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FOR IMMEDIATE RELEASE

FDA APPROVES EXPANDED INDICATION FOR QUDEXY® XR (TOPIRAMATE) EXTENDED-RELEASE CAPSULES TO INCLUDE PROPHYLAXIS OF MIGRAINE HEADACHE IN ADULTS AND ADOLESCENTS

Molecule Most Prescribed by Neurologists for Migraine Prophylaxis Now Available in a Unique 24-hour Formulation

Maple Grove, MN – March 30, 2017 – Upsher-Smith Laboratories, Inc. (Upsher-Smith) today announced that it has received U.S. Food and Drug Administration (FDA) final approval of two supplemental new drug applications (sNDAs) for Qudexy® XR (topiramate) Extended-Release Capsules for use as prophylaxis of migraine headache in adults and adolescents 12 years of age and older. Topiramate is the molecule that neurologists prescribe most frequently for the prevention of migraines[1], and the American Academy of Neurology and the American Headache Society have given topiramate a "top tier" rating for migraine prevention in adults.[2] A study designed to address post-marketing requirements in the United States is planned to evaluate the efficacy and safety of Qudexy XR for the prophylaxis of migraine in pediatric patients ages 6-11. Upsher-Smith was granted tentative approval of its sNDA in April 2016, but was not eligible to receive final approval until after the innovator drug's exclusivity for the adolescent population expired in March 2017.

It has been reported that adherence to migraine prophylaxis medications is as low as 41 percent at two months and declines even further over time.[3] Qudexy® XR capsules offer adolescents and adults with migraines a once-daily prophylactic medication that can be taken morning or night, with or without food. The capsules have also been approved for administration by opening and sprinkling the contents onto a small amount of soft food, which may be helpful to patients who have difficulty swallowing whole capsules. Qudexy® XR has been specifically engineered to deliver a smooth pharmacokinetic profile and shown to reduce the peak-to-trough fluctuation of topiramate plasma concentrations that are associated with immediate-release topiramate.[1,4]

"Topiramate is a first-line, Level A migraine medication, and the expanded indication for migraine prevention in adolescent and adult patients for once-daily Qudexy® XR is a great addition to our treatment options," said Brian D. Loftus, MD, Board Certified in Headache Medicine, President of the Southern Headache Society. "Qudexy® XR capsules can be swallowed whole or opened and the beads sprinkled onto a spoonful of soft food that is swallowed. The unique

extended-release formulation of Qudexy® XR will allow for smoother delivery of topiramate than was previously possible."

Qudexy® XR is also 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 and 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.

A savings and support program is available to patients who have been prescribed Qudexy® XR. The Access Pathways™ Program offers co-pay assistance and administrative support to help patients start, stay and save on Qudexy® XR therapy. To learn more, please visit QudexyXR.com or call 1-855-282-4887 Monday-Friday from 8:00 a.m. – 7:00 p.m. (EST).

WHAT IS QUDEXY XR?

Qudexy® XR (topiramate) Extended-Release Capsules is a prescription medicine used for:

- **Migraine:** To prevent migraine headaches in adults and adolescents 12 years and older.
- **Monotherapy Epilepsy:** Initial monotherapy to treat certain types of seizures (partial-onset seizures and primary generalized tonic-clonic seizures) in adults and children 2 years and older.
- **Adjunctive Epilepsy:** Adjunctive therapy 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.

WHAT IMPORTANT SAFETY INFORMATION SHOULD I KNOW ABOUT QUDEXY XR?

Qudexy® XR should not be taken by patients with metabolic acidosis who are also taking a medicine called metformin.

What should I tell my healthcare provider BEFORE starting Qudexy XR?

Tell your healthcare provider if you take any medicines that impair or decrease thinking, concentration, or muscle coordination; medicines used to prevent seizures; any other carbonic anhydrase inhibitors; or birth control pills. Qudexy XR may make birth control pills less effective.

Qudexy XR can cause serious side effects, including:

- **Serious eye problems**, including blurred or sudden decrease in vision and increased pressure in the eye, which can lead to permanent vision loss.
- **Decreased sweating and fever,** especially in hot weather which may result in hospitalization; children are especially susceptible to these effects.
- **Increased acid level in the blood (metabolic acidosis)**, which may lead to brittle or soft bones (osteoporosis, osteomalacia, osteopenia), kidney stones, slowed rate of growth in children and fetal harm. Metabolic acidosis may or may not cause symptoms. Symptoms may include feeling tired, decreased appetite, change in heartbeat, or trouble thinking clearly.
- **High ammonia level in the blood**, which can affect mental activities, slow alertness and cause tiredness and vomiting. This can also happen when Qudexy XR is taken with a medicine called valproic acid.

- **Kidney stone formation,** which may be reduced by increasing fluid intake while taking Qudexy XR**.**
- **Low body temperature.** Taking Qudexy XR while taking valproic acid may cause a drop in body temperature to less than 95°F with associated symptoms of tiredness, confusion, or coma.
- **Effects on thinking and alertness.** Qudexy XR may affect thinking, and 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.**
- **Fetal harm**. Taking Qudexy XR while pregnant increases the fetus risk of cleft lip and/or cleft palate and of being small for gestational age. Alternative treatment or effective birth control should be used. Discuss with your healthcare provider.
- **Suicidal thoughts and actions**. Like other antiepileptic drugs, Qudexy XR may cause suicidal thoughts and actions in a very small number of people, about 1 in 500. Tell your healthcare provider right away if you experience these effects, or any symptoms of depression or mood changes.

Tell your healthcare provider right away if you have any of the above symptoms, are planning to become pregnant, or if you become pregnant while taking Qudexy XR.

The most common side effects of Qudexy XR include: tingling of the arms and legs (paresthesia), not feeling hungry, weight loss, nervousness, nausea, speech problems, tiredness, dizziness, sleepiness/drowsiness, a change in the way foods taste, upper respiratory tract infection, slow reactions, difficulty with memory, fever, abnormal vision, diarrhea, and pain in the abdomen. These are not all the possible side effects of Qudexy XR. For more information, ask your healthcare provider or pharmacist.

Before taking Qudexy XR, tell your healthcare provider 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 healthcare provider about the best way to feed your baby if you take Qudexy XR.

Qudexy XR should not be taken while drinking alcohol, as this can cause serious side effects such as severe sleepiness, dizziness, and an increase in seizures.

Patients taking Qudexy XR should not drive, swim, climb, or operate heavy machinery until it is known how Qudexy XR affects them. Qudexy XR can slow thinking and motor skills and may affect vision. Some patients with epilepsy taking Qudexy XR will continue to have unpredictable seizures.

Do not stop Qudexy XR without first talking to a healthcare provider. If you have epilepsy and you stop taking Qudexy XR suddenly, you may have seizures that do not stop.

This is the most important information to know about Qudexy XR, but is not comprehensive. For more information, talk to your healthcare provider and read

the Medication Guide for Qudexy XR. You can also visit www.upsher-smith.com for the full Prescribing Information 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.

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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References

1. Data on file. Maple Grove, MN: Upsher-Smith Laboratories, Inc; 2015.
2. Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78(17): 1337-1345.
3. Hepp Z, Bloudek LM, Varon SF. Systemic review of migraine prophylaxis adherence and persistence. *J Manage Care Pharm.* 2014;20(1):22-23.
4. Qudexy XR [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, Inc; March 2017.

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