ONO PHARMA

Press Release

Ono Received Manufacturing and Marketing Approval in Japan for XCOPRI® Tablets for the Treatment of Patients with Partial-onset Seizures, With or Without Secondary Generalized Seizures

- Ono Received manufacturing and marketing approval in Japan for the treatment of patients with partial-onset seizures, with or without secondary generalized seizures.
- Adjunctive therapy with XCOPRI significantly improved the primary endpoint, the percent change in seizure frequency, and demonstrated a manageable safety profile.
- XCOPRI is expected to provide an additional treatment option for patients with partial-onset seizures.

Osaka, Japan, September 16, 2026—Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President and COO: Toichi Takino; "Ono") today announced that Ono received manufacturing and marketing approval of XCOPRI® (generic name: cenobamate) Tablets 12.5 mg, 50 mg, 100 mg, 200 mg ("XCOPRI") for the treatment of patients with partial-onset seizures, with or without secondary generalized seizures.

This approval is based on the results of a multinational Phase 3 clinical study (YKP3089C035) conducted in Asian patients with uncontrolled partial-onset (focal) seizures despite treatment with antiseizure medications (ASMs). In this study, adjunctive therapy with XCOPRI showed a statistically significant improvement in the median percent change in seizure frequency, the primary endpoint, compared with existing treatment alone. A manageable safety profile was also observed.

About YKP3089C035

YKP3089C035 was a randomized, double-blind, placebo-controlled, multinational Phase 3 clinical study conducted in South Korea, China, and Japan. In this study, the efficacy and safety of XCOPRI as adjunctive therapy was evaluated in adult patients aged 18–70 with uncontrolled partial-onset (focal) seizures on 1-3 ASMs. Patients were randomly allocated in a 1:1:1:1 ratio to adjunctive placebo or adjunctive XCOPRI 100, 200, or 400 mg once daily.

All dosage groups of XCOPRI achieved the primary efficacy endpoint, showing a significant reduction in the median percent change in seizure frequency during the 6-week maintenance phase compared with the placebo group. XCOPRI 400 mg group showed a 100% reduction in the median seizure frequency during the maintenance period (Placebo: 25.9% vs XCOPRI: 42.6% for 100 mg, 78.3% for 200 mg, and 100% for 400 mg). In the secondary endpoints for efficacy, all dosage groups of XCOPRI showed significantly higher seizure-free rate* compared with the placebo group (Placebo: 2.6% vs XCOPRI: 12.4% for 100 mg, 30.1% for 200 mg, and 52.4% for 400 mg). The most common adverse events with the incidence of 20% or more in XCOPRI groups were dizziness and somnolence.

The results of this study were presented in a poster session at the 2024 Annual Meeting of the American Epilepsy Society (AES).[1]

*The maximum rate of seizure-free, which aligns with the goal in epilepsy treatment, in adjunctive therapy with existing ASMs is reported to be around 6.4%.[2]

About Epilepsy

Epilepsy is a chronic brain disorder in which seizures are triggered by abnormal excitability of nerve cells in the brain. In Japan, approximately 1 million people are estimated to have epilepsy, which generally requires long-term drug therapy.[3] Thirty percent of epilepsy patients do not achieve adequate seizure control with existing ASMs.[4,5] Epilepsy is a disease with high unmet medical needs for which new ASMs are still anticipated.

Overview of XCOPRI® Tablets

<table>
<tr><td>Product name</td><td>XCOPRI® Tablets 12.5 mg/50 mg/100 mg/200 mg</td></tr>
<tr><td>Generic name (JAN)</td><td>Cenobamate</td></tr>
<tr><td>Indication</td><td>Patients with partial-onset seizures, with or without secondary generalized seizures</td></tr>
<tr><td>Dosage and administration</td><td>The usual adult starting dose is 12.5 mg of cenobamate administered orally once daily. Thereafter, the dose should be increased by 1 step at intervals of at least 2 weeks to 100 to 200 mg once daily as the maintenance dose. The dose may be adjusted according to the patient's condition. The dose should be increased to >200 mg by 50 mg at intervals of at least 2 weeks, and the maximum dose should be 400 mg once daily.
(Dose Titration Schedule up to 200 mg)
<table>
<tr><th>Regimen</th><th>Dose</th></tr>
<tr><td>1</td><td>12.5 mg</td></tr>
<tr><td>2</td><td>25 mg</td></tr>
<tr><td>3</td><td>50 mg</td></tr>
<tr><td>4</td><td>100 mg</td></tr>
<tr><td>5</td><td>150 mg</td></tr>
<tr><td>6</td><td>200 mg</td></tr>
</table></td></tr>
<tr><td>Manufacturer/distributor</td><td>Ono Pharmaceutical Co., Ltd.</td></tr>
<tr><td>Approval date</td><td>September 16, 2026</td></tr>
</table>

About XCOPRI

Although the precise mechanism by which XCOPRI exerts its therapeutic effects remains unknown, XCOPRI reduces repetitive neuronal firing by inhibiting voltage-dependent sodium currents. In addition, XCOPRI positively modulates γ-aminobutyric acid type A ($GABA_A$) ion channels. Based on its clinical results, XCOPRI has demonstrated efficacy and is expected to become a new treatment option that has been associated with seizure freedom in a proportion of patients in clinical studies, which is consistent with the goal of epilepsy treatment. As of September 2026, XCOPRI is approved as a treatment for partial-onset seizures in more than 45 countries or regions worldwide, including in the U.S. and Europe (where it is marketed as ONTOZRY®).

In Japan, Ono is conducting Phase 3 clinical study of XCOPRI for the treatment of primary generalized tonic-clonic (PGTC) seizures in adolescents and adults as well as Phase 3 clinical study

for the treatment of pediatric patients with partial-onset seizures.

About Partnership with SK Biopharmaceuticals Co., Ltd.

In 2020, Ono entered into a licensing agreement with SK Biopharmaceuticals Co., Ltd. (headquartered in Gyeonggi-do, South Korea) which originally discovered and developed the anti-seizure medication (ASM) XCOPRI. Through this agreement, Ono has obtained the exclusive rights to develop and commercialize XCOPRI in Japan. SK Biopharmaceuticals and its U.S. subsidiary, SK Life Science Inc., are global pharmaceutical companies focused on the research, development, and commercialization of treatments for central nervous system (CNS) disorders. Their pipeline includes 7 development compounds for CNS diseases, including epilepsy. In addition, SK Biopharmaceuticals is actively engaged in early-stage oncology research. Further information can be found on the SK Biopharmaceuticals website (www.skbp.com/eng) and the SK Life Science Inc. website (www.SKLifeScienceInc.com).

References:

1. Sunita N Misra, Louis Ferrari, Zhen Hong, et.al., A Randomized, Double－Blind, Placebo－Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Adjunctive CENOBAMATE in Asian Patients with Focal Seizures. AES 2024.
2. French JA. Cenobamate for focal seizures — a game changer? Nat Rev Neurol. 2020;16:133-
3. Japan Epilepsy Association (JEA)（accessed on August 26, 2025）
   Available at https://www.jea-net.jp/epilepsy
4. Yushi Inoue. The Guideline Development Committee of the Japan Epilepsy Society. Report of the Guideline Development Committee of the Japan Epilepsy Society: Guidelines for the Pharmacological Treatment of Epilepsy in Adults. Epilepsy Research. 2005;23:249-53.
5. Brodie MJ, Barry SJ, Bamagous GA, Norrie JD, Kwan P. Patterns of treatment response in newly diagnosed epilepsy. Neurology. 2012;78:1548-54.

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