

EDITORIALS

Payer Perspective of the American Academy of Sleep Medicine Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia

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INTRODUCTION

The recently published clinical practice guideline of the American Academy of Sleep Medicine (AASM) for the pharmacologic management of chronic insomnia (“the guideline”)¹ represents the first comprehensive, evidence-based analysis of individual agents commonly used in the treatment of chronic insomnia. This guideline includes specific recommendations for or against the use of many commonly prescribed and over-the-counter medications. These recommendations were developed using the GRADE methodology (Grading of Recommendations, Assessment, Development, and Evaluation). The quality of evidence, benefits versus harms of the treatment, and values and preferences were all considered from the perspective of clinicians and their patients.

These values and perspectives may, at times, differ from those of a payer. Therefore, in light of the clinical and economic implications of these recommendations, it is of great importance that they be interpreted by payers in an appropriate context, and with a clear understanding of the strengths and limitations of this process. This publication addresses appropriate interpretation of the guideline by payers, in an effort to promote sound decision-making in the pharmacologic management of insomnia.

GENERAL USE

As stated in the guideline, the recommendations define principles of practice that should meet the needs of most adult patients, when pharmacologic treatment of chronic insomnia is indicated. The guideline should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of management that may reasonably be used to obtain comparable results. Pharmacologic treatment of chronic insomnia is but one arm of a comprehensive approach to chronic insomnia. Management should also incorporate thorough patient evaluation, including identification of comorbidities (medical, psychiatric, substance use, or other sleep disorders), assessment of sleep-wake schedule, and cognitive and behavioral factors that contribute to the chronicity of the insomnia syndrome. A previous AASM clinical guideline²

recommended cognitive-behavioral therapy for insomnia as an initial intervention for chronic insomnia. It also advised that, when medication is used, it should, whenever possible, be supplemented with cognitive-behavioral therapy for insomnia. Most investigations that are included in the current analysis address relatively short-term use (e.g., 1 day to 5 w). Some studies^{3,4} have shown that long-term treatment with newer-generation benzodiazepene receptor agonist hypnotics can be safe and effective under properly controlled conditions. Considerations for long-term use have been described elsewhere.⁵

The literature review, meta-analyses, and recommendations contained in the guideline are based only on United States Food and Drug Administration (FDA)-approved doses. However, FDA-recommended dosages may be (and, in some cases, have been) changed as new data regarding efficacy or adverse events emerge. Therefore, the dosages on which the guideline recommendations are based should not be interpreted as a recommendation for the use of a specific dosage in clinical practice. Numerous factors including, but not limited to, age, sex, comorbidities, and concurrent use of other medications may affect dosage recommendations. Additionally, it should be understood that the efficacy of these medications in populations with major comorbidities is not addressed in the guideline. The presence of such comorbidities, especially psychiatric disorders, may significantly influence the pharmacotherapeutic approach to insomnia.

SPECIFIC RECOMMENDATIONS

The recommendations for individual medications are summarized in Table 4 of the guideline.¹ Payers should be aware of several factors in interpreting these recommendations. As discussed in the guideline, the current standard for assessment of “efficacy” of hypnotic medications is the analysis of specific sleep outcome variables such as reduction of sleep latency or wake after sleep onset. Although these are reasonable metrics and have a certain degree of face validity, they may well fall short of reflecting the full picture of clinical improvement. Other considerations such as quality of sleep or daytime function may be equally or more important in

evaluating clinical improvement, and could affect clinical decision-making.

The strength of a recommendation is expressed using two categories: “STRONG” and “WEAK”, for or against a particular patient care strategy, in this case hypnotic use for insomnia. By definition, a “STRONG” recommendation is one that clinicians should, under most circumstances follow. However, this guideline contains exclusively “WEAK” recommendations. A “WEAK” recommendation reflects a lower degree of certainty in the outcome and appropriateness of a specific patient care strategy (i.e., using a specific hypnotic). Therefore, a “WEAK” recommendation requires that clinicians use their clinical knowledge and experience and assess the individual patient’s values and preferences in determining the best course of action. Importantly a “WEAK” recommendation *against* a hypnotic agent is not a recommendation that the hypnotic agent should never be used; it too requires clinicians to use their knowledge and experience and evaluate the needs of the individual patient. A “WEAK” recommendation primarily indicates that either the available evidence is insufficient and fails to provide convincing support in favor of (or against) this patient care strategy (hypnotic medication), or that the balance of benefits versus harms and patient values and preferences are such that the use of the hypnotic agent cannot be confidently recommended for use in all patients. It is noteworthy that clinical guidelines from a variety of specialties are replete with weak recommendations for commonly employed therapies, for many of the same reasons.^{6–8}

The quality of the evidence on which many of the recommendations are based is “low” or “very low,” indicating low certainty that the estimated effects seen in the published literature will occur in all patients. It is also important to understand that the overwhelming majority of clinical trials for the efficacy of pharmacologic agents are, of necessity, industry-sponsored. Therefore, the likelihood of publication bias would reduce the confidence in the estimated effect; as a result, there is an almost across-the-board downgrading of evidence from “high” quality to “moderate” quality, before other factors are even considered. Identification of heterogeneity and/or imprecision of the data results in further downgrading to “low” or “very low” quality.

It is also essential for payers to recognize that all of the recommendations made in the guideline are based on available data that met statistical requirements for evidence grading. As a result of the variability in data-reporting formats across studies, particularly among older investigations, numerous trials were not included in our analysis. While findings of efficacy, or lack thereof, may reflect the true biological efficacy of a given medication, the reported outcomes are clearly a function of data availability, study population, methodology, and quality of evidence.

These limitations affect all of the recommendations contained in the guideline, to some extent, and have substantial bearing on the final recommendations. Therefore, it is incumbent on payers to view recommendations with these limitations in mind, and to recognize that, in the context of this guideline, a recommendation “against” use is often more reflective of a lack of quality data, as opposed to high-quality data demonstrating

a true absence of effect. The choice of sleep-promoting medication is ultimately a matter of clinical judgment based on patient profile and preferences, prior response, and consideration of adverse effects. Finally, clinicians and payers should bear in mind that certain medications, such as ramelteon or melatonin, may have limited or no indications for treatment of chronic insomnia *per se* but may be effective for insomnia complaints that are a function of other sleep disorders.

CONCLUSIONS

With increased understanding of the elements of the GRADE methodology, future research may provide stronger levels of recommendations regarding hypnotic use in the management of chronic insomnia. To reduce the uncertainty resulting from the possibility of publication bias, increased nonindustry-sponsored research will be needed. Improvement in the standardization of assessing sleep outcomes and reporting of adverse effects will be essential for future clinical practice guidelines. Finally, there continues to be uncertainty regarding the appropriate metrics for assessing the efficacy of a treatment intervention in the management of chronic insomnia. Further research may lead to an understanding of nonconventional measures such as improvement or resolution of the “insomnia syndrome,” which suggests a more patient-centered approach. This could include metrics of improved daytime cognitive, emotional, and psychomotor function.

In clinical decision-making multiple factors are weighed when determining the appropriate course of therapy. These include but are not exclusive of patient history, previous therapeutic interventions, response to intervention, availability of therapy, cost, and patient preference. The current guideline is an additional tool to aid the clinician and patient in making the best decision for the patient.

CITATION

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