Xyrem® (sodium oxybate) – Expanded indication

- On October 29, 2018, Jazz Pharmaceuticals announced the FDA approval of Xyrem (sodium oxybate), for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
    - Previously, Xyrem was approved for the treatment of cataplexy or EDS in patients with narcolepsy with dosing recommendations only provided for adult patients.
- The approval of Xyrem's expanded indication was based on a randomized-withdrawal study evaluating the efficacy of Xyrem in pediatric patients aged 7 years or older. A total of 106 patients were enrolled and 63 were randomized to either continued treatment with Xyrem or placebo. The primary efficacy measure was the change in frequency of cataplexy attacks. In addition, the efficacy of Xyrem in the treatment of EDS was evaluated using the Epworth Sleepiness Scale score.
    - Patients randomized to placebo experienced an increase in the median number of weekly cataplexy attacks vs. patients randomized to continued treatment with Xyrem (median change from baseline: 12.7 vs. 0.3, respectively; $p < 0.0001$).
    - Patients randomized to receive placebo also experienced an increase in the median Epworth Sleepiness Scale score vs. patients randomized to continued treatment with Xyrem (median change from baseline: 3 vs. 0, respectively; $p = 0.0004$).
- The most common adverse reactions in pediatric patients (≥ 5%) with Xyrem use were enuresis, nausea, headache, vomiting, decreased weight, decreased appetite, and dizziness.
- Xyrem carries boxed warnings for central nervous system depression and abuse and misuse. Xyrem is available only through a restricted program called the Xyrem REMS Program.
- The recommended starting pediatric dosage for Xyrem, titration regimen, and maximum total nightly dosage are based on patient weight. The dosage may be gradually titrated based on efficacy and tolerability. Xyrem is administered orally twice nightly as follows:

Patient weight (kg)	Initial dosage*		Maximum weekly dosage increase		Maximum recommended dosage	
	Take at bedtime:	Take 2.5 to 4 hours later:	Take at bedtime:	Take 2.5 to 4 hours later:	Take at bedtime:	Take 2.5 to 4 hours later:
< 20**	Insufficient information to provide specific dosing recommendations					
20 to < 30	≤ 1 g	≤ 1 g	0.5 g	0.5 g	3 g	3 g
30 to < 45	≤ 1.5 g	≤ 1.5 g	0.5 g	0.5 g	3.75 g	3.75 g
≥ 45	≤ 2.25 g	≤ 2.25 g	0.75 g	0.75 g	4.5 g	4.5 g

* For patients who sleep > 8 hours per night, the first dose of Xyrem may be given at bedtime or after an initial period of sleep.
** If Xyrem is used in patients ≥ 7 years of age who weigh < 20 kg, a lower starting dosage, lower maximum weekly dosage increases, and lower total maximum nightly dosage should be considered.

- Refer to the Xyrem drug label for dosing recommendations in adults.