Cannabinoid Therapeutics

Clinical Evidence Reference for UK Prescribers

Working draft, non-promotional, for clinical decision-making under MHRA Specials and licensed-medicine pathways.

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Section 1: How to Use This Reference

This reference summarises the clinical evidence base for cannabidiol (CBD) and tetrahydrocannabinol (THC) across the principal indications where cannabinoid therapies are considered in UK practice. It identifies, for each indication, which molecule has the prevailing evidence, the strength of that evidence, and any UK-licensed product available.

It is intended to support prescriber decision-making, not to recommend treatment. Individual prescribing decisions remain the responsibility of the treating clinician and must consider patient-specific factors, contraindications, and licensing status.

References require independent verification before clinical or regulatory submission.

Section 2: Evidence Grading

Level	Description
1	Multiple Phase 3 RCTs and/or regulatory approval in the indication
2	Single adequately powered Phase 3 RCT
3	Phase 2 RCT(s), or meta-analysis of moderate-quality trials
4	Open-label, observational cohort, or single small RCT
5	Preclinical or mechanistic only

Section 3: Master Evidence Matrix

Indication	Prevailing molecule	Evidence level	UK licensed product	Key refs
Dravet syndrome	CBD	1	Epidyolex	1, 2, 3, 4
Lennox-Gastaut syndrome	CBD	1	Epidyolex	1, 2, 3, 4
Tuberous sclerosis complex	CBD	1	Epidyolex	3, 4
MS-related spasticity	CBD : THC (1:1)	1	Sativex	20, 21
Chemotherapy-induced N&V	THC (synthetic)	1	Nabilone (Cesamet)	16, 17, 18
AIDS-related wasting	THC	2	Dronabinol (Specials)	16, 17, 18
Schizophrenia (adjunct)	CBD	3	None licensed	5, 6, 7, 8
Social anxiety / acute performance anxiety	CBD	3	None licensed	9, 10, 11
Generalised anxiety disorder	CBD	4	None licensed	9, 10, 11
Cancer pain	CBD : THC	3	Sativex (off-label)	18, 22, 23, 24
Chronic neuropathic pain	CBD : THC	3	Sativex (off-label)	18, 22, 23, 24
Tourette's syndrome	THC	3	Nabilone (off-label)	19
Opioid / cannabis use	CBD	3	None licensed	13, 14

disorder				
PTSD	CBD (emerging)	4	None licensed	12, 25
Parkinson's disease (RBD, motor)	CBD (weak)	4	None licensed	small RCTs
Autism (irritability, behaviour)	CBD-rich	4	None licensed	15
Insomnia disorder	CBD (emerging)	4	None licensed	26
Traumatic brain injury / TBI sequelae	CBD (investigational)	5	None licensed	27

Prevailing molecule is an evidence-strength judgement, not a treatment recommendation.

Section 4: Indication-by-Indication Detail

4.1 Drug-resistant epilepsies (Dravet, LGS, TSC)

CBD has the strongest evidence base of any cannabinoid in any indication. Three Phase 3 RCTs led to UK and EU approval of Epidyolex (cannabidiol oral solution) at 10 to 25 mg/kg/day. THC is contraindicated; pro-convulsant risk and absence of paediatric safety data.

Verdict: CBD has strongest evidence; licensed in indication. Level 1.

References: 1, 2, 3, 4

4.2 Multiple sclerosis spasticity

Sativex (THC:CBD 1:1, oromucosal spray) is licensed in UK for MS-related spasticity inadequately responsive to other antispastics. Two pivotal Phase 3 RCTs and an enriched-design responder trial. CBD monotherapy has no robust evidence here. THC monotherapy is not licensed for this indication.

Verdict: CBD:THC combination has strongest evidence. Level 1.

References: 20, 21

4.3 Chemotherapy-induced nausea and vomiting

Nabilone (synthetic THC analogue) and dronabinol (synthetic THC) are both supported by Phase 3 RCTs and meta-analyses, with nabilone licensed in the UK as Cesamet. CBD has no licensed CINV indication and limited data.

Verdict: THC analogue has strongest evidence. Level 1.

References: 16, 17, 18

4.4 AIDS-related anorexia and wasting

Dronabinol is FDA-approved (Marinol) on the basis of Beal 1995/1997 trials. Not licensed in UK; available via Specials or import on consultant authorisation. CBD has no clinical evidence for appetite stimulation.

Verdict: THC analogue has strongest evidence. Level 2.

References: 16, 17, 18

4.5 Cancer pain

Mixed picture. Earlier Phase 2/3 trials of Sativex (Johnson 2010, Portenoy 2012) showed modest benefit; subsequent Phase 3s (Lichtman 2018) failed primary endpoints in advanced cancer. CBD monotherapy is not supported. UK use is off-label and increasingly contested.

Verdict: Evidence signal exists; mixed Phase 3 results. Level 3.

References: 18, 22, 23, 24

4.6 Chronic neuropathic pain

Whiting 2015 meta-analysis and subsequent reviews show modest effects for CBD:THC combinations on central neuropathic pain. CBD monotherapy data are weak. THC monotherapy at therapeutic doses is poorly tolerated in non-cancer neuropathic pain. UK guidance does not support routine cannabinoid prescribing for chronic pain; exceptional specialist/research use only.

Verdict: Evidence signal exists; UK guidance caution. Level 3.

References: 18, 22, 23, 24

4.7 Schizophrenia

Leweke 2012 (CBD vs amisulpride; comparable efficacy with better tolerability) and McGuire 2018 (CBD adjunct, 600 to 800 mg/day; positive primary endpoint) support CBD as adjunctive therapy. Boggs 2018 was negative at lower dose. THC is contraindicated and is associated with psychosis-onset.

Verdict: CBD has only positive evidence; THC contraindicated. Level 3.

References: 5, 6, 7, 8

4.8 Social anxiety / acute performance anxiety

CBD has multiple acute-dosing RCTs in social anxiety (Bergamaschi 2011, Crippa 2011, Linares 2019) showing reductions in anticipatory and performance anxiety at 300 to 600 mg single doses. No chronic-dosing Phase 3 data. THC at low doses can be anxiolytic but at higher doses is anxiogenic and triggers panic attacks.

Verdict: CBD has small acute-dose RCT support; not licensed. Level 3.

References: 9, 10, 11

4.9 Generalised anxiety disorder

No chronic-dosing Phase 3 data for CBD in generalised anxiety disorder. Evidence extrapolated from acute social anxiety studies; chronic GAD efficacy not established. THC is unsuitable due to anxiogenic risk at higher doses.

Verdict: CBD has emerging signal; chronic efficacy not established. Level 4.

References: 9, 10, 11

4.10 PTSD

Limited prospective RCT evidence. Elms 2019 case series (11 patients, oral CBD adjunctive) and Bonn-Miller 2021 open-label data suggest CBD reduces PTSD symptom severity. Smoked cannabis observational work is methodologically weaker and confounded by THC.

Verdict: CBD has emerging signal; investigational only. Level 4.

References: 12, 25

4.11 Tourette's syndrome

Muller-Vahl small Phase 2 work supports nabilone (THC analogue) for tic reduction. CBD has minimal data. Off-label use under specialist supervision.

Verdict: THC analogue has limited supportive data. Level 3.

References: 19

4.12 Insomnia

Neither CBD nor THC has robust Phase 3 evidence in primary insomnia. Narayan 2024 pilot RCT (150 mg nightly CBD) provides initial controlled data supporting Level 4/Emerging. THC reduces sleep latency acutely but disrupts architecture and shows tolerance. CBD is the preferred molecule where a cannabinoid is considered.

Verdict: CBD has emerging pilot data; THC not preferred. Level 4.

References: 26

4.13 Parkinson's disease

Small RCTs (Chagas 2014; Peball 2020 in REM sleep behaviour disorder) suggest CBD may help non-motor symptoms; motor evidence is weaker. THC has no evidence base here.

Verdict: CBD has weak signal; non-motor symptoms only. Level 4.

References: 15

4.14 Substance use disorders

Hurd 2019 (heroin cravings, Phase 2 RCT) and Freeman 2020 (cannabis use disorder, Phase 2) are the principal positive CBD signals. THC is contraindicated in addiction medicine.

Verdict: CBD has emerging Phase 2 support; THC contraindicated. Level 3.

References: 13, 14

4.15 Autism spectrum disorder

Aran 2019 RCT of CBD-rich extract (CBD:THC 20:1) in children with severe autism showed modest improvements in disruptive behaviour and anxiety. THC monotherapy not appropriate.

Verdict: CBD-enriched has weak signal; specialist supervision essential. Level 4.

References: 15

4.16 Traumatic brain injury / TBI sequelae

CBD is the preferred investigational molecule based on neuroprotective and anti-inflammatory rationale. Aychman 2023 review supports CBD neuroprotective rationale but does not establish human efficacy. Evidence base is primarily preclinical/mechanistic.

Verdict: CBD investigational (preclinical); THC unsuitable. Level 5.

References: 27

Section 5: UK Regulatory Framing

Within UK practice, cannabinoid-based therapies sit across three regulatory categories that prescribers should explicitly identify before prescribing.

Licensed medicines (full UK marketing authorisation): Epidyolex (cannabidiol; specific epilepsy indications), Sativex (nabiximols; MS spasticity), Cesamet (nabilone; CINV).

Cannabis-based products for medicinal use (CBPM) under the Misuse of Drugs Regulations 2018, Schedule 2: any product containing THC above trace levels that is unlicensed. Prescribing restricted to specialists on the GMC Specialist Register; mandatory entry on the national CBPM registry.

Pure CBD pharmaceutical-grade products with negligible THC that fall outside the CBPM legal definition and are therefore unlicensed medicines under the broader MHRA Specials framework, not subject to Schedule 2 obligations or the Specialist Register restriction. *Note: this regulatory position should be confirmed by formal legal opinion before being relied on externally.*

Specials prescribing requires: a particular patient under specialist care; a clinically appropriate special need not met by a licensed medicine; the prescribing physician's clinical responsibility; compliance with MHRA reporting, batch-traceability, and pharmacovigilance obligations.

Section 6: References

References require independent verification. Several have been compiled from secondary sources and DOIs are not included; cross-check against PubMed before any prescriber-facing or regulatory use.

1. Devinsky O et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. NEJM 2017;376(21):2011-2020.

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22. Johnson JR et al. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of THC:CBD extract and THC extract in patients with intractable cancer-related pain. J Pain Symptom Manage 2010;39(2):167-179.

23. Portenoy RK et al. Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain. J Pain 2012;13(5):438-449.

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25. Elms L et al. Cannabidiol in the Treatment of Post-Traumatic Stress Disorder: A Case Series. J Altern Complement Med. 2019.

26. Narayan AJ et al. Cannabidiol for moderate-severe insomnia: a randomized controlled pilot trial of 150 mg nightly dosing. J Clin Sleep Med. 2024;20(5):753-763.

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Section 7: Caveats and Limitations

References require independent verification. Several have been compiled from secondary sources and DOIs are not included; cross-check against PubMed before any prescriber-facing or regulatory use.

Evidence levels reflect strength of clinical evidence, not appropriateness in individual cases. A Level 1 indication does not mean cannabinoids are first-line. A Level 4 indication does not preclude appropriate Specials use.

The prevailing-molecule verdict is an answer to a narrow question: where adequate evidence exists, which cannabinoid has the stronger data. Full clinical decision-making must consider patient-specific factors, contraindications, drug interactions (particularly CBD-CYP450 interactions), and licensing status.

THC contraindications apply across most psychiatric indications: personal or family history of psychotic disorders, active substance use disorder, pregnancy, severe cardiovascular disease.

CBD-class hepatic monitoring per Epidyolex labelling: baseline and periodic LFTs given documented transaminase elevations at high doses, particularly with concomitant valproate.

Inclusion in this matrix does not imply suitability for prescribing under the UK Specials framework; each case requires patient-specific clinical justification and product-specific regulatory review.

This document is non-promotional and does not constitute medical advice.