

Emerging preclinical evidence supports a potential role for cannabidiol in the management of sickle cell disease

Arne M. de Kreuk,^{1,2} Matthew A. Howard,³ Kate Gardner^{2,4} and Olivia S. Kowalczyk³

¹King’s College Hospital NHS Foundation Trust; ²Faculty of Life Sciences & Medicine, King’s College London; ³Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King’s College London; ⁴Guy’s and St Thomas’ Hospital NHS Foundation Trust and ⁵Functional Imaging Laboratory (FIL), Department of Imaging Neuroscience, University College London, London, UK

Correspondence: A.M. de Kreuk
arne.dekreuk@nhs.net

Received: February 15, 2026.
Accepted: May 20, 2026.
Early view: May 28, 2026.

<https://doi.org/10.3324/haematol.2026.300736>

©2026 Ferrata Storti Foundation
Published under a CC BY-NC license



Supplementary tables

Table S1 Clinical effects, side effects, drug interactions and toxicity of cannabinoids

Aspect	CBD	THC
Psychoactive effects	Non-psychoactive	Psychoactive, causes typical 'high'
Medical use	Anti-epileptic Anxiolytic Analgesic	Anti-emetic Anti-anorexiant Spasmolytic Analgesic
Main undesirable symptoms	Tiredness Dizziness Reduced appetite Dry mouth Diarrhoea Abdominal discomfort Headache Sedation	Euphoria Anxiety Paranoia Psychosis Impaired attention/memory. Cognitive impairment Red eyes Increased appetite
Drug interactions	CYP2C19/3A4 interactions: Increased levels of some antiepileptics/SSRIs Additive sedation	CYP2C9/3A4 interactions: Additive sedation with alcohol/opioids
Liver toxicity	Dose-related liver function tests elevation, especially with valproate	Not typical at usual doses
Cardiovascular side effects	Occasional hypotension	Tachycardia, blood pressure changes
Dependence risk	Low risk	Clear risk of cannabis use disorder
Pregnancy	Potential risk	Significant risk
Infections	Potentially increased risk	No added risk other than due to smoking

Abbreviations: CBD, cannabidiol; THC, Δ 9-tetrahydrocannabinol

Table S2 Dosing strategies and prescribing of medicinal cannabinoids

Medicinal cannabinoids encompass both licensed, pharmaceutical-grade, cannabinoids and unlicensed medicinal cannabinoids. For details on approved indications and prescribers' responsibilities, in particular for off-label use and unlicensed use, we refer to country-specific official regulatory documents.

Region	Unified policy?	Regulatory body	Most relevant document
United Kingdom (UK)	Yes	NICE / MHRA	NICE NG144 (2019)
European Union	No, fragmented by member	EMA	EU Directive 2001/83/EC
United States of America (USA)	No, fragmented by state	FDA / DEA	FDA — Regulation of Cannabis and Cannabis-Derived Products (updated regularly)

Licensed, pharmaceutical-grade cannabinoids

Current key pharmaceutical-grade cannabinoids approved by the US FDA and/or MHRA in the UK include:

Drug Name	Active Ingredient	Dosing range	Approval Status & Indication	Characteristics
Epidiolex (USA) / Epidyolex (UK)	CBD	5-20 mg/kg daily	FDA-approved for seizures associated with LGS & Dravet syndrome (and later for TSC) MHRA/UK license for TSC, and LGS/Dravet syndromes in children aged ≥ 2 yrs	Plant-derived, highly purified CBD (THC concentration less than 0.005%)
Marinol / Syndros	Dronabinol	2.5-10 mg twice daily	FDA-approved for AIDS-related anorexia, and for nausea/vomiting from chemotherapy when other treatments fail	Synthetic single-molecule THC
Cesamet	Nabilone	2-6 mg daily	FDA-approved for chemotherapy-induced nausea & vomiting when conventional antiemetics fail.	Synthetic single-molecule THC
Sativex (nabiximols)	Approx 1:1 THC + CBD mix	THC: 2.7-32.4 mg daily CBD: 2.5-30 mg daily	Licensed in the UK (and other countries) via MHRA for adult spasticity due to Multiple sclerosis; not FDA-approved in the USA	Plant-derived

For clinical guidelines on prescribing medicinal cannabinoids, we refer to the [Clinical Practice Guidelines for Cannabis and Cannabinoid-Based Medicines in the Management of Chronic Pain and Co-Occurring Conditions](#) (Cannabis and Cannabinoid Research, 2024; 9(2): 669–687. DOI: [10.1089/can.2021.0156](#)).

For both licensed and off-label indications, medicinal cannabinoids are typically prescribed using a titration strategy:

- Initiate at the lowest dose within the recommended dosing range
- Up-titrate at intervals of 3–7 days, guided primarily by tolerability and adverse effects
- Avoid dose escalation beyond that required to achieve the desired clinical response, and do not exceed the upper limit of the recommended dosing range

Non-licensed medicinal cannabis prescribing guidance recommends against pure THC preparations but suggests either CBD-predominant formulations (up to 1:10 THC to CBD), or full spectrum cannabis, typically a 1:1 mix of THC and CBD. **THC is the dose-limiting component of these preparations and should not exceed 40 mg/day.**

Abbreviations: CBD, cannabidiol; THC, Δ^9 -tetrahydrocannabinol; NICE, National Institute for Health and Care Excellence; MHRA, Medicines & Healthcare products Regulatory Agency; EMA, European Medicines Agency; FDA, Food and Drug Administration; DEA, Drug Enforcement Administration; LGS, Lennox-Gastaut Syndrome; TSC, Tuberous Sclerosis Complex

Table S3 Summary of pharmacokinetics of cannabidiol in single-dose studies, based on a systematic review by Moazen-Zadeh et al¹

Route	T _{max} (h)	C _{max} (ng/mL)	AUC _(0-t) (h x ng/mL)	AUC _(0-inf) (h x ng/mL)	T _{1/2} (h)
Inhalation Dose: 2–100 mg	0.00–0.60	0.42–120.77	6.18–76.77	9.03 (one study only)	1.10–31.00
Oromucosal Dose: 5–50 mg	1.00–5.01	0.38–12.90	0.69–61.64	1.59–70.98	1.44–10.86
Oral Dose: 0.42–6000 mg	0.59–10.45	0.22–1628	0.47–9390.94	3.32–8669	1.09–70.3

Abbreviations: PK, pharmacokinetics; T_{max}, time to maximum concentration; C_{max}, maximum plasma concentration; AUC_(0-t), area under the curve (from time zero to the last measurable concentration of the drug); AUC_(0-inf), area under the curve (from time zero extrapolated to infinity from the last measurable concentration); T_{1/2}, elimination half-life time

1. Moazen-Zadeh E, Chisholm A, Bachi K, Hurd YL. Pharmacokinetics of Cannabidiol: A Systematic Review and Meta-Regression Analysis. Cannabis and Cannabinoid Research. 2024;9(4):939-966.

Table S4 Summary of factors affecting pharmacokinetics of cannabidiol in single-dose and multiple-dose studies, based on a systematic review by Moazen-Zadeh et al¹

Factor	PK parameters affected	Key findings
Route of administration		
Inhalation versus oral	T_{max}	Inhalation was associated with lower T_{max} (faster absorption) compared with oral administration. No significant difference was found for C_{max} , $AUC_{(0-t)}$, or $AUC_{(0-inf)}$, suggesting comparable overall bioavailability.
Oromucosal versus oral	C_{max} , $AUC_{(0-t)}$, $AUC_{(0-inf)}$	Oromucosal administration was consistently associated with lower C_{max} , AUC_{0-t} , and AUC_{0-inf} than oral administration, indicating lower bioavailability. No significant difference in T_{max} between the two routes was observed.
CBD Dose		
Higher dose	C_{max} , $AUC_{(0-t)}$, $AUC_{(0-inf)}$	Higher CBD dose was consistently associated with higher C_{max} , AUC_{0-t} , and AUC_{0-inf} across all models, as expected. Doses above 100 mg were only studied using the Epidiolex formulation, limiting comparison across formulations at higher doses.
Formulation		
Nanocarriers* and oil-based versus Epidiolex® formulation**	T_{max}	Nanotech and oil-based formulations were associated with a lower T_{max} than Epidiolex, indicating faster onset of action. Including formulation in models notably improved model fit for T_{max} .
Dietary (fed/fasted) status		
Fed versus fasted (for oromucosal and oral formulations)	C_{max} , $AUC_{(0-t)}$	Fed status was associated with higher C_{max} and AUC_{0-t} compared with fasting, consistent with (reportedly up to 4-5 times) increased bioavailability due to longer intestinal transit time and enhanced lymphatic absorption of this lipophilic compound. No significant effect on T_{max} or AUC_{0-inf} was detected.

Sex assigned at birth		
Female versus male	T_{max} , C_{max} , $T_{1/2}$	A higher proportion of female participants was associated with lower T_{max} (faster absorption) in oral administration models, higher C_{max} across all models, and longer $T_{1/2}$ in oral administration models. This suggests faster onset and longer duration of CBD in women, possibly related to sex differences in CYP450 enzyme activity and clearance rates.
Duration of PK session (varying between 6 and 168 hours)		
Long versus short session	$AUC_{(0-t)}$, $AUC_{(0-inf)}$, $T_{1/2}$	Longer PK session duration was associated with higher AUC_{0-inf} and $T_{1/2}$ across all models, and higher AUC_{0-t} in models including all routes. This reflects the long terminal half-life of cannabinoids; half-lives exceeding 60 hours were reported in a study with a 168-hour session duration.

*Nanocarriers are liposomes or oil droplets dispersed in water that increase the surface area and enhance intestinal absorption.

** Epidiolex is a an oil-based formulation in 10% ethanol.

Abbreviations: PK, pharmacokinetics; T_{max} , time to maximum concentration; C_{max} , maximum plasma concentration; $AUC_{(0-t)}$, area under the curve (from time zero to the last measurable concentration of the drug); $AUC_{(0-inf)}$, area under the curve (from time zero extrapolated to infinity from the last measurable concentration); $T_{1/2}$, elimination half-life time; CBD, cannabidiol

1. Moazen-Zadeh E, Chisholm A, Bachi K, Hurd YL. Pharmacokinetics of Cannabidiol: A Systematic Review and Meta-Regression Analysis. Cannabis and Cannabinoid Research. 2024;9(4):939-966.