Xcopri® (cenobamate) – New drug approval

- On November 21, 2019, the FDA announced the approval of SK Biopharmaceuticals' Xcopri (cenobamate), for the treatment of partial-onset seizures in adult patients.

- Seizures can cause uncontrolled movements, abnormal thinking or behavior, and abnormal sensations. Movements can be violent, and changes in consciousness can occur. Seizures occur when clusters of nerve cells (neurons) in the brain undergo uncontrolled activation. A partial-onset seizure begins in a limited area of the brain.

- While the precise mechanism by which Xcopri exerts its therapeutic effect is unknown, Xcopri is believed to reduce repetitive neuronal firing by inhibiting voltage-gated sodium currents.

- The efficacy of Xcopri was established in two randomized, double-blind, placebo-controlled studies in adult patients with partial-onset seizures. In study 1 (N = 221), patients received Xcopri 200 mg/day or placebo. In study 2 (N = 434), patients received Xcopri 100 mg/day, 200 mg/day, 400 mg/day, or placebo. The primary efficacy outcome in study 1 and study 2 was the percent change from baseline in seizure frequency per 28 days in the treatment period.

    — In study 1, a statistically significant 55.6% reduction in median seizure frequency was observed with Xcopri 200 mg/day vs. 21.5% reduction with placebo ($p < 0.0001$).
    — In study 2, Xcopri 100 mg/day, 200 mg/day, or 400 mg/day had statistically significant 36.3%, 55.2%, and 55.3% reductions in median seizure frequency, respectively, vs. a 24.3% reduction with placebo ($p = 0.006$ for 100 mg/day; $p < 0.001$ for 200 mg/day and 400 mg/day).

- Xcopri is contraindicated in patients with hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri and in patients with familial short QT syndrome.

- Warnings and precautions for Xcopri include drug reaction with eosinophilia and systemic symptoms (DRESS)/multiorgan hypersensitivity, QT shortening, suicidal behavior and ideation, neurological adverse reactions, and withdrawal of antiepileptic drugs.

- The most common adverse reactions (≥ 10% and more frequently than placebo) with Xcopri use were somnolence, dizziness, fatigue, diplopia, and headache.

- The recommended oral dosage and titration of Xcopri, which should not be exceeded because of the potential for serious adverse reactions is provided in the table below.

Initial dosage	
Week 1 and 2	12.5 mg once daily
Titration regimen	
Week 3 and 4	25 mg once daily
Week 5 and 6	50 mg once daily
Week 7 and 8	100 mg once daily
Week 9 and 10	150 mg once daily
Maintenance dosage	

Continued . . .

Week 11 and thereafter	200 mg once daily
Maximum Dosage	
If needed based on clinical response and tolerability, dose may be increased above 200 mg by increments of 50 mg once daily every two weeks to 400 mg	400 mg once daily

- SK Biopharmaceuticals plans to launch Xcopri in the second quarter of 2020, following scheduling review by the DEA, which typically occurs within 90 days of FDA approval. Xcopri will be available as 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg tablets.