



NEW & UPCOMING NARCOLEPSY TREATMENTS

Created by:

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WELCOME!

We are so glad you are here. This toolkit is designed for people living with narcolepsy and their loved ones to offer new tools, tips, and perspectives on navigating narcolepsy. Project Sleep created this toolkit as part of the **Narcolepsy Nerd Alert** series.

Narcolepsy Nerd Alert is an educational series diving deeper into specific topics relevant to narcolepsy. Each month, Project Sleep broadcasts a live event via Facebook, hosted by Julie Flygare, JD, Project Sleep's President & CEO.

After each live broadcast, we create a corresponding toolkit (like this one!) to capture our collective knowledge to help others down the road. Quotes featured throughout the toolkit are from panelists and audience members who joined us for the live broadcast.

PLEASE NOTE

The **Narcolepsy Nerd Alert** series is intended for educational and awareness purposes and is not a substitute for medical attention. If anything in this toolkit sparks questions for you about your medical management, please bring those questions to your sleep doctor or narcolepsy specialist.



MEET OUR GUEST



Dr. Anne Marie Morse is a board-certified and fellowship-trained pediatric neurologist specializing in sleep medicine at Geisinger Health System. Her clinical interests include sleep-wake disorders in neurologic disease, narcolepsy and hypersomnia disorders, and neuroimmunology. Her research interests include sleep-wake disorders in neurologic disease, hypersomnia disorders, and sleep-wake disorder phenotyping.

Dr. Morse earned her degree in osteopathy from Rowan University. She completed her residency and child neurology fellowship at the State University of New York, Downstate Medical Center. She completed another fellowship in sleep medicine at the Albert Einstein College of Medicine of Yeshiva University, Montefiore Medical Center. Dr. Morse is certified by the American Board of Psychiatry and Neurology in neurology with special qualification in child neurology.

“New and upcoming narcolepsy treatment options is a great, versatile topic, and the discussion is so needed — it provides hope.

- Dr. Anne Marie Morse

MEET THE HOST



Julie Flygare, JD, currently serves as President & CEO of [Project Sleep](#). She was diagnosed with narcolepsy with cataplexy in 2007 while in law school. Julie is an internationally recognized patient-perspective leader, an accomplished advocate, and the award-winning author of *Wide Awake and Dreaming: A Memoir of Narcolepsy*.



NEW & UPCOMING NARCOLEPSY TREATMENTS

Medical management of narcolepsy is continuously evolving.

On October 27, 2021, special guest Dr. Anne Marie Morse, DO joined host Julie Flygare to discuss new options and exciting possibilities on the horizon.

- Watch the [New & Upcoming Narcolepsy Treatments](#) Video
- Learn more about the [Narcolepsy Nerd Alert Series](#)



WHAT TREATMENT APPROACHES HAVE HELPED YOU MANAGE NARCOLEPSY?



It is so important to empower patients with education. And using education to have better shared decision making with your provider is critical.

- DR. ANNE MARIE MORSE



CURRENT TREATMENTS

Dr. Morse gave an overview of the different types of medications that are used to treat narcolepsy today.

In the American Academy of Sleep Medicine's recommendations for treatment of narcolepsy, there are different tiers of approach: from first-line, to second and third-line treatments used when other medications aren't as effective as desired.

Generally, these treatments approaches can be broken down into a few categories: **alerting agents**, **oxybate therapies**, **stimulants**, and **antidepressants** used primarily to treat cataplexy. Specific information about each treatment option is listed in the table below:

Drug	Mechanism of action	Indication
Alerting Agents		EDS
<i>Modafinil</i>	DA reuptake inhibitor	
<i>Armodafinil</i>	DAT inhibitor	
<i>Pitolisant</i>	H ₃ -receptor antagonist/inverse agonist Increased H synthesis and release	EDS, cataplexy
<i>Solriamfetol</i>	DA and NE reuptake inhibitor DAT and NET inhibitor	EDS
Oxybate Therapy		EDS, cataplexy, fragmented sleep
<i>Sodium Oxybate</i>	GABA _B -receptor agonist	
<i>Low Sodium Oxybate</i>		
Stimulants		Narcolepsy
<i>Methylphenidate</i>	DA reuptake inhibitor DAT inhibitor	
<i>Amphetamine</i>	DAT inhibitor DA reuptake inhibitor Increased DA release	Narcolepsy
Antidepressants		Primarily for cataplexy
<i>Venlafaxine</i>	5-HT and NE reuptake inhibitor 5-HT reuptake inhibitor	
<i>Fluoxetine</i>		
<i>Citalopram</i>	5-HT reuptake inhibitor	
<i>Clomipramine</i>	5-HT, DA and NE reuptake inhibitor	

Note: EDS is an acronym for Excessive Daytime Sleepiness.



ALERTING AGENTS & STIMULANTS

- Alerting agents include modafinil and armodafinil, and pitolisant and soriamfetol are newer options.
- Stimulants include methylphenadates and amphetamines.
- Pitolisant is a histamine-directed treatment to improve excessive daytime sleepiness and cataplexy.

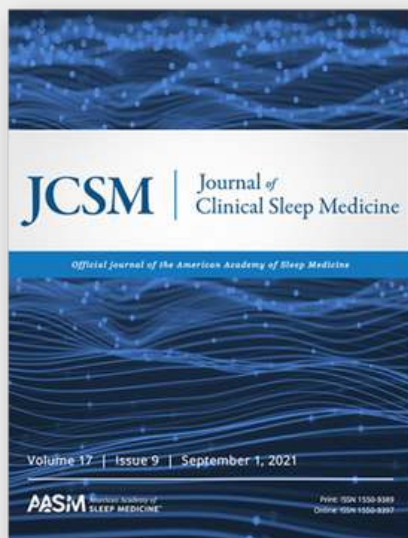
OXYBATE THERAPY

- Taken at night to improve excessive daytime sleepiness and cataplexy.
- Sodium oxybate has been used for a long time, and now low sodium oxybate is available.

ANTIDEPRESSANTS

- Reduce likelihood of experiencing cataplexy by adjusting norepinephrine.
- Considered second-line treatment for cataplexy.

LEARN MORE ABOUT TREATMENT OPTIONS:



Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline



The increased number of treatment options we have today is a reflection of slowly but progressively improving awareness and investment.

- DR. ANNE MARIE MORSE



TREATMENTS IN DEVELOPMENT

Dr. Morse provided a brief explanation and some updates on treatments for narcolepsy that may be available in the future. Treatments under development are listed in the table below:

DRUG	Mechanism of Action	Symptom Impact
FT218	GABA _B -receptor agonist (oral once nightly)	EDS, cataplexy, fragmented sleep
TAK-925	Hypocretin/orexin 2 receptor selective agonist (intravenous)	EDS, cataplexy
TAK-861	Hypocretin/orexin 2 receptor selective agonist (oral)	EDS, cataplexy
TAK-994	Hypocretin/orexin 2 receptor selective agonist (oral)	EDS, cataplexy STOPPED DUE TO SAFETY CONCERNS
SUVN-G3031	H ₃ -R inverse agonist	EDS, cataplexy
AXS-12	NE reuptake inhibitor 5-HT reuptake weak inhibitor	Primarily for cataplexy
THN-102	DA reuptake inhibitor DAT inhibitor Inhibitor of astroglial connexins	EDS
Clarithromycin	Negative allosteric modulator of GABA _A receptor	EDS

“As of October 2021, many of these drugs are in phase one or phase two studies. This means they are being evaluated for safety, tolerability, and appropriate dosing. Later they'll undergo randomized controlled trials to say, 'This is the effect we are seeing consistently,' and get FDA approval.

- Dr. Morse



FT218

- This is a once nightly oxybate therapy.
- As of October 2021, the Phase 3 trial is complete and currently under review by the FDA, and it is available through an open label extension study.

TAK-925, TAK-861, & TAK-994

- These are orexin agonists.
 - Orexin, also known as hypocretin, is the neurotransmitter many people with type 1 narcolepsy, or narcolepsy with cataplexy, are deficient in. This deficiency is responsible for symptoms of type 1 narcolepsy.
 - Orexin agonists aim to mimic the function of orexin.
- As of October 2021, all orexin agonists are in early-phase studies.

“ The unfortunate news about TAK-994 is the clinical trial has been stopped due to a safety concern. This does not mean TAK-925 and TAK-861 may not come to fruition as treatment options.

- Dr. Morse

SUVN-G3031

- A histamine-directed treatment similar to already-approved pitolisant.
- In Phase 2 trials as of October 2021.

AXS-12

- This is reboxetine, a norepinephrine reuptake inhibitor.

THN-102

- A combination of modafinil and flecainide, which has historically been used to help people with cardiac rhythm problems and may help with sleep regulation.

CLARITHROMYCIN

- This is an antibiotic used to treat idiopathic hypersomnia, which is being extended for use in narcolepsy.
- It is shown to have an alerting effect in people with central disorders of hypersomnolence.



Clinical trials used in drug development are often described by phase. These phases are defined by the Food and Drug Administration (FDA):

Early Phase 1	exploratory trials conducted before traditional phase 1 trials to investigate how or whether a drug affects the body. They involve very limited human exposure to the drug and have no therapeutic or diagnostic goals (for example, screening studies, microdose studies).
Phase 1	clinical trials that focus on the safety of a drug. They are usually conducted with healthy volunteers , and the goal is to determine the drug's most frequent and serious adverse events and, often, how the drug is broken down and excreted by the body. These trials usually involve a small number of participants.
Phase 2	clinical trials that gather preliminary data on whether a drug works in people who have a certain condition/disease (that is, the drug's effectiveness). For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.
Phase 3	clinical trials that gather more information about a drug's safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These studies typically involve more participants.
Phase 4	clinical trials occurring after FDA has approved a drug for marketing. They include postmarket requirement and commitment studies that are required of or agreed to by the study sponsor. These trials gather additional information about a drug's safety, efficacy, or optimal use.
Not Applicable	trials without FDA-defined phases, including trials of devices or behavioral interventions. (CLINICALTRIALS.GOV)

“ I'm the most impatient patient, but understanding the development phases and how well-studied each of these treatments are — it gives you respect for such a lengthy and rigorous process.

- Julie

“ Pharmaceutical companies don't develop drugs alone. They seek out expert opinions to help in understanding, 'Is this the right study design? Are we looking at the right outcomes? Are we looking at the right patient population?' So it's not something that can happen overnight.

- Dr. Morse



PARTICIPATING IN CLINICAL RESEARCH

“ New treatment options can't come to market without people with narcolepsy being part of the process. We're thankful to all the people with narcolepsy who participate in research and clinical trials.

- Julie

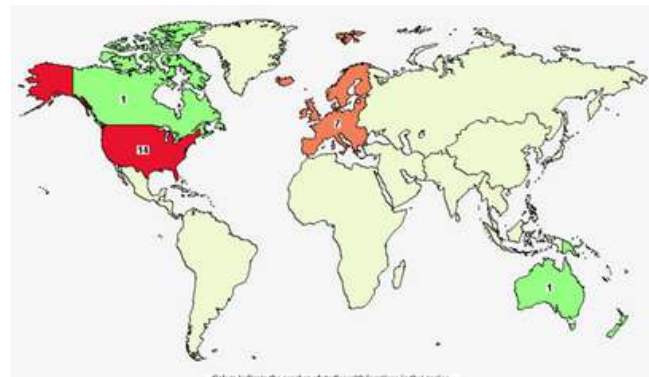
- Participating in research and clinical trials can have many benefits, such as opportunities to try new medications, expert support from research staff, learning more about your own experience with narcolepsy, and contributing to the broader narcolepsy community.
- Opportunities to participate in research and clinical trials are highlighted on Project Sleep's "Participate in Research" webpage.
- Announcements about clinical trials are often shared on social media by nonprofits like Project Sleep, Wake Up Narcolepsy, Narcolepsy Network, or the Hypersomnia Foundation, or by the group organizing the research.
- Visit ClinicalTrials.gov and search for narcolepsy or idiopathic hypersomnia to find current opportunities to participate in clinical trials.

“ I think sometimes people are unaware there are clinical research opportunities, which don't necessarily need to be occurring in the office where you're seeing your provider.

- Dr. Morse

ClinicalTrials.gov

A service of the U.S. National Institutes of Health





NON-PHARMACOLOGICAL APPROACHES

Medication is one part of an integrated treatment approach. Project Sleep emphasizes "four pillars" of narcolepsy treatment: medication, naps, social support, and lifestyle adjustments.

- **Naps** are shown to improve daytime sleepiness, alertness, and reaction time. See our [Narcolepsy and Napping Nerd Alert](#) for an in-depth discussion on the importance and complexity of napping as part of narcolepsy treatment.
- **Social Support** is a crucial part of treatment for many people with narcolepsy.
 - Connecting with other people with narcolepsy via support groups and social media is a good reminder that you're not alone.
 - Therapy can be helpful in processing and dealing with a chronic condition.
- **Lifestyle Adjustments** can be an important part of narcolepsy treatment.
 - Dr. Morse says for every patient, "looking at sleep habits and making sure they have optimal sleep hygiene and good bedtime routines" is a priority.
 - Diet and exercise play a role in how symptoms present because of normal, biological processes associated with food and physical activity.

“ I thought if my medications were working well, I wouldn't have to nap. I've found that while I have benefits from medications, napping has continued to be an important part of my treatment.

- Julie

“ It is okay to seek support. No one is born equipped for something that completely changes their expectations.

- Dr. Morse

“ I've tried many medication options, along with naps, support groups, and strength training. Checked all pillar boxes!

- Matt

"Take these twice a day
They'll keep you wide awake
You'll focus on everything
trivial
They'll wonder what's wrong
with your face"

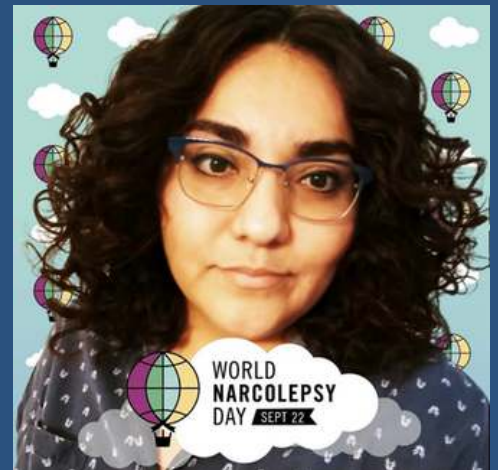
They said I was a sleeping
beauty
Always in a trance
A state of eternal confusion
But when can we have that
dance? @mysleepystories

@mysleepystories



@MYSLEEPYSTORIES
AMANDA IN SCOTLAND

To buy myself time with my eyes open wide;
I medicate in hopes to freeze time and extend my daylight.
I buy off the shelf, what I can't make myself.
Is this script made for me?
Perhaps we shall see.
I'm feeling it now, freedom each time.
When I take the pill, it's like I can fly.
Damn it, I'm crying.
The fog has dissolved.
My icy skin thawed.
To feel this sunshine brings tears to my eyes.
Is this what it's like to be alive?



ANA E. LARA
POET & PROJECT SLEEP BOARD MEMBER



RESOURCES

Here are some of our favorite resources. We look forward to hearing what our fellow #NarcolepsyNerds find most useful!

PATIENT ORGANIZATIONS

- Major US Organizations:
 - [Hypersomnia Foundation](#)
 - [Narcolepsy Network](#)
 - [Project Sleep](#)
 - [Wake Up Narcolepsy](#)
- International Organizations:
 - Listed on Project Sleep's [World Narcolepsy Day webpage](#)

RESOURCES

- AASM's [Hypersomnia Clinical Practice Guideline](#) (Sept. 2021)
- Project Sleep's ["Participate in Research" webpage](#)
- [Clinicaltrials.gov](#)
- [WakeUpandLearn.org](#)
- ["Narcolepsy and Napping" Nerd Alert](#)
- Lauren Selfridge's ["Therapists + Coaches Who Get It" Directory](#)
 - This is a resource to help you find support for full-hearted living with chronic illness and health challenges.
 - Please keep in mind that this directory is an *information sharing resource only*. The listed coaches and clinicians are not screened or endorsed by Lauren Selfridge Consulting or Project Sleep. Please do some research by checking out their websites and contacting professional licensing entities in your state to verify a coach's credentials or therapist's licensure, good standing, and eligibility to practice in your state.



THANK YOU!

We are grateful that you took the time to check out this toolkit!

Project Sleep is a 501(c)(3) nonprofit organization dedicated to raising awareness about sleep health and sleep disorders.

More resources at: www.project-sleep.com

