieved immediately. It may take some years before the

suggested volumes are reached. For modelling and costing purposes, the analysis assumes that volumes will start low initially, and potentially increase over time before eventually reaching the levels suggested. The assumed profile²² is as follows:

Year	1	2	3	4	5	6	7	8	9	10
Caseload as percentage of eventual steady state	0.25	0.5	1	2	5	10	20	40	70	100

65. This means that average volumes over the ten-year period may be around a quarter of the eventual figure. Actual timing will depend on licensing approvals, NICE assessments and capacity being achieved, and may be faster or slower than this. Nevertheless, it is unlikely that large numbers of patients could expect to receive a currently unlicensed drug immediately. Clinicians would be expected to be cautious in their prescribing and consider MHRA and NHS England guidance, including any changes to that guidance as further evidence becomes available.

Gross cost to the NHS of CBPM treatment

66. The estimated cost of treatment captures the following three components:

- Time spent on medical assessment or approval for CBPM use.
- Expenditure on CBPM treatment itself (comprising both medicine and care costs).
- Time/expenditure associated with dealing with any side effects or harms.

67. Average costs are based on assumptions about how each condition might be treated on average, for example how many appointments might be required with GPs or consultants. The specific methodology, assumptions and limitations of these estimates are described in detail in Annex 2, and should be considered alongside the summary provided here, owing to the considerable uncertainty associated with these estimates. The estimated average cost for each medical condition are presented in Table 4 below. These are gross costs, funded through existing resources.

Table 4 - Estimated average gross costs per case of patients receiving CBPM, by medical condition, (£), 2018.

Gross cost →	One-off	Annual	10-year (undiscounted)	10-year (discounted at 3.5% ²³)
Condition ↓				
MS pain / spasticity	1,000	6,000	61,000	52,600
CINV	1,000	1,000	3,000 ¹	3,000
DS / LGS	1,000	13,000	131,000	112,900
HIV/AIDS appetite / weight loss	1,000	6,500	66,000	56,900
Chronic pain adults	1,000	6,000	61,000	52,600

Source: DHSC, 2018.

Note: (1) The ten-year estimates assume that treatment begins in year 1. In practice, some treatments may not be available immediately and only a proportion of the ten-year cost will be incurred during the first ten years. Chemotherapy is assumed to last up to two years only.

68. Estimates of total cost for the selected conditions can in principle be estimated by multiplying the estimated volume in each year by the estimated average cost for each medical condition, adjusted for any delay before treatment becomes available. As shown in Table 5, this would provide a discounted upper limit estimated gross cost, before cost-effectiveness is considered, of £3,698 million across all five medical conditions, with a range from £739 million to £12,335 million over ten years. As stated previously, it will take time to reach a steady state, and costs in the early years may be significantly lower. The discounted figures shown take this into account.

²² DHSC modelling assumption. The actual profile will depend on the speed with which licensing and guidance can be developed.

²³ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/685903/The_Green_Book.pdf

69. Such analysis is illustrative, and makes the unrealistic assumption that all conditions and cases are judged to be cost-effective. Only a subset will meet that test, and in such cases the gross cost, both in terms of the potential for side effects for the patient and to the NHS, should be outweighed by benefits. Where NICE advises interventions are not cost-effective, there would be little or no NHS prescription. It should be noted that these figures do not include any potential savings to public health services, for example if CBPM replace existing treatment, or if health improvements from CBPM leads to patients requiring less treatment, for example fewer hospital admissions from a reduction in seizures for patients with epilepsy.

Table 5, Estimated potential gross cost of CBPM, by medical condition, in the unlikely event of treatment being recommended as cost-effective in all cases, over 10 years, 2018.

Condition	Estimated potential gross cost (£m) over 10 years			Notes
	Low	Central	High	
MS pain / spasticity	2	21	98	This table assumes that all relevant cases will be judged to be cost-effective.
CINV	0	1	4	
DS / LGS	5	13	19	
HIV/AIDS appetite / weight loss	0	2	12	In practice only a proportion will be, and illustrative scenarios of 0, 10, 25, 50 and 75 per cent of these numbers should be considered.
Chronic pain adults	732	3,661	12,203	
Total	739	3,698	12,335	

Source: DHSC, 2018.

70. These estimates assume a gradual introduction, with volumes, costs and benefits being low in the early years, rising later, on the assumption that appropriate licensing, cost-effectiveness recommendations and guidance are developed. As previously identified, this expenditure does not represent an additional financial cost to the NHS, as funding for CBPM will be reallocated from within existing resources, and only if cost-effective.

71. Actual cost-effectiveness will vary between and within conditions. Table 5 presents a potential maximum, with a large uncertainty margin, but the proportion of this that will actually be incurred is unknown. Because only cost-effective treatments will be funded, the more CBPM prescriptions made and the higher the costs, the greater too will be the expected net benefits from rescheduling CBPM.

72. The above covers patients actually prescribed CBPM. In addition, there may be ongoing costs of £1,000 per case for assessments which conclude that CBPM are unsuitable. The total cost of this will depend on the proportion of assessments prescribing CBPM, and the higher that proportion is, the lower the extra cost. If guidance advises that CBPM are not cost-effective in some situations, such that assessments are not required, there will no extra cost. Any costs which are incurred will be funded from within existing resources.

73. Similarly, it is possible that some patients will use CBPM for a trial period but then clinicians may conclude that the treatment is unsuccessful and should be terminated. Again, there may be costs incurred with no longer-term benefit. This cannot be quantified robustly on current evidence but may be significant. It would be reasonable to assume that as evidence and experience improve over time, decisions to assess patients and/or try new treatments may become more efficient.

Patients

74. As previously identified, funding for CBPM will be reallocated from existing NHS resources. This will create an opportunity cost to patients in terms of foregone health benefits elsewhere. However, CBPM will only be funded where it is cost-effective, so any spending on CBPM should replace spending on less cost-effective treatments elsewhere in the healthcare system. This means that the increase in health benefits from CBPM should be greater than the foregone health benefits from the treatment that it has displaced. Also, the net increase in health benefits should be greater at higher volumes of CBPM prescribed.

Enforcement agencies

75. There may be ongoing costs for police forces and the Border Force, if they need to spend additional time trying to distinguish between genuine CBPM and illicit cannabis products.
76. The smoking of cannabis will remain prohibited when CBPM are rescheduled, which may make it easier for enforcement officers to distinguish between illegal use of cannabis and CBPM, and therefore mitigate some of these costs. Also, police forces and the Border Force already have experience of distinguishing between the medicinal and illegal use of controlled substances, for example for substances such as benzodiazepines, which can be legally prescribed as medicines but may also be subject to misuse.
77. However, these costs may still be substantial given that cannabis is the main drug of misuse which is encountered by the police and the Border Force. For example, in 2016/17 police forces in England and Wales made a total of 96,604 seizures of cannabis, representing 73 per cent of all drug seizures, and the Border Force made 3,175 seizures of cannabis, representing 48 per cent of all drug seizures in that year²⁴. Due to a lack of data on how much additional time this might take for enforcement agencies, this cost has not been quantified. However, if it takes police and Border Force officers an additional 30 minutes per cannabis seizure to identify whether the item is medicinal cannabis, this would represent an additional cost of £1.1 million per year (assuming an average labour cost per hour of £23 for police/immigration officers, as previously identified).

Home Office

78. Companies and individuals in England, Wales and Scotland are required to apply to the Home Office (or to DH NI in Northern Ireland) for a licence if they wish to produce, supply, possess, import or export controlled drugs. If the rescheduling of CBPM leads to an increase in the number of licence applications, then this would impose additional costs on the Home Office Drugs and Firearms Licensing Unit (DFLU), in terms of additional time and resources for conducting compliance visits for all new licensees, responding to enquiries, refusing spurious registrations and the processing of the domestic and import/export applications.
79. In the UK, cannabis cultivation licenses have not currently been issued for the purpose of CBPM, and therefore it is likely that raw cannabis or oils will need to be imported. There may be a potential increase of high-THC cannabis cultivation licence applications (and a corresponding increase in enquiries), to enable the UK to manufacture without needing to import the raw materials. However, based on input from DFLU, it is not known how, where and what products will be obtained in practice (for example, raw cannabis or oils). This cost therefore cannot be estimated with any certainty.
80. However, it is unlikely that there will be a significant increase in the number of domestic schedule 2 possess, supply and produce licence applications, as CBPM are likely to be handled by wholesalers/distributors and manufacturers who already operate with schedule 2 controlled drugs, and thus already hold the required licence.

BENEFITS

Business

81. The rescheduling of CBPM may have a long-term benefit to the economy and employment if it leads to a growth in UK-based companies producing CBPM, in order to more efficiently serve the new UK market. However, it is not possible to identify with any certainty whether this benefit would occur, or to quantify how large any such benefit might be. Also, there may well be an offsetting impact to the economy if CBPM replace existing medicines which are produced in the UK, as there could be a fall in the economic output of these businesses.

²⁴ <https://www.gov.uk/government/statistics/seizures-of-drugs-in-england-and-wales-financial-year-ending-2017>

Health-related benefits

82. There are three types of health-related benefits that may arise from the use of CBPM:
- A net improvement in the patient's health outcomes, taking into account any risks or side-effects.
 - A saving in treatment costs if CBPM produce a net health improvement which reduces the need for future treatment (for example, in the case of a patient with severe epilepsy if it reduces the frequency of seizures, and therefore reduces the number of hospital admissions).
 - A saving in treatment costs if the CBPM replaces existing medication.
83. Research suggests that CBPM will provide health benefits for several conditions in certain situations. The CMO's recent report summarises the evidence and makes clear that it is of variable quantity and quality²⁵. The Expert Panel has advised that the size of any health benefit is less certain and will vary on a case-by-case basis.
84. Treatment by CBPM may or may not be cost-effective. Even if research suggests they could help, that does not necessarily mean that traditional treatments would be less effective. Focusing on the benefits for those patients for whom existing treatments have failed necessarily reduces the number of cases and amount of evidence available.
85. Any spending on CBPM will replace spending on less cost-effective treatments elsewhere in the healthcare system. This means that there should be a net increase in health benefits if CBPM is prescribed, and this increase should be greater at higher volumes of prescriptions.
86. The limitations of the evidence base are significant and mean that the health-related benefits of CBPM cannot currently be quantified with any certainty. Instead, two breakeven values have been assessed in this analysis, for each medical condition. The first breakeven value is the required reduction in treatment costs (either through CBPM replacing existing medicines, or through a reduced need for future treatment due to health improvements) to outweigh the gross costs of CBPM. This analysis only considers the health-related costs and does not include the wider costs such as those related to familiarisation, as familiarisation costs cannot be disaggregated by medical condition with any certainty (and they may relate to other medical conditions outside of the five specific conditions that have been examined in this IA).
87. The second breakeven value is the required improvement in health outcomes in order to outweigh the gross costs of CBPM. This has been assessed by using the available evidence to estimate the improvement in quality-adjusted life years (QALYs), a measure which captures improvements in quality and duration of life, for each of the five conditions. The monetary value of one QALY is assumed to be £60,000, as recommended in the Green Book guidance on appraisal and evaluation²⁶. However, because NHS resources are finite, any investment would displace spending elsewhere and create an opportunity cost.
88. Instead of using a value of £60,000 per QALY, this impact assessment uses the central assumption that the NHS as a whole generates additional health gain for patients at the rate of 1 Quality Adjusted Life Year (QALY) for every additional £15,000 spent. This is standard for DHSC impact assessments and is based on research at the Centre of Health Economics in York²⁷. This assumption is used to estimate the opportunity cost of spending NHS resources on the policy proposal (in this case investing in cannabis-based products for medicinal use). If a policy leads to more health gain being generated for the same level of resource (or the same level of health gain for less money) then it is cost effective. The reverse is also true. The actual health foregone will

²⁵https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/722010/CMO_Report_Cannabis_Products_Web_Accessible.pdf

²⁶ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/685903/The_Green_Book.pdf The value of £60,000 represents the perceived value to the public of improved health. A lower value of £15,000 is used by NICE and others to judge cost-effectiveness, given that any investment must also compare favourably with other potential uses of funding within the NHS. The £15,000 value is used in the break-even analysis in this IA, to reflect the opportunity cost.

²⁷ <https://www.york.ac.uk/che/research/teehta/health-opportunity-costs/>

depend on the treatment foregone to fund the policy. This cannot be known, so the average from the York research is chosen.

89. The methodology, assumptions and limitations of the breakeven analysis are described in detail in Annex 3, and should be considered alongside the brief summary provided here, due to the considerable uncertainty associated with this type of analysis. The results of this analysis are summarised in Table 6 below.

Table 6 – The required benefits of CBPM, to outweigh the gross costs, (£), 2018.

Condition	Total savings in treatment costs required per patient (over 10 years, £ discounted)	(or) QALY health improvement required per patient (over 10 years, discounted)
MS pain / spasticity	52,600	3.5
CINV	3,000	0.2
DS / LGS	112,900	7.5
HIV/AIDS appetite / weight loss	56,900	3.8
Chronic pain	52,600	3.5

90. These results indicate that, for example, if the use of CBPM for MS pain results in a reduction of treatment costs of more than £52,600 per patient, or alternatively in a health improvement of more than 3.5 QALYs per patient, then there would be an overall benefit to society from this treatment. The lowest breakeven values are for chemotherapy, where a cost reduction of £3,000 or a health improvement of 0.2 QALYs is required in order for the benefits to outweigh the costs of treatment, while the highest breakeven values are for Dravet and Lennox-Gastaut Syndromes which have higher expected costs.
91. In practice, if the health improvement from a given treatment is low, then higher cost savings would be required for the benefits to outweigh the costs (and vice versa). Annex 3 provides an assessment of whether the breakeven values in Table 6 might be feasible, given the evidence currently available. In isolation, the QALY values required to justify cost-effectiveness are high, and it is likely that both cost savings and QALY gains will be needed to justify any intervention. At the very least, it would be more difficult to achieve and demonstrate cost-effectiveness. Recommendations from NICE will be prepared in due course and this may help identify where intervention is, or isn't, likely to be cost-effective. Given limitations around the evidence base, this may be done through a narrative comparing CBPM with alternatives. Traditional cost-effectiveness analysis may also be provided in the longer term.
92. This analysis should be regarded as an approximate illustration of the balance of costs and benefits required, given that it is based on uncertain cost figures, timing and given the limited evidence on the specific benefits of CBPM when used as a treatment after other interventions have been unsuccessful.

Carers

93. An improvement in health outcomes for patients may also have wider consequential benefits for the family and unofficial carers of those patients, by reducing their caring workload. However, this benefit cannot be quantified as the magnitude of this benefit is considerably uncertain.

Society

94. The rescheduling may lead to increased UK research into CBPM, as these products can be tested more easily. This may lead to economic benefits for UK businesses and health benefits to patients if this research leads to new and improved CBPM. It is not possible to identify with any certainty whether and when this benefit would occur, or to quantify how large any such benefit might be. In principle, research is ongoing and could lead to more effective treatment, lower costs, better understanding and management of risks, and improved health and wellbeing, over the medium term.

F. Risks

OPTION 1

95. If patient access to CBPM continues to be restricted, there is the potential for patient healthcare to deteriorate as their clinical need is not met.

OPTION 2

96. By placing CBPM into Schedule 2 of the 2001 Regulations there will be fewer controls on its use within healthcare in the UK. This wider availability has the potential to lead to increased diversion into the illicit market. However, measures in regulations will be put in place to ensure that the risk of diversion is minimised. For example, for CBPM that have not gone through the MHRA's licensing process, the decision to prescribe can only be made by a doctor on the Specialist Register of the General Medical Council.
97. The potential demand for CBPM may be high and need careful management to avoid over or under-prescription. The analysis in the IA demonstrates the large patient volumes that could arise without adequate procedures and controls being in place. There are risks around ensuring referrals from primary care are only made in circumstances where prescription is likely to be appropriate. Prescription can still only be made by, or under the direction of, a doctor on the GMC Specialist Register, so the risk is more about inefficiency and managing patient expectations than inappropriate prescribing. Finally, there is a risk around how demand is met over time. The estimated volumes assume that all appropriate demand is met, but in practice it may take time (possibly years) for all patients to be prioritised, seen and assessed. Early volumes may be lower.
98. There are currently few providers known that meet the quality requirements that MHRA guidance will set out. Prescriptions will be of unlicensed products, at least in the short-term, and be supplied using the current 'special medicines' routes. While actors in the supply chain are very familiar with the process, costs per supply are likely to be high as manufacturers/importers are unlikely to be able to benefit from economies of scale under these restrictions. Competition and therefore price will be dependent on prescription volumes and the supplier base widening over time. Costs, to the NHS, of any medicines that obtain a marketing authorisation will be negotiated via normal commissioning arrangements following assessment by NICE.
99. There is evidence²⁸ of the potential harms from use of CBPM. For example, tetrahydrocannabinol (THC) is the principal mind-altering constituent of cannabis, and its short-term effects can include increased heart rate, anxiety, coordination problems, slower reaction times and memory loss. High use may also be associated with an increased longer-term risk of psychosis and schizophrenia, particularly if taken from a young age.
100. There is a risk that longer-term serious issues emerge within the health sector from wider use of CBPM. This formed part of the rationale for the Expert Panel currently in place to advise the Home Secretary on licence applications requiring treatment with CBPM to be given only if other treatments are unsuccessful. NICE are intending to produce a patient decision tool to help them make informed decisions about the benefit / risk trade-off, particularly when some harms may be longer-term or less well evidenced.
101. NHS England is ensuring that appropriate guidance is available to prescribers in advance of the relevant regulations coming into force. DHSC has commissioned the National Institute for Health and Care Excellence (NICE) to develop more detailed prescribing guidelines.
102. There is significant uncertainty around the volume of patients that will be prescribed CBPM, and around the net change in healthcare benefits resulting from the reallocation of healthcare spending from other treatments to CBPM. It is assumed that there will be a positive net change as healthcare spending is allocated according to cost-effectiveness, but there is a risk that actual costs and benefits may differ from expectations.

G. Enforcement

103. The enforcement of CBPM will be subsumed by the measures already in place to tackle the illicit possession, sale or production of other Schedule 2 controlled drugs. Enforcement of the legislation will be undertaken by police forces, Border Force, the Crown Prosecution Service and other

²⁸ For example, reviewed by NASEM at <https://www.nap.edu/read/24625/chapter/1#xii>

relevant agencies responsible for enforcing the legislative and regulatory framework for controlled drugs in the UK.

104. The MHRA regulates medicines in the UK, and will therefore be responsible for regulating CBPM. They are responsible for: (a) ensuring that medicines, meet applicable standards of safety, quality and efficacy; (b) ensuring that the supply chain for medicines is safe and secure; (c) helping to educate the public and healthcare professionals about the risks and benefits of medicines leading to safer and more effective use and; (d) influencing UK, EU and international regulatory frameworks so that they are risk-proportionate and effective at protecting public health.²⁹
105. The General Medical Council regulates doctors and can investigate concerns about inappropriate practice, for example with respect to the prescribing of medicines.

H. Summary and Recommendations

106. Table 7 outlines the costs and benefits of the proposed changes for Option 2. Option 2 is the preferred option as it permits the use of CBPM in healthcare in the UK, while continuing to prevent the illegal misuse of cannabis.

Table 7 Option 2, Gross Costs and Benefits, discounted, total over 10 years

Costs	£m	Benefits	£m
Familiarisation costs to private-only doctors on the Specialist Register.	0.04	All non-monetised Improvement in health and wellbeing outcomes for those receiving CBPM, and their carers.	
Familiarisation costs to NHS doctors on the Specialist Register.	0.6		
Familiarisation costs to other NHS specialists.	0.4	Health-related cost savings if CBPM replace existing medicines, and if the health improvement leads to lower treatment costs.	
Familiarisation costs to GPs	0.3		
Familiarisation costs to police officers and immigration enforcement officers.	0.4	Potential growth in UK-based companies cultivating and producing CBPM.	
Non-monetised costs			
Familiarisation costs to NHS or private doctors prescribing CBMP under direction.			
Opportunity cost in terms of foregone health benefits elsewhere in the healthcare system, as cannabis treatment displaces other healthcare spending.			
Increase in licensing activity by the Home Office, to process additional high-THC cannabis cultivation licence applications.			
Some patients may experience side effects from CBPM and require additional care.			
Additional time spent by enforcement agencies			

²⁹ <https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/about>

distinguishing between medicinal and illegal use of cannabis.			
Total cost	1.8	Total benefit	0.0
Net present value			-1.8

Source: Home Office and DHSC internal analysis, 2018.

107. This negative NPV is not a fair reflection because only the familiarisation costs are quantified while the ongoing costs and all benefits are not. In practice, there is reasonable evidence of medical benefit which will deliver a QALY gain, and potentially treatment cost savings, in a wide range of situations and conditions. Such benefits may or may not be sufficient to be cost-effective, and NICE guidance will make recommendations on this in due course. The policy intention is that CBPM are prescribed in specific circumstances only, when cost-effective to do so, rather than as a general remedy. That means not only that volumes may be limited, but also that those patients receiving treatment are those most likely to see the greatest benefit, and hence the best cost-effectiveness.
108. The numbers also reflect only the five medical conditions described in the text. If eligibility is wider or different from that, the picture will change. Nevertheless, the five conditions are designed to provide a representative picture. The list of five is used without prejudice to any final decisions on cost-effectiveness or eligibility.
109. Although it is not possible to quantify the benefits at this time because of the level of uncertainty, the evidence suggests it is reasonable to believe a benefit could be achieved. It is also reasonable to expect that the benefits may outweigh the costs for some patients. In practice, it will be up to doctors on the Specialist Register or those working under their direction to decide whether CBPM should be prescribed in any particular case, taking into account the balance of benefits and costs and official guidance.
110. Costs may be high if prescription is adopted in a wide range of cases, albeit mitigated by potential savings, and the possibility of a gradual stepping up of patient assessments over time. Risks of side effects also need to be considered.
111. Continued monitoring is required to confirm in which circumstances prescription is likely to be most successful, so that guidance and hence cost-effectiveness can be improved over time.

I. Implementation

112. The Government plans to implement the rescheduling of CBPM under the 2001 Regulations via the negative resolution procedure, subject to Parliament's approval. The DH NI plans to implement the changes via negative resolution, subject to the approval of the Northern Ireland Assembly. These changes are intended to be implemented in autumn 2018.
113. Changes to the regulations will be complemented by prescriber guidelines informed by clinical/professional bodies as follows:
- a. NHS England guidance will provide support and guidance to clinicians in the prescribing of CBPM.
 - b. NICE are due to produce clinical guidelines on the prescribing of CBPM use in humans to support specialist clinicians' prescribing decisions. This guidance is expected by October 2019.
 - c. In the interim, NHS England have asked the British Paediatric Neurology Association (BPNA) to develop clinical advice on the use of CBPM in paediatric patients with epilepsy.
 - d. The Royal College of Physicians (RCP) has been asked to develop additional advice around the prescribing of these products in other indications.
 - e. MHRA guidance sets out the requirements for the manufacture, import, distribution and supply of CBPM. 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.

- f. Police guidance will be developed to help with the enforcement of the illegal use of cannabis. This will aim to help the police identify between a medicinal product and a non-medicinal product.
- g. Border Force guidance will be in place to assist with the monitoring of imported CBPM.

J. Monitoring and Evaluation

114. As part of its statutory duties under the 1971 Act, the ACMD keeps the situation relating to the misuse of drugs under review. Following on from their short-term advice, the ACMD have been asked to conduct a full review of CBPM, with advice to be provided by July 2019. They are also intending to review the use of synthetic cannabinoids.
115. Taking into account evidence provided in the forthcoming full ACMD review, the Home Secretary has committed to reviewing the changes to these regulations in two years from the date of commencement. This is an evolving field and it is clear that as further clinical research progresses and experience is gained changes in practice may be needed. This review will be an opportunity to review the operation of the amendments and to consider the effect of any further ACMD recommendations.
116. The effectiveness of the new regime will be monitored by the CQC for England, and the healthcare regulatory bodies for Wales, Scotland and Northern Ireland. The Health Act 2006 also established the role of Accountable Officers with responsibility to establish and ensure appropriate arrangements to comply with misuse of drugs legislation. Accountable officers have a duty to establish local intelligence networks to analyse prescribing practices in their area and ensure that their areas have processes for establishing an incident panel if serious concerns are raised about controlled drugs.
117. The existing regime for unlicensed medicines requires that any person selling or supplying a 'special medicine' must keep records of any suspected adverse drug reaction (ADR); make these records available to the MHRA and report serious suspected ADRs to the MHRA electronically within 15 days. MHRA may consider further measures to maintain and improve vigilance

K. Feedback

118. Information gathered from the monitoring and evaluation process will inform future ACMD advice on the classification, designation and scheduling of CBPM, including any future legitimate uses of cannabis.

Impact Assessment Checklist

The impact assessment checklist provides a comprehensive list of specific impact tests and policy considerations (as of October 2015). Where an element of the checklist is relevant to the policy, the appropriate advice or guidance should be followed. Where an element of the checklist is not applied, consider whether the reasons for this decision should be recorded as part of the Impact Assessment and reference the relevant page number or annex in the checklist below.

The checklist should be used in addition to [HM Treasury's Green Book guidance](#) on appraisal and evaluation in central government.

Economic Impact Tests

Does your policy option/proposal consider...?	Yes/No (page)
Business Impact Target The Small Business, Enterprise and Employment Act 2015 (s. 21-23) creates a requirement to assess the economic impacts of qualifying regulatory provisions on the activities of business and civil society organisations. [Better Regulation Framework Manual] or [Check with the Home Office Better Regulation Unit]	Not in scope of BIT

GLOSSARY

UK Law: The Schedules

The 2001 Regulations determine in what circumstances it is lawful to possess, supply, produce, export and import controlled drugs. The authorised scope of activity will depend on the schedule to which the controlled drug is assigned. There are five schedules. Schedule 1 contains those drugs that are considered to have little or no therapeutic value and are subjected to the most restrictive control. Schedule 5 contains drugs that are considered to have therapeutic value and are commonly available as over the counter medicines.

Schedule 1

Drugs belonging to this schedule are thought to have no therapeutic value and therefore cannot be lawfully possessed or prescribed. These include LSD, MDMA (ecstasy) and cannabis. Schedule 1 drugs may be used for the purposes of research but a Home Office licence is required.

Schedule 2 & 3

The drugs in these schedules can be prescribed and therefore legally possessed and supplied by pharmacists and doctors. They can also be possessed lawfully by anyone who has a prescription. It is an offence contrary to the 1971 Act to possess any drug belonging to Schedule 2 or 3 without prescription or lawful authority. Examples of schedule 2 drugs are methadone and diamorphine (heroin). Schedule 3 drugs include subutex and most of the barbiturate family.

The difference between Schedule 2 and Schedule 3 drugs is limited to the application of the 2001 Regulations concerning record keeping and storage requirements in respect of schedule 2 drugs.

Schedule 4 (i) & (ii)

Schedule 4 was divided into two parts by the 2001 Regulations [as amended by the Misuse of Drugs (Amendment No. 2) Regulations 2012].

Schedule 4(i) controls most of the benzodiazepines. Schedule 4(i) drugs can only be lawfully possessed under prescription. Otherwise, possession is an offence under the 1971 Act.

Schedule 4(ii) drugs can be possessed as long as they are clearly for personal use. Drugs in this schedule can also be imported or exported for personal use where a person himself carries out that importation or exportation. The most common example of a schedule 4(ii) drug is steroids.

Schedule 5

Schedule 5 drugs are sold over the counter and can be legally possessed without a prescription.

Annex 1 – methodology for estimating the number of patients who may be prescribed cannabis

The intention is for cannabis-based medicinal products (CBPM)³⁰ to be prescribed only following treatment with or consideration of existing licensed medicines. In other words, CBPM should be seen as a subsequent treatment rather than a primary one. Subject to clinical judgment, other treatments will be offered first, and only if they prove unsuccessful will CBPM then be prescribed.

Any prescription should normally be given only where products are licensed, recommended as cost-effective and supported with detailed clinical guidance.

Several different medical conditions and circumstances are likely to be in scope. It is not possible to consider every possible situation in detail, and so the analysis focuses on five specific medical conditions only. These conditions were chosen with reference to the recent Chief Medical Officer evidence review³¹ but chosen independently within DHSC to provide a varied but representative picture of the types of cases where CBPM might be prescribed. The list contains a mix of conditions identified in the CMO's review as having conclusive or substantial evidence of potential medical benefit, conditions where the evidence of benefit is more limited, and conditions where CBPM are available overseas.. The conditions are:

- Multiple Sclerosis (MS) – pain or muscle spasticity.
- Chemotherapy-induced nausea and vomiting (CINV).
- Severe treatment-resistant epilepsy in children - specifically Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS) only.
- Chronic pain in adults.
- Appetite and weight loss associated with HIV/AIDS.

This is NOT a definitive list, but merely an illustration designed to inform the cost-benefit analysis and decision-making generally. Formal guidance will be issued in due course specifying which conditions, and criteria within those conditions, are in scope. That list may be narrower, broader or otherwise different from the five conditions listed. It may also change over time. The list of five is not intended to change any existing guidance and is used without prejudice to any future decisions.

Patient volumes are subject to significant uncertainty, both in terms of the volumes themselves, and in terms of when prescriptions are likely to be made. The approach taken identifies the number of patients with each condition, and then narrows that down to a subset where CBPM might be prescribed. In this way, evidence is used to inform the forecasts as far as possible, while acknowledging uncertainty.

The typical approach identifies:

- How many patients have the underlying condition (such as multiple sclerosis)?
- Of those, what proportion have symptoms which could be mitigated by CBPM?
- Of those, what proportion have severe and chronic symptoms?
- Of those, what proportion have intractable symptoms where other treatments had been tried without success?
- Of those, what proportion might be prescribed CBPM, once individual circumstances, risks, and any other criteria have been considered?³²

Finally, a judgement is required on the proportion of cases likely to meet cost-effectiveness criteria. This judgement is applied generically in the form of several illustrative scenarios, once baseline figures for each individual condition have been obtained.

The result is typically a wide range estimate for the final number of patients. There is no guarantee that the actual number of patients will fall within the range quoted, however based on the available evidence,

³⁰ The ACMD review will consider whether a more refined listing of cannabis and cannabis-based products should be produced.

³¹ <https://www.gov.uk/government/publications/cannabis-scheduling-review-part-1>

³² This does assume an idealised scenario where there is a specialist clinician who is content to prescribe, and there are no issues with product licences.

the ranges should provide a plausible indication. The approach used also helps to identify which assumptions the results are most sensitive to. The following sections set out the detailed rationale behind the assumptions used to estimate volumes for each medical condition, with references to source material where appropriate.

On the timing side, the analysis assumes that while volumes will eventually reach a steady state, it may take some years to reach that level. The following profile³³ is assumed for all medical conditions:

Table A.1 – Assumed profile of patient volumes

Year	1	2	3	4	5	6	7	8	9	10
Caseload as percentage of eventual steady state	0.25	0.5	1	2	5	10	20	40	70	100
Increment	0.25	0.25	0.5	1	3	5	10	20	30	30

This affects both the volumes directly, and the expected costs/benefits over the ten-year appraisal period. The 30 per cent of people added in year 9, for example, would only incur two years of costs and benefits within the ten-year timeframe (and another eight years afterwards).

The following analysis is tentative and uses material beyond that included in the CMO review. This is necessary to develop cost and benefit scenarios, but is less robust.

Multiple sclerosis – chronic pain and/or muscle spasticity

In the specific case of MS, existing guidance from NICE advises that treatment with Sativex (the one currently licensed CBPM) is not cost-effective. This IA does not alter that advice, but nonetheless recognises that additional medical products may be licensed in future, costs and benefits may change and evidence may improve. MS is included as an example medical condition accordingly. Current evidence of benefit in tackling MS pain and spasticity is mixed. For example, it is conclusive or substantial for improving patient-reported MS spasticity symptoms, but limited for improving clinician-measured MS spasticity symptoms.

The number of people diagnosed with MS in the UK is estimated at 130,000.³⁴ This includes a wide range of severities but a distinction can be made between relapsing/remitting illness and progressive/worsening illness. Each category accounts for about 50 per cent of cases. The progressive half can be further split into 15 per cent primary progressive (where the condition has always been progressive) and 35 per cent secondary progressive (where the condition was previously relapsing/remitting but has worsened).³⁵

On this basis, one could argue that between 15 and 50 per cent of cases are relatively serious and the rest relatively less so. The former category might, if other conditions are met, be more disposed to an eventual cannabis prescription.³⁶

The next question is whether those with relatively more serious illness are likely to experience symptoms of pain and spasticity (the symptoms that might be most amenable to cannabis). Evidence suggests that 20 per cent of MS patients experience spasticity, and 33 per cent pain.³⁷ These rates may be higher for those with progressive illness. For illustration the calculation assumes the rate will be double, namely that progressive patients will experience spasticity 40 per cent of the time, and pain around 70 per cent of the time.³⁸ By adding an assumption that the majority of those with spasticity will also experience pain, and adjusting for that overlap, the incidence for “spasticity and/or pain” might be around 80 per cent.³⁹

³³ DHSC modelling assumption.

³⁴ Research paper - Incidence and prevalence of multiple sclerosis in the UK 1990-2010: a descriptive study in the General Practice Research Database (McKenzie et al, Dundee University). This quoted 127,000 cases of which 110,000 had a more certain diagnosis, with annual growth of 2.4 per cent. That implies around 130,000 in 2018.

³⁵ The figures in this paragraph are based on NHS Choices data at <https://www.nhs.uk/conditions/multiple-sclerosis/>

³⁶ This modelling assumption is tentative and would benefit from refinement as the availability of evidence improves.

³⁷ MS Society. <https://www.mssociety.org.uk/about-ms>

³⁸ DHSC modelling assumption for illustration. Subject to refinement as evidence improves.

³⁹ Ditto. Assumes 30 out of the 40 with spasticity also experience pain, and hence that 10 of them do not. That 10 per cent is then added to the 70 with pain to give 80 per cent experiencing one or both.

However, some of these symptoms may be acute rather than chronic. The precise proportion is unknown (and the distinction is somewhat arbitrary) but for analysis purposes the calculation assumes that a majority, between 50 and 100 per cent of those with these symptoms will have chronic symptoms.⁴⁰

Other treatments may still be effective. Some survey evidence suggests that 20 per cent of MS patients have tried cannabis.⁴¹ However, that does not necessarily provide a good estimate of how many would reach the stage of last resort. Other treatment may or may not have been successful, and they may or may not have benefited from cannabis. The current legal restrictions may have further distorted the figure. For illustration, the analysis assumes that between 10 and 30 per cent would reach the stage of last resort.⁴²

Finally, only a proportion of these people might be prescribed CBPM. Individual assessments of suitability and risks would be required, applying clinical guidance which is still being developed. A robust figure is not available, but the analysis assumes between 20 and 50 per cent of those at this final stage would be deemed suitable for prescription.⁴³ A determination of cost-effectiveness might reduce the figure further, possibly significantly.

Evidence from the Republic of Ireland is limited because of the relatively short term since cannabis treatment has been permitted. They have estimated that around 10 per cent of MS patients would experience moderate to severe spasticity which did not respond to existing treatment, and that 60 per cent of those might benefit from long-term CBPM treatment. That would represent a prescription ratio of 1 in 16, similar to the upper estimate below. See the summary in Table A.2.

Table A.2 - Methodology for estimating the number of patients who may receive CBPM for MS, before cost-effectiveness is considered

	Lower estimate	Upper estimate	Central estimate
Number of MS patients in UK	130,000		
Of which, serious cases (%)	15	50	32.5
Of which, relevant symptoms (%)	80	80	80.0
Of which, chronic symptoms (%)	50	100	75.0
Of which, intractable (%)	10	30	20.0
Of which, prescribed CBPM (%)	20	50	35.0
Overall proportion qualifying (rounded)	1 in 800	1 in 16	1 in 75
Implied volume (eventual steady state)	150	8,000	1,700

It is accepted that this range is very wide, but that reflects the uncertainty. There are three possibilities:

- As a very tentative central estimate of volume, prior to cost-effectiveness being considered, 1,700 cases a year might be a workable assumption.
- If CBPM prescription is restricted to the most serious cases, and applied only in the most exceptional circumstances, the volume of cases is likely to be around 150 cases each year.
- If CBPM are prescribed more broadly, with less restrictive definitions of what qualifies, around 8,000 cases might be expected.

These estimates may be refined as detailed guidance is prepared and evidence to support the underlying assumptions improves. In the meantime, they should be treated as indicative only.

⁴⁰ DHSC modelling assumption for illustration.

⁴¹ MS Society, 2014.

⁴² DHSC modelling assumption.

⁴³ Ditto.

Chemotherapy-induced nausea and vomiting (CINV)

Chemotherapy is a relatively short-term treatment, and it is assumed that symptoms such as nausea will only occur during, or close to, a course of treatment. As such, the annual number of cancer cases, rather than total accumulative caseload is a better measure of potential demand.

Around 360,000 cancer cases are newly diagnosed each year, and around 28 per cent of them are treated with chemotherapy.⁴⁴ That gives around 100,000 cases as a starting point.

Research suggests that, indicatively, 63 per cent of people suffer nausea or vomiting as a response to chemotherapy.⁴⁵ A range of 50 to 75 per cent caters for sampling error and limited coverage in the original research.

Such symptoms may be minor or severe, and it is assumed that more minor symptoms would be either untreated, handled with conventional treatments or were themselves the (improved) result of conventional treatment for more severe symptoms. Only the more severe and sustained symptoms are assumed to qualify for potential CBPM treatment. Research is very limited but in the study referenced, five per cent of cases with vomiting as a side effect were classed as grade III or IV, meaning more severe. While this proportion is tentative, it suggests the rate may be quite low. For illustration, a range of between two and eight per cent is suggested as plausible.

Finally, only a proportion of these people might be prescribed CBPM. As usual, individual assessments of suitability and risks would be required. A robust figure is not available, but the analysis assumes between 10 and 30 per cent of those at this stage would be deemed suitable for prescription.⁴⁶

Evidence from the Republic of Ireland, although limited, also indicates that a relatively low number of cases is plausible. If their expected frequency were extrapolated to the UK population, one might expect around 100 cases each year, towards the lower end of the suggested range below. See summary in Table A.3.

Table A.3 - Methodology for estimating the number of patients who may receive CBPM for chemotherapy-induced nausea and vomiting, before cost-effectiveness is considered

	Lower estimate	Upper estimate	Central estimate
Number of new cancer cases in UK each year	360,000		
Of which, treated with chemotherapy	100,000		
Of which, nausea/vomiting (%)	50	75	63.0
Of which, severe / intractable (%)	2	8	5.0
Of which, prescribed CBPM (%)	10	30	20.0
Overall proportion qualifying (rounded)	1 in 1,000	1 in 50	1 in 150
Implied volume (eventual steady state)	100	2,000	600

Again, this range is wide and uncertain. Potential results include:

- As a very tentative central estimate of volume, prior to cost-effectiveness being considered, 600 cases a year might be a workable assumption.
- If severe symptoms occur very rarely and CBPM prescription is applied only in the most exceptional circumstances, the volume of cases may be around 100 per year.
- If severe symptoms occur more often, or CBPM are prescribed more broadly, with less restrictive but still stringent definitions of what qualifies, around 2,000 cases might be expected.

⁴⁴ Estimated new cases of cancer (all types) in 2015 as quoted at <https://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence>

⁴⁵ Indicative estimate taken from Australian study <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5634543/>

⁴⁶ DHSC modelling assumption. Not based on hard evidence. Needs to be refined.

These estimates may be refined as detailed guidance is prepared and evidence to support the underlying assumptions improves. In the meantime, they should be treated as indicative only.

Treatment-resistant epilepsy in children

For analysis purposes, two specific conditions are considered: Dravet Syndrome and Lennox-Gastaut Syndrome. These are two of the most treatment-resistant forms seen in children. Evidence of benefit in epilepsy generally is lacking, but these particular syndromes have attracted attention in the UK with a small number of high-profile cases. In the US, Epidiolex (a form of cannabidiol containing very limited THC and therefore not considered a controlled drug) has recently been licensed to treat patients with these syndromes and may be licensed in the EU soon. It is possible, notwithstanding the limited evidence, that CBPM might be considered here. With both syndromes it is assumed that, at least initially, only under 18s would be eligible for CBPM. Any final policy may differ from this.

Drawing on NICE findings⁴⁷, the number of patients is estimated as follows:

- Dravet Syndrome – incidence rate of between 1 in 19,000 to 1 in 40,000 live births. Around 17-36 cases per annual cohort. Onset during first year of life. 20 per cent mortality at an average age of eight. This implies total caseload at any point in time, for children age 0 to 17, of around 300 to 600 cases.
- Lennox-Gastaut Syndrome – incidence and prevalence are less certain because LGS can be defined in a number of ways. NICE draw on evidence⁴⁸ suggesting one to two per cent of childhood epilepsies are LGS, which might imply total under-18 caseload of 600 to 1,200 cases.⁴⁹ Other estimates exist and the figure is uncertain. Onset at average age of four. 5 per cent mortality. Allowing for the uncertainty, the analysis uses a wide range of around 500 to 1,500 cases.

The total number of cases across the two conditions is estimated at 800 to 2,100 with 1,500 as a central estimate. Adult survivors are not considered in this calculation, but might form an additional (and possibly larger) group where CBPM could be considered. Those prescribed CBPM as children might continue, and survivors who had already reach adulthood might be considered from scratch.

For children to qualify for CBPM, the assumption is that they would:

- Experience severe and frequent symptoms of a chronic nature.
- Have intractable symptoms, with other treatments proving ineffective.
- Be considered suitable for CBPM.

The likelihood of these tests being met is unknown, but for illustrative purposes the analysis assumes:

- A large majority, between 70 and 90 per cent, will have qualifying symptoms.
- A large majority, between 70 and 90 per cent, will have intractable symptoms.
- Around half of those, between 30 and 70 per cent, will be deemed suitable for prescription.

These proportions are not based on clinical evidence, but are intended to give an indication of final volumes that can be refined as evidence improves. The evidence on benefits is currently incomplete and for some cases the likelihood of prescription may be low in the short term.

Evidence from the Republic of Ireland has tended to focus on a broader definition of epilepsy than used in this document. They note correctly that other treatment-resistant syndromes exist and eligibility may be defined more broadly. On Dravet Syndrome and Lennox-Gastaut Syndrome specifically, they have predicted that a high proportion (up to half) might be considered suitable for CBPM prescription. This is towards the upper end of the indicative ranges in Table A.4. See the summary in Table A.4.

⁴⁷ <https://www.nice.org.uk/guidance/gid-ta10274/documents/draft-scope-pre-referral>

⁴⁸ https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Ing=EN&Expert=2382

⁴⁹ The Epilepsy Society (<https://www.epilepsysociety.org.uk>) estimates 1 in 200 children are affected by epilepsy. There are around 12 million children in the UK aged under 18, implying 60,000 with epilepsy. 1 to 2 per cent of such case is 600 to 1,200.

Table A.4 - Methodology for estimating the number of patients who may receive CBPM for treatment-resistant epilepsy in children, before cost-effectiveness is considered

	Lower estimate	Upper estimate	Central estimate
Number of children with treatment-resistant epilepsy (defined as either Dravet Syndrome or Lennox-Gastaut Syndrome)	1,500		
Of which, chronic / severe (%)	70	90	80.0
Of which, intractable (%)	70	90	80.0
Of which, prescribed CBPM (%)	30	70	50.0
Overall proportion qualifying (rounded)	1 in 7	1 in 2	1 in 3
Implied volume (eventual steady state)	200	750	500

Again, this range is wide and uncertain. The analysis is intended more as a starting point for future refinement than a definitive forecast. The possible outcomes are:

- As a very tentative central estimate of volume, prior to cost-effectiveness being considered, 500 cases a year might be a workable assumption.
- If severe untreatable symptoms occur very rarely and CBPM prescription applied only in the most exceptional circumstances, the volume of cases may be around 250 per year.
- If severe symptoms occur more often, or CBPM are prescribed more broadly, with less restrictive but still stringent definitions of what qualifies, around 750 cases might be expected.

These estimates may be refined as detailed guidance is prepared and evidence to support the underlying assumptions improves. In the meantime, they should be treated as indicative only.

Appetite or weight loss associated with HIV/AIDS

The total number of patients in the UK currently expected to have HIV is 90,000.⁵⁰ This includes both diagnosed and undiagnosed cases.

For such patients to qualify for CBPM, the assumption is that they would:

- Experience loss of appetite and/or weight loss.
- Experience severe symptoms.
- Have intractable symptoms, with other treatments proving ineffective.
- Be considered suitable for CBPM.

The likelihood of these tests being met is unknown, but for illustrative purposes the analysis assumes:

- Around a fifth, between 10 and 30 per cent, would experience appetite/weight loss.
- Around a fifth, between 10 and 30 per cent, would have severe symptoms.
- Around a tenth, between 5 and 15, per cent would have intractable symptoms.
- Around half of those, between 30 and 70 per cent, would be suitable for prescription.

These proportions are not based on clinical evidence, but are intended to set out a framework, and give an indication of final volumes, that can be refined as evidence improves. See summary in Table A.5.

⁵⁰ Terence Higgins Trust <https://www.tht.org.uk/hiv-and-sexual-health/about-hiv/hiv-statistics>

Table A.5 - Methodology for estimating the number of patients who may receive CBPM for appetite or weight loss associated with HIV/AIDS, before cost-effectiveness is considered

	Lower estimate	Upper estimate	Central estimate
Number of HIV patients	90,000		
Of which, appetite or weight loss (%)	10	30	20
Of which, severe (%)	10	30	20
Of which, intractable (%)	5	15	10
Of which, prescribed CBPM (%)	30	70	50
Overall proportion qualifying (rounded)	1 in 7,000	1 in 100	1 in 500
Implied volume (eventual steady state)	13	900	180

This range is wide and very uncertain. The analysis is intended more as a starting point for future refinement than a definitive forecast. Possible outcomes include:

- As a very tentative central estimate of volume, prior to cost-effectiveness being considered, 180 cases a year might be a workable assumption.
- If severe untreatable symptoms occur very rarely and CBPM prescription applied only in the most exceptional circumstances, the volume of cases may be just a dozen or so per year.
- If severe symptoms occur more often, or CBPM are prescribed more broadly, with less restrictive but still stringent definitions of what qualifies, around 900 cases might be expected.

These estimates may be refined as detailed guidance is prepared and evidence to support the underlying assumptions improves. In the meantime, they should be treated as indicative only.

Chronic pain in adults

This final category is the hardest to define because it may cover a large variety of conditions, severities and prognoses. Injuries, illnesses and disabilities - of many different kinds - are all potentially included. Evidence of medical benefit is of variable quality.

As a starting point, research has estimated that 43 per cent of the UK population suffers from chronic pain, which is about 28 million people.⁵¹

Of those, the same research suggests one in six, about four to five million may have severe (Grade IV) symptoms. It might be reasonable to focus attention on those. Extending to Grade III (which is still serious) would increase volumes.

Assumptions are required for the proportion of those who might:

- Have intractable symptoms, with other treatments proving ineffective.
- Have a type of chronic pain that CBPM could potentially treat. This test can also be used to exclude any conditions already considered elsewhere (such as MS-related pain) to avoid double-counting.
- Be considered suitable for CBPM.

The likelihood of these tests being met is unknown, and the uncertainty here is greater than with other medical conditions because of the wide scope of chronic pain.

Evidence overseas may provide some indications, but the differing circumstances and definitions of chronic pain limit the scope. For example, in the US, Minnesota has 7,000 patients with “intractable pain” registered for cannabis use. In Colorado there are 80,000 patients registered with “severe pain”. Both states have populations of around 5.5 million (only residents are eligible) implying that anything from 0.1 to 1.5 per cent of the population might register for CBPM.⁵²

⁵¹ <https://bmjopen.bmj.com/content/6/6/e010364>

⁵² <http://www.health.state.mn.us/topics/cannabis/about/stats.html> <https://www.colorado.gov/pacific/cdphe/medicalmarijuana>

While the UK population, circumstances, prescribing system and clinical criteria may be very different, the fact remains that the number of people living with chronic pain is very large, and depending on the developing guidance, may produce a large population seeking cannabis as a potential therapy.

For illustrative purposes the analysis assumes:

- A majority of those, between 50 and 90 per cent, will have a type of pain that CBPM could treat (and which is not considered elsewhere, such as MS-related pain).
- A significant proportion, between 20 and 60 per cent, will have intractable symptoms.
- Around a quarter, between 15 and 35 per cent, will be deemed suitable for CBPM once risks of side effects and other factors are considered.

These proportions are not based on clinical evidence, but are intended to set out a framework, and give an indication of final volumes, that can be refined as evidence improves. The proposed values deliver a ranged outcome similar to the range seen in the US states mentioned. See summary in Table A.6.

Table A.6 - Methodology for estimating the number of patients who may receive CBPM for chronic pain, before cost-effectiveness is considered

	Lower estimate	Upper estimate	Central estimate
Number of people with chronic pain	28 million		
Of which, severe (%)	14	18	16
Of which, qualifying type of pain (%)	50	90	70
Of which, intractable (%)	20	60	40
Of which, prescribed CBPM (%)	15	35	25
Overall proportion qualifying (rounded)	1 in 500	1 in 30	1 in 90
Implied volume (eventual steady state)	60,000	1,000,000	300,000

Again, this range is wide and very uncertain. The analysis is intended more as a starting point for future refinement than a definitive forecast. Potential results include:

- As a very tentative central estimate of volume, prior to cost-effectiveness being considered, 300,000 cases a year might be a workable assumption for an eventual steady state.
- If cannabis prescription is applied only in the most exceptional circumstances, the volume of cases may be around 60,000 per year.
- If cannabis is prescribed more broadly, with less restrictive but still stringent definitions of what qualifies, around 1 million cases might be expected.

It may take time for these volumes to be reached, as it will not be possible to assess all potential patients overnight. This applies to all conditions, but particularly to chronic pain because of the large population involved. The assumption made is that the volumes shown would be reached after ten years, with much lower numbers early on. Timing may be different from this, depending on patient demand and capacity constraints.

These estimates may be refined as detailed guidance is prepared and evidence to support the underlying assumptions improves. In the meantime, they should be treated as indicative only. They emphasise the importance of having appropriate processes, rules and controls in place, to ensure prescription is given only when appropriate and volumes are properly managed.

Table A.7 - Estimated number of patients prescribed CBPM, in the (unlikely) event of cannabis-based treatment being recommended as cost-effective in all cases

Condition	Prevalence (relative to the total number with the underlying condition)	Volume (eventual steady state) (number of cases per year receiving CBPM in the UK) ⁵³	
	Central estimate	Central estimate	Indicative Range
MS pain / spasticity	1 in 75	1,700	150 to 8,000
CINV	1 in 150	600	100 to 2,000
DS / LGS	1 in 3	500	200 to 750
HIV/AIDS appetite / weight loss	1 in 500	180	13 to 900
Chronic pain adults	1 in 90	300,000	60,000 to 1.0m

Ostensibly these are annual forecasts, with the numbers representing a mix of new and repeat prescription patients. A more detailed time breakdown, including an assessment of any 'bedding in' period as new rules are introduced, is not yet available. The assumption of a ten-year period for chronic pain volumes to be attained, while assuming other conditions will be processed more quickly, is a partial attempt to reflect the likely situation. Other medical conditions (such as Tourette Syndrome) may be deemed eligible for cannabis, and so the tabulated figures are not exhaustive.

The estimates for chronic pain are particularly uncertain and will be heavily influenced by the definitions and prescribing criteria adopted. A stringent and highly selective approach may limit numbers below the range quoted, and the opposite may be true if very broad criteria are used.

Cost-effectiveness adjustment

As reproduced in the main text, a further adjustment is required to isolate those cases judged to be cost-effective. This proportion is not known, and will be informed by NICE guidance in due course. In principle, cost-effectiveness recommendations may refer to any combination of particular:

- Cannabis-based medicines or products.
- Doses or delivery mechanisms.
- Medical conditions.
- Symptoms or severity of symptoms within those conditions.
- Patient history with other treatments and their effect.
- Patient characteristics, such as age or risk factors.

It is not as simple as saying (for example) that treating chronic pain would be judged cost-effective, or treating chemotherapy would not. Nor is it possible to rank the different medical conditions in a robust objective way. Instead, the analysis considers a range of illustrative scenarios, corresponding to the proportion of cases judged cost-effective being 0, 10, 25, 50, 75 and 100 per cent of the numbers shown in Table A.7 above. Actual volumes may be different. A summary is given in Table A.8.

⁵³ Although the analysis typically refers to the UK, it is possible that there may be a different system in place in Northern Ireland. Excluding Northern Ireland would reduce the numbers slightly.

Table A.8 - Central estimates of potential patient volumes, adjusted for cost-effectiveness (CE)

Scenario →	Percentage of cases where CBPM are recommended as cost-effective					
	0%	10%	25%	50%	75%	100%
MS pain / spasticity	0	170	425	850	1,275	1,700
CINV	0	60	150	300	450	600
DS / LGS	0	50	125	250	375	500
HIV appetite / weight loss	0	18	45	90	135	180
Chronic pain adults	0	30,000	75,000	150,000	225,000	300,000

All these numbers are subject to the additional uncertainty margins listed in Table A.7. The zero scenario is not intended to imply that no cases at all will be deemed to be cost-effective, but simply that certain conditions or circumstances may be. In such a situation, cannabis treatment on the NHS would be exceptional, and likely based on unique individual circumstances. Actual cost-effectiveness will vary between and within conditions. Because this determination has not yet generally been completed, and will continue to be reviewed as new products are licensed and evidence gathered, the IA leaves the volumes as illustrative scenarios rather than a definitive forecast.

Annex 2 – methodology for assessing the gross costs of CBPM

The estimated health-related costs of CBPM includes the following components:

- Time spent on medical assessment or approval for CBPM use.
- Expenditure on CBPM treatment itself (comprising both medicine and care costs).
- Time/expenditure associated with dealing with any side effects.

The analysis concentrates on numbers which are indicative but plausible given the limited evidence available. The material also focuses on potential costs per case. The total cost is subject to additional uncertainty arising from the potential range of patient volumes. All cost estimates are gross, and are expected to be funded from within existing resources provided CBPM are cost-effective.

Cost of medical assessments

The decision to prescribe is a critical one and all patients will need a clinical assessment to judge the suitability of CBPM intervention. The precise procedure will be fully defined in future guidance. As an interim approach, assumptions are made as follows:⁵⁴

- Each patient will only need to be assessed once initially (subsequent monitoring is covered later).
- The assessment will be carried out at consultant level.
- The consultant will already have some familiarity with the case.
- The assessment will require the patient to be physically present.
- The assessment will take place during existing treatment where possible, minimising the need for additional hospital or home visits.
- The decision reached at assessment will be final (where a patient does not agree with the decision made by a specialist they are entitled to seek a second opinion, but this is not costed in this IA).

A consultant-led outpatient face-to-face appointment costs the NHS £138 on average.⁵⁵ However it is variable according to condition, severity and specialty. Costs for children are typically higher (for example neurology costs £152 for adults and £329 for children). Amounts will be higher in complex cases (for example £401 is quoted for complex cases of HIV).

Allowing for cases to be complex, relatively unusual, a novel medical product, some inflation since these figures were calculated, involvement of other staff and an allowance for associated administration, the analysis in this IA assumes that all assessments will cost the NHS £1,000. This may be refined in the light of experience.

An assessment may or may not recommend prescription. The number of assessments will therefore exceed the number of patients prescribed CBPM. Any follow-up assessment, after prescription, would be an additional cost and is covered as part of CBPM costs generally in the following sections.

Cost of prescriptions

On the assumption that CBPM would be dispensed through the normal pharmacy network, costs will arise as follows:

- The cost of issuing prescriptions is assumed, initially, to be included within the £1,000 figure for clinical assessment. Repeat prescriptions might require additional administration on the part of clinicians, but this is assumed to be low in the context of the ongoing medical care costs generally and subsumed within those figures.⁵⁶

⁵⁴ DHSC working assumptions.

⁵⁵ National reference costs 2016/17 <https://improvement.nhs.uk/resources/reference-costs/> These statistics provide estimates of the cost to the NHS of various procedures. The tables for CL (consultant-led) procedures are used here. Costs may have risen slightly since 2016/17.

⁵⁶ DHSC modelling assumption.

- Pharmacies will incur a time cost in processing prescriptions. This may be covered (from their perspective) because they can claim a £2.53 dispensing fee per prescription.⁵⁷ However, these fees would be debited to the NHS. In practice, there may be some additional upfront cost in sourcing the medicine initially, with the fee more likely to cover repeat demand. The costs of the medicine will also include import licences and importers fees if imported into the UK. Reimbursement of the cost of all of this and the fee will be chargeable to the NHS either through the CCG or direct.
- There would be a one-off familiarisation cost to pharmacies but this is expected to be relatively low, given that there are already established and familiar procedures for dealing with Schedule 2 prescriptions. Some time may be required to become familiar with the specific medication.
- Patients and their families/carers may need to hand in and collect prescriptions.
- The number of prescriptions per patient will be variable, depending primarily on the condition(s) for which they are being treated.

Cost of medication

This comprises the cost of the medication itself plus any costs associated with administering the treatment to patients if done under medical supervision. In practice, costs will vary case by case and the concept of an average cost, even for people with the same underlying condition, is difficult to estimate. Even if dosage is known, the actual cost of medical products in the UK may depend on patient volumes, negotiation with suppliers on price, expected efficacy, cost-effectiveness and other factors.

Until products are put on the UK market, any discussion of prices would be commercially confidential, and not necessarily suitable for inclusion in a published impact assessment. In Wales, but not the rest of the UK, the NHS does currently provide Sativex, a CBPM, for use with Multiple Sclerosis. The list price is £375 for 30ml (around 270 sprays). Maximum dosage is twelve sprays per day, but the median is eight, giving a daily cost of £11 and an annual cost of £4,000, rising to £6,000 for the highest dosage.⁵⁸

In the absence of more definitive information, this impact assessment takes the above as a baseline and assumes that cannabis-based medication will cost, indicatively:

- £5,000 per patient per year for continuous therapy, and proportionately less for non-continuous use.
- Some potential for extra cost if treatment is given under supervision, although the marginal effect of this on top of existing treatment may be low.⁵⁹
- Some potential for extra cost if treatment is given to children, and especially young children, where procedures may take extra time and require more nursing care.
- Potential for reduced cost if treatment proves unsuccessful and is terminated earlier than expected.
- Actual costs will vary by case.

Actual costs may vary between medical conditions, and may differ significantly from this estimate, higher or lower, but the above is based on the current cost of care with Sativex, and provides a reasonable ballpark within which to work.

DHSC does have access to some commercially sensitive price information which cannot be published. The estimates quoted are explicitly not based on such information and no inferences should be drawn linking the two.

⁵⁷ Comprises a basic fee of £1.25, plus an additional fee of £1.28 for drugs listed under Schedule 2, which cannabis is expected to be. <https://psnc.org.uk/dispensing-supply/endorsement/fees-allowances/>.

⁵⁸ NHS England. Cost will vary with number of doses, up to a maximum of twelve sprays (which would cost £16.67 per day). As stated, the median is lower. Also see <https://www.medicines.org.uk/emc/product/602/smpc>

⁵⁹ The NHS National schedule of reference costs quotes a wide range of cost for medicine administration, typically as a standalone procedure. It is assumed that the marginal cost above existing treatment will be low, and not add significantly to the medicine cost. <https://improvement.nhs.uk>

Cost of side effects

The risk of CBPM side effects may be significant, if not precisely known at this time. The ACMD and NASEM have both found clear evidence for cannabis (as opposed to CBPM specifically), of (for example) increased risk of schizophrenia, respiratory symptoms, increased risk of road traffic accidents and heightened probability of substance abuse. Such effects may occur in either the short or longer term. The CMO's review mentioned that cannabis is an addictive and harmful drug. The risks attached to CBPM specifically will be further evaluated and incorporated into guidance in due course.

Against any potential risk, patients with intractable symptoms may have no viable alternatives left to them, poor quality of life and/or a low life expectancy, such that the risks may be viewed in a favourable context. If side effects are severe, and incurred only while CBPM are taken, one might revert to traditional treatments. If less severe, one might persist with CBPM on the basis that the benefits justify that. The CMO's review noted that when taking prescribing decisions, doctors must balance the potential for harm against the potential for benefit for individual patients.

For analysis purposes, and acknowledging that each case will be different, this impact assessment presents crude estimates of side effect costs as a proportion of the CBPM cost. In principle, one could assign a probability and cost value to such side effects. For example, if the chance of side effects were hypothetically estimated at 25 per cent, with a consequential cost of £2,000, that would add £500 on average to the cost of the treatment. While estimates of this type are intended to be plausible, the evidence is limited and they should be treated as indicative only.

The risks and consequences vary with each condition, and actual estimates are discussed separately in the following sections.

Costs for specific conditions

Each of the five representative medical conditions is discussed separately below.

Multiple Sclerosis – muscle spasticity and pain

MS may lead to a wide range of symptoms including pain, muscle spasms, incontinence, impaired mobility and weakness, difficulty chewing or swallowing, speech difficulties, problems with memory and thinking, and emotional disturbances. Patients may receive multiple interventions and medicines to manage these effects.⁶⁰

With conventional treatments, the total cost for a patient with intractable symptoms may be significant. Medicine costs may be high (multiple symptoms may require multiple drugs costing thousands of pounds, and hospital visits may be expensive. A very rough figure of £50,000 per patient per year may be plausible, albeit with considerable variation between cases.⁶¹

In the case of MS, patients in Wales may already be prescribed Sativex, the only currently-licensed CBPM. It costs £4,000 to £6,000 per year, plus some medical supervision, but if no improvement is seen within four weeks, treatment is suspended. For simplicity this IA assumes that any patient treated with Sativex would not be eligible for another CBPM, and would effectively not be affected by any proposed rescheduling in the rest of the UK.

If a patient were considered for new CBPM, a clinical assessment would be required and this is assumed to cost £1,000. Treatment would then typically take the form of an oral cannabidiol, taken daily. Precise costs outside Wales may depend on the volume of patients, but the baseline Sativex-based annual cost of £5,000 provides a reasonable estimate, plus some potential for medical supervision.

⁶⁰ <https://www.nhs.uk/conditions/multiple-sclerosis>

⁶¹ Costs will vary as stated. NHS reference costs (<https://improvement.nhs.uk>) may provide some indication, but there is no "MS figure" as such. Research in the US notes that costs may have increased over time. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4451044/>

There is a risk of side effects and these may (based on Sativex⁶²) include dizziness, drowsiness, diarrhoea, fatigue, nausea, headache and a dry mouth. Some of these effects may diminish as tolerance improves. The majority of these side effects are assumed to occur only while CBPM are taken, though some (such as psychosis) may persist. For modelling purposes, these side effects are assumed to cost around £1,000 per year on average.⁶³

In summary:

- Cost of assessment for potential CBPM use = £1,000 one-off.
- Cost of CBPM = £5,000 per year.
- Potential cost of side effects = £1,000 per year.
- Total cost = £61,000 over ten years, or £6,100 per year, before discounting.

Chemotherapy-induced nausea and vomiting

Unlike many of the other conditions, the side effects of chemotherapy are usually acute rather than chronic. A typical course of chemotherapy may consist of between four and six cycles of treatment, with each cycle lasting one to four weeks. Side effects can occur before, during or after treatment, but typically in fairly close proximity to that treatment.⁶⁴ That implies a very variable, but time limited, period during which nausea and vomiting might occur.

As usual, a patient being considered for CBPM intervention will undergo a clinical assessment, costing an estimated £1,000. The intervention itself is likely to involve oral medication taken close to and during chemotherapy, ideally while under medical supervision. Typical treatment might be required for around three weeks for each cycle, and 15 weeks across the full course of four to six cycles. On a proportionate basis, using the Sativex-based £5,000 per full year benchmark, that could cost around £1,500 in total, or £300 per cycle. Actual costs will depend on the actual drugs used, patient volumes, discussion with suppliers and other factors. If given under medical supervision, costs may be higher.

Research suggests there may be a significant risk of both physical and mental side effects, which although typically short-term, could cause problems in some cases. The most common side effects may be dizziness and drowsiness, with each being experienced by around half of patients. Nearly all patients experience at least one side effect.⁶⁵ Given that the majority of side effects are temporary and may be manageable without further medical intervention, the additional cost to the NHS of dealing with them is assumed to be relatively low. Indicatively, the side effects might add £500.⁶⁶

In summary:

- Cost of assessment for potential CBPM use = £1,000 one-off.
- Cost of CBPM = £1,500 per course (one-off).
- Potential cost of side effects = £500 per course (one-off).
- Total cost = £3,000 per patient on average (one-off, spread over two years).

Treatment-resistant epilepsy in children (Dravet Syndrome, Lennox-Gastaut Syndrome only)

Traditional treatment focuses on improving life for the individual primarily through anti-epileptic drugs.⁶⁷ Learning difficulties and associated care needs are common too⁶⁸

⁶² <https://www.medicines.org.uk/emc/product/602/pil>

⁶³ DHSC modelling assumption. Notionally assumes a 25% chance of side effects, with a consequential cost of £4,000 should they occur. This is illustrative and may be refined over time.

⁶⁴ <https://www.nhs.uk/conditions/chemotherapy/>

⁶⁵ <https://www.rxlist.com/cesamet-side-effects-drug-center.htm#professional>

⁶⁶ DHSC modelling assumption. Indicative. Not based on hard evidence.

⁶⁷ <https://www.nice.org.uk/guidance/cg137/chapter/1-Guidance#pharmacological-treatment>. See 1.9.9. and 1.9.10.

⁶⁸ <https://www.epilepsy.org.uk/info/syndromes/>

The cost of this treatment may be high⁶⁹, although in practice there may be wide variation between cases and considerable uncertainty. If a patient were considered for CBPM, a clinical assessment would be required and this is assumed to cost £1,000.

Treatment might take the form of an oral cannabidiol, taken daily, with the dose varying with body weight.⁷⁰ The annual cost of such treatment is initially estimated using the Sativex benchmark, at £5,000, plus some allowance for medical supervision. However, because the patients are children, costs may be above average in this case. An arbitrary doubling to £10,000 is assumed, but evidence needs to be strengthened.⁷¹

In the case of childhood epilepsy, the most common side effects may include drowsiness, digestive disorders and potentially convulsions. While not insignificant, such effects may not be dissimilar from those caused by the underlying condition. For modelling purposes, the chance of side effects is estimated at 25 per cent, with a consequential cost of £12,000 – which would represent a 25 per cent increase in conventional treatment costs.⁷² That gives a net annual cost increase of £3,000 for the typical patient. These assumptions are not based on firm evidence and are intended to be refined as research improves.

In summary:

- Cost of assessment for potential CBPM use = £1,000 one-off.
- Cost of CBPM = £10,000 per year.
- Potential cost of side effects = £3,000 per year.
- Total cost = £131,000 over ten years, or £13,100 per year, before discounting.

The latter bullet does assume that the child survives for at least 10 years.

Appetite or weight loss associated with HIV/AIDS

Stage 3 HIV (otherwise known as AIDS) develops when HIV has significantly weakened the immune system. Symptoms include weight loss, skin problems, recurrent infections and chronic diarrhoea, nausea and vomiting.⁷³

The cost of Stage 3 care, on an annual basis, is estimated at £16,000.⁷⁴ If a patient were considered for CBPM to manage appetite and weight loss, a clinical assessment would be required and this is assumed to cost £1,000.

Treatment is assumed to be similar for chemotherapy-induced nausea, except that CBPM would be taken continuously, rather than in cycles with gaps in between. On this basis, the annual cost might be around £5,000 for the medicine itself, with a duration of three years. Any medical supervision might cost more.

Side effects, if severe, and incurred only while CBPM are taken, might cause a patient to revert to traditional treatments. If less severe, one might persist with CBPM on the basis that the benefits justify that.

The additional cost to the NHS of dealing with the side effects is unknown but potentially mitigated by the possibility that the patient may already be receiving significant traditional treatment. Indicatively, the side effects might add 25 per cent to the course cost.⁷⁵

⁶⁹ A rough estimate of £48,000 has been produced by DHSC analysts, based on a range of reference costs for medication, hospital visits (including A&E), inpatient episodes and other items.

⁷⁰ Research is ongoing, but recent material includes <https://onlinelibrary.wiley.com/doi/full/10.1002/acn3.621>

⁷¹ Firm figures are not available. The analysis simply tries to indicate that medical costs and supervision may be above average in this type of case, even if some treatment can be administered at home. It is possible that costs may exceed the £10,000 figure in some cases.

⁷² DHSC modelling assumption. Indicative. Not based on hard evidence.

⁷³ <https://www.nhs.uk/conditions/hiv-and-aids/>

⁷⁴ Based on NHS reference costs for HIV disease with multiple interventions. £15,800. <https://improvement.nhs.uk>

⁷⁵ DHSC modelling assumption. Indicative. Not based on hard evidence.

In summary:

- Cost of assessment for potential CBPM use = £1,000 one-off.
- Cost of CBPM = £5,000 per year, including some staffing.
- Potential cost of side effects = £1,500 per year.
- Total cost = £66,000 over ten years, or £6,600 per year, before discounting.

Chronic pain in adults

The wide range of conditions and types of chronic pain make it difficult to describe traditional care in terms of an average or typical case. In principle, all adult ages, all parts of the body and variable duration of symptoms are possible. Back pain generally and joint pain in older age groups are common, but only two examples of the category generally.

Conventional treatment may take several forms, and may be focused on helping the patient manage or reduce the pain rather than eliminating it. Opioids such as morphine may be prescribed, although not necessarily with successful outcomes. NICE provide a fuller discussion.⁷⁶ Given the nature of the symptoms – severe pain of chronic nature, the costs of care, and to patient wellbeing, may be significant, albeit not quantifiable on a generalised basis.

If a patient were considered for CBPM to help reduce or manage the pain, a clinical assessment would be required and this is assumed to cost £1,000. Treatment might take a number of forms – inhaler, tablets, oil and so on. Costs would be variable depending on the nature of the precise condition, but the assumption is that treatment would be required more or less continuously.⁷⁷

An indicative cost of £5,000 per year is assumed, based on the Sativex benchmark. Medical supervision may not always be required but might add additional cost in some cases. Side effects, if the treatment is continued, may be significant – but equally traditional opioid treatment carries potential side effects too, and the marginal change in risk may be moderate. The analysis assumes an additional 10 to 20 percent in cost for side-effect management, which is around £1,000.

In summary:

- Cost of assessment for potential CBPM use = £1,000 one-off.
- Cost of CBPM = £5,000 per year.
- Potential cost of side effects = £1,000 per year.
- Total cost = £61,000 over ten years, or £6,100 per year, before discounting.

Summary

A summary of the indicative gross costs of CBPM for each condition are as follows:

Table A.9 - Estimated average gross costs per case of patients receiving CBPM, by medical condition, (£), 2018.

Condition	One-off (£)	Annual (£)	Total (10 years) (£ undiscounted)	Total (10 years) (£ discounted at 3.5%)
MS pain / spasticity	1,000	6,000	61,000	52,600
CINV	1,000	1,000	11,000	9,600
DS / LGS	1,000	13,000	131,000	112,900
HIV weight loss	1,000	6,500	66,000	56,900
Chronic pain	1,000	6,000	61,000	52,600

⁷⁶ <https://www.nice.org.uk/advice/ktt21/chapter/Evidence-context>

⁷⁷ DGSC Modelling assumption – based simply in the chronic nature of the condition.

These numbers represent gross costs of treatment, before any savings that might accrue are considered. The chemotherapy figure covers up to two years of treatment (the typical course), while the others are assumed to last for ten years. Actual costs for any individual case may vary widely from these indicative averages.

Furthermore, any such costs would be funded by existing NHS budgets. This means there is no net increase in expenditure. There may be an opportunity cost in terms of foregone benefits elsewhere, but because of the cost-effectiveness constraint, any such cost should be outweighed by the benefits of CBPM.

Annex 3 – methodology for assessing the health-related benefits of cannabis rescheduling

There are three types of health-related benefits that may arise from the use of CBPM:

- A net improvement in the patient's health outcomes, taking into account any risks or side-effects.
- A saving in treatment costs if CBPM produce a net health improvement which reduces the need for future treatment (for example, in the case of a patient with severe epilepsy if it reduces the frequency of seizures, and therefore reduces the number of hospital admissions).
- A saving in treatment costs if the cannabis-based medicine replaces existing medication. This is expected to be less significant than the other two benefits, as in some cases the medication replaced may not be especially expensive.

Research suggests that CBPM will provide health benefits for several conditions in certain situations. The CMO's recent review summarised the evidence and made clear that it is of variable quality⁷⁸.

Although the existence of a benefit for many patients may be supported by evidence, the size of the benefit is less certain and will vary on a case-by-case basis. Focusing on the benefits for those patients for whom traditional treatments have failed necessarily reduces the number of patients in the sample, and hence the amount of evidence available.

The limitations of the evidence base mean that the health-related benefits of CBPM cannot currently be quantified with any certainty. Instead, a breakeven analysis has been undertaken, to identify the likely magnitude of health-related benefits that may be required to outweigh the gross costs. This does not alter the fact that any costs will be met from within existing resources, but instead notes that the need for reallocation will be reduced by any CBPM-related savings or benefits.

Two breakeven values have been assessed in this analysis, for each medical condition. The first breakeven value is the required reduction in treatment costs (either through CBPM replacing existing medicines, or through a reduced need for future treatment due to health improvements) in order to outweigh the costs of CBPM. This analysis only considers the health-related costs, and does not include the wider costs such as those related to familiarisation, as familiarisation costs cannot be disaggregated by medical condition with any certainty (and they may relate to other medical conditions outside of the five specific conditions that have been examined in this IA).

The second breakeven value is the required improvement in health outcomes in order to outweigh the gross costs of CBPM. This has been assessed by using the available evidence to estimate the improvement in quality-adjusted life years (QALYs), a measure which captures improvements in quality and duration of life, for each of the five conditions. The monetary value of one QALY is assumed to be £60,000, as recommended in the Green Book guidance on appraisal and evaluation⁷⁹. However, as explained in the main text, a value of £15,000 per QALY is used to assess cost-effectiveness, given that any investment needs to provide a better net benefit than alternative uses of funding within the NHS.

In the sections below, the breakeven values for each of the five medical conditions are identified, and are assessed against the available evidence regarding the health-related benefits of CBPM.

Multiple Sclerosis – muscle spasticity and pain

The evidence behind CBPM for MS-related muscle spasticity and pain is mixed. The CMO's review cited the NASEM report which found conclusive or substantial evidence that oral cannabinoids are effective for improving patient-reported MS spasticity symptoms, and limited evidence for improving clinician-measured MS spasticity symptoms. The CMO's review also mentioned the Australian Government Department of Health Medicinal Cannabis Review that found low to moderate quality evidence for treating symptoms of pain in MS.

⁷⁸https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/722010/CMO_Report_Cannabis_Products_Web_Accessible.pdf

⁷⁹

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/685903/The_Green_Book.pdf

The size of any benefit is uncertain (based on Expert Panel advice). Quantified estimates for spasticity impact are not available. Meta-analysis of research contained in Australian guidance⁸⁰ suggests a reduction in pain of around 30 per cent might be plausible in some patients, with related improvements in mental wellbeing and quality of life generally. However, the quality of evidence supporting this is described as very low to moderate, and compares the effect of various CBPM against a placebo, rather than in comparison to other potential treatments.

A proportional reduction in some or all symptoms is unlikely to provide a like for like reduction in cost (because some costs may be fixed) or improvement in health, but some improvement might be observed.

A comprehensive benefits analysis and QALY assessment are not available at the current time. By way of illustration, for the benefits to fully cover the costs of CBPM, they would need to total around £6,000 per year on average. That could be achieved by:

- Existing treatment costs falling by £6,000, or around (10 to 15 percent).
- Cannabis delivering an improvement in health worth 0.4 QALYs per year.
- Some combination of these two effects.

The plausibility of such benefits should be viewed alongside the potential for a possible reduction in spasticity-related symptoms and the (weakly evidenced) possibility of a 30 per cent reduction in pain. The cost figure, although presented as a point estimate, is subject to uncertainty.

Cancer – chemotherapy-induced nausea and vomiting (CINV)

The evidence that oral cannabinoids are effective for CINV is mentioned in the CMO's review in reference to the NASEM report⁸¹ as "conclusive or substantial". The size of that benefit is unknown (Expert Panel advice). A proportional reduction in some or all symptoms is unlikely to provide a like for like reduction in cost (because some costs may be fixed) or improvement in health, but some improvement might be observed.

A detailed benefits analysis and QALY assessment, is not available at the current time. By way of illustration, for the benefits to fully cover the costs of CBPM, they would need to total around £3,000 per patient on average. That could be achieved by:

- Existing treatment costs falling by £3,000.
- Cannabis delivering an improvement in health worth 0.2 QALYs per patient.
- Some combination of these two effects.

The plausibility of such benefits should be viewed alongside the evidence that the chance of a health gain is high, although its size is uncertain. The cost figure, although presented as a point estimate, is subject to uncertainty.

Treatment-resistant epilepsy in children (Dravet Syndrome and Lennox-Gastaut Syndrome only)

Assessing benefits for this category is hampered by the conditions being relatively rare, and research being based on small samples. The CMO review did not comment on the evidence for these syndromes specifically, but did note that Epidiolex has recently been licensed as a treatment in the US. The Republic of Ireland considers severe, refractory (treatment-resistant) epilepsy as a potential condition for CBPM treatment under expert supervision, provided the patient has failed to respond to standard anticonvulsant medications.

The size of any benefit is unknown. One recent piece of research with Dravet Syndrome patients found that the frequency of seizures reduced by 70 per cent, the number of seizure-free days increased by 50

⁸⁰ <https://www.tga.gov.au/medicinal-cannabis-guidance-documents> and <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-chronic-non-cancer-pain-australia> specifically.

⁸¹ <https://www.nap.edu/read/24625/chapter/1>

per cent and quality of life improved by 56 per cent.⁸² However this research used a small sample, was industry-funded and acknowledged itself that the research design and nature of existing treatment may impact on accuracy. There was also some uncertainty over optimal dosage (indeed confirming that was a research objective). Such evidence is therefore not conclusive, and in any case found wide variation between individual cases.

Indicative conventional treatment costs are £48,000 per year for conventional therapy and £13,100 per year for CBPM. Health improvements are unlikely to provide a like for like reduction in cost (because some costs may be fixed) but a reduction in the variable cost component might be observed.

To offset CBPM treatment costs of (on average) £13,100 per year, one would need to see either:

- Treatment costs fall by £13,100, which is a 25 per cent saving.
- Health improvements worth 0.9 QALYs per year.
- Some combination of the above.

If 25 per cent savings are plausible, it would be reasonable to expect the financial costs and savings to balance out. If such savings are conservative, one might expect CBPM to be cost-saving. If exaggerated, one would expect CBPM to increase costs on a net basis, although such a rise might still be cost-effective if health gains were achieved alongside.

Those health gains will best be considered with reference to the symptom reduction evidence. An improvement of 0.9 QALYs per year is unlikely to be achieved, as that would imply a return to near perfect health, but a lesser improvement, alongside some possible savings, may be plausible. Such reductions may also generate a better prognosis for later life and indeed life expectancy. The cost figure, although presented as a point estimate, is subject to uncertainty.

Appetite or weight loss associated with HIV/AIDS

The CMO's review mentioned conclusions from NASEM's report⁸³ that there is limited evidence that cannabis and oral cannabinoids are effective for increasing appetite and decreasing weight loss associated with HIV/AIDS. Even if some improvement in symptoms can be expected, the size of that benefit, and any side effects, are less clear (Expert Panel advice).

To offset the estimated costs of (on average) £6,600 per year would require either:

- Treatment costs to fall by £6,600, which is a 40 per cent saving.
- Health improvements worth 0.4 QALYs per year.
- Some combination of the above.

Given the limited nature of the evidence, it seems more likely that both savings and health improvements would be required to justify CBPM-based intervention in this case. Alternatively, more selective treatment may be an option. The cost figure, although presented as a point estimate, is subject to additional uncertainty. Further investigation is recommended.

Chronic pain in adults

Evidence for the effectiveness of cannabis for the treatment of adult chronic pain was described in the CMO's review as conclusive or substantial, based on evidence from NASEM⁸⁴. The Cochrane Review⁸⁵ noted that evidence for the treatment of neuropathic pain was not of high quality, but nonetheless advised that the evidence suggested CBPM could provide a medical benefit for a range of symptoms compared to placebo (along with some potential side effects). In practice, clinical advice will be developed to recommend the specific circumstances in which patients would be eligible, or not, for CBPM.

⁸² <https://onlinelibrary.wiley.com/doi/full/10.1002/acn3.621>

⁸³ <https://www.nap.edu/read/24625/chapter/1>

⁸⁴ <https://www.nap.edu/read/24625/chapter/1#xii>

⁸⁵ https://www.cochrane.org/CD012182/SYMPT_cannabis-products-adults-chronic-neuropathic-pain

This IA assumes that some improvement in symptoms can be expected, but that the scope of the chronic pain category itself, and the circumstances in which such improvement might occur, remain unclear.

As with MS, meta-analysis of research⁸⁶ suggests a reduction in pain of around 30 per cent might be plausible in some patients, with related improvements in mental wellbeing and quality of life generally. A proportional reduction in some or all symptoms is unlikely to provide a like for like reduction in cost (because some costs may be fixed) or improvement in health, but some improvement might be observed.

For the benefits to fully cover the costs of CBPM, they would need to total around £6,000 per year on average. That could be achieved by:

- Existing treatment costs falling by £6,000.
- CBPM delivering an improvement in health worth 0.4 QALYs per year.
- Some combination of these two effects.

Wider benefits, such as reductions in health-related work absence, should also be considered. The plausibility of such benefits should be viewed alongside the potential for a 30 per cent reduction in pain-related symptoms. The cost figure, although presented as a point estimate, is subject to additional uncertainty.

The overall results of the breakeven analysis are presented in the table below:

Table A.10 – Total savings in treatment or QALY health improvement required in order to offset the costs of CBPM

Condition	Total savings in treatment costs required per patient (over 10 years, £ discounted)	(or) QALY health improvement required per patient (over 10 years, discounted)
MS pain / spasticity	52,600	3.5
CINV	3,000	0.2
DS / LGS	112,900	7.5
HIV/AIDS weight loss	56,900	3.8
Chronic pain	52,600	3.5

Interventions may or may not be deemed cost-effective when NICE provides formal recommendations. The QALY values required to generate a cost-effective intervention are, in isolation, quite high for some conditions. While such a health gain may be possible in some cases, it is likely that both cost savings and health gains will be required to justify cost-effectiveness in those situations where NICE recommend prescription will be worthwhile.

⁸⁶ <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-chronic-non-cancer-pain-australia>