MMV-098-061620-43

SYLLABUS AND COURSE GUIDE

Laying to Rest Challenges in Managing Excessive Daytime Sleepiness in Patients with Obstructive Sleep Apnea or Narcolepsy – *An Augmented Reality Experience*

www.cmeoutfitters.com/sleep20
#SleepAR

FACULTY
Richard K. Bogan, MD, FCCP, FAASM
Michael J. Thorpy, MD

Recorded on Monday, June 15, 2020
Credit Expiration Date: Tuesday, June 15, 2021

This continuing education activity is provided by

CME Outfitters

INFORMATION FOR PARTICIPANTS

Statement of Need

Excessive daytime sleepiness (EDS) is a common symptom of obstructive sleep apnea (OSA) and narcolepsy. EDS is often associated with traffic accidents and occupational incidents, cognitive impairments, and increased risk of medical and psychiatric comorbidities, resulting in poorer quality of life (QoL) and increased mortality. Yet, the burden of EDS is often underestimated and devising effective strategies for management poses a significant challenge.

Advances in sleep medicine have offered increasingly detailed insight into the physiology of the sleep-wake cycle and its associated neurotransmitters. Subsequently, recent clinical trials have revealed the efficacy and safety of novel therapies in improving outcomes in patients with OSA or narcolepsy experiencing EDS. Translating these data into evidence-based practices is critical to reduce the burden of EDS.

This virtual symposium will examine the impact of EDS on clinical outcomes, QoL, and psychosocial functioning as well as the subsequent need for early detection and effective treatment. In order to apply the latest scientific updates in sleep medicine, this symposium will feature Augmented Reality, enabling expert faculty to walk clinicians through the core physiological mechanisms involved in sleep and the means by which current and novel therapies exert their clinical impact. By navigating recent clinical trial data on these therapies, clinicians should be better able to apply the latest evidence to practice, optimizing the management of EDS in patients with narcolepsy or OSA.

Learning Objectives

At the end of this CME/CE activity, participants should be able to:

- Recognize the burden of EDS in patients with OSA or narcolepsy.
- Apply the science of sleep to novel treatments for EDS to optimize treatment selection.
- Integrate efficacy and safety data into treatment decisions for EDS in patients with OSA or narcolepsy to improve QoL and functioning.

The following learning objectives pertain only to those requesting CNE or CPE credit:

- Recognize the burden of EDS in patients with OSA or narcolepsy.
- Explain the science of sleep for novel treatment decisions for EDS in patients with OSA or narcolepsy to improve QoL and functioning.
- Recognize the burden of EDS in patients with OSA or narcolepsy.

Target Audience

Sleep specialists, pulmonologists, psychiatrists, neurologists, PCPs, PAs, NPs, nurses, and pharmacists

Financial Support

Supported by an educational grant from Jazz Pharmaceuticals, Inc.

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Note to PAs: PAs may claim a maximum of 1.5 Category 1 credits for completing this activity. NCCPA accepts *AMA PRA Category 1 Credit™* from organizations accredited by ACCME or a recognized state medical society.

CNE Credit (Nurses)

Provider approved by the California Board of Registered Nursing, Provider Number CEP 15510, for 1.5 contact hours.

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Universal Activity Number: Enduring: 0376-0000-20-010-H01-P
Type: knowledge-based

ABIM/MOC Credit

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.5 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Learning Formats: Enduring material

ABPN MOC Credit

ABPN Diplomates may select any CME activity relevant to their practice to count towards ABPN MOC requirements.

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Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

MIPS Improvement Activity

This activity counts towards MIPS Improvement Activity requirements under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). Clinicians should submit their improvement activities by attestation via the CMS Quality Payment Program website.

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Post-tests, credit request forms, and activity evaluations must be completed online (requires free account activation), and participants can print their certificate or statement of credit immediately (75% pass rate required). This website supports all browsers except Internet Explorer for Mac. For complete technical requirements and privacy policy, visit https://www.cmeoutfitters.com/privacy-and-confidentiality-policy.

There is no fee for participation in this activity. The estimated time for completion is 90 minutes. Questions? Please call **877.CME.PROS**.

FACULTY BIOS & DISCLOSURES

Richard K. Bogan, MD, FCCP, FAASM

Dr. Bogan is the President of Bogan Sleep Consultants, LLC. He is serving as Chief Medical Officer of SleepMed, Inc., the largest sleep diagnostic company in the United States. He is also Associate Clinical Professor at the University of South Carolina School of Medicine and Associate Clinical Professor at the Medical University of South Carolina in Charleston, S.C.

Dr. Bogan received his bachelor's degree in chemistry from Wofford College and his MD degree from the Medical University of South Carolina in Charleston. He served his internship and residency, as well as Chief Medical Resident, at the University of Alabama Hospital and Clinics in Birmingham. Thereafter, he completed a fellowship and assistant professorship in the Pulmonary Division of the Department of Medicine at the University of Alabama School of Medicine. He has been certified by the American boards of Sleep Medicine, Internal Medicine, and Pulmonary Diseases.

Dr. Bogan has served as principal investigator on numerous clinical trials in the past and continues to do so now. He has a variety of publications and research interests that focus on topics such as narcolepsy, insomnia, sleep apnea, shift work sleep disorder, restless legs syndrome/periodic limb movement disorder, chronic fatigue/fibromyalgia, and circadian rhythm abnormality.

Michael J. Thorpy, MD

Dr. Thorpy is a Professor of Neurology at Albert Einstein College of Medicine and Director of the Sleep-Wake Disorders Center in the Department of Neurology at Montefiore Medical Center, both in New York. In addition to treating patients with sleep disorders, he conducts research in narcolepsy, insomnia and sleep apnea. He is President of the New York State Society of Sleep Medicine, Past President of the Sleep Section of the Academy of Neurology, and Past Secretary of the National Sleep Foundation. In 1993 Dr. Thorpy received the Nathaniel Kleitman Award from the American Academy of Sleep Medicine, one of the field's highest honors, and in 2012 he received the Lifetime Achievement Award from the National Sleep Foundation.

Born in New Zealand, Dr. Thorpy earned his medical degree from the University of Otago Medical School. After receiving postgraduate training in Dunedin, New Zealand; Bombay, India; and London, England, he completed his residency in neurology at the State University of New York in Syracuse and a neuroendocrinology fellowship at Albert Einstein College of Medicine and Montefiore Medical Center. Dr. Thorpy is board certified in sleep disorders medicine.

Dr. Thorpy has published extensively on narcolepsy, insomnia, and sleep disorders. He chaired the first International Classification of Sleep Disorders and has published more than 200 peer-reviewed articles and chapters, including publications in journals such as *The New England Journal of Medicine*. His numerous books include *"The Encyclopedia of Sleep and Sleep Disorders", Parasomnias (2010), Sleepiness (2011), Neuroimaging of Sleep and Sleep Disorders (2012), Genetics of Sleep and Sleep Disorders (2013), Narcolepsy: A Clinical Guide (2016)*, and *SleepMultiMedia*, a computerized textbook of sleep medicine (v11.0 2018).

Dr. Thorpy has given more than 100 television, radio, and print interviews on sleep disorders.

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Dr. Bogan reports that he is a consultant for Harmony Biosciences, LLC; and Jazz Pharmaceuticals, Inc. He participates in industry funded research with Avadel/Flamel Ireland LTD; Axsome Therapeutics, Inc.; Balance; Elsai Inc.; Fresca; Jazz Pharmaceuticals Inc.; and Merck & Co., Inc. He is on the speakers bureau for Jazz Pharmaceuticals, Inc.; and Merck & Co., Inc. He is a shareholder, member of the Board of Directors, and Chief Medical Officer and employee of SleepMed, Inc. He receives other financial or material support as a member of the Board of Directors, First Community Corporation, SC and National Sleep Foundation.

Dr. Thorpy reports he receives research support from Avadel Pharmaceuticals; Axsome Therapeutics, Inc.; Balance Therapeutics; Harmony Biosciences, LLC; Jazz Pharmaceuticals, Inc. and Takeda Pharmaceuticals U.S.A., Inc. He is a consultant for Avadel Pharmaceuticals; Axsome Therapeutics, Inc.; Balance Therapeutics; Eisai Inc.; Harmony Biosciences, LLC; Jazz Pharmaceuticals, Inc. and Takeda Pharmaceuticals U.S.A., Inc.

Tony Graham, MD (peer reviewer) has no disclosures to report.

Mae Ochoa, RPh (peer reviewer) has no disclosures to report.

Kashemi D. Rorie, PhD (planning committee) has no disclosures to report.

Evan Luberger (planning committee) has no disclosures to report.

Jan Perez (planning committee) has no disclosures to report.

Sharon Tordoff (planning committee) has no disclosures to report.

Disclosures were obtained from the CME Outfitters, LLC staff: No disclosures to report.

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LAYING TO REST CHALLENGES IN MANAGING EXCESSIVE DAYTIME SLEEPINESS

An Augmented Reality Experience

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2. Complete your post-test and evaluation at the conclusion of the webcast
3. Be sure to fill in your **ABIM ID number** and **DOB** (MM/DD) on the evaluation, so we can submit your credit to ABIM.

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CME for MIPS Improvement Activity

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- Actively participate by responding to ARS questions and/or asking the faculty questions.
- Complete activity posttest and evaluation at the link provided.
- Over the next 90 days, actively work to incorporate improvements in your clinical practice from this presentation.
- Complete the follow-up survey from CME Outfitters in approximately 3 months

CME Outfitters will send you confirmation of your participation to submit to CMS attesting to your completion of a CME for MIPS Improvement Activity.

CME for MIPS IMPROVEMENT ACTIVITY

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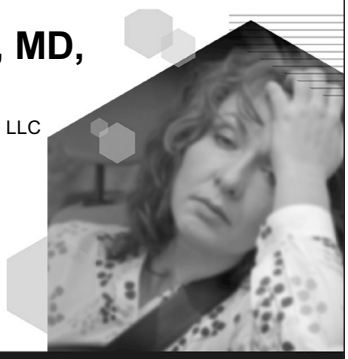

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Learning Objective 1

Recognize the burden of EDS in patients with OSA or narcolepsy.

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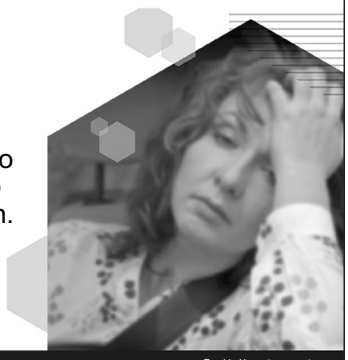
Learning Objective 2

Apply the science of sleep to novel treatments for EDS to optimize treatment selection.



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Learning Objective 3

Integrate efficacy and safety data into treatment decisions for EDS in patients with OSA or narcolepsy to improve QoL and functioning.

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Sleepiness in OSA and Narcolepsy is Nothing to Snooze On

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EDS in OSA and Narcolepsy

- EDS in OSA
  - Despite adequate treatment with CPAP, patients with OSA still have residual EDS[1]
  - The prevalence of residual sleepiness in patients with OSA on CPAP is estimated to be 5% - 10%[2]
- EDS in Narcolepsy[3]
  - Often the first symptom of narcolepsy
  - Identified as the most disruptive symptom by both patients (87.5%) and physicians (92%)

CPAP = continuous positive airway pressure; EDS = excessive daytime sleepiness; OSA = obstructive sleep apnea
1. Foster SN, et al. *Sleep Breath*. 2020 Mar;24(1):143-150.; 2. Launois SH, et al. *Curr Opin Pulm Med*. 2013;19(6):601-698.; 3. Thorpy MJ, et al. *Sleep*. 2019;42(Suppl 1):A236.

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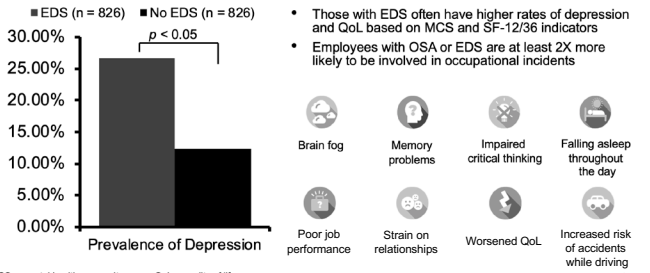
Impact of EDS

An Animated Tour

Provided by #SleepAR CME Outfitters

EDS in OSA and Depressed Mood or QoL



- Those with EDS often have higher rates of depression and QoL based on MCS and SF-12/36 indicators
- Employees with OSA or EDS are at least 2X more likely to be involved in occupational incidents

Brain fog | Memory problems | Impaired critical thinking | Falling asleep throughout the day

Poor job performance | Strain on relationships | Worsened QoL | Increased risk of accidents while driving

MCS = mental health composite score; QoL = quality of life
Leger D, et al. *Sleep Med Rev*. 2020;51:101275.; Gharibi V, et al. *Int J Occup Environ Med*. 2020;11(2):95-107.

Neurotransmitters Involved in the Sleep-Wake Cycle and Their Anatomical Locations

An Animated Tour

Provided by #SleepAR CME Outfitters

Mechanisms of Action of Solriamfetol, Traditional Stimulants, and Other Wake-Promoting Agents

	Affinities and Selectivity
Traditional stimulants (e.g. methylphenidate, dextroamphetamine)	High affinity, non-selective for the DAT, NET, and SERT[1]
Wake-promoting agents (e.g. modafinil)	Low affinity, DAT selective[2]
Solriamfetol	Low affinity, DAT and NET selective[3]
Pitolisant	High affinity, histamine-3 (H3) selective[4]
Sodium oxybate	High affinity, $GABA_B$ selective[5]

DAT = dopamine transporter; NET = noradrenaline transporter; SERT = serotonin transporter
1. Rothman RB, et al. *Synapse*. 2001;39(1):32-41.; 2. Wisor J. *Front Neurol*. 2013;4:139.; 3. Markham A. *Drugs*. 2019;79:785-790.;
4. Center for Drug Evaluation and Research (CDER). *Joint Supervisory Memo – NDA 211150, Pitolisant*. 2019. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/211150Orig1s000SumR.pdf; 5. Available at http://pp.jazzpharma.com/pi/xyrem.ca.PM-en.pdf.

Treatment Decision-Making for EDS in Patients with OSA or Narcolepsy

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FDA-Approved Treatments for EDS

Agent	Indication
Modafinil	Adult patients with excessive sleepiness associated with narcolepsy, OSA, or shift work sleep disorder
Armodafinil	Adult patients with excessive sleepiness associated with narcolepsy, OSA, or shift work sleep disorder
Sodium oxybate	Patients 7 years and older with cataplexy or EDS associated with narcolepsy
Solriamfetol	Adult patients with EDS associated with narcolepsy or OSA
Pitolisant	Adult patients with EDS associated with narcolepsy

*Amphetamines and methylphenidate are approved for ADHD and narcolepsy but not EDS.

ADHD = attention deficit hyperactivity disorder

Drugs@FDA Website.

Interaction of Stimulants with the Sleep-Wake Cycle

An Animated Tour

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Modafinil and Armodafinil: Efficacy

Parameter	Modafinil	Armodafinil
ESS score		
Studies, n (patients)	4 (459)	3 (665)
Change from baseline (95% CI)	-1.94 (-2.67, -1.21)	-2.24 (-3.1, -1.32)
MWT sleep latency, minutes		
Studies, n (patients)	3 (356)	2 (624)
Change from baseline (95% CI)	+3.55 (2.33, 4.78)	+3.60 (2.33, 4.87)

ESS = Epworth Sleepiness Scale; MWT = maintenance of wakefulness test

Sukhal S, et al. *J Clin Sleep Med.* 2015;11(10):1179-1186.; Avellar A, et al. *Sleep Med Rev.* 2016;30:97-107.

Modafinil and Armodafinil: Safety

- Most common AEs (≥ 5%)
  - Headache
  - Nausea
  - Nervousness*
  - Rhinitis*
  - Diarrhea*
  - Back pain*
  - Anxiety*
  - Dizziness
  - Insomnia
  - Dyspepsia*
- Reports of rash, including Stevens-Johnson
- May decrease effectiveness of hormonal contraceptive agents
- May increase heart rate and diastolic and systolic BP

* = ≥ 5% in modafinil but not armodafinil

AE = adverse effect; BP = blood pressure

Volkow ND, et al. *JAMA.* 2009;301(11):1148-1154.; Black JE, et al. *J Clin Sleep Med.* 2010;6(5):458-466.; Drugs@FDA Website.

Stimulants: Safety

- 58 patients who were taking high-dose stimulants for narcolepsy or idiopathic hypersomnia were compared with 58 control patients:[1]
  - High dose stimulants were > 120% recommended maximal doses
  - The prevalence of psychosis, psychiatric hospitalizations, tachyarrhythmias, polysubstance abuse, anorexia and weight loss were significantly increased in the stimulant group
- Greater risk of new-onset psychosis with therapeutic amphetamines[2]
- In 2016, an estimated 5,647,000 persons aged 12 and older reported misuse of prescription stimulants[3]

1. Auger RR, et al. *Sleep*. 2005;28(6):667-672.; 2. Moran LV, et al. *N Engl J Med*. 2019;380(12):1128-1138.;
3. Centers for Disease Control and Prevention [CDC]. *2018 Annual Surveillance Report of Drug-Related Risks and Outcomes*. 2018. https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf.

Novel and Emerging Therapies for EDS in Narcolepsy

Medication	Mechanism of Action	Developmental/ Approval Status
Pitolisant	H_3 receptor antagonist/inverse agonist	FDA-approved Indication: adult patients with EDS associated with narcolepsy
Solriamfetol	Dopamine and norepinephrine reuptake inhibitor	FDA-approved Indication: adult patients with EDS associated with narcolepsy or OSA
JZP-258 (low-sodium oxybate formulation)	$GABA_B$ receptor modulator	Submitted: patients 7 years and older with cataplexy or EDS associated with narcolepsy
FT218 (long-acting sodium oxybate)	$GABA_B$ receptor agonist	Phase III FDA-designated orphan drug: EDS and cataplexy in patients with narcolepsy

GABA = gamma-aminobutyric acid
Thorpy MJ. *CNS Drugs*. 2020;34(1):9-27.

Interaction of Solriamfetol and the Sleep-Wake Cycle

An Animated Tour

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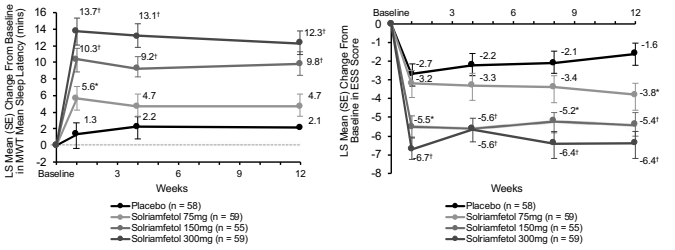
Solriamfetol: Efficacy in Narcolepsy



AEs (≥ 5% and greater than placebo) included headache, nausea, decreased appetite, insomnia, and anxiety.

* $p < .05$; † $p < .0001$ vs. placebo
Thorpy MJ, et al. *Ann Neurol*. 2019;85(3):359-370.

Solriamfetol: Efficacy in Narcolepsy and OSA

Figure A. ESS in 52-Week Maintenance Phase Group

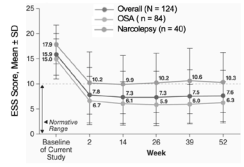
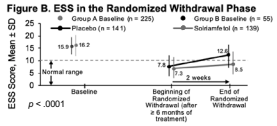


Figure B. ESS in the Randomized Withdrawal Phase



Malhotra A, et al. *Sleep*. 2019;43(2):zsz220.

Figure C. Patient Global Impression of Change (PGI-C) in 52-Week Maintenance Phase Group

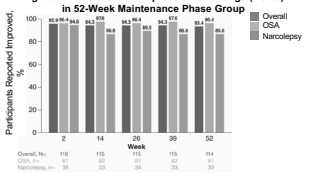
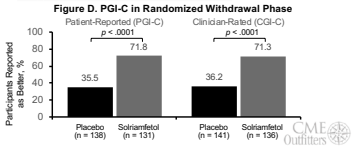


Figure D. PGI-C in Randomized Withdrawal Phase



Solriamfetol: Safety

- In a study of 24 patients with narcolepsy, at 2 hours post-dose, solriamfetol produced significantly lower standard deviation of lateral position (SDLP), or weaving, when driving compared to placebo[1]
- Impact of solriamfetol alone or in conjunction with stimulants on blood pressure and heart rate:
  - At 8 weeks there was no increase in percentage of non-dippers relative to baseline (placebo, 44%; solriamfetol combined [150 and 300 mg doses], 39%[2])
  - Addition of solriamfetol to stimulant therapy did not lead to significant increases in systolic or diastolic blood pressure, heart rate, or mean arterial pressure[3]
- Unlike modafinil/armodafinil and pitolisant, solriamfetol is unlikely to reduce effectiveness of birth control[4]
- Abuse potential comparable to or lower than phentermine in recreational drug users[5]

1. Vinckenbosch F, et al. *Sleep*. 2020;43(Suppl 1):A290; 2. Strollo PJ, et al. *Sleep*. 2020;43(Suppl 1):A293; 3. Meskill GJ, et al. *Sleep*. 2020;43(Suppl 1):A291; 4. Zomorodi K, et al. *J Clin Pharmacol*. 2019;59(8):1120-1129.; 5. Carter LP, et al. *J Psychopharmacol*. 2018;32(12):1351-1361.

Interaction of Pitolisant and the Sleep-Wake Cycle

An Animated Tour

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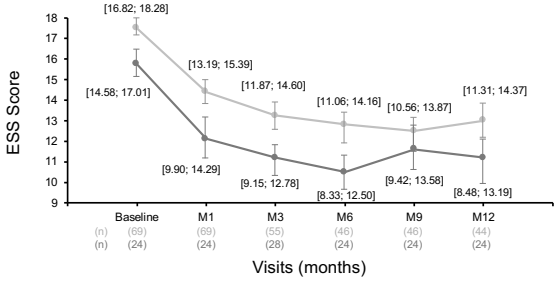
Pitolisant: Efficacy in Narcolepsy



Dauvilliers Y, et al. *Sleep*. 2019;42(11).pii:zsz174.

Pitolisant:* Efficacy in OSA

Parameter	Pitolisant (N-201)	Placebo (N = 67)	*p* value
Final ESS Score	9.1 (4.7)	12.1 (5.8)	< .001
Sleep Diary Variables			
Mean change in daily number of sleep/sleepiness episodes	-1.79	-1.30	.056
Mean change in daily duration of sleep/sleepiness episodes	-47.87	-32.24	.066
Leeds Sleep Evaluation Questionnaire			
Mean change in modified getting to sleep	10.21	2.42	.155
Mean change in quality of sleep	17.70	13	.108
Mean change in Global LSEQ score	17.26	10.69	.005
CGI improvement at end of DB treatment	84%	56%	< .001
Patient Global Opinion			
Improvement at end of DB treatment	86%	61%	< .001
Any treatment-related TEAE	24%	19.4%	.377

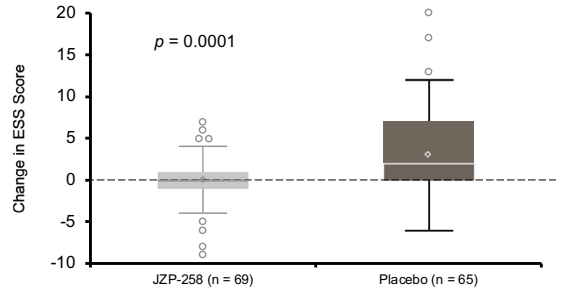
*Pitolisant is not FDA-approved for EDS in OSA
CGI = clinical global impression; TEAE = treatment emergent adverse event
Dauvilliers Y, et al. *Am J Respir Crit Care Med*. 2020;201(9):1135-1145.

Pitolisant: Safety

- AEs (> 5% and twice placebo) include:[1]
  - Nausea
  - Insomnia
  - Anxiety
- Prolongs QT interval; may be greater in patients with hepatic or renal impairment[1]
- May reduce effectiveness of hormonal contraceptives[1]
- In a study of 303 patients (pitolisant = 172; placebo, n = 131) with narcolepsy, no clinically relevant effects on vital signs, laboratory findings, or ECG parameters were noted[2]
- Lower abuse potential compared to phentermine and overall profile to placebo[3]

ECG = electrocardiogram
1. Drugs@FDA Website; 2. Scart-Gres C, et al. *Sleep*. 2019;42(Suppl 1):A244-245.; 3. Setnik B, et al. *Sleep*. 2020;43(4):zsz252.

JZP-258: Efficacy in Narcolepsy



Bogan RK, et al. *Sleep Med*. 2019;64(Suppl 1):S43.;
Foldvary-Schaefer N, et al. American Academy of Neurology (AAN) Annual Meeting; 2020 (canceled).

JZP-258: Safety

AEs, n (%)	SXB Only (n = 52)	SXB + Other Anticataplectics (n = 23)	Other Anticataplectics (n = 36)	Anticataplectic Naïve (n = 90)	Total (N = 201)
Participants with ≥1 AE	31 (59.6)	20 (87.0)	30 (83.3)	72 (80.0)	153 (76.1)
Preferred term in ≥5% of total participants					
Headache	7 (13.5)	3 (13.0)	7 (19.4)	24 (26.7)	41 (20.4)
Nausea	2 (3.8)	1 (4.3)	7 (19.4)	16 (17.8)	26 (12.9)
Dizziness	1 (1.9)	1 (4.3)	6 (16.7)	13 (14.4)	21 (10.4)
Cataplexy*	0	11 (47.8)	6 (16.7)	3 (3.3)	20 (10.0)
Decreased appetite	0	1 (4.3)	2 (5.6)	12 (13.3)	15 (7.5)
Nasopharyngitis	2 (3.8)	1 (4.3)	5 (13.9)	7 (7.8)	15 (7.5)
Influenza	5 (9.6)	3 (13.0)	3 (8.3)	3 (3.3)	14 (7.0)
Diarrhoea	4 (7.7)	0	0	7 (7.8)	11 (5.5)
Vomiting	1 (1.9)	0	4 (11.1)	5 (5.6)	10 (5.0)

Incidences of enuresis and somnambulism were low (3.5% and 2.0% of total participants, respectively)

* = worsening from baseline
SXB = sodium oxybate
Bogan RK, et al. *Sleep Med*. 2019;64(Suppl 1):S43.;
Foldvary-Schaefer N, et al. American Academy of Neurology (AAN) Annual Meeting; 2020 (canceled).

Theoretical Treatment Algorithm for Narcolepsy

- Trial of SXB in all NT1 and NT2 patients if acceptable to patient and no contraindications
  - If SXB not fully effective for EDS, then add solriamfetol
  - If SXB not fully effective for cataplexy then add pitolisant
- If unable to take SXB: Trial of pitolisant
  - If pitolisant not fully effective for EDS, then add solriamfetol
  - If pitolisant not fully effective for cataplexy then add venlafaxine*
- If pitolisant contraindicated or unacceptable, then use solriamfetol
  - After stabilizing on solriamfetol add a NERI, if cataplexy is present, such as venlafaxine
- Rationale: SXB and pitolisant are the only medications that treat both REM abnormalities and EDS

*Venlafaxine is not FDA-approved for cataplexy

NERI = norepinephrine reuptake inhibitor

Maski K, et al. American Academy of Sleep Medicine. https://aasm.org/clinical-resources/practice-standards/guidelines-in-development.; Thorpy MJ, et al. *Ann Neurol*. 2019;85(3):359-370.; Drakatos P, et al. *Sleep Med*. 2017;35:80-84.; Weaver T, et al. *Ann Am Thorac Soc*. 2020 Apr 30. [Epub ahead of print].; Dauvilliers Y, et al. *Sleep*. 2019;42(11):zsz174.

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Conclusions

- The burden of EDS is vast, encompassing diminished QoL, impaired cognitive functioning, poor workplace performance, mood changes, and changes in cortical functioning
- Limitations of long-time first-line therapies such as stimulants have shown issues with safety (e.g., tolerance, rebound, and withdrawal), indicating the need for therapies with a different mechanism of action
- Sodium oxybate is an effective treatment for all the main symptoms of narcolepsy
- Solriamfetol improves EDS associated with narcolepsy or OSA
  - For patients who have just daytime sleepiness, this may be the only medication needed
- Targeting histamine pathways with agents such as pitolisant have demonstrated efficacy in EDS in adults

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SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Identify the potential CNS pathophysiology of EDS in narcolepsy and OSA
- Incorporate into practice, effective treatments with novel mechanisms of action that can reduce the burden of EDS in narcolepsy and OSA while also reducing the risk for abuse

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with Richard K. Bogan, MD, FCCP, FAASM (Chair) and Michael J. Thorpy, MD

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