# **Supplemental Table 1:** Summary of Outcome Definitions Assessed in Efficacy Studies for Each Condition

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| --- | --- |
| Condition | Efficacy outcomes employed within identified studies |
| **Amyotrophic Lateral Sclerosis (ALS)** | Cramp Intensity; Number/frequency of cramps |
| **Autism** | Clinical improvement in symptoms (i.e., measured with Autism Spectrum Quotient, frequency of episodes of hyperactivity, or self-injury) |
| **Cancer** |  |
| Pain | Pain reduction |
| Cachexia | Weight change, appetite, caloric intake |
| Nausea and Vomiting | Frequency of nausea and vomiting episodes |
| **Chronic non-Cancer Pain** | Pain reduction; Quality of Life (QoL) |
| **Crohn’s Disease** | Clinical improvement in symptoms (e.g. measured with Clinical disease activity Index, or Harvey Bradshaw score); frequency of disease-related complications |
| **Epilepsy** | Seizure frequency; Seizure severity; Episodes of status epilepticus; Health-Related Quality of Life (HRQoL); QoL |
| **Glaucoma** | Reduction in intraocular pressure |
| **Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS)** |  |
| Pain | Pain reduction; HRQoL; QoL |
| Other Outcomes | Change in adherence; Viral load suppression |
| **Multiple Sclerosis (MS)** |  |
| Spasticity and Spasm | Frequency of spasms; severity of spasms |
| Pain | Pain reduction; QoL |
| Function Outcomes | Bladder (Incontinence episodes, nocturia episodes); Gait improvement |
| **Parkinson's Disease** | Clinical improvement in symptoms (e.g. measured via motor examination scores, effect on dyskinesias, tremor severity). |
| **Post-Traumatic Stress Disorder (PTSD) and PTSD-Related Anxiety** | Clinical improvement in symptoms (e.g. measured with PTSD Score, nightmare frequency and severity, daytime flashbacks frequency) |
| Condition | Efficacy outcomes employed within identified studies |

**Supplemental Table 2:** Ongoing Randomized Controlled Trials for Medical Cannabis in the United States as of 2020

|  |  |
| --- | --- |
| Condition Studied in the Trial | Initiation Year, Trial Registration Citation |
| Crohn’s Disease\* | 2018 (133) |
| Chronic non-Cancer Pain | 2019 (123) |
| Chronic non-Cancer Pain | 2019 (124) |
| Chronic non-Cancer Pain | 2017 (125) |
| Cancer | 2018 (76) |
| Cancer | 2018 (77) |
| Parkinson’s Disease | 2018 (187) |
| Post-Traumatic Stress Disorder | 2016 (200) |
| Post-Traumatic Stress Disorder | 2016 (201) |
| Post-Traumatic Stress Disorder\*² | 2017 (202) |
| Post-Traumatic Stress Disorder | 2018 (203) |
| Post-Traumatic Stress Disorder | 2019 (204) |

*\* This trial was withdrawn due to inadequate funding.*

*\*² This trial was terminated in November 2019 due to safety concerns following incidents of severe adverse events.*

**Supplemental Table 3:** Dosage and Ratio of Agents in Reviewed Studies by Condition

|  | **Agent** | **Daily dosage / Dosage** | **Ratio/Concentration** |
| --- | --- | --- | --- |
| **Amyotrophic Lateral Sclerosis (ALS)** | **---** | **---** | **---** |
| **Autism** |  |  |  |
| Carey C et al., 2016 (15) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Schapir L et al., 2016 (18) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Stringer S et al., 2016 (21) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Raynal P et al., 2016 (20) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Barchel D et al., 2018 (16) | (THC and CBD) extract | Not specified | High THC: low CBD |
| Aran A et al., 2019 (17) | (THC and CBD) extract | Oil was given 2-3 times a day with doses up-titrated over 2-4 weeks, to effect and tolerability (starting CBD dose was 1mg/kg/day, maximal CBD dose was 10 mg/kg/day) | Low THC: high CBD |
| Pretzsch CM et al., 2019a (22) | CBD | 600 mg | Not specified |
| Pretzsch CM et al., 2019b (23) | CBD | 600 mg | Not specified |
| **Cancer** |  |  |  |
| Elliott DA et al., 2016 (245) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Pergam SA et al., 2017 (48) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Vin-Raviv N et al., 2017 (246) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Rauenzahn S et., 2017 (51) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Hoffman K et al., 2017 (53) | Not specified | Not specified | Not specified |
| Mohite PN et al., 2017 (54) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Fallon MT et al, 2017 (34) | (THC and CBD) extract (nabiximols) | 1:1 (THC (27 mg/mL): CBD (25 mg/mL) (Sativex®)  Study 1: active group on average took 6.3 sprays/day and 7.3 sprays/day in placebo group.  Study 2: 6.3 sprays/day in active group and 6.5 in the placebo group.  Dose range not specified. | Pharmaceutical grade product/ substance |
| **Chronic non-Cancer Pain** |  |  |  |
| Kosiba JD et al., 2019 (78) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Hawley LA et al., 2018 (110) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Reynolds IR et al., 2018 (83) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Piper BJ et al., 2017 (84) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Freisthler B et al., 2018 (85) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Delling FN et al., 2019 (86) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Barlowe TS et al., 2019 (87) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Orr MF et al., 2019 (248) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Mercurio A et al., 2019 (92) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Merlin et al., 2019 (118) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Perron BE et al., 2019 (107) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Rogers AH et al., 2019 (96) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Fales JL et al. 2019, (97) | Cannabis/Marijuana, not specified | Not specified | THC range <5% to  26%;  CBD range <5% to  26% |
| Cohen NL et al., 2016 (98) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Cooke AC et al., 2019 (100) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Nugent SM et al., 2018 (101) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Khelemsky Y et al., 2017 (102) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Boehnke KF et al., 2019 (103) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Bruce E et al., 2018 (68) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Bellnier T et al., 2018 (227) | Cannabis/Marijuana, not specified | 10 mg capsules, every 8 to 12 hours | 1:1 (THC:CBD) |
| Bachhuber M et al., 2019 (250) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| **Crohn’s Disease** |  |  |  |
| Hoffenberg EJ et al., 2018 (129) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Hoffenberg EJ et al., 2019(126) | (THC and CBD) unspecified | Daily dosage not specified;  dose range CBD 1.2-500 mg, THC 1-50 mg | Not specified |
| Mbachi C et al., 2019 (229) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Desai R et al., 2019 (61) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| **Epilepsy** |  |  |  |
| Hess EJ et al., 2016 (134) | Epidiolex® (CBD) | Starting dose 5 mg/kg/day every week up to an initial maximum dose of 25 mg/kg/day  For subjects who continued to have seizures and tolerated CBD at 25 mg/kg/day, the dose was increased to a maximum dose of 50 mg/kg/day at a maximum rate of 5 mg/kg/day each week | Pharmaceutical grade product/ substance |
| Szaflarski JP et al., 2018 (135) | Epidiolex® (CBD) | Starting dose 5 mg/kg/day divided between AM and PM taken approx. 12 h apart.  Dosage was allowed to be titrated in 5-mg/kg/day increments up to a max of 50 mg/kg/day, with adjustments made based on seizure response and tolerability (highest dose 2,000 mg/day) | Pharmaceutical grade product/ substance |
| Thiele E et al., 2018 (136) | Epidiolex® (CBD) | Dose escalation, 2 week titration starting dose 2.5 mg/kg, followed by 12 weeks of maintenance dose (20mg/kg), dose administered in equally divided doses (half in the morning, half in the evening) | Pharmaceutical grade product/ substance |
| Thiele E et al., 2019 (151) | Epidiolex® (CBD) | Titrated from 2.5 to 20 mg/kg/d over a 2‐week titration period.  Doses could be reduced if not tolerated or increased up to 30 mg/kg/d if thought to be of benefit. | Pharmaceutical grade product/ substance |
| Kaplan EH et al., 2017 (149) | Epidiolex® (CBD) | Starting dose of 2 mg/kg/day in twice-daily doses. The dose was increased to 5 mg/kg/day at week 1 and by 5 mg/kg/day each subsequent week as tolerated up to a maximum dose of 25 mg/kg/day. | Pharmaceutical grade product/ substance |
| Gaston TE et al., 2019 (238) | Epidiolex® (CBD) | Participants were weighed at every visit, and weight-based CBD dosing was initiated at 5 mg/kg/day and taken twice daily. At each subsequent clinic visit, CBD could be increased in 5 mg/kg/day increments every 2 weeks up to a maximum dose of 50 mg/kg/day. | Pharmaceutical grade product/ substance |
| Treat L et al., 2017 (152) | (THC and CBD) extract | Not specified | Not specified |
| Porcari G et al., 2018 (150) | CBD | Dose range 0.018-50 mg/kg/day | Low THC:high CBD |
| Szaflarski JP et al., 2019 (139) | Epidiolex® (CBD) | Starting dose 5 mg/kg/day divided between morning and evening dosages that were taken ~ 12 h apart. At each follow-up visit, the dosage was allowed to be titrated in 5 mg/kg/day increments up to a maximum of 50 mg/kg/day with adjustments made based on seizure response and tolerability. | Pharmaceutical grade product/ substance |
| Gaston TE et al., 2017 (157) | Epidiolex® (CBD) | Starting dose 5 mg/kg/day and increased every 2 weeks by 5 mg/kg/day up to a maximum of 50 mg/kg/day. | Pharmaceutical grade product/ substance |
| Devinsky O et al., 2019 (140) | Epidiolex® (CBD) | Titrated from 2.5 to 20 mg/kg/d over a 2‐week period, with their existing medications. Based on response and tolerance, CBD could be reduced or increased up to 30 mg/kg/d. | Pharmaceutical grade product/ substance |
| Szaflarski JP et al., 2018 (141) | Epidiolex® (CBD) | Starting dose at 2‐10 mg/kg/d, titrated to a maximum dose of 25‐50 mg/kg/d. | Pharmaceutical grade product/ substance |
| Sands TT et al., 2019 (142) | Epidiolex® (CBD) | Starting dose 5 mg/kg/day and titrated weekly by 5-mg/kg increments to a dose of 25 mg/kg/day | Pharmaceutical grade product/ substance |
| Wheless JW et al., 2019 (154) | Epidiolex® (CBD) | Single dose (5, 10, or 20 mg/kg) on day 1 and twice-daily dosing on days 4 through 10 (10-mg/kg [cohort 1], 20-mg/kg [cohort 2], or 40-mg/kg [cohort 3] total daily dose) | Pharmaceutical grade product/ substance |
| Knupp KG et al., 2019 (146) | Cannabis/Marijuana, not specified | Daily dose 1 mg/kg/day | Not specified |
| Gaston TE et al., 2019 (144) | Epidiolex® (CBD) | Starting dose CBD 5 mg/kg/day with dose increasing every 2 weeks by increments of 5 mg/kg/day to seizure control or tolerability at in-person visits to a maximum dose of 50 mg/kg/day | Pharmaceutical grade product/ substance |
| Devinsky O et al., 2018 (153) | Epidiolex® (CBD) | 5, 10, or 20 mg/kg/d,  administered twice daily starting at 2.5 mg/kg/d (or equivalent volume for placebo) and increasing by 2.5–5.0 mg/kg every other day to randomized dose, which took 3, 7, and 11 days for the 5, 10, and 20 mg/kg/d doses, respectively. | Pharmaceutical grade product/ substance |
| Devinsky O et al., 2017 (145) | Epidiolex® (CBD) | 5, 10, and 20 mg per kilogram of body weight per day, administered twice daily.  Dose was escalated up to 20 mg per kilogram per day (or equivalent volume of placebo) with the use of a 14-day dosing regimen. | Pharmaceutical grade product/ substance |
| **Glaucoma** | --- | --- | --- |
| **HIV/AIDS** |  |  |  |
| Gamarel KE et al., 2016 (178) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Gross IM et al., 2016 (232) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Thames AD et al., 2016 (175) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Hartzler B et al., 2017 (165) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Kipp AM et al., 2017 (168) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Lorenz DR et al., 2017 (176) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Noorhasan M et al., 2017 (166) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Okafor CN et al., 2017 (167) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Sinha S et al., 2017 (173) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Vidot DC et al., 2017 (161) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Adams JW et al., 2018 (177) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Lee JY et al., 2018 (169) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Mannes ZL et al., 2018 (162) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Thompson AB et al., 2018 (163) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Lorenz DR et al., 2019 (239) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Bruce D et al., 2019 (170) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Zhang Y et al., 2018 (172) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| Jolley SE et al., 2019 (164) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| **Multiple Sclerosis (MS)** | --- | --- | --- |
| **Parkinson’s Disease** |  |  |  |
| NCT02818777, 2016 (186) | CBD | Starting dose 5 mg/kg/day and increased by 2.5-5 mg/kg at 3-5 day intervals to a target dose of 20 mg/kg/day | Not specified |
| Kindred JH et al., 2017 (189) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| NCT03582137, 2018 (187) | CBD | Targeted dose 2.5 mg/kg/day | Not specified |
| Reynolds IR et al., 2018 (83) | Cannabis/Marijuana, not specified | Not specified | Not specified |
| **Post-Traumatic Stress Disorder (PTSD)** |  |  |  |
| NCT03008005, 2016 (200) | Marinol® (dronabinol; THC) | 5 mg or 10 mg, once daily | Pharmaceutical grade product/ substance |
| NCT02759185, 2016 (201) | Cannabis, wholeplant | Up to 1.8 grams per day smoked ad libitum, for a 3-week period | Arm 1) High THC:low CBD  Arm 2) Low THC:high CBD  Arm 3) High THC:high CBD  Arm 4) Placebo |
| NCT03518801, 2018 (203) | CBD | Not specified | Not specified |
| NCT04080427, 2019 (204) | Marinol® (dronabinol; THC) | 7.5 mg, single oral dose | Pharmaceutical grade product/ substance |