P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

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Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** Electronic Medicines Compendium (eMC). Epidyolex® 100 mg/ml oral solution: summary of product characteristics. 2026. Available from: https://www.medicines.org.uk/emc/product/10781/smpc/print (Accessed 19 August 2026). **3.** European Medicines Agency. Epidyolex® 100 mg/ml oral solution: summary of product characteristics. 2026. Available from: https://www.ema.europa.eu/en/documents/product-information/epidyolex-epar-product-information_en.pdf (Accessed 19 August 2026). **4.** Ebert N, et al. *Kidney Int*. 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant*. 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int*. 2024;105(4S): S117–S314. **7.** Inker LA, et al. *N Engl J Med*. 2021;385(19):1737–1749.

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Epidyolex® is approved in the EU for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, in conjunction with clobazam, in patients ≥2 years of age; it is additionally approved in the EU for the adjunctive treatment of seizures associated with tuberous sclerosis complex in patients ≥2 years of age.

Clinical trial ID: GWCP18057

POSTER | ANNOTATED POSTER | AUDIO

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Introduction

- Highly purified, plant-derived cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US], 100 mg/mL oral solution) is approved for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), and tuberous sclerosis complex (TSC)[1–3]
- A *post hoc* analysis of safety laboratory results from three double-blind, randomised, placebo-controlled studies of CBD in paediatric and adult patients with LGS or DS, and a phase 1 randomised withdrawal study in healthy participants, showed an ~10% increase in serum creatinine concentration following CBD administration[1–3]
- In healthy participants, the increase was observed within 1 to 2 weeks of initiating CBD, after which it stabilised, and concentrations returned to baseline following CBD discontinuation[1–3]
  - Reversibility of serum creatinine increases was not assessed in LGS or DS CBD studies
- It was unknown whether the observed increase in serum creatinine reflected a reduction in glomerular filtration rate (GFR)[1–3]
- Iohexol is a non-radioactive contrast agent; its plasma clearance is a validated method for measuring GFR and is not affected by limitations of creatinine-based measures[4–6]
- In this phase 1, open-label, single-site study (GWCP18057), the potential cause of the increase in serum creatinine was explored by assessing the effect of repeated-dose CBD administration on measured GFR (mGFR) using iohexol plasma clearance

Methods

Participants

- This study included healthy male and female participants, aged 18–60 years, with a body mass index of 18.5–30.0 kg/m^2, and a minimum body weight of 50.0 kg from a single centre in the US

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

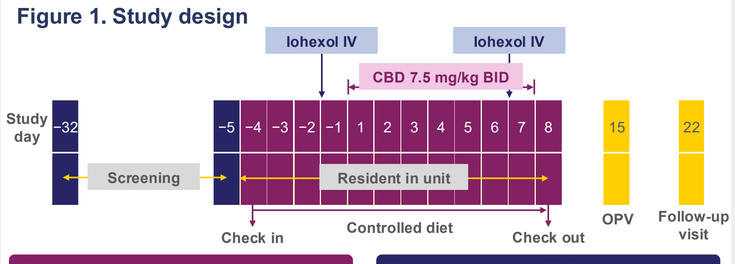
Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design



Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

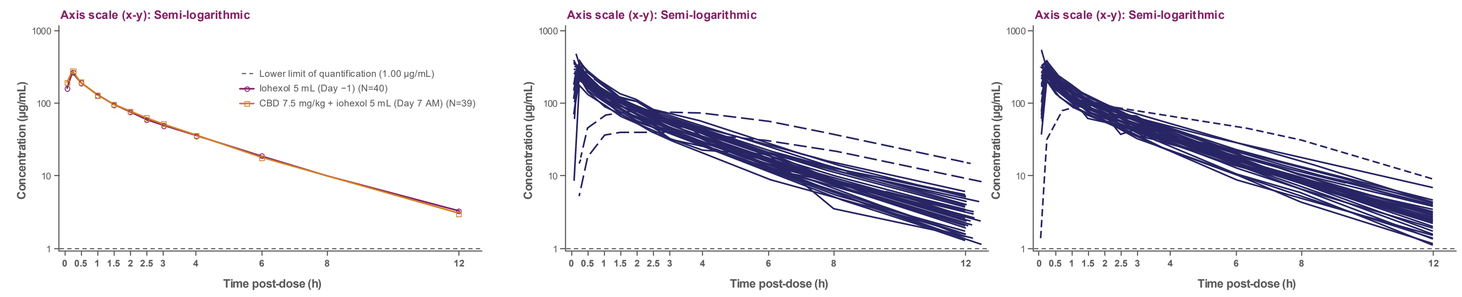
[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021)).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

A. Iohexol mean profiles Day −1 and Day 7 | B. Iohexol individual profiles Day −1 | C. Iohexol individual profiles on Day 7



- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m^2)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m^2)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

Pharmacokinetic parameters of iohexol

Table 2. Summary of iohexol plasma pharmacokinetic parameters

Parameter[a]		Iohexol 5 mL (Day −1)[b] (N=40)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM)[b] (N=39)
AUC_{0-last} (h·µg/mL)	Mean (SD)	479.0 (86.7)	485.0 (81.6)
	Geomean (CV%)	471.0 (18.7)	478.0 (17.3)
	Median (min–max)	475.0 (313.0–659.0)	471.0 (328.0–673.0)
AUC_{∞} (h·µg/mL)	Mean (SD)	490.0 (90.8)	494.0 (85.1)
	Geomean (CV%)	482.0 (18.8)	487.0 (17.6)
	Median (min–max)	484.0 (316.0–678.0)	481.0 (333.0–687.0)
$\%AUC_{extrap}$	Mean (SD)	2.3 (2.2)	1.9 (0.9)
	Geomean (CV%)	1.8 (65.3)	1.7 (48.5)
	Median (min–max)	1.7 (0.7–11.2)	1.7 (0.7–5.3)
C_{max} (µg/mL)	Mean (SD)	277.0 (77.9)	285.0 (65.4)
	Geomean (CV%)	261.0 (43.8)	277.0 (25.7)
	Median (min–max)	284.0 (40.6–467.0)	274.0 (91.9–542.0)
T_{max} (h)	Mean (SD)	0.4 (0.6)	0.3 (0.2)
	Geomean (CV%)	NC (NC)	NC (NC)
	Median (min–max)	0.3 (0.1–3.0)	0.3 (0.1–1.5)
$t_{1/2}$ (h)	Mean (SD)	2.2 (0.3)	2.2 (0.2)
	Geomean (CV%)	2.2 (14.4)	2.1 (10.7)
	Median (min–max)	2.2 (1.8–3.4)	2.1 (1.8–2.8)

[a]Pharmacokinetic parameters were summarised descriptively; no formal statistical comparisons were performed. [b]40 received at least one dose of iohexol, and 39 received at least one dose of both iohexol and CBD; the participant who only received iohexol was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria.
AUC, area under the plasma concentration–time curve; AUC_{0-last}, AUC from time 0 until the last quantifiable concentration; AUC_{extrap}, AUC that is extrapolated (predicted); AUC_{∞}, AUC from time 0 extrapolated to infinity; CBD, cannabidiol; C_{max}, maximum measured plasma concentration; CV, coefficient of variation; NC, not calculated; SD, standard deviation; T_{max}, time to maximum observed plasma concentration; $t_{1/2}$, terminal elimination half-life.

- The geometric mean values of iohexol maximum measured plasma concentration (C_{max}), area under the curve $(AUC)_{0-last}$, AUC_{∞}, $\%AUC_{extrap}$, and terminal half-life, as well as median time to maximum plasma concentration (T_{max}) values were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

Pharmacokinetic parameters of CBD and its metabolites

Table 3. Summary of CBD and CBD metabolite plasma pharmacokinetic parameters

Parameter[a]		CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM)[b] (N=39)		
		CBD	7-OH-CBD	7-COOH-CBD
$AUC_{0-\tau}$ (h·ng/mL)	Mean (SD)	1920.0 (691.0)	1140.0 (457.0)	69,200.0 (38,500.0)
	Geomean (CV%)	1800.0 (37.4)	1060.0 (43.1)	58,800.0 (69.5)
C_{max} (ng/mL)	Mean (SD)	412.0 (199.0)	184.0 (60.2)	6800.0 (3530.0)
	Geomean (CV%)	374.0 (45.6)	174.0 (37.2)	5910.0 (63.5)
MR_{AUC}	Mean (SD)	—	0.6 (0.3)	37.2 (22.8)
MR_{Cmax}	Mean (SD)	—	0.5 (0.2)	18.4 (11.2)
T_{max} (h)	Median (min–max)	3.0 (1.5–6.1)	3.0 (1.5–6.1)	4.0 (0–6.1)

[a]Pharmacokinetic parameters were summarised descriptively; no formal statistical comparisons were performed.
[b]38 participants had valid observations.
7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; AUC, area under the plasma concentration–time curve; $AUC_{0-\tau}$, AUC over a dosing interval, where tau is the dosing interval; CBD, cannabidiol; C_{max}, maximum measured plasma concentration; CV, coefficient of variation; MR_{AUC}, metabolite-to-parent ratio based on $AUC_{0-\tau}$; MR_{Cmax}, metabolite-to-parent ratio based on C_{max}; SD, standard deviation.

- Steady-state plasma CBD, 7-hydroxy-CBD (7-OH-CBD), and 7-carboxy-CBD (7-COOH-CBD) pharmacokinetic parameters (**Table 3**) were consistent with historical data[1,2]
  - Median T_{max} was similar for CBD and 7-OH-CBD (3.0 hours), with a slightly longer T_{max} observed for 7-COOH-CBD (4.0 hours)
  - Metabolite-to-parent ratio (MR) based on $AUC_{0-\tau}$ (MR_{AUC}) and MR_{Cmax} were higher for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)
Body mass index, kg/m^2		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m^2		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)