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 1. Overview of dosing and reported safety events from published clinical trials (interventional studies) enrolling children investigating cannabidiol (CBD)

Indication (Reference)	Cannabis product type	Sample size and age range	Starting daily CBD dose	Mean (std) or median CBD dose taken/day	Maximum* daily CBD dose	Reported serious adverse events (SAEs) and AEs (%)
Dravet syndrome and drug-resistant seizures (15)	purified CBD (Epidiolex)	n=120, 2 to 18 years old	5 mg/kg	Not reported	20 mg/kg	SAEs: Status epilepticus (4.9%), elevated transaminases (>3xULN) (4.9%) AEs: Somnolence (36%), diarrhea (31%), decreased appetite (28%), fatigue (20%), pyrexia (15%), convulsions (15%), vomiting (15%), lethargy (13%), upper respiratory tract infection (11%)
Lennox-Gastaut syndrome (18)	purified CBD (Epidiolex)	n=171, 2 to 55 years old	2.5 mg/kg	Not reported	20 mg/kg	SAEs: Increased serum AST/ALT (>3xULN) levels (4.6%) Increased GGT concentrations (3.4%), pneumonia and acute respiratory failure (2.3%) AEs: Somnolence (14%), diarrhea (13%)
Lennox-Gastaut syndrome (20)	purified CBD (Epidiolex)	n=225, 2 to 55 years old	2.5 mg/kg	Not reported	10 mg/kg 20 mg/kg	SAEs: Reported in 33 patients (13 at each CBD dose and 7 in placebo) increased seizures during weaning (0.65%), nonconvulsive status epilepticus (0.65%), elevated transaminases (>3xULN) (9%), lethargy (0.65%), constipation (0.65%), worsening chronic cholecystitis (0.65%) AEs: Somnolence (CBD10 21%, CBD20 30%), decreased appetite (CBD10 16%, CBD20 26%), diarrhea (CBD10 10%, CBD20 15%), upper respiratory tract infection (CBD10 10%, CBD20 13%), pyrexia (CBD10 9%, CBD20 12%), vomiting (CBD10 6%, CBD20 12%), mild nasopharyngitis (CBD10 4%, CBD20 11%), status epilepticus (CBD10 10%, CBD20 5%)
CDKL5 deficiency disorder and Aicardi, Dup15q, and Doose syndromes (21)	purified CBD (Epidiolex)	n=55, 1 to 30 years old	5 mg/kg	29.6 (±12.2) mg/kg/day	25 mg/kg 50 mg/kg	SAEs: None reported AEs: Somnolence (66%), increase in seizure frequency (33.3%)

Tuberous sclerosis complex (22)	purified CBD (Epidiolex)	n=224, 1 to 65 years old	5 mg/kg	CBD25: 24 mg/kg/day CBD50: 36 mg/kg/day	25 mg/kg 50 mg/kg	SAEs: Reported in 28 patients, 16 patients on CBD50, 10 patients on CBD25, and 2 receiving placebo. Increased serum ALT (CBD25 3%, CBD50 3%) level, increased serum AST level (CBD25 3%, CBD50 3%), status epilepticus (CBD25 3%, CBD50 0%), gastroenteritis viral (CBD25 3%, CBD50 0%), increased transaminases (CBD25 0%, CBD50 3%), vomiting (CBD25 3%, CBD50 0%), abdominal pain (CBD25 0%, CBD50 1%), acute respiratory failure (CBD25 1%, CBD50 0%), angioedema (CBD25 0%, CBD50 1%), increased blood bilirubin (CBD25 1%, CBD50 0%), dehydration (CBD25 0%, CBD50 1%), diarrhea (CBD25 0%, CBD50 1%), electrolyte imbalance (CBD25 1%, CBD50 0%), fatigue (CBD25 1%, CBD50 0%), gastroenteritis (CBD25 0%, CBD50 1%), generalized tonic−clonic seizure (CBD25 0%, CBD50 1%), hypophagia (CBD25 1%, CBD50 0%), laceration (CBD25 0%, CBD50 1%), liver injury (CBD25 1%, CBD50 0%), malaise (CBD25 1%, CBD50 0%), nausea (CBD25 1%, CBD50 0%), acute otitis media (CBD25 1%, CBD50 0%), pneumonia (CBD25 1%, CBD50 0%), aspiration pneumonia (CBD25 1%, CBD50 0%), rash (CBD25 1%, CBD50 0%), erythematous rash (CBD25 1%, CBD50 0%), macular rash (CBD25 0%, CBD50 1%), seizure (CBD25 1%, CBD50 1%), toxicity to various agents (CBD25 0%, CBD50 1%), type IV hypersensitivity reaction (CBD25 1%, CBD50 0%) and urticaria (CBD25 0%, CBD50 1%) AEs: Diarrhea (CBD25 31%, CBD50 56%), somnolence (CBD25 13%, CBD50 26%), decreased appetite (CBD25 20%, CBD50 23%), increased serum AST level (CBD25 11%, CBD50 19%), vomiting (CBD25 17%, CBD50 18%), pyrexia (CBD25 19%, CBD50 16%), nasopharyngitis (CBD25 15%, CBD50 15%), seizures (CBD25 7%, CBD50 11%), upper respiratory tract infection (CBD25 8%, CBD50 10%), constipation (CBD25 11%, CBD50 7%), cough (CBD25 11%, CBD50 4%)
Drug-resistant epileptic encephalopathy (28)	CBD-enriched extract	n=59, 2 to16 years	2 mg/kg twice daily in children	median (range)	25 mg/kg	SAEs: None reported

	(Rideau 25:1, Aphria)		weighing ≤ 45 kg 5 mg/kg per day (weight > 45 kg)	18 (1 to 25) mg/kg/day		AEs: Drowsiness (30.5%), decreased appetite (28.8%), diarrhea (25%) behavioural disturbances (22%), weight loss (18%), vomiting (15%)
Drug-resistant epilepsy (26)	purified CBD (Epidiolex)	n=33, 2 to 16 years	5 mg/kg	Not reported	25 mg/kg	SAEs: None reported AEs: Drowsiness (57.8%), diarrhea (34.4%), somnolence (27.5%), agitation (13.8%)
Lennox-Gastaut syndrome (45)	purified CBD (Epidiolex)	n=366, 2 to 55 years old	2.5 mg/kg	24 mg/kg	30 mg/kg/day	SAEs: Convulsion (11.7%), status epilepticus (11.5%), pneumonia (8.2%) aspiration pneumonia (4.4%), vomiting (3.6%), pyrexia (3%), acute respiratory failure (2.7%), urinary tract infection (2.5%), hypoxia (2.5%), respiratory failure (2.2%), serum ALT levels increased (1.9%), sepsis (1.6%), serum AST levels increased (1.6%), hepatic enzyme increased (1.6%, mental status changes (1.6%), respiratory distress (1.6%), diarrhea (1.4%), dehydration (1.4%), acute kidney injury (1.4%), ileus (1.4%), hypotension (1.1%), weight decreased (1.1%) AEs: Convulsion (38.5%), diarrhea (38.3%), pyrexia (34.4%), somnolence (29.2%), vomiting (29.2%), upper respiratory tract infection (27.9%), decreased appetite (25.4%), cough (17.2%), weight decreased (16.7%), pneumonia (15.6%), urinary tract infection (13.9%), ear infection (13.7%), sinusitis (13.4%), nasal congestion (12.6%), insomnia (10.9%), fatigue (10.4%)
Developmental and epileptic encephalopathies (27)	Transdermal CBD (4.2 % topical CBD gel)	n=48, 3 to 18 years old	250 mg (weight 25 kg or less) 500 mg (weight above 25 kg)	Not reported	750 mg (weight 25 kg and below) 1000 mg (weight above 25 kg)	SAEs: None reported AEs: Upper respiratory tract infection (42%), nasopharyngitis (21%), somnolence (13%), vomiting (10%)
Fragile X (59)	Transdermal CBD	n= 20 6 to 17 years old	50 mg	Not reported	250 mg	SAES: None reported AEs: Gastroenteritis (25%), vomiting (10%), upper respiratory tract infection (10%), mouth ulceration (5%), paraesthesia oral (5%),

						diarrhea (5%), application site dryness (5%), application site rash (5%), influenza (5%), viral infection (5%), viral upper respiratory tract infection (5%), otitis media (5%), tonsillitis (5%), limb injury (5%), eosinophil count abnormal (5%), neck pain (5%), pain in extremity (5%), dizziness (5%), lethargy (5%), psychomotor hyperactivity (5%), enuresis (5%), stereotypy (5%), nightmare (5%), pruritus (5%), eczema (5%), pruritic rash (5%)
Intellectual disabilities and severe behavioural problems (54)	purified CBD	n=8 8 to 16 years old	5 mg/kg	7.8 (±2) mg/kg/day	20 mg/kg	SAEs: None reported AEs: Treatment emergent symptoms reported on MOSES

ALT Alanine aminotransferase; AST Aspartate aminotransferase; CBD Cannabidiol; MOSES Monitoring of Side Effects Scale; SAEs Serious adverse events; ULN Upper limit of normal