Cost-Effectiveness of Cannabidiol Add-on Therapy Versus Placebo for the Treatment of Seizures in Tuberous Sclerosis Complex

Sally Bowditch[1] | Colin Burke[2] | Catriona Crossan[2] | Matthew Hemstock[2] | Emma Tyas[2] | Dawn Lee[2]

[1]Jazz Pharmaceuticals, Inc., London, UK; [2]Lumanity Inc., Sheffield, UK

Poster EE16

KEY POINTS

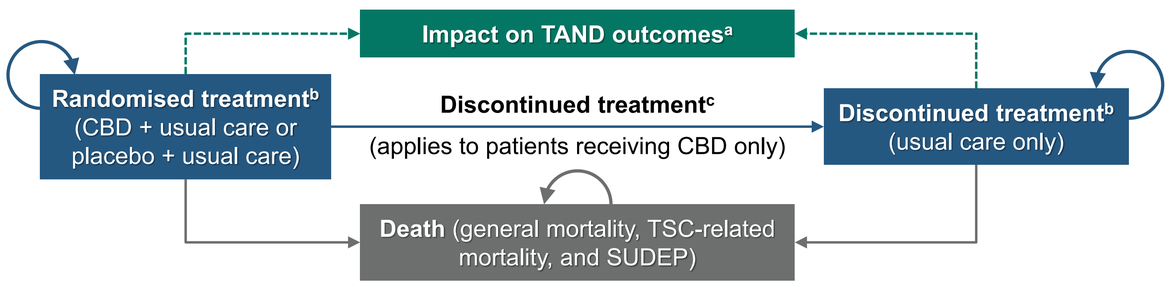
- Based on an incremental cost-effectiveness ratio (ICER) threshold of £20,000–30,000 for England and Wales, compared with placebo, add-on treatment with highly purified cannabidiol (CBD) medicine (Epidyolex®) is a cost-effective treatment option in patients with tuberous sclerosis complex (TSC)-associated epilepsy.
- Base-case ICER was £12,876 and reduced to £10,730 following application of a disease severity modifier of 1.2 for quality-adjusted life years (QALYs); seizure-free days had the largest impact, equating to 74% of QALY gains.
- Results were robust to sensitivity and scenario analyses, and cost-effectiveness was highly likely at both £20,000 (65.9%) and £30,000 (88.4%) thresholds.

INTRODUCTION

- TSC is a rare disorder characterised by benign tumours in multiple organ systems, most commonly occurring in the brain and resulting in neurological disease manifestations.[1]
- TSC commonly results in an early onset and highly treatment-resistant epilepsy with a substantial unmet need for treatments offering early, effective seizure control with an acceptable safety profile.[1,2]
- This analysis evaluated the cost-effectiveness of plant-derived highly purified CBD medicine (Epidyolex®; 100 mg/mL oral solution), versus placebo, in patients aged ≥2 years with treatment-refractory TSC-associated seizures managed according to usual care.

METHODS

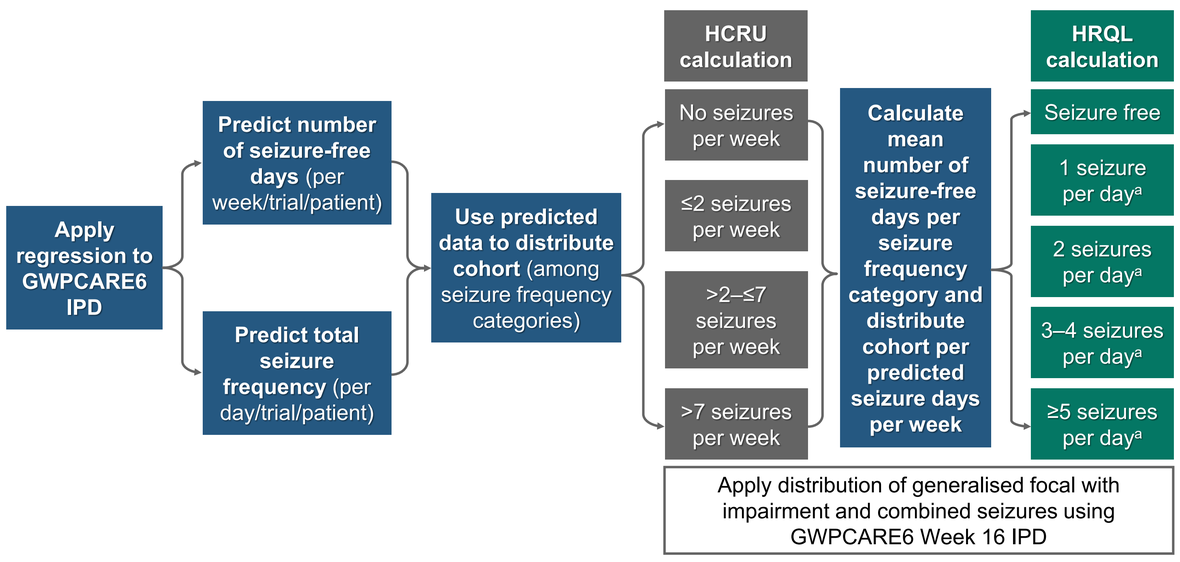
- A cohort-level cost-effectiveness model was developed using a National Health Service (NHS) perspective, with a lifetime horizon (assumed to be 82 years) to determine the average costs and QALYs per patient associated with changes in seizure frequency and seizure-free days for patients treated with CBD (average of 12 mg/kg/day) or placebo.



[a]TAND outcomes included intellectual disability, delayed development, behavioural issues, autism spectrum disorder, attention deficit hyperactivity disorder, and anxiety disorders; [b]cohort population distributions based on IPD data from the 16-week treatment period of GWPCARE6; [c]discontinuation rates were applied based on the 16-week GWPCARE6 and 72-week OLE study; discontinuation of treatment is a transition once patients enter the alive health state on treatment with CBD. Circular lines represent patients remaining in the health state for the alive health states (blue boxes) and following mortality (grey box). Dotted lines represent the modelled effect of treatment on TAND outcomes in early childhood based on changes in seizure frequency. CBD, cannabidiol; IPD, individual patient-level data; OLE, open-label extension; SUDEP, sudden unexplained death in epilepsy; TAND, tuberous sclerosis complex-associated neuropsychiatric disorders; TSC, tuberous sclerosis complex.

- Three health states were modelled using a cycle length of 7 days; health states were derived using two mixed-effects regression models (negative binomial regression for seizure frequency on seizure days and binomial regression for seizure-free days) utilising patient-level data from GWPCARE6, a double-blind, placebo-controlled, randomised trial.
- Health states were categorised into sub-health states to allow different healthcare resource utilisation (HCRU) and health-related quality of life (HRQL) values to be applied per category.

Model process diagram



[a]Seizure frequency per day categories are aligned to HRQL data collected by seizure type (including generalised seizures [tonic-clonic, tonic, clonic, or atonic] and focal seizures with impairment of consciousness/awareness). The model includes the costs for HCRU, including primary care visits, outpatient visits, hospitalisation, additional support (e.g., educational – children only), and institutionalisation (residential care – adults only). HCRU, healthcare resource utilisation; HRQL, health-related quality of life; IPD, individual patient-level data.

- HCRU was collected using a Delphi panel study, and HRQL was collected using vignettes in the general population using time trade-off (TTO) methods.
- Base-case analysis parameters included annual HCRU, effect of treatment on development of TSC-associated neuropsychiatric disorders (TAND), patient and caregiver utilities, and TSC-related excess mortality rates.
- CBD discontinuation and stopping rates (applied to the model every 6 months for 2 years to reflect discontinuation resulting from non-response over time) were calculated from GWPCARE6 and the subsequent OLE. The impact of the new National Institute for Health and Care Excellence (NICE) disease severity modifier was also examined.
- The uncertainty of parameters and the effect on the model results was assessed via one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA).
- To test the robustness of the base-case analysis, scenario analyses were conducted for structural and methodological assumptions, including stopping rule rates.

RESULTS

- In the base-case analysis, compared with placebo, treatment with CBD resulted in an ICER of £12,876 that reduced to £10,730 following application of the disease severity modifier.
- When determining the impact of health state parameters on QALY gains, the increase in seizure-free days accounted for 74% of the benefit attributed to use of CBD versus placebo.

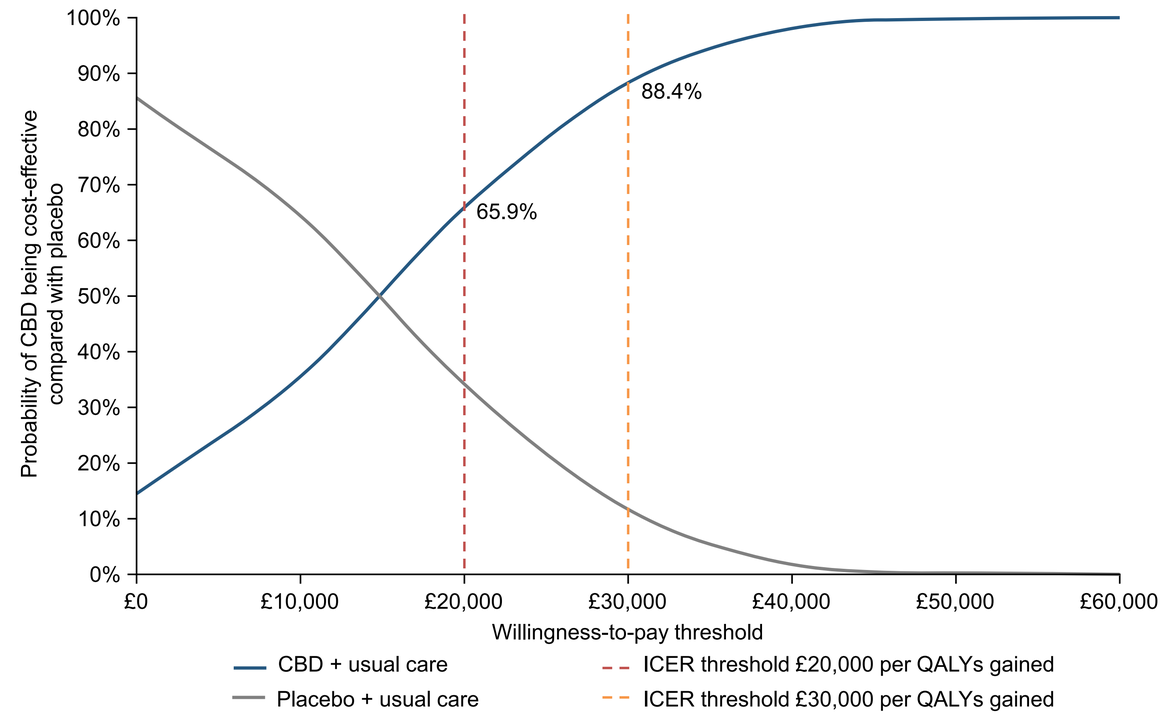
Base case and key scenario analyses

- Results were robust to sensitivity (OWSA and PSA) and key scenario analyses.
- Within the OWSA, the ICER was most sensitive to variation of the stopping rule assessment rate applied at 6 months for patients with a seizure frequency ≥7 seizures per week (highest seizure frequency category); the ICER ranged from £10,279 to £15,318.
- The most influential scenario, resulting in a dominant ICER, was the inclusion of social and educational care resource use.

Scenario	Base-case setting	Scenario detail	Impact on base-case ICER
Base-case ICER		**NA**	**£12,876**
Application of disease severity modifier	Excluded	Application of a severity modifier of 1.2 is applied to all QALYs	£10,730
Time horizon (years)	Lifetime	30	£12,842
Age group for TAND benefit	Patients aged 2–6 years	Applied to all patients	£4674
Duration of modelled TAND benefit (years)	Lifetime	5	£14,203
Patient HRQL source	Lo 2022 (vignette study)[3]	Tritton 2019 (EQ-5D)[4]	£12,535
		Vergeer 2019 (HUI-3)[5]	£13,346
Number of caregivers	2	3	£10,101
Resource use	Excluded	Inclusion of resource costs related to social care and education support	Dominant
Subsequent treatment with everolimus (applied to a proportion of patients in both arms)	Everolimus is included	Everolimus is not included	£13,550
CBD dose	12 mg/kg/day	10 mg/kg/day	£7326

CBD, cannabidiol; EQ-5D, EuroQol-5D; HRQL, health-related quality of life; HUI-3; Health Utilities Index-3; ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life year; TAND, tuberous sclerosis complex-associated neuropsychiatric disorders.

Cost-effectiveness acceptability curve from the PSA



CBD, cannabidiol; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Disclosures: This analysis was sponsored by Jazz Pharmaceuticals, Inc. Medical writing, editorial, and formatting assistance was provided to the authors by Sam Mason of Selene Medical Communications, Macclesfield, UK and funded by Jazz Pharmaceuticals, Inc. All authors met the ICMJE authorship criteria and had full access to relevant data. Neither honoraria nor payments were made for authorship. CB, CC, MH, ET, and DL have consulted for, conducted studies funded by, or received honoraria from GW Pharmaceuticals companies, now part of Jazz Pharmaceuticals, Inc.; SB is an employee of Jazz Pharmaceuticals, Inc. CBD is approved as Epidyolex® in the UK and 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 UK, and the EU for the adjunctive treatment of seizures associated with tuberous sclerosis complex in patients ≥2 years of age.
References: **1.** Curatolo P et al. *Lancet Neurol.* 2015; 14(7):733–45; **2.** French JA et al. *Epilepsia.* 2013; 54(Suppl. 4):3–12; **3.** Lo SH et al. *Pharmacoecon Open.* 2022; 6(1):105–21; **4.** Tritton T et al. *Epilepsy Behav.* 2019; 92:213–20; **5.** Vergeer M et al. *Epilepsia Open.* 2019; 4(4):581–92.

Contact Information: medinfo@gwpharm.com.
Clinical Trial ID: NCT02544763 and NCT02544750 (GWPCARE6)

Presented: International Society for Pharmacoeconomics and Outcomes Research, Europe; Vienna, Austria; 6–9 November 2022

To obtain a PDF of this poster:
- Scan the QR code or
- Visit www.gwqrcodes.com/538081
- Charges may apply. No personal information is stored.