Oveporexton for Narcolepsy: Effectiveness and Value

Public Meeting — May 14, 2026

Meeting materials available at: https://icer.org/assessment/narcolepsy-2026

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- **Jimi Olaghere,** Sickle Cell Disease Advocate; Entrepreneur, Sugarloaf Capital
- **Stuart A. Winston, DO,** Cardiologist in the Sub-Specialty of Cardiac Electrophysiology, Trinity Health IHA Medical Group, Ann Arbor, MI; Physician Lead, Professional Enhancement Program, Trinity Health IHA Medical Group, Ann Arbor, MI

Patient Experts

Tammy Anderson, Executive Director, Wake Up Narcolepsy

- *Tammy Anderson is a full-time employee of Wake Up Narcolepsy. Wake Up Narcolepsy receives grants/sponsorships from Jazz Pharmaceuticals, Harmony Biosciences, Avadel, and Takeda Pharmaceuticals to support patient programming. These grants represent approximately 80% of the funding received through pharmaceutical grants/sponsorships for the most recent year.*

Emily Clegg Barker, PhD, Freelance Medical Communicator; Person with Narcolepsy; Patient Advocate

- *Dr. Barker has received honoraria from Jazz Pharmaceuticals and compensation for supporting advisory boards from Jazz Pharmaceuticals and Centessa Pharmaceuticals. Dr. Barker volunteers with Wake Up Narcolepsy as a peer support facilitator.*

Clinical Experts

Luis Ortiz, MD, Sleep Medicine Physician, John Hopkins All Children's Hospital; Assistant Professor of Pediatrics, John Hopkins University School of Medicine

- *Dr. Ortiz has received fees for serving on advisory boards for Harmony Biosciences, Jazz Pharmaceuticals, and Avadel regarding pitolisant and oxybate products.*

Thomas Scammell, MD, Professor of Neurology, Harvard Medical School

- *Dr. Scammell has received consulting fees from Takeda, Jazz Pharmaceutical, Harmony Biosciences, Avadel Pharmaceuticals, and Merck over the last three years. He also serves on the medical advisory board for Wake Up Narcolepsy and Narcolepsy Network.*

ICER Speakers

Sarah K. Emond, MPP
President & CEO, ICER

Grace Lin, MD
Evidence Author,
Medical Director for HTA, ICER

Foluso Agboola, MBBS, MPH
Senior Vice President of Research, ICER

Linda Luu, MSc
Lead Modeler and Research Scientist, Department of Pharmacy, University of Washington

Why are we here today?

“Imagine living 72 hours without sleep, and the rest of the world still expects you to perform as if you got 8 hours of sleep. That is what living with narcolepsy is like. There is never a moment when I feel fully awake or alert. My daily life revolves around managing my symptoms. It requires so much physical and emotional energy that I’ve had to reconsider what responsibilities I can realistically take on; while many of my friends are starting families, I have chosen not to have children.”

Patient stories from ICER Share Your Story submission

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - What are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

GALLUP

APRIL 1, 2025

In U.S., Inability to Pay for Care, Medicine Hits New High

Rates among Hispanic, Black adults and those with lower incomes worsen markedly since 2021

FIERCE Healthcare

FINANCE

Only 1 in 4 employers able to 'absorb' increasing health benefit costs without impacting business

By Cailey Gleeson · Apr 29, 2026 1:00pm

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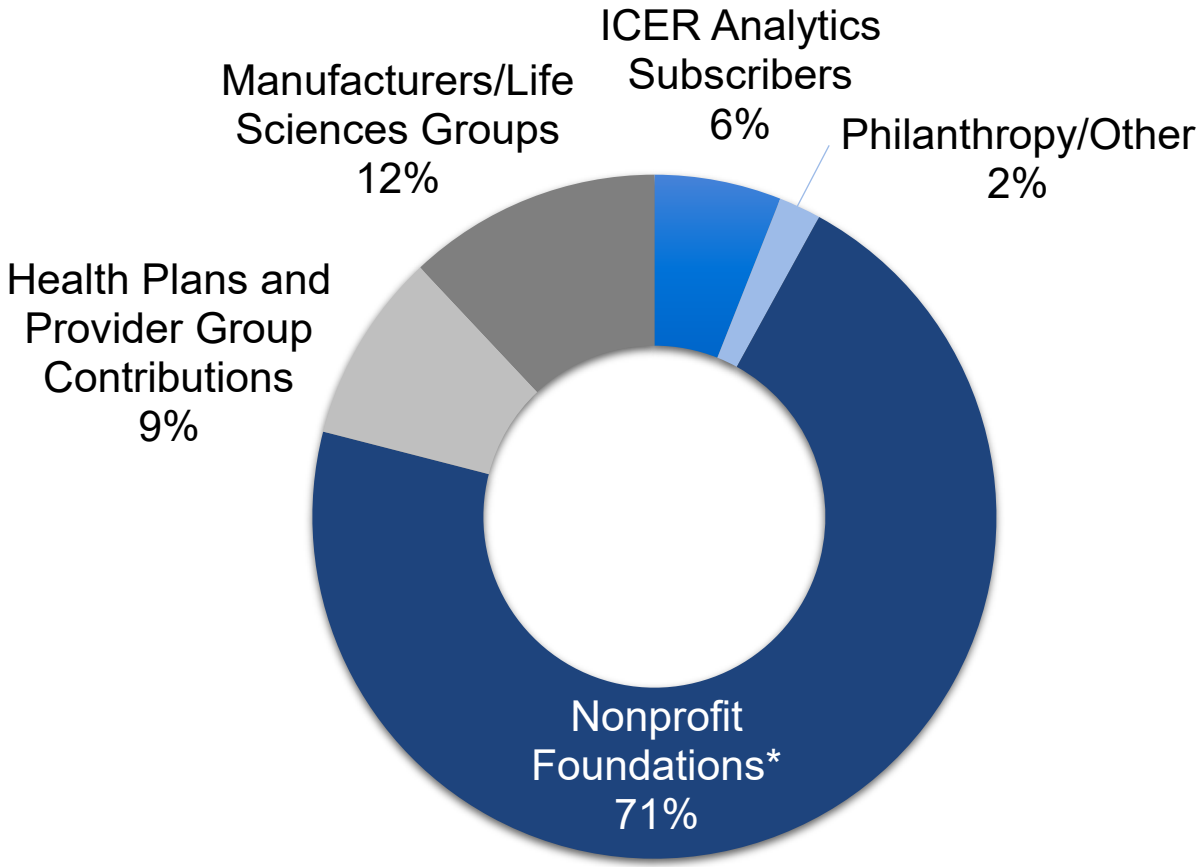
https://www.modernhealthcare.com/insurance/mh-healthy-workers-company-insurance-premiums/

Organizational Overview

2026 Funding and Managing COIs



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ICER Policy Summit and non-report activities only

*ICER received significant funding from Arnold Ventures and the Peterson Center on Healthcare, LLC (represented on our "Sources of Funding" page under "Non-profit Foundations").

How Was the ICER Report Developed?

Guidance from patients, clinical experts, manufacturers, and other stakeholders

Evidence analysis in collaboration with the **University of California, San Francisco** and cost-effectiveness modeling in collaboration with the **University of Washington**

- **Tammy Anderson,** Executive Director, Wake Up Narcolepsy
- **Kiran Maski, MD, MPH**, Associate Professor, Neurology, Boston Children's Hospital
- **Katherine Sharkey, MD, PhD**, Professor of Psychiatry and Behavioral Medicine and of Internal Medicine, Wake Forest University School of Medicine
- **Sonya Snedecor, PhD,** Chief Simplicity Officer, Science Clarity

Structured to support **Midwest CEPAC** voting and policy discussion

Value Assessment Framework: Long-Term Value for Money

Agenda (CT)

10:00 AM	Meeting Convened and Opening Remarks
10:15 AM	Presentation of the Clinical Evidence
10:55 AM	Presentation of the Economic Model
11:35 AM	Manufacturer Feedback on Economic Modeling
11:50 AM	Public Comments and Discussion
12:15 PM	Lunch Break
1:00 PM	Midwest CEPAC Deliberation and Vote
1:55 PM	Break
2:10 PM	Policy Roundtable Discussion
3:40 PM	Reflections from Midwest CEPAC
4:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Grace Lin, MD, MAS

Medical Director, Health Technology Assessment, ICER

Professor of Medicine and Health Policy, University of California, San Francisco

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Key Team Members

Team Member	Title
Grace Lin, MD, MAS	Evidence Author; Medical Director, Health Technology Assessment, ICER; Professor of Medicine, UCSF
Dmitriy Nikitin, MSPH	Senior Research Lead, ICER
Sol Sanchez, BA	Research Assistant, ICER

Disclosures

- Financial support provided to UCSF from ICER for this report. GL also reports receiving research grant funding from the National Institutes of Health, Mt. Zion Health Fund, GRAIL, Inc., and the California Health Benefits Research Program.
- DN and SS are employees of ICER and have no conflicts to disclose.

Narcolepsy Background

- Chronic neurological disorder characterized by sleep-wake cycle disruptions
- Affects 1 in 2000 people, males and females equally
- Onset usually in adolescence or young adulthood
- Two types
  - Narcolepsy Type 1 (NT1): characterized by loss of orexin-producing neurons in hypothalamus and low orexin levels
  - Narcolepsy Type 2 (NT2): unknown etiology, normal orexin levels

Symptoms of NT1

- Excessive daytime sleepiness (EDS)
- Daytime “sleep attacks”
- Disrupted nighttime sleep (fragmented night sleep, sleep paralysis)
- Cataplexy (sudden loss of muscle control)
- Hallucinations (going to/coming out of sleep)
- Cognitive impairment

Diagnosis of NT1

- Diagnosis is established by history of ≥3 months of excessive daytime sleepiness (EDS) and at least one of the following:
  - Cataplexy
  - Low orexin levels in cerebrospinal fluid
  - Abnormal Multiple Sleep Latency Test (MSLT)
- HLA-DQB1*06:02 allele strongly associated with NT1; positive blood test supports diagnosis
- Diagnosis can be delayed for years; usually requires specialist (neurologist or pulmonologist specializing in sleep medicine)

Standard of Care and Management

- Currently no treatments that address underlying cause of NT1
- Daytime naps and consistent sleep schedule are important
- Polypharmacy is common
  - Wake-promoting agents (e.g., modafinil, methylphenidate) address EDS but not cataplexy
  - Anticataplexy agents (e.g., antidepressants such as venlafaxine)
  - Agents to address both EDS and cataplexy (e.g., sodium oxybate, pitolisant)
- Even with combination therapy, most people living with NT1 not satisfied with treatment

Insights from Discussions with Patients

- Symptoms of NT1 affects all aspects of daily life
- Cataplexy episodes can be embarrassing and unpredictable
- Diagnosis is often delayed, specialists are hard to find
- Large impact on caregivers
- Current treatment usually involves multiple medications
  - College can be a particular challenge since some treatments are controlled substances
  - Insurance coverage can be a substantial barrier

Oveporexton

- First-in-class selective orexin-receptor-2 (OX2R) agonist
- Oral medication, 1 or 2 mg twice daily
- New drug application accepted in February 2026, decision expected by third quarter of 2026

Scope of Review

- To examine the clinical effectiveness and safety of oveporexton as monotherapy for the treatment of adults with NT1 compared with the following treatment options:

  (1) No pharmacological treatment, represented by the placebo arms evaluated in the clinical trials

  (2) Combination therapy of modafinil/armodafinil with venlafaxine

  (3) Sodium oxybate

  (4) Pitolisant

Outcomes of Interest

- Daytime symptoms (e.g., Epworth Sleepiness Scale [ESS] Score, Maintenance of Wakefulness [MWT], cataplexy events)
- Nighttime symptoms (e.g., sleep paralysis, sleep-related hallucinations)
- Work or school performance
- Quality of life measures (e.g., HRQoL, cognitive and fatigue symptoms)
- Adverse events associated with treatment, including discontinuation

Clinical Evidence

Key Clinical Trials - Oveporexton

- Two Phase III randomized, controlled trials (FirstLight, RadiantLight), one Phase II trial, all enrolling patients with NT1
- Approximately 100 patients in each Phase III trial
- Baseline mean ESS score 17-19 (normal ≤10)
- Baseline mean MWT of 4-6 minutes
- Baseline median weekly cataplexy rate of 11-27

ESS: Epworth Sleepiness Scale, MWT: Maintenance of Wakefulness Test, NT1: narcolepsy type 1

Meta-Analysis: Oveporexton Trials

Outcome	Meta-Analysis Results Oveporexton versus Placebo
MWT, Mean Difference (95% CI), Minutes	19.59 (17.3 to 21.88)
ESS, Mean Difference (95% CI), Points	-9.84 (-11.58 to -8.10)
Treatment Response (ESS ≤10), RR (95% CI)	5.64 (3.45 to 9.23)

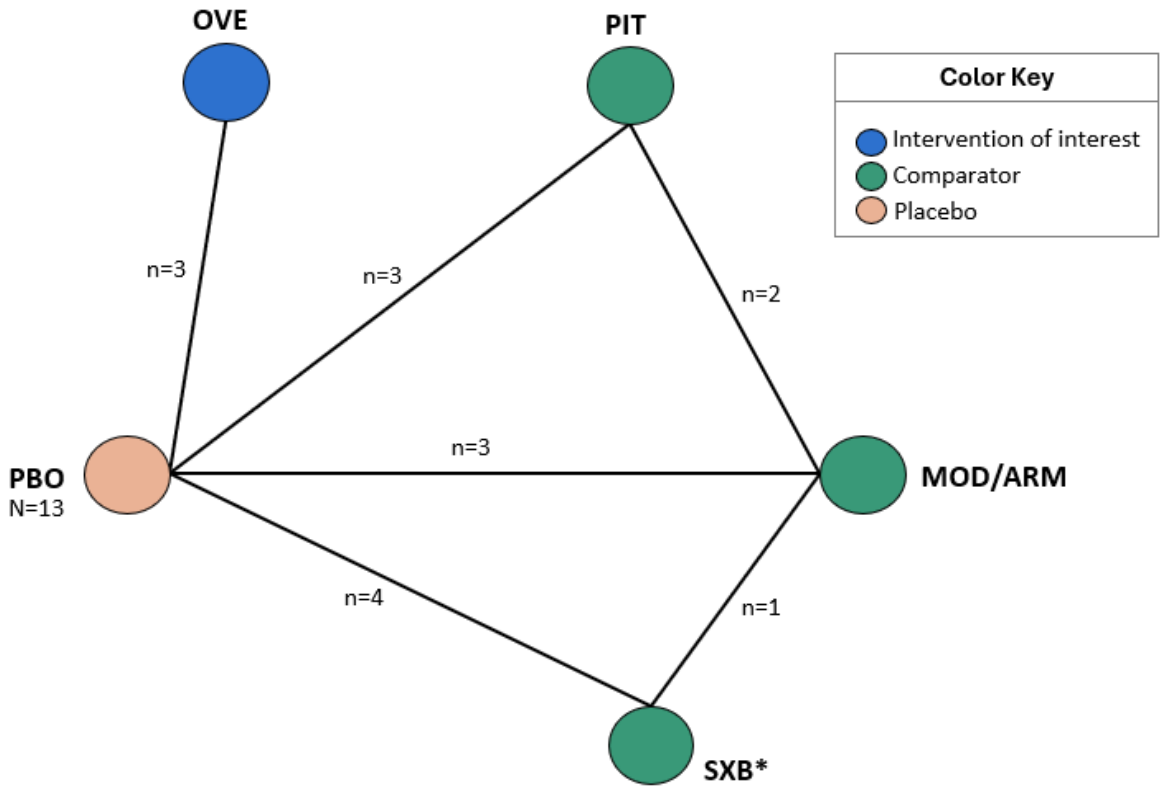
CI: confidence interval, ESS: Epworth Sleepiness Scale, MWT: Maintenance of Wakefulness Test, RR: risk ratio

Cataplexy and Other Patient-Important Outcomes

- Oveporexton decreases weekly cataplexy attacks by 62-75% compared with placebo
- Treatment with oveporexton resulted in:
  - Clinically significant improvement in combined outcome of sleepiness, cataplexy, hallucinations, and disrupted nighttime sleep
  - Improved memory and cognition
  - Improved health-related quality of life

Network Meta-Analysis: Oveporexton versus Active Comparators

- 13 trials, including the following comparators: modafinil/armodafinil (3), sodium oxybate (5), pitolisant (3), oveporexton (2)
- Combined data from high sodium oxybate forms due to similar efficacy for primary outcome
- Trial follow-up ranged from 4-13 weeks



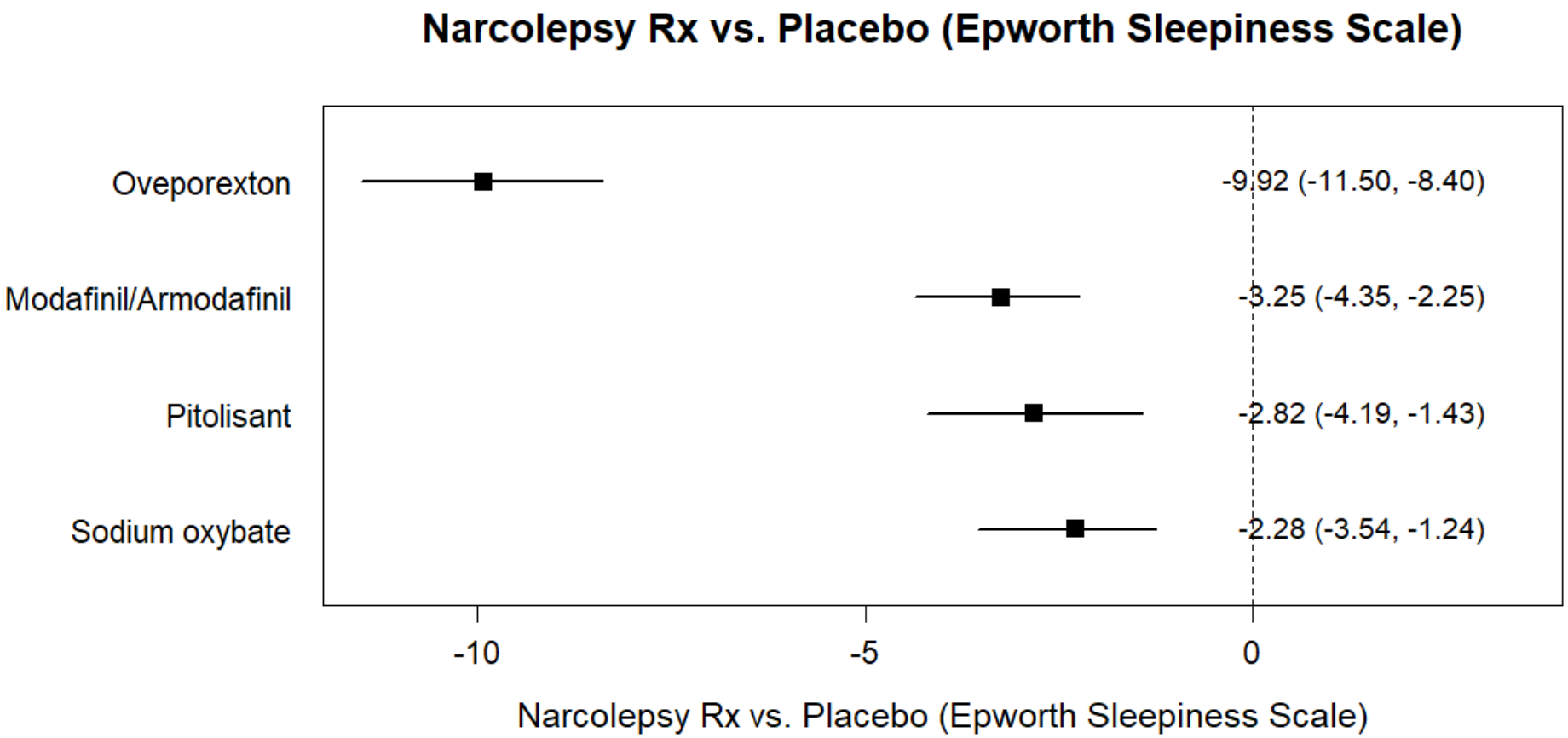
* Studies in our network included the once and twice nightly formulations, but not the mixed salts/low-sodium formulation.

MOD/ARM: modafinil/armodafinil, N: number, OVE: oveporexton, PBO: placebo, PIT: pitolisant, SXB: sodium oxybates

NMA Outcome – Maintenance of Wakefulness (minutes)

Oveporexton				
14.99 (10.04, 20.24)	Sodium Oxybate			
15.56 (11.07, 20.35)	0.6 (-3.73, 4.88)	Modafinil/Armodafinil		
18.48 (12.96, 23.92)	3.5 (-1.98, 8.48)	2.93 (-1.57, 6.97)	Pitolisant	
20.01 (16.32, 23.99)	**5.01 (1.63, 8.38)**	**4.43 (1.76, 7.15)**	1.51 (-2.22, 5.78)	Placebo

NMA Outcome – Daytime Sleepiness



Limitations of Comparisons versus Active Treatment

- Sodium oxybates are grouped together, data comes from higher sodium forms
- Not able to compare on cataplexy and other patient-important outcomes
- Some studies included both NT1 and NT2 patients
- Different trial protocols – e.g., washout versus withdrawal studies, differences in MWT protocols – introduce uncertainty into NMA results

MWT: Maintenance of Wakefulness Test, NMA: network meta-analysis, NT1: narcolepsy type 1, NT2: narcolepsy type 2

Harms - Oveporexton

Key Points

- Pooled safety review of oveporexton trials showed drug was well tolerated
- Most common adverse events were frequent urination and insomnia
- Low rates of serious adverse events (1%) and discontinuation (2.6%)
- No evidence of drug-induced liver injury
- Long-term extension trial has not found any new harms

Controversies and Uncertainties

Key Points

- Oveporexton studied as monotherapy, uncertain whether there will be need for combination therapy in real-world use
- Efficacy of oveporexton versus current combination therapies is not known
- Combining sodium oxybate products may not capture all unique benefits from the different forms and dosages
- Lack of subgroup data, especially children

Benefits Beyond Health and Special Ethical Priorities

Key Points

- Current treatments do not address the underlying orexin deficiency characteristic of NT1
- Treatment with oveporexton is likely to improve caregiver quality of life if treatment allows persons living with NT1 the ability to participate more fully in daily activities, work, etc.

Public Comments Received

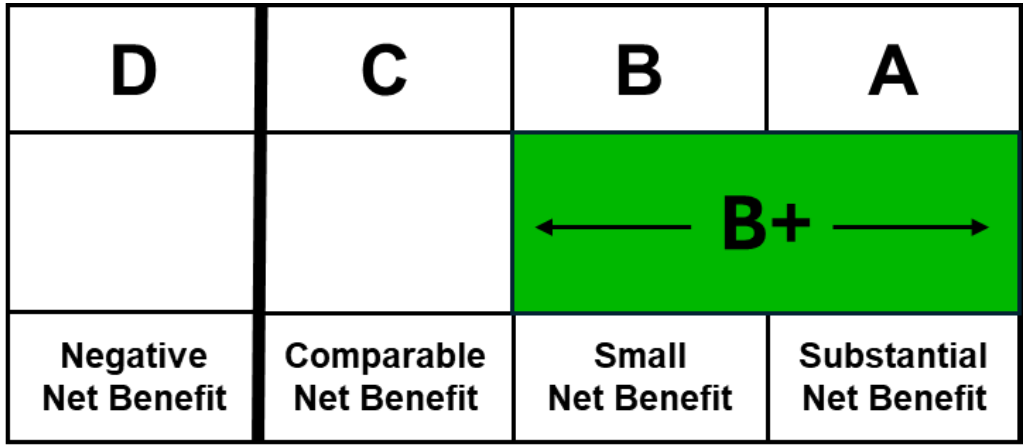
- Sodium oxybate products have differing properties, and thus combining them for the NMA analysis is not appropriate
  - Efficacy is similar across forms
  - Trials included in NMA are from higher sodium forms
- Oveporexton was studied as monotherapy; there is no evidence that NT1 patients will need combination therapy

Summary

- Narcolepsy is a chronic neurological disease with lifelong effects on daily life activities.
- Oveporexton is the first drug to address the underlying orexin deficiency characteristic of NT1.
- Treatment with oveporexton resulted in larger improvements in daytime sleepiness than active comparator drugs, as well as reducing cataplexy.
- Harms of oveporexton appear minimal but long-term studies are needed to confirm.

Evidence Ratings of Oveporexton in People with NT1

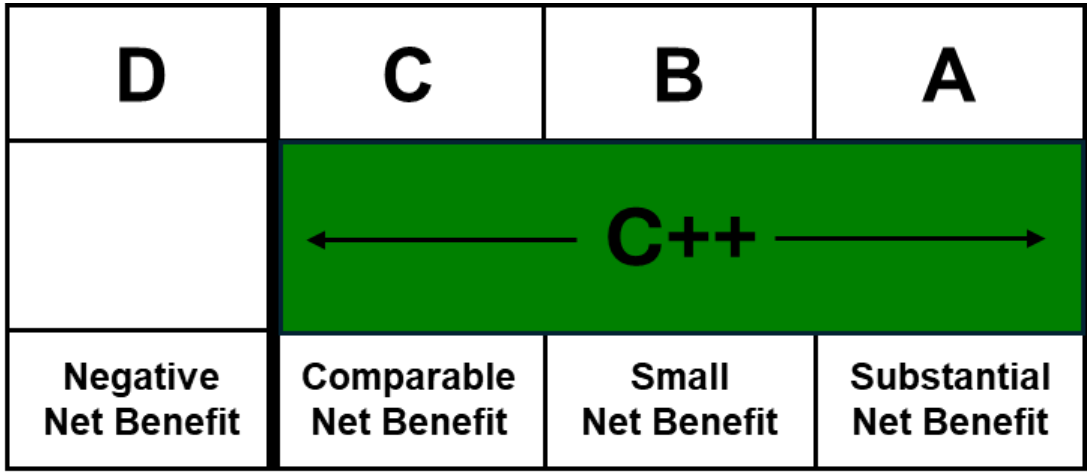
Oveporexton *versus* **Placebo**



At least a small net health benefit, and possibly substantially better

Evidence Ratings of Oveporexton in People with NT1

Oveporexton *versus* **Modafinil + venlafaxine**
Sodium oxybate
Pitolisant



At least as good, and possibly somewhat to substantially better

Questions?

Presentation of the Economic Model

Linda Luu, MSc

Research Scientist

University of Washington

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Key Team Members

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Marie Phillips, BA	Health Economics Research Assistant, ICER

Disclosures

Financial support provided to the University of Washington from the Institute for Clinical and Economic Review (ICER)

JC has received consulting fees from Takeda, not related to Narcolepsy.

Other members have no conflicts to disclose.

Objective

To evaluate the lifetime cost-effectiveness of oveporexton compared to:

(1) Combination therapy of modafinil with venlafaxine

(2) Sodium oxybate

(3) Pitolisant

(4) No pharmacological treatment

for the treatment of Narcolepsy Type 1 (NT1) in adults.

Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
Narcolepsy Type 1	10.4	25%
Other Example Conditions		
Hemophilia	10.9	22%
Multiple Sclerosis	18.9	52%
Osteoporosis	2.6	19%

evLY: equal value of life years

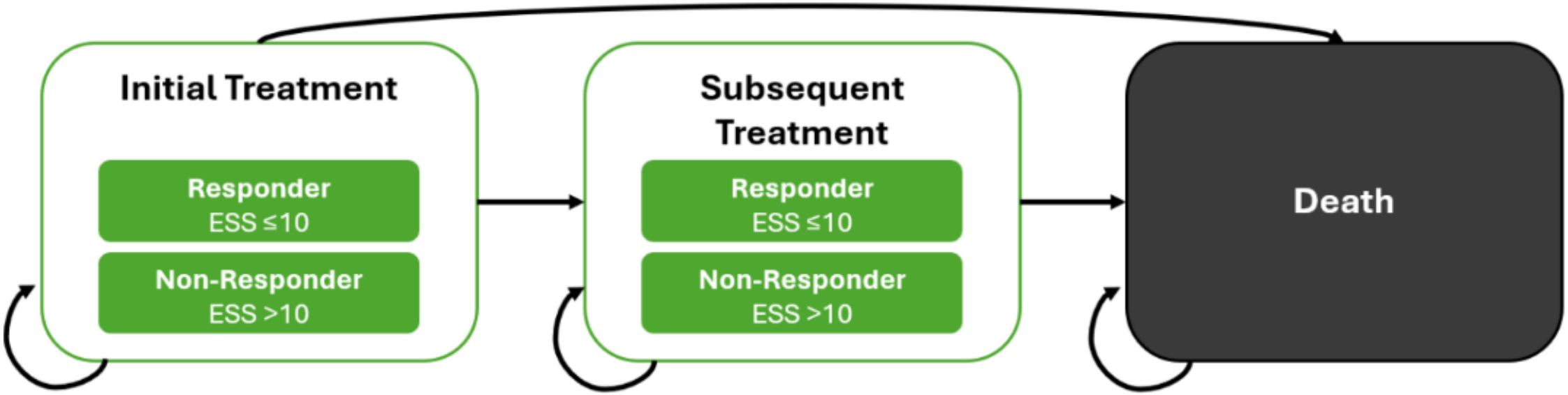
Methods in Brief

Methods Overview

Domain	Approach
Model	Markov Model
Setting	United States
Perspective	Health Care Sector Perspective and Modified Societal Perspective
Time Horizon	Lifetime
Discount Rate	3% per year (costs and outcomes)
Cycle Length	3 months
Primary Outcome	Total costs, QALYs and evLYs, Cost per QALY gained, Cost per evLY gained

evLY: equal value of life years, QALY: quality-adjusted life years

Model Schematic



Initial treatment may be oveporexton, modafinil + venlafaxine, sodium oxybate, pitolisant, or no pharmacological treatment.

Health state utilities are treatment-based and not impacted by responder status.

Model Characteristics

- Based on patient population in 2 mg twice daily and placebo arms of the FirstLight and RadiantLight trials

Baseline Characteristic	Value	Source
Mean (SD) Age, Years	30.4 (10.9)	The FirstLight and RadiantLight Trials
Female, %	56.6	
Mean (SD) ESS Score	18.1 (3.3)	

Key Assumptions

Assumption	Rationale
1. **Treatment effectiveness remains constant over the lifetime.**	• Limited long-term data on treatment effect
2. **Patients discontinuing initial treatment transition to a subsequent treatment basket.**	• No robust evidence to inform specific switching patterns
3. **Venlafaxine affects only cataplexy; modafinil affects only EDS and drives HRQoL changes.**	• No evidence to model synergistic effects • Literature on HRQoL in narcolepsy identifies sleepiness, but not cataplexy, as a significant driver (Vignatelli 2011, Raggi 2019, Dodel 2007)

Key Assumptions

Assumption	Rationale
4. Patients achieving response (ESS ≤10) have no EDS and incur non-drug and productivity costs equal to controls without narcolepsy.	• Insufficient evidence to model costs at a more granular level • Healthcare use and productivity expected to improve as EDS resolves
5. Treatments have no impact on mortality in the base.	• Insufficient evidence that any narcolepsy treatment reduces disease-related mortality

Key Model Inputs: Response

- **Responder:** ESS ≤10 (no EDS)
- **Non-responder:** ESS >10 (mild–severe EDS)

Treatment	Responders	Source
Oveporexton	81%	ICER NMA
Modafinil + Venlafaxine	40%	ICER NMA
Sodium Oxybate	56%	REST-ON
Pitolisant	32%	ICER NMA
No Pharmacological Treatment	15%	ICER NMA

EDS: excessive daytime sleepiness, ESS: Epworth Sleepiness Scale, NMA: Network Meta-Analysis

Key Model Inputs: Discontinuation

Treatment	1st Cycle		Up to 2 Years		Source
	AE	LOE	AE	LOE	
Oveporexton	2.76%	0%	1.09%	0%	FirstLight, RadiantLight, Phase II LTE
Modafinil + Venlafaxine	5.66%	2.20%	2.64%	3.85%	US Modafinil in Narcolepsy Multicenter Study Group 1998 and 2000, Mitler 2000, Moldofsky 2000
Sodium Oxybate	21.19%	1.87%	1.45%	0.43%	Ahmed 2005, Black 2006, REST-ON, Mayer 2018, Bogan 2023, Roy 2024
Pitolisant	2.17%	9.86%	2.80%	5.29%	HARMONY 1, HARMONY CTP, HARMONY 3

Note: All displayed rates are for 3 months

- After 2 years: 0.39% AE / 0.39% LOE, applied to all treatments (HARMONY 3)

AE: adverse event, LOE: lack of efficacy, LTE: long term extension

Key Model Inputs: Subsequent Treatment

- Mixture of comparator treatments with proportions based on survey data (Ortiz 2025)
- Patients could retry initial treatment in the subsequent treatment state
- Treatment effectiveness assumed equal in initial versus subsequent treatment

Treatment	Proportion	Source
Modafinil + Venlafaxine	38%	Ortiz 2025
Sodium Oxybate	32%	
Pitolisant	11%	
No Pharmacological Treatment	19%	

Key Model Inputs: Treatment Costs

Intervention (Dosage)	WAC	Net Annual Cost	Source
Oveporexton (2 mg BID)	$171.12/mg*	$250,000*	IPD Analytics
Modafinil (200 mg)	$0.0063/mg	$460.22	RedBook
Venlafaxine (75 mg)	$0.0060/mg	$164.36	
Sodium Oxybate (3.75 g BID)	$58.54/g	$160,363	
Pitolisant (Wakix®)	$25.06/mg	$216,392	RedBook with 17.6% discount from SSR Health

*Placeholder Price

BID: twice daily, g: grams, mg: milligrams, WAC: wholesale acquisition cost

Key Model Inputs: Annual Costs

Non-Drug Costs

Parameter	Non-Responders Mean (SD)	Responders Mean (SD)	Source
Outpatient Care	$9,245 (14,854)	$4,934 (8,686)	Doane 2025
Emergency Room	$2,822 (7,916)	$1,742 (6,215)	
Hospitalization	$25,749 (72,889)	$16,647 (76,399)	

Mild to Severe EDS: ESS >10, No EDS: ESS ≤10

Productivity Costs (Scenario Analysis)

Parameter	Non-Responders Mean (SD)	Responders Mean (SD)	Source
Absenteeism	$12,267 (19,314)	$6,191 (12,048)	Doane 2025
Presenteeism	$18,814 (16,460)	$11,913 (13,971)	

Mild to Severe EDS: ESS >10, No EDS: ESS ≤10

EDS: excessive daytime sleepiness, ESS: Epworth Sleepiness Scale, SD: standard deviation

Key Model Inputs: Utilities

- Age-specific utilities from the US population (Jiang 2021), adjusted by a multiplier for NT1 with no pharmacological treatment

Treatment	Base Case Utility (Trial-Based)	Source	Scenario Utility (ESS-Based)	Source (Scenario)
Oveporexton	0.960	FirstLight, RadiantLight	0.912	ICER NMA, Cambron-Mellot 2022
Modafinil + Venlafaxine	0.781	Beusterien 1999, Ara 2009	0.844	
Sodium Oxybate	0.776	Bogan 2016, Ara 2009	0.844	
Pitolisant	0.771	Harmony CTP	0.844	
No Pharmacological Treatment	0.760	FirstLight & RadiantLight	0.760	

Note: Utilities displayed are for the mean baseline age of 30

ESS: Epworth Sleepiness Scale, NMA: network meta-analysis, NT1: Narcolepsy Type 1

Key Model Inputs: Mortality

- Elevated mortality rates were applied to all patients regardless of treatment and response status
- Scenario analyses removed elevated mortality from:
    1. Responders
    2. All patients

Mortality Parameter	Value (95% CI)	Source
SMR Males	1.56 (1.43–1.72)	Ohayon 2014
SMR Females	1.43 (1.31–1.57)	Ohayon 2014
All-Cause Mortality	Varies by age and sex	US Life Tables

CI: confidence interval, SMR: standardized mortality ratio, US: United States

Results

Base-Case Results: Versus Active Comparators

Drug	Intervention Acquisition Costs*†	Subsequent Treatment Acquisition Costs†	Total Cost*	QALYs	evLYs	LYs
Oveporexton	$3,884,000	$649,000	$5,192,000	20.11	20.11	24.05
Modafinil + Venlafaxine	$9,600	$1,055,000	$1,809,000	17.29	17.29	24.05
Sodium Oxybate	$2,456,000	$318,000	$3,503,000	17.25	17.25	24.05
Pitolisant	$2,268,000	$791,000	$3,816,000	17.20	17.20	24.05

*For oveporexton, results are based on a placeholder price
†Results have been slightly revised since the report was posted and will be updated in the final evidence report.

Base-Case Results: Versus Active Comparators

Incremental Results

Treatment	Comparator	Cost per QALY Gained*	Cost per evLY Gained*	Cost per Life Year Gained*
Oveporexton	**Modafinil + Venlafaxine**	$1,201,000	$1,201,000	No difference in life years
	Sodium Oxybate	$589,000	$589,000	No difference in life years
	Pitolisant	$472,000	$472,000	No difference in life years

*Based on placeholder price for oveporexton

Base-Case Results: Versus No Treatment

Drug	Intervention Acquisition Costs*	Total Cost*	QALYs	evLYs	LYs	Cataplexy Attacks†
Oveporexton	$3,883,898	$4,573,789	19.99	19.99	24.05	23,093
No Pharmacological Treatment	$0	$857,381	16.88	16.88	24.05	39,832

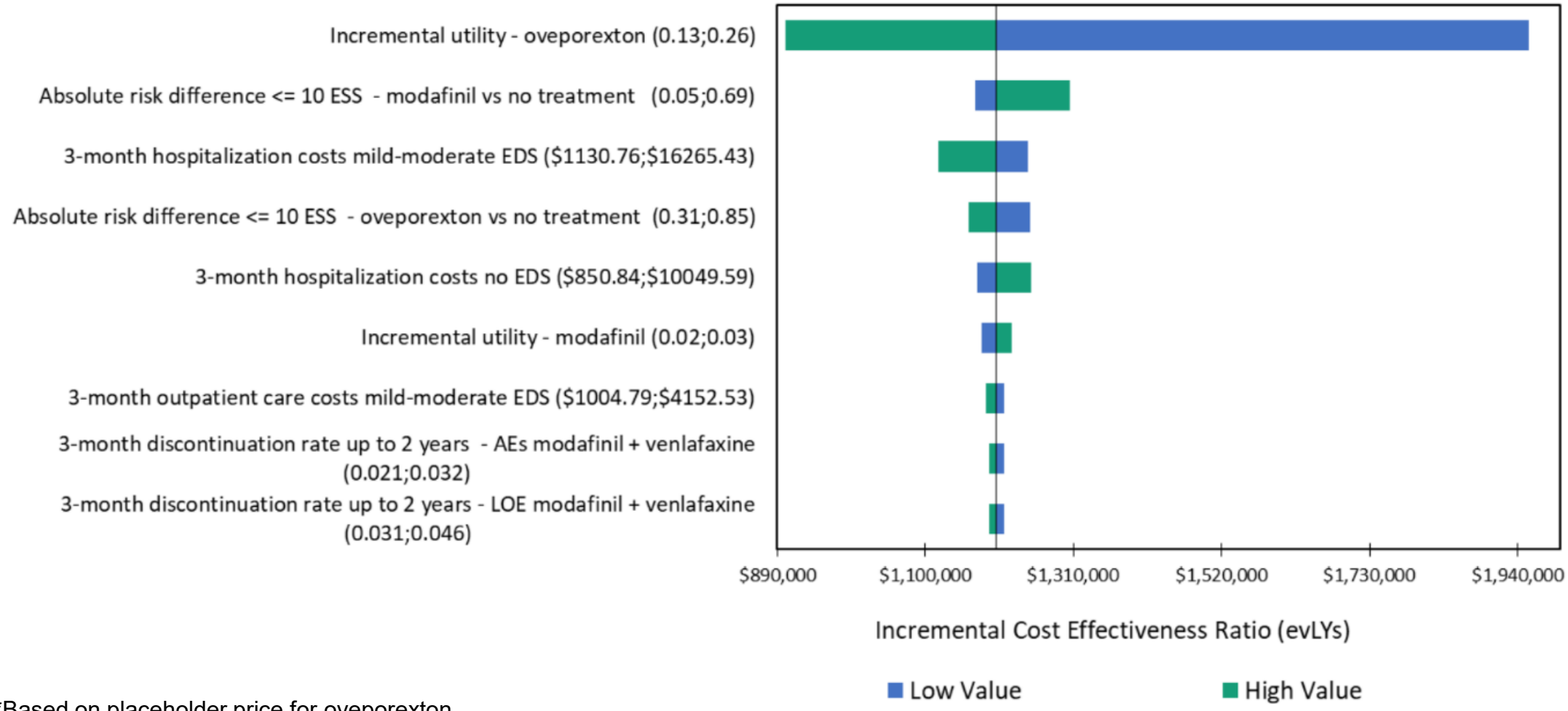
*For oveporexton, results are based on a placeholder price
†Cataplexy Attacks are undiscounted

Incremental Results

Treatment	Comparator	Cost per QALY Gained*	Cost per evLY Gained*	Cost per Life Year Gained*
Oveporexton	**No Pharmacological Treatment**	$1,196,000	$1,196,000	No difference in life years

*Based on placeholder price for oveporexton

One Way Sensitivity Analyses



*Based on placeholder price for oveporexton

AEs: adverse events, EDS: excessive daytime sleepiness, ESS: Epworth Sleepiness Scale, evLYs: equal value of life years, LOE: lack of efficacy

Probabilistic Sensitivity Analysis

Treatment	Comparator	Cost-Effective at $50,000 per evLY*	Cost-Effective at $100,000 per evLY*	Cost-Effective at $150,000 per evLY*
Oveporexton	Modafinil + Venlafaxine	0%	0%	0%
	Sodium Oxybate	0%	0%	0%
	Pitolisant	0%	0%	0%
	No Pharmacological Treatment	0%	0%	0%

*Based on placeholder price for oveporexton

Scenario Analyses

1. Modified societal perspective (with productivity costs)
2. Exclusion of unrelated healthcare costs
3. ESS-based utilities
4. Sodium oxybate market share weighting
5. Sodium oxybate real-world dosing (8.25 g daily)
6. Removal of excess mortality in responders
7. Removal of excess mortality in all patients

Scenario Analyses: Incremental Results (evLY)

- ESS-based utilities roughly doubled to tripled incremental cost effectiveness ratios versus base case
- All other scenarios had results within ~10% of base case

Scenario	Modafinil + Venlafaxine	Sodium Oxybate	Pitolisant
Base Case	$1,200,000	$589,000	$472,000
ESS-Based utilities	$3,200,000	$1,600,000	$1,300,000

*Based on placeholder price for oveporexton

Health Benefit Price Benchmark (HBPB)

Annual Price Benchmark for Oveporexton Compared to Modafinil + Venlafaxine

Annual Prices Using	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold
QALYs Gained	$50,400	$59,400
evLYs Gained	$50,400	$59,400

Limitations

- Trial-based utilities derived from different instruments (SF-6D mapping, EQ-5D VAS) may respond differently to the same clinical change; ESS-based scenario yielded higher incremental cost effectiveness ratios
- Cardiovascular, mental health, caregiver, and broader life course impacts not directly captured due to insufficient evidence — likely underestimates NT1 burden
- Differing protocols across trials and lack of combination treatment data introduce uncertainty in comparator effectiveness

ESS: Epworth sleepiness Scale, NT1: narcolepsy type 1, SF-6D: Short Form 6-Dimension, VAS: visual analog scale

Comments Received

- Updated oveporexton placeholder price from $175,000 to $250,000 annually based on new estimates from IPD Analytics
- Added scenario analyses for sodium oxybate: market share-weighted distribution and real-world dosing
- Expanded Uncertainties and Controversies section to address "no treatment" framing, unmodeled NT1 burden (CVD, mental health, caregiver burden, life course)

Conclusions

- Oveporexton showed meaningful clinical benefit, with gains in QALYs and evLYs relative to all comparators.
- At a placeholder price of $250,000 annually, oveporexton exceeds commonly cited cost-effectiveness thresholds across all comparisons.

Questions?

Sodium Oxybates (Scenario Analyses)

- Scenario analyses
  1. Weighted distribution of all sodium oxybate products based on market share (Takeda)
  2. Real-world dosing: 2/3 patients on 9 g, 1/3 split between 6 g and 7.5 g (clinical expert input)

Sodium Oxybate Product	WAC/g	Discount from WAC	Net Price per Year	Market Share
Generic	$58.54	--	$160,363	29%
XYREM®	$82.88	29.7%	$159,595	8%
XYWAV®	$78.33	29.7%	$150,846	52%
LUMRYZ™	$76.98	42.5%	$121,254	11%

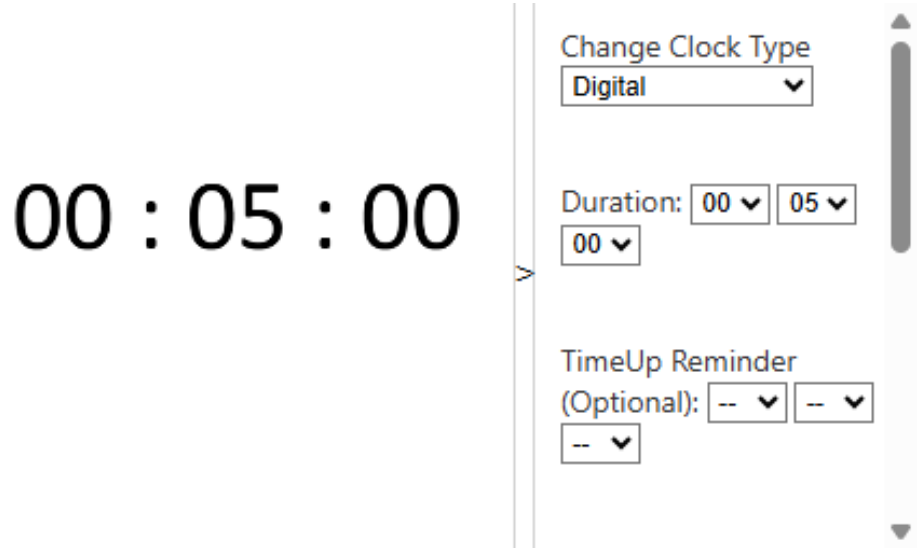
Note: WAC prices from RedBook, discounts for XYREM and XYWAV from SSR Health, discount for LUMRYZ from IPD Analytics

Manufacturer Feedback on Economic Modeling

Phil Naughten, PharmD
Head of US Value and Evidence Generation, Takeda Pharmaceuticals

Conflicts of Interest:

- *Dr. Phil Naughten is a full-time employee of Takeda Pharmaceuticals.*

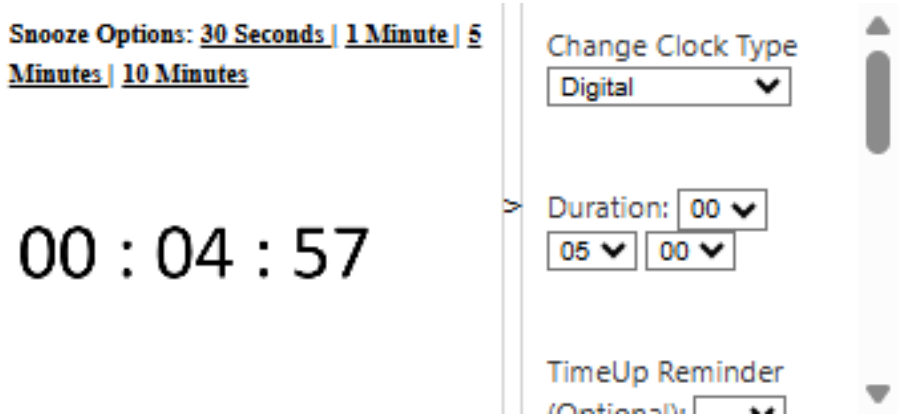


Public Comment and Discussion

Emily Clegg Barker, PhD
Freelance Medical Communicator; Person with Narcolepsy; Patient Advocate

Conflicts of Interest:

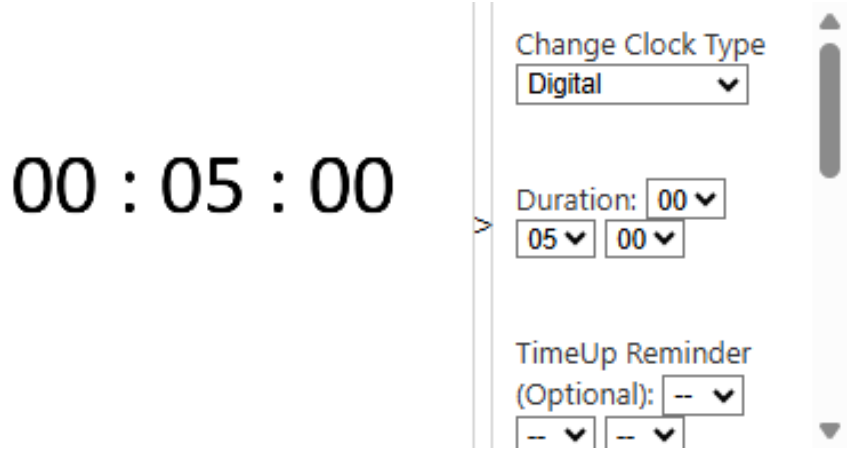
- *Dr. Barker has received honoraria from Jazz Pharmaceuticals and compensation for supporting advisory boards from Jazz Pharmaceuticals and Centessa Pharmaceuticals. Dr. Barker volunteers with Wake Up Narcolepsy as a peer support facilitator.*



Matthew Horsnell
Patient Advocate, Wake Up Narcolepsy

Conflicts of Interest:

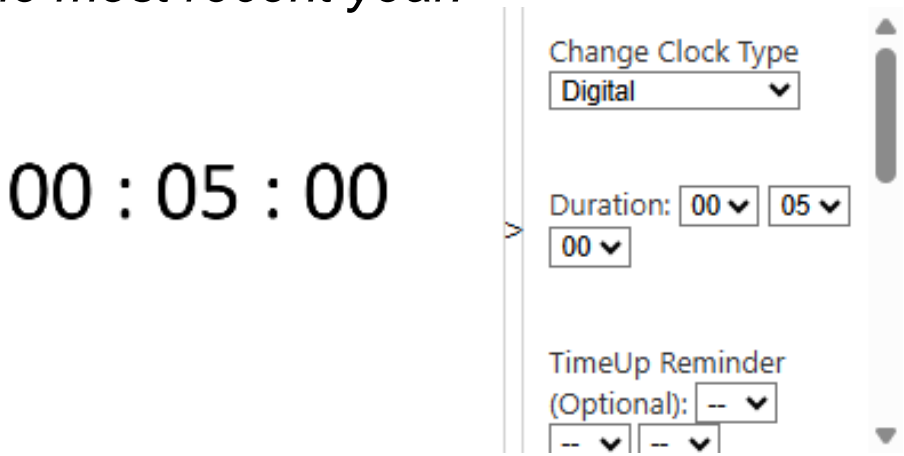
- *Matthew Horsnell has received consulting fees from Avadel Pharmaceuticals and honoraria from Harmony Biosciences. Matthew Horsnell is a patient volunteer for the Hypersomnia Foundation, Project Sleep, and Wake Up Narcolepsy.*



Anne Samarawickrama
Trustee, Wake Up Narcolepsy

Conflicts of Interest:

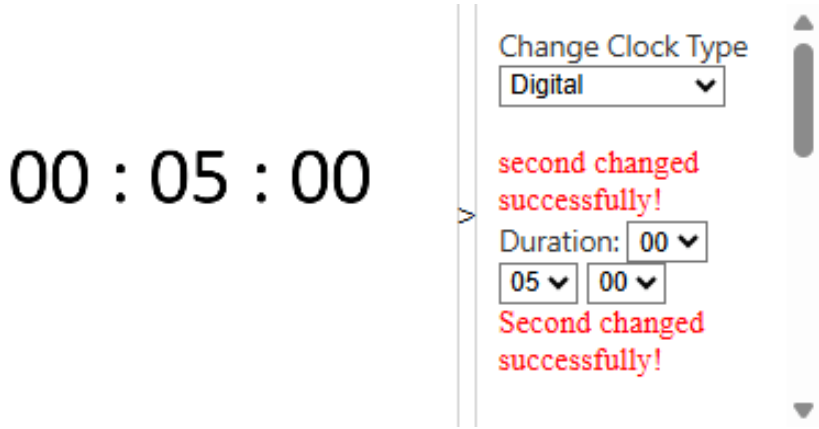
- *Wake Up Narcolepsy receives grants/sponsorships from Jazz Pharmaceuticals, Harmony Biosciences, Avadel, and Takeda Pharmaceuticals to support patient programming. These grants represent approximately 80% of the funding received through pharmaceutical grants/sponsorships for the most recent year.*



Audelia Wittbrodt
Patient; Peer Support Volunteer, Wake Up Narcolepsy and Dysautonomia International

Conflicts of Interest:

- *Audelia Wittbrodt is a patient volunteer for the Dysautonomia International and Wake Up Narcolepsy.*

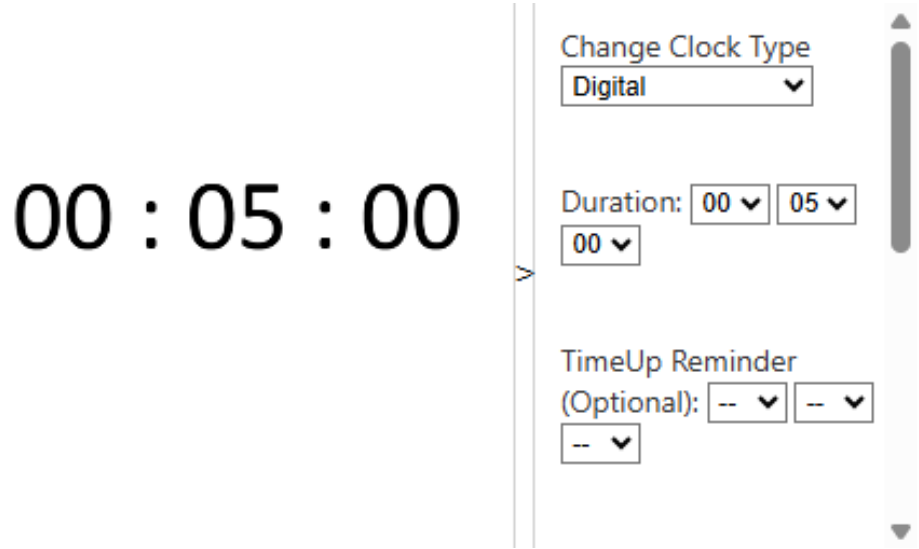


Manufacturer Public Comment and Discussion

Phil Naughten, PharmD
Head of US Value and Evidence Generation, Takeda Pharmaceuticals

Conflicts of Interest:

- *Dr. Phil Naughten is a full-time employee of Takeda Pharmaceuticals.*



Lunch

Meeting will resume at 1:00 PM CT

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Voting Questions

Patient Population for All Questions: Adults with Narcolepsy Type 1

Special Ethical Priorities

To help inform judgements of overall long-term value for money, please answer the following questions:

1. Are there particular obligations to people with this condition because of disease severity and/or unmet need with currently available therapies?

2. Are there particular obligations to people with this condition because it disproportionately affects those from a racial/ethnic group that have not been equitably served by the healthcare system?

3. Apart from issues around disease severity/unmet need and race/ethnicity, are there other particular obligations to people with this condition?

Clinical Evidence

4. Is the current evidence adequate to demonstrate that the net health benefit of oveporexton is greater than that of no pharmacological treatment?

5. Is the current evidence adequate to demonstrate that the net health benefit of oveporexton is greater than that of modafinil with venlafaxine?

6. Is the current evidence adequate to demonstrate that the net health benefit of oveporexton is greater than that of sodium oxybate?

7. Is the current evidence adequate to demonstrate that the net health benefit of oveporexton is greater than that of pitolisant?

Benefits Beyond Health

To help inform judgements of overall long-term value for money, please answer the following questions about oveporexton when compared to sodium oxybates, modafinil plus venlafaxine, pitolisant and no pharmacological treatment:

8. Is oveporexton likely to improve caregivers' quality of life and/or ability to pursue their own education, work, and family life?

9. If payment/cost were not an issue, would oveporexton be likely to improve access to treatment because of its method of delivery and/or treatment setting?

Break

Meeting will resume at 2:10 PM CT

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Tammy Anderson Executive Director, Wake Up Narcolepsy	Tammy Anderson is a full-time employee of Wake Up Narcolepsy. Wake Up Narcolepsy receives grants/sponsorships from Jazz Pharmaceuticals, Harmony Biosciences, Avadel, and Takeda Pharmaceuticals to support patient programming. These grants represent approximately 80% of the funding received through pharmaceutical grants/sponsorships for the most recent year.
Emily Clegg Barker, PhD Freelance Medical Communicator; Person with Narcolepsy; Patient Advocate	Emily Clegg Barker has received honoraria from Jazz Pharmaceuticals and compensation for supporting advisory boards by Jazz Pharmaceuticals and Centessa Pharmaceuticals. She volunteers with Wake Up Narcolepsy as a peer support facilitator.
Becky Faustgen, PharmD Manager, Clinical Pharmacy, UnitedHealthcare	Becky Faustgen is a full-time employee of UnitedHealthcare.
Phil Naughten, PharmD Head of US Value and Evidence Generation, Takeda Pharmaceuticals	Phil Naughten is a full-time employee of Takeda Pharmaceuticals.
Luis Ortiz, MD Sleep Medicine Physician, John Hopkins All Children's Hospital Assistant Professor of Pediatrics, John Hopkins University School of Medicine	Luis Ortiz has received fees for serving on advisory boards for Harmony Biosciences, Jazz Pharmaceuticals, and Avadel regarding pitolisant and oxybate products
Thomas Scammell, MD Professor of Neurology, Harvard Medical School	Over the last three years, Thomas Scammell has received consulting fees from Takeda, Jazz Pharmaceuticals, Harmony Biosciences, Avadel Pharmaceuticals, and Merck.
Emily Tsiao, PharmD, BCPS Senior Clinical Pharmacist, Trend Management Strategies and Programs, Premera Blue Cross	Emily Tsiao is a full-time employee of Premera Blue Cross.

Midwest CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around June 8, 2026
    - Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/narcolepsy-2026/

Adjourn

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