Transcript Details
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Incorporating Pharmacologic Management of Insomnia Into a Sleep Routine

Announcer
You are listening to ReachMD. This medical industry feature, titled “Incorporating Pharmacologic Management of Insomnia Into a Sleep Routine,” is sponsored by Idorsia Pharmaceuticals.

This program is intended for healthcare providers, and our speaker today is a paid consultant and is presenting on behalf of Idorsia Pharmaceuticals. Your host is Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Joining me today to discuss the importance of routine in the management of insomnia is Dr. Paul Doghramji. Dr. Doghramji is Senior Family Physician at Collegeville Family Practice and Medical Director at Ursinus College in Collegeville, Pennsylvania. Dr. Doghramji, thank you for joining us today.

Dr. Doghramji:
Pleasure to be here, Dr. Turck.

Dr. Turck:
Insomnia is the most common sleep disorder in the United States, and its prevalence has become even more prominent during the COVID-19 pandemic. A number of studies in the United States showed that about a third of patients seen by primary care physicians have insomnia. Dr. Doghramji, how do you approach discussing sleep with your patients to gain a better understanding of their insomnia?

Dr. Doghramji:
Well, first, it's worth noting that while insomnia is very prevalent, sleep health is rarely assessed in the clinic, even though there was strong evidence showing the benefits of good sleep, and its impact on many health outcomes. This is why discussions around sleep should occur on a regular basis with our patients. But we know these conversations don't happen as frequently as they should. So to demystify the conversation around sleep with patients, I ask my patients about their nights and days, as we know that insomnia impacts both. I'll ask about their nighttime symptoms, how is their sleep quality, how long do they sleep, when did they go to sleep, etcetera. Of equal importance, do they feel alert during the day, do they experience any struggles with work, school, or even their personal and professional relationships because of their insomnia. Then, in addition to ruling out any other medical conditions that might be disturbing their sleep, I'll further probe them to better understand what behaviors may be contributing to their insomnia.

Dr. Turck:
You bring up an interesting point, Dr Doghramji—insomnia doesn’t only impact the night but also the day. What do you consider as the most common daytime and nighttime behaviors that may contribute to the cycle of insomnia?

Dr Doghramji:

When patients struggle to stay alert or focused during the day, they tend to address it by drinking coffee—sometimes four to five cups of coffee a day—or they will take late afternoon naps. As we get closer to nighttime, other things that may negatively affect sleep are late dinners or alcohol consumption. Let’s also not forget the effect of blue light—whether it’s being glued to a cellphone or watching TV before going to bed, the blue light emitted from these screens has been known to negatively affect our ability to go to sleep. These common behaviors and others, such as inconsistent bed and wake times, can further impact sleep patterns. A first step in addressing insomnia can be modification of these behaviors, or developing healthy sleep hygiene. This is often part of cognitive behavioral therapy

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for insomnia, or CBT-I. We know that access to CBT-I may be an issue for many patients, but you can advise your patients with insomnia on how to modify the behaviors I just described as part of building a healthy sleep routine.

Dr. Turck:
Thank you for these insights, Dr. Doghramji. And in addition to addressing sleep hygiene with your patients, when do you consider recommending a pharmacologic treatment?

Dr. Doghramji:
Well generally speaking, pharmacologic treatment is recommended for patients who are unable to start or complete CBTI, and for those who found it to be ineffective. Where appropriate, a pharmacologic treatment can be given in combination with CBTI. Therefore, the appropriate insomnia management strategy would depend on your patient's history and where they are on their insomnia journey.

Dr. Turck:
Now, let's move on to discuss a recent advancement in the treatment of insomnia which is Quviviq, or daridorexant. Dr. Doghramji, can you tell us more about it?

Dr. Doghramji:
Sure. Quviviq is a treatment option for adult patients with insomnia characterized by difficulty with sleep onset and/or sleep maintenance. In other words, patients who have consistent trouble falling asleep and/or staying asleep. It is contraindicated in patients with narcolepsy. One of the characteristics of Quviviq is that it was designed and studied with consistent nightly use. It was approved by the FDA in January 2022 and became available in May 2022. It is available in 50-milligram and 25-milligram doses taken no more than once per night.

Now, let me share some details about the Quviviq clinical program. The safety and efficacy of Quviviq were evaluated in two multicenter randomized, double-blind, placebo-controlled parallel group studies over 3 months, followed by a 40-week extension safety study. The first study had 930 patients that were randomized to placebo, Quviviq 25 milligrams, or Quviviq 50 milligrams. The second study had 617 patients, and evaluated Quviviq 25 milligrams and placebo. The extension safety study further evaluated 662 patients and consisted of patients treated with Quviviq 25 milligrams, Quviviq 50 milligrams, or placebo. Some of the patients receiving Quviviq 25 milligrams previously received placebo.

Overall, in study 1, Quviviq showed statistically significant improvements versus placebo in nighttime symptoms. And in a single study, which was study 1, there were statistically significant reductions in patient-reported daytime symptoms with Quviviq 50 milligrams versus placebo. Quviviq 25-milligram did not show significant improvement compared with placebo in daytime sleepiness in either study 1 or study 2 at either time point.

Dr. Turck:
Can you tell us some more about the nighttime and daytime endpoints of the clinical trials?

Dr. Doghramji:
Absolutely. There were two coprimary nighttime efficacy endpoints measured objectively by polysomnography. The first was latency to persistent sleep, which is a measure of sleep onset, or the time needed to fall asleep. And the second was wake after sleep onset, a measure of sleep maintenance, which was used to observe the additional time patients spent asleep after onset. In study 1, both Quviviq 50 milligrams and 25 milligrams showed statistically significant improvements versus placebo at month 1 and month 3 in the time it took patients to fall asleep, and in reducing the time patients spent awake after onset. Additionally, both doses of Quviviq showed statistically significant improvement versus placebo in subjective total sleep time, a patient-reported key secondary endpoint in the study.

So to summarize, the nighttime endpoints efficacy, patients treated with Quviviq fell asleep faster, stayed asleep longer, and gained more total sleep time compared with patients treated with placebo.

Now moving to daytime symptoms, these were measured with the insomnia, daytime symptoms and impact questionnaire, or IDSIQ, sleepiness domain score. As its name suggests, this tool evaluated daytime symptoms in patients with insomnia with 14 items of daytime functioning across three domains, sleepiness, mood, and alert or cognition. The change from baseline in the IDSIQ sleepiness domain score at months 1 and 3 was a key secondary endpoint in the Quviviq clinical trials. In one well controlled study, Quviviq 50 milligrams showed statistically significant reductions in the patient reported IDSIQ sleepiness score at months 1 and 3 versus placebo. Quviviq 25 milligrams did not show significant reductions in daytime sleepiness versus placebo in either study at either time point.

Dr. Turck:
Thank you for that. Let's now discuss the safety profile. Dr. Doghramji, what can you tell us about it?

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Dr. Doghramji:
Quviviq has demonstrated safety profile with consistent nightly use. In study 1 and through 3 months of treatment, reported adverse reactions with - with Quviviq were comparable between doses and with placebo. The most common adverse reaction reported in greater than or equal to percent of patients and greater than placebo was headache, reported enough to 7% of patients with Quviviq and 5% with placebo. Next-day somnolence or fatigue was reported in up to 6% of patients on Quviviq and 4% with placebo. The other common adverse reactions were dizziness and nausea, which occurred in up to 3% of patients on Quviviq and 2% of patients on placebo, respectively. The safety profile in the 40-week safety extension study was consistent with study 1 and 2. Over 12 months of treatment, there was no evidence of physical dependence, withdrawal, or rebound insomnia upon discontinuation.

Now, for more information, please listen to the important safety information at the end of this discussion.

Dr. Turck:
Now that we know about the efficacy and safety of Quviviq with consistent nightly use, what are some considerations when treating with Quviviq, along with a healthy sleep hygiene routine that we discussed earlier?

Dr. Doghramji:
Let's talk about dosing. The recommended dosage is 25 milligrams or 50 milligrams once nightly. There is no designated starting dose or titration requirement. Greatest efficacy was seen with the 50-milligram dose compared with placebo. For patients with moderate hepatic impairment, and those who take a moderate CYP3A4 inhibitor, the recommended dose is Quviviq 25 milligrams. It's important to avoid concomitant use of Quviviq with strong inhibitors of CYP3A4 and with strong or moderate, CYP3A4 inducers, and Quviviq is not recommended to patients with severe hepatic impairment.

Now, there are a few considerations to keep in mind for nightly treatment with Quviviq along with good sleep hygiene. If you recall, consistent bedtime and wake time are important. Therefore, patients should take Quviviq once per night 30 minutes before going to bed, and with at least 7 hours of sleep prior to planned awakening. In addition, time to sleep onset may be delayed if Quviviq is taken with or soon after a meal, which aligns with a good sleep hygiene routine of not eating close to bedtime. We should also advise patients not to consume alcohol when taking Quviviq as alcohol may negatively impact sleep and may lead to side effects when taken with the drug.

To summarize, building a good bedtime routine is an important part of insomnia management into which Quviviq can be incorporated as a treatment option when appropriate.

Now we will review additional important safety information for Quviviq.

Announcer:
INDICATION

QUVIVIQ (daridorexant) is indicated for the treatment of adult patients with insomnia characterized by difficulties with sleep onset and/or sleep maintenance.[11]

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS

- QUVIVIQ is contraindicated in patients with narcolepsy.[11]

WARNINGS AND PRECAUTIONS
Central Nervous System (CNS) Depressant Effects and Daytime Impairment

- QUVIVIQ can impair daytime wakefulness. CNS depressant effects may persist in some patients up to several days after discontinuing QUVIVIQ. Advise patients about the potential for next-day somnolence. Driving ability was impaired in some subjects taking QUVIVIQ 50 mg. Risk of daytime impairment is increased if QUVIVIQ is taken with less than a full night of sleep or at a higher than recommended dose. Caution patients against driving or activities requiring complete mental alertness. Dosage Adjustments of QUVIVIQ and CNS depressants may be necessary when administered together. Use with other insomnia drugs is not recommended. Advise patients not to consume alcohol in combination with QUVIVIQ [11]

Worsening of Depression/Suicidal Ideation

- Patients with psychiatric disorders including insomnia are at increased risk of suicide. In primarily depressed patients treated with hypnotics, worsening of depression, suicidal thoughts and actions have been reported. Administer with caution in patients exhibiting symptoms of depression. Monitoring suicide risk and protective measures may be required[11]

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Sleep Paralysis, Hypnagogic/Hypnopompic Hallucinations, and Cataplexy-Like Symptoms

- Sleep paralysis, and hypnagogic/hypnopompic hallucinations, including vivid and disturbing perceptions, can occur with QUVIVIQ. Symptoms similar to mild cataplexy have been reported with orexin receptor antagonists[11]

Complex Sleep Behaviors

- Complex sleep behaviors, including sleep-walking, sleep-driving, and engaging in activities while not fully awake, have been reported with the use of hypnotics, including orexin receptor antagonists, such as QUVIVIQ. This can occur in hypnotic-naïve or in hypnotic-experienced persons. These events may occur following the first or subsequent use of hypnotics, with or without the concomitant use of alcohol and other CNS depressants. Discontinue QUVIVIQ immediately if a patient experiences a complex sleep behavior[11]

Patients with Compromised Respiratory Function

- Consider the effects of QUVIVIQ on respiratory function in patients with compromised respiratory function. QUVIVIQ has not been studied in patients with moderate obstructive sleep apnea (OSA) requiring CPAP, severe OSA or severe chronic obstructive pulmonary disease (COPD)[11]

Need to Evaluate for Comorbid Diagnoses

- Initiate treatment only after careful evaluation of the patient. Re-evaluate for comorbid conditions if insomnia fails to remit after 7 to 10 days of treatment. Worsening insomnia or new cognitive or behavioral abnormalities may be the result of an underlying psychiatric or medical disorder and can emerge during treatment with QUVIVIQ[11]

MOST COMMON ADVERSE REACTIONS

- The most common adverse reactions (reported in ≥ 5% of patients treated with QUVIVIQ and at an incidence ≥ placebo) were headache and somnolence or fatigue[11]

DRUG INTERACTIONS

- **CYP3A4 Inhibitors:** The recommended dose of QUVIVIQ is 25 mg when used with a moderate CYP3A4 inhibitor. Concomitant use of QUVIVIQ with a strong inhibitor of CYP3A4 is not recommended.[11]
- **CYP3A4 Inducers:** Concomitant use of QUVIVIQ with a strong or moderate inducer of CYP3A4 is not recommended.[11]

USE IN SPECIFIC POPULATIONS

Pregnancy and Lactation

- There are no available data on QUVIVIQ use in pregnant women or on the presence of daridorexant in human milk, the effects on the breastfed infant, or the effects on milk production. Monitor infants exposed to QUVIVIQ through breastmilk for excessive sedation[11]

Geriatric Use

- Because QUVIVIQ can increase somnolence and drowsiness, patients, particularly the elderly, are at higher risk of falls[11]

Hepatic Impairment

- QUVIVIQ is not recommended in patients with severe hepatic impairment. Reduce the dose in patients with moderate hepatic impairment[11]

DRUG ABUSE AND DEPENDENCE

- QUVIVIQ is a Schedule IV controlled substance. Follow patients with a history of abuse or addiction to alcohol or other drugs carefully[11]

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PLEASE SEE THE FULL PRESCRIBING INFORMATION FOR QUVIVIQ AND LEARN MORE AT WWW.QUVIVIQHCP.COM

Dr. Turck:
Thank you, Dr. Doghramji, for enlightening us about the importance of routine in both sleep behaviors and management strategies. It was great speaking with you today.

Dr. Doghramji:
Well thank you again for having me. I hope our listeners found this helpful.

Dr. Turck:
I'm Dr. Charles Turck. And thank you for listening.

Announcer
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