Xywav® (calcium/magnesium/potassium/sodium oxybates) – New indication

- On August 12, 2021, Jazz Pharmaceuticals announced the FDA approval of Xywav (calcium/magnesium/potassium/sodium oxybates), for the treatment of idiopathic hypersomnia (IH) in adults.
    - Xywav is a schedule III controlled substance.
- Xywav is also approved for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy.
- IH is a neurologic sleep disorder characterized by chronic excessive daytime sleepiness. An estimated 37,000 people in the U.S. have been diagnosed with IH and are actively seeking healthcare.
- The approval of Xywav for the new indication was based on a double-blind, placebo-controlled, randomized-withdrawal study in IH adult patients. The study enrolled 154 patients with 115 evaluable for efficacy data. The primary endpoint was the change in Epworth Sleepiness Scale (ESS) score, as a measure of reduction in excessive daytime sleepiness from the end of the stable dose period (SDP) to the end of the double-blind, randomized withdrawal period (DB RWP). The ESS is an 8-item self-reported questionnaire by which patients rate their perceived likelihood of falling asleep during usual daily life activities (maximum score of 24).
    - Patients taking stable doses of Xywav who were withdrawn from Xywav and randomized to placebo during DB RWP experienced significant worsening in ESS score vs. patients randomized to continue treatment with Xywav ($p < 0.0001$) across all dosing regimens (median change in ESS was 8.0 vs. 0.0 for placebo and Xywav, respectively).
- Xywav carries a boxed warning for central nervous system depression and abuse and misuse.
- The recommended dose and regimen of Xywav for the treatment of IH should be individualized based on clinical presentation. Xywav can be administered orally as a twice nightly or once nightly regimen. The recommended starting dose, titration guidance, and maximum nightly doses appear in the table below.
    - The increase in the total nightly dose should not exceed 1.5 g/week. During titration, the dosing regimen may be changed between twice nightly and once nightly, as needed based on efficacy and tolerability.
    - Doses higher than 9 g per night or single dose administrations higher than 6 g have not been studied and should not be administered.

Dosing regimen	Starting nightly dose	Titration increments	Maximum total nightly dose
Twice nightly	≤ 4.5 g per night divided into two doses (eg, 2.25 g each)	≤ 1.5 g per night per week (divided into two doses)	9 g (divided into two doses)
Once nightly	≤3 g per night	≤1.5 g per night per week	6 g

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- Refer to the Xywav drug label for dosing for narcolepsy.