Xywav™ (calcium, magnesium, potassium, and sodium oxybates) Oral Solution Testimony

My name is Deb Profant, Director of Global Value for Jazz Pharmaceuticals. Xywav was approved in July of 2020 for the treatment of cataplexy or excessive daytime sleepiness (abbreviated EDS) in patients 7 years of age and older with narcolepsy and was approved in August 2021 for the treatment of idiopathic hypersomnia in adults. For narcolepsy patients, the recommended dosage range for Xywav in adults is 6 g to 9 g per night orally. For patients transitioning from sodium oxybate, Xywav is initiated at the same gram-for-gram dose and regimen as sodium oxybate with an option for additional titration to balance efficacy and tolerability as needed (XywavI [package insert] 2020). At the maximum recommended dosage of 9 grams nightly, sodium intake with Xywav is reduced by 1509 mg (92%) in comparison with sodium oxybate (Xyrem®), and exposure to each of the other cations is within the adult recommended daily allowance (HHS/USDA 2015). Distinct from sodium oxybate, Xywav does not have a warning regarding high sodium content or subsequent precautions around monitoring patients with heart failure, hypertension, or impaired renal function. (Xywav [package insert] 2020).

Sodium intake may be particularly relevant for patients with narcolepsy due to their increased risk of cardiovascular disease based on their disrupted nighttime sleep and their lack of nocturnal blood pressure dipping. Studies have demonstrated a diagnosis of narcolepsy is associated with an increased prevalence of cardiovascular, metabolic, and psychiatric comorbidities (Thorpy 2014; Black 2017; Ohayon 2013; Cohen 2018; Jennum 2013). Specifically, hypertension, obesity, diabetes, and dyslipidemia are generally more prevalent among patients with a narcolepsy diagnosis relative to matched, non-narcolepsy controls (Thorpy 2014; Black 2017; Ohayon 2013; Cohen 2018; Jennum 2013). In the general population, it has been well-established that chronic, excessive sodium consumption is associated with increased risk of hypertension and cardiovascular disease (HHS/USDA 2015; Grillo 2019; Mente 2014; Eckel 2014; Whelton 2018).

In the Xywav phase 3 narcolepsy clinical trial, the most common adverse reactions in adults were headache, nausea, dizziness, decreased appetite, parasomnia, diarrhea, hyperhidrosis, anxiety, and vomiting. (Xywav [package insert] 2020).

Xywav is a schedule III controlled substance and has a black box warning associated with central nervous system depression and abuse and misuse. Xywav is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XYWAV and XYREM REMS (Xywav [package insert] 2020). Please refer to the full Prescribing Information for more details Xywav [package insert] 2020; XYREM [package insert] 2020.

XYWAV is a lower-sodium formulation of oxybate, without cardiovascular warnings or precautions in the label. Xywav allows patients with narcolepsy to benefit from oxybate therapy while providing a clinically relevant reduction in daily sodium intake. The results of the phase 3 clinical trial for XYWAV in narcolepsy demonstrated efficacy in terms of excessive daytime sleepiness and the frequency of cataplexy attacks, as well as a safety profile consistent with that of sodium oxybate (Bogan RK 2020)

I respectfully request that the prior authorization criteria for Xywav be the same as the prior authorization criteria for Xyrem so that patients with narcolepsy can have access to treatment with the optimal oxybate formulation.

REFERENCES

Black J, Reaven NL, Funk SE, et al. Medical comorbidity in narcolepsy: findings from the Burden of Narcolepsy Disease (BOND) study. Sleep Med. 2017;33:13-18.

Bogan RK, Thorpy MJ, Dauvilliers Y, et al. Efficacy and Safety of JZP-258 in a Phase 3, Placebo-Controlled Blind Randomized Withdrawal Study in Adults With Narcolepsy With Cataplexy. *Sleep*, zsaa206, https://doi.org/10.1093/sleep/zsaa206

Cohen A, Mandrekar J, St louis EK, Silber MH, Kotagal S. Comorbidities in a community sample of narcolepsy. Sleep Med. 2018;43:14-18.

Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(25 Suppl 2):S76-S99.

Grillo A, Salvi L, Coruzzi P, Salvi P, Parati G. Sodium intake and hypertension. Nutrients. 2019;11(9).

Jennum P, Ibsen Rikke, Knudsen S, Kjellberg J. Comorbidity and Mortality of Narcolepsy: A Controlled Retro- and Prospective National Study. Sleep. 2013;36:835-840.

Mente A, O'Donnell MJ, Rangarajan S, et al. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med. 2014;371(7):601-11

Ohayon MM. Narcolepsy is complicated by high medical and psychiatric comorbidities: a comparison with the general population. Sleep Med. 2013;14(6):488-492.

Thorpy MJ, Dauvilliers Y. Clinical and practical considerations in the pharmacologic management of narcolepsy. *Sleep Med*. 2015;16(1):9-18.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines/.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in Hypertension. 2018 Jun;71(6):e140-e144]. Hypertension. 2018;71(6):e13-e115.

Xyrem [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2020.

Xywav [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2021.