

Where different sites or populations or arms have different maximum doses, all are listed. *Maximum allowable dose based on the study protocol.

Note: Escalation and de-escalation intervals range from 1 mg/kg to 10 mg/kg of CBD per every other day or week of treatment. SAEs and all safety events are reported based on available published data only.

eTable 2. Overview of dosing and reported safety events from published clinical trials (interventional studies) enrolling children investigating CBD and other cannabinoids, including THC

Indication Reference	Cannabis product type	Sample size (n) Age range	Starting daily CBD dose	Mean or median (std or range) CBD dose taken/day	Maximum daily CBD dose	Starting daily THC dose	Mean (std) or median THC dose taken/day	Maximum daily THC dose	Reported serious adverse events (SAEs) and AEs (%)
Dravet syndrome (39)	CBD-enriched extract (50:1 TIL-150 oil)	n=19 1 to 18 years old	2 mg/kg	13.3 (7 to 16) mg/kg/day	16 mg/kg	0.04 mg/kg	0.27 mg/kg	0.32 mg/kg	SAEs: None reported AEs: Somnolence (89.5%), increased seizures (21%), diarrhea (31.6%), constipation (26.3%), gagging (15.8%), poor balance (42.1%), sleep disturbance (21%), mood change (21%), upper respiratory tract infection (21%), urinary tract infection (10.5%), anorexia (52.6%), increased appetite (15.8%)
Treatment-resistant epileptic encephalopathy (43)	CBD-enriched extract (20:1 oil)	n=7 1 to 10 years old	2 to 3 mg/kg	Not reported	12 mg/kg	0.1 mg/kg	Not reported	0.6 mg/kg	SAEs: Two participants required hospitalization unrelated to the study drug AEs: No clinically significant adverse events directly attributed to cannabinoids were encountered
Refractory epileptic encephalopathy (36)	CBD-enriched extract (25 mg/mL CBD, <2 mg/mL THC)	n=12 2 to 18 years old	2 mg/kg	12.2 (5.3 to 19.4) mg/kg	19.4 mg/kg	<0.08 mg/kg	Not reported	<0.8 mg/kg	SAEs: None reported AEs: None reported

Autism spectrum disorder (48)	CBD-enriched extract (20:1 oil) purified CBD	n=150 5 to 21 years old	1 mg/kg	CBD enriched extract: 5.7 (±2.6) mg/kg purified CBD: 5.9 (± 2.7) mg/kg	420 mg	0.05 mg/kg	-	21 mg	SAEs: None reported AEs: Somnolence (CBD-EE 27%, pure 24%), decreased appetite (CBD-EE 24%, pure 22%), weight loss (CBD-EE 12%, pure 13%), tiredness (CBD-EE 25%, pure 34%), euphoria (CBD-EE 20%, pure 19%), anxiety (CBD-EE 20%, pure 27%)
Chemotherapy-induced nausea and vomiting (62)	Synthetic THC (Nabilone)	n=40 3 to 18 years old	-	-	-	single dose	-	1 mg	SAEs: dizziness (11.1%), increased appetite (11%) AEs: Drowsiness (67%), dizziness (50%), mood alteration (14%), ocular swelling (8%)
Spasticity due to cerebral palsy or traumatic non-progressive CNS injury (51)	THC and CBD (Nabiximols)	n=72 8 to 18 years old	-	5.82 sprays (14.55 mg)	12 sprays (30 mg)	-	5.82 sprays (15.71 mg)	12 sprays (32.4 mg)	SAEs: Change in seizure profile (8%), food aversion and retching (4%), viral respiratory tract infection (4%) AEs: Retching (12.8%), vomiting (12.8%), constipation (2.1%), gastroenteritis (8.5%), lower respiratory tract infection (8.5%), upper respiratory tract infection (8.5%), somnolence (12.8%)

ALT Alanine aminotransferase; AE Adverse event; AST Aspartate aminotransferase; CBD Cannabidiol; CNS central nervous system; EE Enriched extract; GGT Gamma-glutamyl transferase; SAE Serious adverse event; Std Standard deviation; THC Delta-9-tetrahydrocannabinol