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FOR IMMEDIATE RELEASE

UPSHER-SMITH GRANTED TENTATIVE FDA APPROVAL FOR QUDEXY® XR (TOPIRAMATE) EXTENDED-RELEASE CAPSULES FOR PROPHYLAXIS OF MIGRAINE HEADACHE IN ADULTS

Maple Grove, MN – June 9, 2016 – [Upsher-Smith Laboratories, Inc.](http://www.upsher-smith.com) (Upsher-Smith) announced that the U.S. Food and Drug Administration (FDA) has granted tentative approval for its supplemental new drug application (sNDA) for [Qudexy® XR \(topiramate\) extended-release capsules](#) for use as prophylaxis of migraine headache in adults.

“Topiramate is the molecule prescribed most frequently by neurologists for the prevention of migraines. However, there are currently no extended-release topiramate formulations approved for migraine prophylaxis in the US,” said William Pullman, MB, BS, BMedSc, PhD, FRACP, Chief Scientific Officer and Biotech Research Institute Division President, Upsher-Smith. “We look forward to bringing this treatment option to the migraine community, and will continue to work with the FDA to gain final approval.”

Qudexy® XR is currently approved for use as initial monotherapy in patients two years of age and older with partial-onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients two years of age or older with partial-onset or primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome. Qudexy® XR has been available in the United States since June 2014.

INDICATIONS

Qudexy® XR (topiramate) Extended-Release Capsules is a prescription medicine used to treat certain types of seizures (partial-onset seizures and primary generalized tonic-clonic seizures) and with other medicines to treat certain types of seizures (partial-onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome) in adults and children 2 years and older.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about Qudexy XR?

You should discuss the potential benefits and risks of Qudexy XR with your doctor.

Qudexy XR may cause serious eye problems that can lead to permanent loss of vision if not treated. You should call your doctor right away if you have any new eye symptoms, including any new problems with your vision. **Qudexy XR may cause decreased sweating and fever**, which you should monitor and call your doctor right away if you have a high fever, a fever that does not go away, or decreased sweating develops. **Qudexy XR can increase the level of acid in your blood** (metabolic acidosis), which can lead to complications if left untreated. Your doctor should do a blood test to measure the level of acid in your blood before and during your treatment with Qudexy XR. **Do not take Qudexy® XR if you** have been told you have a problem with your blood called metabolic acidosis and are taking a medicine called metformin at the same time.

What should I tell my doctor BEFORE starting Qudexy XR?

Before taking Qudexy XR, tell your doctor about all of your medical conditions, including if you:

- have had depression, mood problems, or suicidal thoughts or behavior;
- have kidney problems, kidney stones, or are getting kidney dialysis;
- have a history of metabolic acidosis (too much acid in the blood);
- have liver problems;
- have weak, brittle or soft bones (osteomalacia, osteoporosis, osteopenia, or decreased bone density);
- have lung or breathing problems;
- have eye problems, especially glaucoma;
- have diarrhea;
- have a growth problem;
- are on a diet high in fat and low in carbohydrates, which is called a ketogenic diet;
- are having surgery; are pregnant or plan to become pregnant;
- or if you are breastfeeding. The medicine in Qudexy XR (topiramate) passes into your breast milk. It is not known if the medicine, topiramate, that passes into breast milk can harm your baby. Talk to your doctor about the best way to feed your baby if you take Qudexy XR.

Also tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take metformin (e.g., Glucophage); valproic acid (e.g., Depakene or Depakote); any medicines that impair or decrease your thinking, concentration, or muscle coordination; birth control pills; medicines used to prevent seizures; or any other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide, or dichlorphenamide). Qudexy XR may make your birth control pills less effective. Ask your doctor if you are not sure if your medicine is listed above.

What should I watch for AFTER starting Qudexy XR?

Qudexy XR can cause serious side effects, including:

- **Eye problems.** Serious eye problems include blurred vision, sudden decrease in vision with or without eye pain and redness, and a blockage of fluid that may cause increased pressure in the eye (secondary angle closure glaucoma). If left untreated, these can lead to permanent vision loss.
- **Decreased sweating and fever.** People, especially children, should be watched for signs of decreased sweating and fever, especially in hot temperatures. Some people may need to be hospitalized for this condition.
- **Increased acid level in your blood (metabolic acidosis).** This may or may not cause symptoms. Symptoms may include feeling tired, decreased appetite, change in heartbeat, or trouble thinking clearly. If left untreated, metabolic acidosis can cause brittle or soft bones

(osteoporosis, osteomalacia, osteopenia), kidney stones, can slow the rate of growth in children, and may harm your baby if you are pregnant.

- **High blood ammonia levels.** High ammonia in the blood can affect mental activities, slow alertness, cause tiredness, or cause vomiting. This can also happen when Qudexy XR is taken with a medicine called valproic acid (e.g., Depakene® and Depakote®).
- **Kidney stones.** Drink plenty of fluids when taking Qudexy XR to decrease your chances of getting kidney stones.
- **Low body temperature.** Taking Qudexy XR when you are also taking valproic acid may cause a drop in body temperature to less than 95°F, tiredness, confusion, or coma.
- **Effects on thinking and alertness.** Qudexy XR may affect how you think, and can cause confusion, and problems with concentration, attention, memory, or speech. Qudexy XR may cause depression or mood problems, tiredness, and sleepiness.
- **Dizziness or loss of muscle coordination.**

Call your doctor right away if you have any of the above symptoms.

The most common side effects of Qudexy XR include: tingling of the arms and legs (paresthesia), not feeling hungry, weight loss, nervousness, speech problems, tiredness, dizziness, sleepiness/drowsiness, slow reactions, difficulty with memory, fever, and abnormal vision. These are not all the possible side effects of Qudexy XR. For more information, ask your doctor or pharmacist.

Like other antiepileptic drugs, Qudexy XR may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Call a doctor right away if you have any of these symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying;
- attempts to commit suicide;
- new or worse depression or anxiety;
- feel agitated or restless;
- experience panic attacks;
- trouble sleeping (insomnia);
- new or worse irritability;
- feel or act aggressive, angry, or violent;
- act on dangerous impulses;
- an extreme increase in activity and talking (mania);
- other unusual changes in behavior or mood.

Qudexy XR can harm your unborn baby. All women of childbearing age should talk to their doctors about possible alternative treatments. If you take Qudexy XR during pregnancy, your baby has a higher risk for birth defects called cleft lip and cleft palate. These defects can begin early in pregnancy, even before you know you are pregnant. If the decision is made to use Qudexy XR, you should use effective birth control (contraception) unless you are planning to become pregnant. **Tell your doctor right away if you become pregnant while taking Qudexy XR.**

Do not stop Qudexy XR without first talking to a doctor. If you have epilepsy and you stop taking Qudexy XR suddenly, you may have seizures that do not stop. Your doctor will tell you how to stop taking Qudexy XR slowly.

What should I avoid while taking Qudexy XR?

Do not drink alcohol while taking Qudexy XR. Qudexy XR and alcohol can cause serious side effects such as severe sleepiness and dizziness and an increase in seizures.

Do not drive a car, swim, climb, or operate heavy machinery until you know how Qudexy XR affects you. Qudexy XR can slow your thinking and motor skills, and may affect vision. Even when taking Qudexy XR, some patients with epilepsy will continue to have unpredictable seizures.

How should I take Qudexy XR?

Take Qudexy XR exactly as your doctor tells you to. You may swallow Qudexy XR capsules whole or, if you cannot swallow the capsule whole, you may carefully open the Qudexy XR capsule and sprinkle the medicine on a spoonful of soft food like applesauce. Swallow the food and medicine mixture right away. Do not store the food and medicine mixture to use later or crush or chew the food and medicine mixture before swallowing.

This is the most important information to know about Qudexy XR. For more information, talk to your health care provider and read the [Medication Guide](#) for Qudexy XR. You can also visit www.upsher-smith.com or call 1-888-650-3789.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see [full Prescribing Information](#) at www.QudexyXR.com

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About Upsher-Smith

Upsher-Smith Laboratories, Inc., founded in 1919, is a growing, fully integrated pharmaceutical company dedicated to its mission of delivering high-value, high-quality therapies and solutions which measurably improve individuals' lives. As a family-owned pharmaceutical company, we are able to adapt and thrive in a dynamic healthcare environment. Our world is constantly evolving, and we are continually adapting to the ever-changing needs of patients, physicians, pharmacists, and healthcare organizations. Where there is a need, we will work to deliver solutions that simplify access to treatment, deliver better health outcomes, and enhance life. Upsher-Smith has a particular focus on developing therapies for people living with central nervous system (CNS) conditions, such as seizure disorders. For more information, visit www.upsher-smith.com.

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