SK life science

XCOPRI® (cenobamate tablets) for the Treatment of Partial-Onset Seizures in Adults

About XCOPRI® (cenobamate tablets)

An FDA-approved anti-epileptic drug (AED) for the treatment of partial-onset seizures in adults

Expected to be available in the U.S. in the second quarter of 2020, following scheduling review by the U.S. Drug Enforcement Administration (DEA)

Marks the first time a Korean company has independently brought a compound from discovery to U.S. FDA approval

Understanding Epilepsy & Partial-Onset Seizures

Epilepsy is a disorder of the brain characterized by seizures, and it affects approximately 3 million adults in the U.S.[1] A person is considered to have epilepsy if they experience two or more unprovoked seizures separated by at least 24 hours, or after one seizure with a high risk for more.[2] Uncontrolled seizures harm health, impair quality of life and increase health care costs.[1]

Although there are many different kinds of seizures, the most common type is partial-onset seizures, which begin in a single area of the brain and affect 60% of people with epilepsy.[3]

More than a dozen new anti-epileptic drugs (AEDs) have been introduced over the past two decades, but overall treatment outcomes for people with epilepsy have not changed significantly.[4] Approximately 40% of adult patients with partial-onset seizures have inadequate control of seizures after treatment with 2 AEDs, highlighting the need for new, innovative therapies and better disease management.[4]

The FDA approval of XCOPRI is based on results from two global, randomized, double-blind, placebo-controlled studies and a large, global, multicenter, open-label safety study that enrolled adults with uncontrolled partial-onset seizures, taking 1-3 concomitant AEDs.

More than **1,900** patients were enrolled across the three studies.

XCOPRI® (cenobamate tablets) Efficacy

In the randomized studies (Study 013 and Study 017), XCOPRI demonstrated significant reductions in seizure frequency compared to placebo.

Study 013

221 patients enrolled in Study 013 and were randomized to 200 mg of XCOPRI® (cenobamate tablets) or placebo for 12 weeks (6-week titration phase and 6-week maintenance phase).

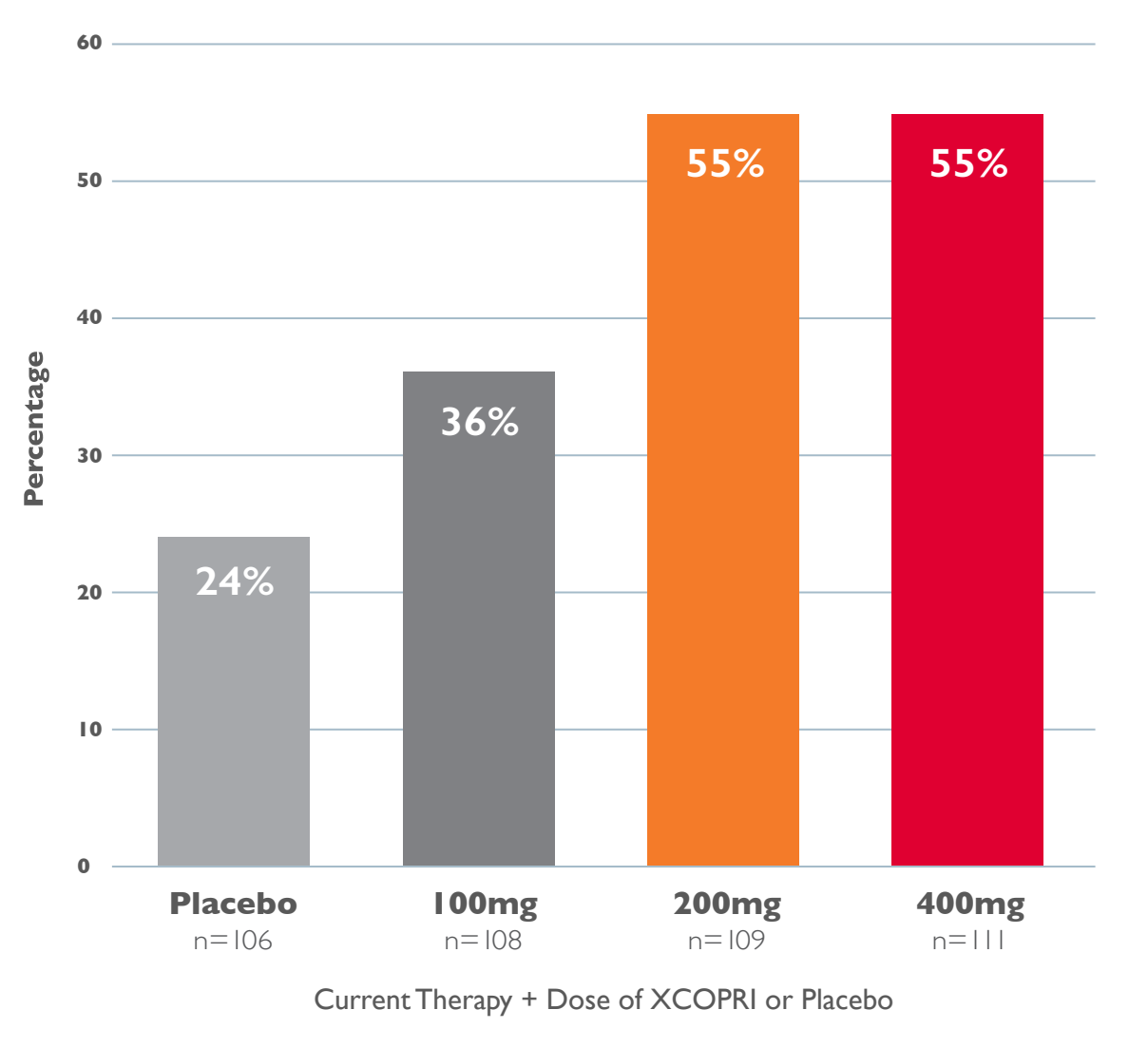
56% **reduction in median seizure frequency** with XCOPRI (n=113) compared to a **22%** reduction with placebo (n=108), which was statistically significant.

28% **of patients taking XCOPRI (n=106) had zero seizures** during the maintenance phase, compared with **9%** of placebo patients (n=102), based on a post-hoc analysis.

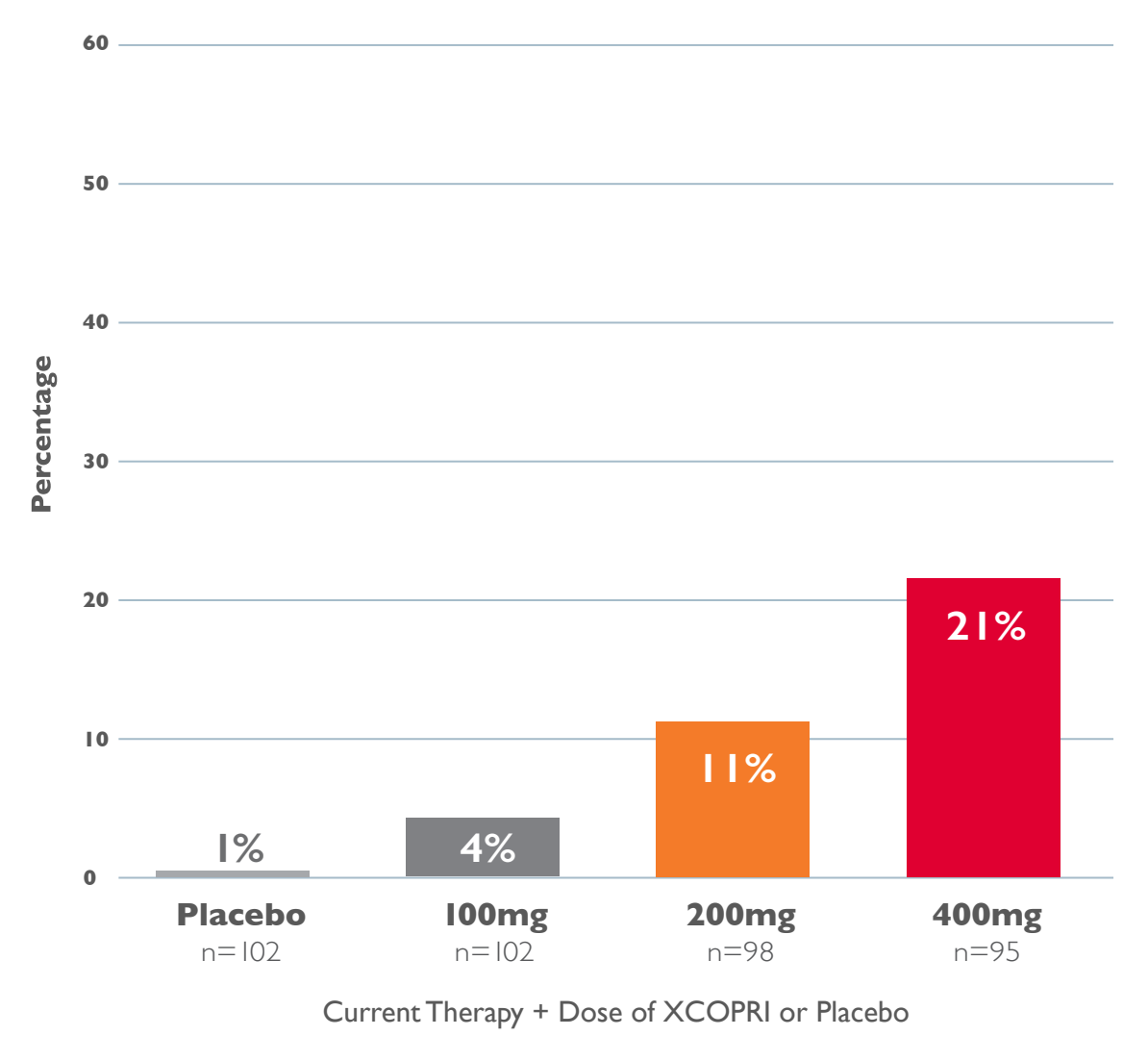
Study 017

434 patients enrolled in Study 017 and were randomized to 100 mg, 200 mg or 400 mg of XCOPRI® (cenobamate tablets) or placebo for 18 weeks (6-week titration phase and 12-week maintenance phase).

Median percentage reduction in seizure frequency during the 18-week treatment period



Percentage of patients who had zero seizures during the 12-week maintenance phase



Safety Profile

Serious reactions associated with XCOPRI include:

- drug reaction with eosinophilia and systemic symptoms (DRESS)
- QT shortening
- suicidal behavior and ideation
- neurological adverse reactions

The most common (≥10% and greater than with placebo) treatment-emergent adverse events associated with XCOPRI include:

- somnolence (sleepiness)
- dizziness
- fatigue
- diplopia (double vision)
- headache

How XCOPRI® (cenobamate tablets) May Work

While the precise mechanism by which XCOPRI exerts its therapeutic effect is unknown, it is believed to reduce repetitive neuronal firing by inhibiting voltage-gated sodium currents. It is also a positive allosteric modulator of the γ-aminobutyric acid ($GABA_A$) ion channel.

Patient Access and Availability of XCOPRI® (cenobamate tablets)

XCOPRI is expected to be available in the U.S. in the second quarter of 2020, following scheduling review by the U.S. Drug Enforcement Administration (DEA), which typically occurs within 90 days of FDA approval.

SK life science is committed to supporting patients taking XCOPRI, and will introduce a new patient access program to help patients get started and stay on track with their medicine.

Media Inquiries
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IMPORTANT SAFETY INFORMATION AND INDICATION FOR XCOPRI® (cenobamate tablets) CX

INDICATION:
XCOPRI is a prescription medicine used to treat partial-onset seizures in adults 18 years of age and older.

It is not known if XCOPRI is safe and effective in children under 18 years of age.

DO NOT TAKE XCOPRI IF YOU:

- Are allergic to cenobamate or any of the other ingredients in XCOPRI.
- Have a genetic problem (called Familial Short QT syndrome) that affects the electrical system of the heart.

XCOPRI CAN CAUSE SERIOUS SIDE EFFECTS, INCLUDING:
Allergic reactions: XCOPRI can cause serious skin rash or other serious allergic reactions which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions. Call your healthcare provider right away and go to the nearest emergency room if you have any of the following: swelling of your face, eyes, lips, or tongue, trouble swallowing or breathing, a skin rash, hives, fever, swollen glands, or sore throat that does not go away or comes and goes, painful sores in the mouth or around your eyes, yellowing of your skin or eyes, unusual bruising or bleeding, severe fatigue or weakness, severe muscle pain, frequent infections, or infections that do not go away. **Take XCOPRI exactly as your healthcare provider tells you to take it. It is very important to increase your dose of XCOPRI slowly, as instructed by your healthcare provider.**

QT shortening: XCOPRI may cause problems with the electrical system of the heart (QT shortening). Call your healthcare provider if you have symptoms of QT shortening including fast heartbeat (heart palpitations) that last a long time or fainting.

Suicidal behavior and ideation:
Antiepileptic drugs, including XCOPRI, may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Call your health care provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you: thoughts about suicide or dying; attempting to commit suicide; new or worse depression, anxiety, or irritability; feeling agitated or restless; panic attacks; trouble sleeping (insomnia); acting aggressive; being angry or violent; acting on dangerous impulses; an extreme increase in activity and talking (mania); or other unusual changes in behavior or mood.

Nervous system problems: XCOPRI may cause problems that affect your nervous system. Symptoms of nervous system problems include: dizziness, trouble walking or with coordination, feeling sleepy and tired, trouble concentrating, remembering, and thinking clearly, and vision problems. **Do not drive, operate heavy machinery, or do other dangerous activities until you know how XCOPRI affects you.**

Do not drink alcohol or take other medicines that can make you sleepy or dizzy while taking XCOPRI without first talking to your healthcare provider.

DISCONTINUATION:
Do not stop taking XCOPRI without first talking to your healthcare provider. Stopping XCOPRI suddenly can cause serious problems. Stopping seizure medicine suddenly in a patient who has epilepsy can cause seizures that will not stop (status epilepticus).

DRUG INTERACTIONS:
XCOPRI may affect the way other medicines work, and other medicines may affect how XCOPRI works. **Do not start or stop other medicines without talking to your healthcare provider.** Tell healthcare providers about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

PREGNANCY AND LACTATION:
XCOPRI may cause your birth control medicine to be less effective. **Talk to your health care provider about the best birth control method to use.**

Talk to your health care provider if you are pregnant or plan to become pregnant. It is not known if XCOPRI will harm your unborn baby. Tell your healthcare provider right away if you become pregnant while taking XCOPRI. You and your healthcare provider will decide if you should take XCOPRI while you are pregnant. If you become pregnant while taking XCOPRI, talk to your healthcare provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic medicine during pregnancy. You can enroll in this registry by calling 1-888-233-2334 or go to www.aedpregnancyregistry.org.

Talk to your health care provider if you are breastfeeding or plan to breastfeed. It is not known if XCOPRI passes into breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking XCOPRI.

COMMON SIDE EFFECTS:
The most common side effects in patients taking XCOPRI include dizziness, sleepiness, headache, double vision, and feeling tired.

These are not all the possible side effects of XCOPRI. Tell your healthcare provider if you have any side effect that bothers you or that does not go away. For more information, ask your healthcare provider or pharmacist. **Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088** or at www.fda.gov/medwatch.

DRUG ABUSE:
Scheduling of XCOPRI is pending review by the U.S. Drug Enforcement Administration (DEA).

[1] Centers for Disease Control and Prevention. Active Epilepsy and Seizure Control in Adults — United States, 2013 and 2015. https://www.cdc.gov/mmwr/volumes/67/wr/mm6715a1.htm?s_cid=mm6715a1. Accessed November 2019.
[2] Epilepsy Foundation. About Epilepsy: The Basics. https://www.epilepsy.com/learn/about-epilepsy-basics. Accessed November 2019.
[3] National Institute of Neurological Disorders and Stroke. The Epilepsies and Seizures: Hope through Research. https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Epilepsies-and-Seizures-Hope-Through#3109_9. Accessed November 2019.
[4] Chen Z, Brodie MJ, Liew D, Kwan P. Treatment outcomes in patients with newly diagnosed epilepsy treated with established and new antiepileptic drugs: a 30-year longitudinal cohort study. https://www.ncbi.nlm.nih.gov/pubmed/29279892. Published online December 26, 2017.