INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Obstructive Sleep Apnea***
-April 2026-

Summary/Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) conducted a clinical review of Obstructive Sleep Apnea (OSA) focusing on epidemiology, pathophysiology, diagnosis, guideline-directed management, and clinical outcomes evidence. Non-pharmacologic therapies, primarily Positive Airway Pressure and Mandibular Advancement Devices, remain the standard of care. Medication classes currently evaluated in the context of OSA include wake-promoting agents (modafinil, armodafinil, solriamfetol, pitolisant) and novel disease-modifying therapies, notably the dual GIP/GLP-1 receptor agonist tirzepatide. Clinical guidance included recommendations from the American Academy of Sleep Medicine (AASM) and 2025 Department of Veterans Affairs/Department of Defense (VA/DoD).[1,2] **No modifications** to the IHS National Core Formulary resulted from this review. Agents reviewed may be re-evaluated in the future as additional clinical trial data and updated practice guidelines emerge.

Discussion:
Obstructive Sleep Apnea is characterized by repeated upper airway collapse during sleep, leading to oxygen desaturation, sleep fragmentation, and severe cardiometabolic consequences. Epidemiological data, including findings from the Sleep Heart Health Study and the Strong Heart Study, indicate American Indian and Alaska Native populations demonstrate 1.7 times higher odds of moderate-to-severe OSA compared to non-Hispanic White cohorts.[3,4] This is driven heavily by a disproportionate burden of risk factors such as obesity and cardiometabolic disease. Diagnosis and severity stratification rely on polysomnography or home sleep apnea testing to determine the Apnea-Hypopnea Index (AHI).

Management strategies reviewed emphasize that mechanical clearance of the airway using positive airway pressure (PAP) therapy remains the standard first-line treatment for moderate-to-severe OSA, particularly for symptom control such as reducing daytime sleepiness and improving quality of life.[1] However, clinical trial evidence highlights adherence as a significant limitation when utilizing continuous positive airway pressure (CPAP) for secondary prevention of cardiovascular events. In both the SAVE and RICCADSA trials, routine CPAP assignment did not significantly reduce major cardiovascular events in the intention-to-treat populations, a failure largely attributed to low average adherence (mean 3.3 hours per night in the SAVE trial).[5,6] When evaluating adherence thresholds of 4 or more hours per night, the evidence is mixed: the RICCADSA trial demonstrated a statistically significant reduction in primary cardiovascular risk among the adherent subgroup, whereas the adherence analysis from the SAVE trial only suggested possible benefits for certain cerebrovascular outcomes, without a statistically significant reduction in the primary cardiovascular endpoint.

Pharmacologic management was reviewed across two paradigms: symptom management and disease modification. Wake-promoting agents were evaluated for the treatment of residual excessive daytime sleepiness. Trials such as TONES 3 (solriamfetol) and HAROSA II (pitolisant in CPAP) demonstrated significant improvements in Epworth Sleepiness Scale scores.[7,8] However, AASM and VA/DoD guidelines position these medications as strictly adjunctive therapies for symptom control, emphasizing they are not replacements for primary airway management.[2]

The review evaluated emerging disease-modifying therapies, targeting metabolic causes of OSA. The SURMOUNT-OSA trials investigated once-weekly tirzepatide in patients with moderate-to-severe OSA and obesity.[9] Tirzepatide demonstrated a statistically significant and clinically meaningful absolute reduction in AHI (a reduction of up to 29.3 events per hour) and substantial weight loss compared to placebo, establishing it as a highly effective pharmacologic intervention regardless of concurrent PAP therapy.

Additionally, investigational oral neuromuscular therapies like AD109 (atomoxetine/aroxybutynin) were discussed following the completion of the Phase 3 SynAIRgy and LunAIRo trials, which demonstrated an approximately 50 percent reduction in AHI. However, the VA/DoD guidelines currently suggest against the routine use of atomoxetine/oxybutynin combinations.[2]

Findings:
The review reinforced that the management of OSA requires a foundational approach of mechanical airway support alongside evidence-based weight management. Current recommendations by major guidelines center on optimizing adherence to PAP or oral appliances.

Notably, the dual GIP/GLP-1 receptor agonist tirzepatide recently received approval from the U.S. Food and Drug Administration (FDA) for the treatment of moderate-to-severe OSA in adults with obesity. While primary clinical practice

guidelines have not yet been fully updated to position systemic metabolic agents above mechanical devices in the treatment algorithm, the VA/DoD guidelines align with this therapeutic approach by formally recommending evidence-based weight management as a core, concurrent component of OSA therapy.

Tirzepatide (Zepbound®) is currently listed on the National Core Formulary for weight management, with recommended local adoption of use criteria. Because the FDA indication for OSA applies specifically to patients with comorbid obesity (a Body Mass Index of 30 or greater), individuals who are clinical candidates for tirzepatide (Zepbound®) for OSA may meet the eligibility criteria under the existing weight management formulary pathways. Therefore, the NPTC determined that the current formulary structure is sufficient to provide access to this therapy for the appropriate patient population.

Wake-promoting agents remain positioned as adjuncts for residual symptoms and were not recommended for addition to the National Core Formulary. Investigational oral neuromuscular agents require further longitudinal data and FDA review. Based on the available evidence, guideline sequencing, and therapeutic coverage already present on the formulary for weight management, no modifications to the National Core Formulary were warranted. The NPTC will continue to monitor the clinical landscape as real-world evidence and updated guidelines become available.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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