Once-Daily

Qudexy® XR

(topiramate) extended-release capsules

Update your topiramate

Give your patients options with Qudexy® XR.

Please see complete Important Safety Information inside and accompanying full Prescribing Information.

A century of serving patients

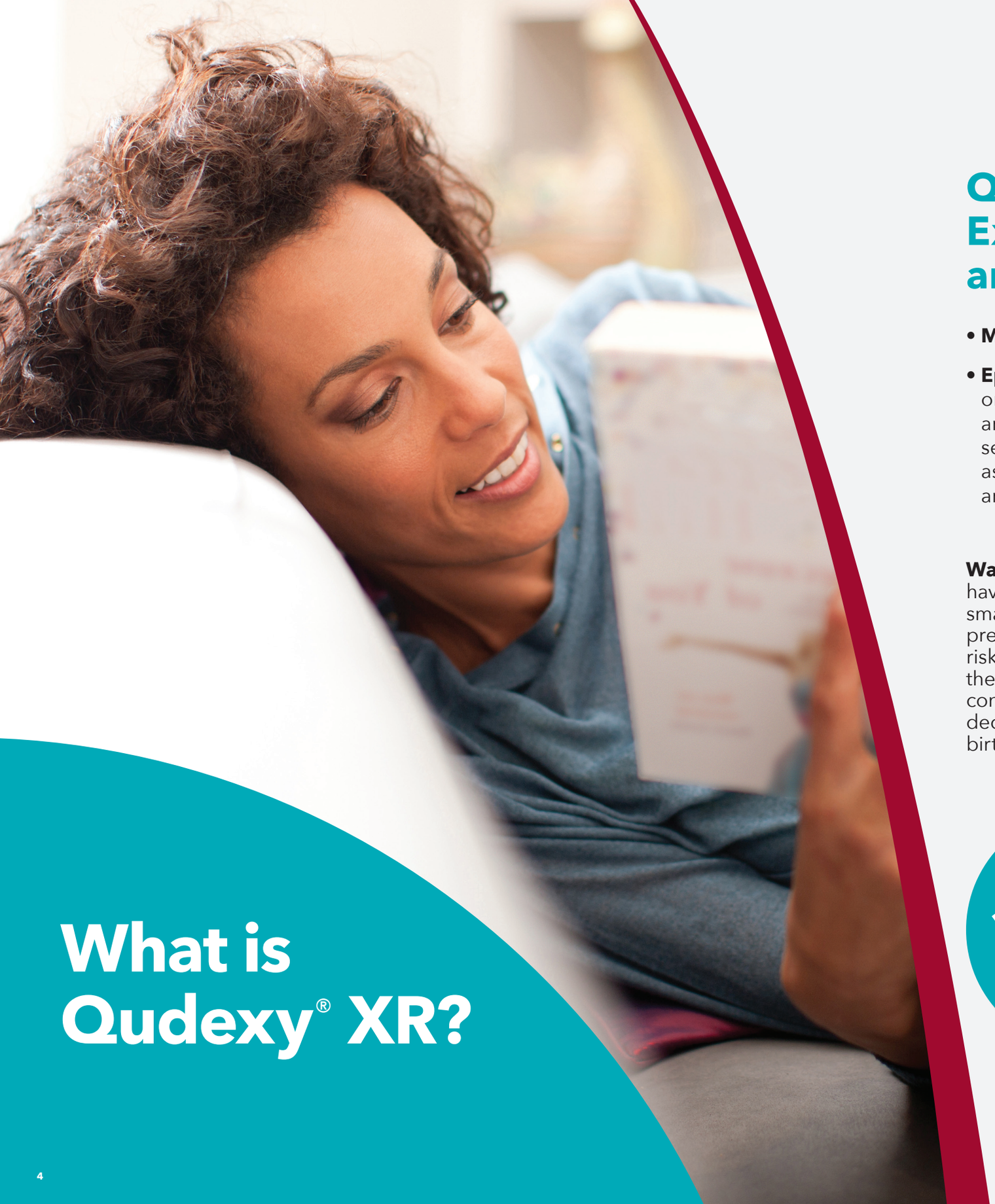
Upsher-Smith Laboratories, LLC has never wavered in our desire to offer people high-quality products that could help improve their health and lives. As we celebrate a century of serving patients, we take pride in providing attentive customer service, having strong industry relationships and being dedicated to uninterrupted supply.

Qudexy® XR demonstrates our commitment to deliver affordable options to patients and healthcare professionals, and we'll continue to develop innovative treatments for the next 100 years.

UPSHER-SMITH

Partners in Health Since 1919

CELEBRATING 1919 100 2019 YEARS



What is Qudexy® XR?

Qudexy® XR (topiramate) Extended-Release Capsules are indicated for:

- **Migraine:** Prophylaxis of migraine in patients 12 years and older.
- **Epilepsy:** Initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years and older. Adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut Syndrome in patients 2 years and older.

Warning: Fetal Toxicity. Infants exposed to topiramate *in utero* have an increased risk of cleft lip and/or cleft palate and of being small for gestational age. Qudexy® XR should be used during pregnancy only if the potential benefit outweighs the potential risk. All women of childbearing potential should be informed of the potential hazard to the fetus and counseled to use effective contraception, keeping in mind that there is a potential for decreased contraceptive efficacy when using estrogen-containing birth control with topiramate.

100%

Qudexy® XR is the only 100% extended-release bead formulation of topiramate.[1]

Please see complete Important Safety Information on pages 14–15 and accompanying full Prescribing Information.

Give your patients options

Qudexy® XR gives your patients options that immediate-release topiramate tablets don't.

Once-Daily
Qudexy® XR
(topiramate) extended-release capsules

	Qudexy® XR[2]	Immediate-release topiramate tablets[1]
100% extended-release bead formulation	✓	–
Once-daily dosing	✓	–
Smooth pharmacokinetic profile	✓	–
FDA-approved sprinkle administration option in all strengths	✓	–
Platinum Pass™ savings card $0 co-pay offer*	✓	–
Five dosage strengths, including 150 mg**	✓	–

* Restrictions apply. Medicare, Medicaid, and other federal and state health care program patients are not eligible.
** Recommended dosage for migraine prophylaxis is 100 mg once daily.

Please see complete Important Safety Information on pages 14–15 and accompanying full Prescribing Information.

Convenient to take

Upsher-Smith formulated Qudexy® XR with patient adherence in mind.[1,2]

Extended-release

Qudexy® XR is an extended-release medication. It provides a slow, continuous release of medication into the body.

Direct switch

Qudexy® XR requires no change in total daily dose when converting from immediate-release topiramate to once-daily dosing with Qudexy® XR

Flexible dosing

Qudexy® XR comes in five dosage strengths, including a unique 150 mg capsule.**

** Recommended dosage for migraine prophylaxis is 100 mg once daily.

Once-daily dosing

Qudexy® XR gives your patients all-day medication coverage with just one daily dose and a sprinkle option.

Once-Daily
Qudexy® XR
(topiramate) extended-release capsules

The most common topiramate adverse reactions in adult and pediatric epilepsy patients were: paresthesia, anorexia, weight loss, speech disorders/related speech problems, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, and fever.

The most common topiramate adverse reactions in adult and adolescent migraine patients were: paresthesia, anorexia, weight loss, difficulty with memory, taste perversion, diarrhea, hypoesthesia, nausea, abdominal pain, and upper respiratory tract infection.

Please see complete Important Safety Information on pages 14–15 and accompanying full Prescribing Information.

Simple to prescribe

Upsher-Smith is dedicated to reducing the administrative hassles and cost barriers of prescribing medications. It's why we created the Access Pathways® Program.

ACCESS PATHWAYS®
PROGRAM

Access Pathways® provides savings and support services for patients.

Platinum Pass™

Eligible patients pay $0 per prescription with the Platinum Pass™ savings card.

Call 1-855-282-4887 to request a Platinum Pass™ savings card for your patients today!

Qudexy® XR
(topiramate) extended-release capsules

Accessible

The Platinum Pass™ savings card buys down a one-month supply for a commercially insured claim to $0,* even if the commercial payer has rejected the prior authorization or the product is not covered.

Affordable

Patients can present their Access Pathways® Platinum Pass™ savings card for Qudexy® XR or its authorized generic to their pharmacist for instant savings. Patients pay $0 per prescription, regardless of coverage.*

*Restrictions apply. Medicare, Medicaid, and other federal and state health care program patients are not eligible.

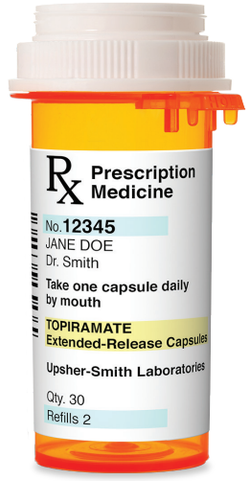
Once-Daily
Qudexy® XR
(topiramate) extended-release capsules

=

UPSHER-SMITH Once-Daily
Topiramate
Extended-Release Capsules

Helping more patients access the medication they need

Topiramate Extended-Release Capsules are the authorized generic of Qudexy® XR. It's the same medication as Qudexy® XR, just with a different name.



- **Identical** to Qudexy® XR
- **Same** active and inactive ingredients
- **Same** manufacturing process
- **Same** savings and support program

Please see complete Important Safety Information on pages 14–15 and accompanying full Prescribing Information.

For more information, visit
hcp.QudexyXR.com

Once-Daily

Qudexy® XR

(topiramate) extended-release capsules

INDICATIONS

Qudexy® XR (topiramate) Extended-Release Capsules are indicated for:

- **Migraine:** Prophylaxis of migraine in patients 12 years and older.
- **Epilepsy:** Initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years and older. Adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut Syndrome in patients 2 years and older.

IMPORTANT SAFETY INFORMATION

WARNINGS & PRECAUTIONS

- **Acute Myopia and Secondary Angle Closure Glaucoma.** A syndrome consisting of acute myopia associated with secondary angle closure glaucoma has been reported in patients receiving topiramate, with symptoms typically occurring within 1 month of therapy initiation. The primary treatment to reverse symptoms is discontinuation of Qudexy XR as rapidly as possible. If left untreated, elevated intraocular pressure can lead to serious sequelae, including permanent vision loss.
- **Visual Field Defects.** Visual field defects have been reported in patients receiving topiramate independent of elevated intraocular pressure. If visual problems occur at any time during topiramate treatment, consideration should be given to discontinuing the drug.
- **Oligohydrosis and Hyperthermia.** Oligohydrosis, resulting in hospitalization in some cases, has been reported in association with topiramate use. The majority of reports have been in pediatric patients, but all patients should be monitored closely for evidence of decreased sweating and increased body temperature, especially in hot weather. Caution should be used when Qudexy XR is prescribed with other drugs that predispose patients to heat-related disorders.
- **Metabolic Acidosis.** Qudexy XR can cause hyperchloremic, non-anion gap metabolic acidosis due to its inhibitory effect on carbonic anhydrase. Conditions that predispose patients to acidosis may be additive to the bicarbonate lowering effects of topiramate. Measurement of baseline and periodic serum bicarbonate during topiramate treatment is recommended. If metabolic acidosis develops and persists, consideration should be given to reducing the dose or discontinuing topiramate (using dose tapering).
- **Suicidal Behavior and Ideation.** Antiepileptic drugs (AEDs), including Qudexy XR increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Patients, their caregivers, and families should be informed of these risks, and behaviors of concern should be immediately reported to healthcare providers.
- **Cognitive/Neuropsychiatric Adverse Reactions.** Immediate-release topiramate can cause, and therefore, Qudexy XR is expected to cause, cognitive/neuropsychiatric adverse reactions. In adults, the most frequent of these can be classified into three general categories: cognitive-related dysfunction, psychiatric/behavioral disturbances, and somnolence/fatigue. In pediatric epilepsy trials, adverse reactions included psychomotor slowing, difficulty with concentration/attention, speech disorders/related speech problems, and language problems. In migraine prophylaxis controlled trials, the most common cognitive adverse reaction was difficulty with memory. Patients should use caution when operating machinery including automobiles. Depression and mood problems may occur.
- **Fetal Toxicity.** Topiramate can cause fetal harm when administered to a pregnant woman. Data from pregnancy registries indicate that infants exposed to topiramate *in utero* have an increased risk of cleft lip and/or cleft palate and of being small for gestational age. Qudexy XR should be used during pregnancy only if the potential benefit outweighs the potential risk. All women of childbearing potential should be informed of the potential hazard to the fetus and counseled to use effective contraception, keeping in mind that there is a potential for decreased contraceptive efficacy when using estrogen-containing birth control with topiramate.
- **Withdrawal of Antiepileptic Drugs.** Antiepileptic drugs, including Qudexy XR, should be gradually withdrawn to minimize the potential for seizures or increased seizure frequency.
- **Hyperammonemia and Encephalopathy.** Topiramate treatment can cause hyperammonemia, with and without encephalopathy. The risk for hyperammonemia with topiramate appears dose-related. Hyperammonemia has been reported more frequently when used concomitantly with valproic acid. Patients with inborn errors of metabolism or reduced mitochondrial activity may have an increased risk of hyperammonemia. Measure ammonia if encephalopathic symptoms occur.
- **Kidney Stones**. Topiramate increases the risk of kidney stones. Topiramate is a carbonic anhydrase inhibitor. Carbonic anhydrase inhibitors can promote stone formation by reducing urinary citrate excretion and by increasing urinary pH. The concomitant use of Qudexy XR with any other drug producing metabolic acidosis, or potentially in patients on a ketogenic diet, may create a physiological environment that increases the risk of kidney stone formation, and should therefore be avoided. Increased fluid intake increases the urinary output, lowering the concentration of substances involved in stone formation. Hydration is recommended to reduce new stone formation.
- **Hypothermia with Concomitant Valproic Acid Use**. Hypothermia has been reported in association with topiramate use with concomitant valproic acid, both in the presence and in the absence of hyperammonemia. Consideration should be given to stopping topiramate or valproate in patients who develop hypothermia.

USE IN SPECIFIC POPULATIONS

- Nursing Mothers: Topiramate is excreted in human milk. The effects of topiramate on milk production are unknown. Diarrhea and somnolence have been reported in breastfed infants whose mothers receive topiramate treatment. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Qudexy XR and any potential adverse effects on the breastfed infant from Qudexy XR or from the underlying maternal condition.
- Females of Reproductive Potential: Women of childbearing potential who are not planning a pregnancy should use effective contraception because of the risks to the fetus of oral clefts and of being small for gestational age.
- Pregnancy: Increased risk of cleft lip and/or palate and for being small for gestational age.
- Patients with Renal Impairment: One-half of the usual adult dose is recommended.
- Patients Undergoing Hemodialysis: To avoid rapid drops in topiramate plasma concentration, a supplemental dose of topiramate may be required.
- Geriatric use: Dosage adjustment may be necessary for elderly with impaired renal function.

DRUG INTERACTIONS

- Antiepileptic Drugs: Concomitant administration of phenytoin or carbamazepine with topiramate resulted in a clinically significant decrease in plasma concentrations of topiramate. A dosage adjustment may be needed. Concomitant administration of valproic acid and topiramate has been associated with hypothermia and hyperammonemia with or without encephalopathy.
- CNS Depressants: Qudexy XR should be used with extreme caution if used in combination with alcohol and other CNS depressants.
- Oral Contraceptives: The possibility of decreased contraceptive efficacy and increased breakthrough bleeding may occur.
- Lithium: Lithium levels should be monitored when co-administered with high-dose Qudexy XR.
- Other Carbonic Anhydrase Inhibitors: Patients should be monitored for the appearance or worsening of metabolic acidosis when Qudexy XR is given concomitantly with another carbonic anhydrase inhibitor.
- Hydrochlorothiazide (HCTZ): The addition of HCTZ to Qudexy XR may require a decrease in the Qudexy XR dose.
- Pioglitazone: When Qudexy XR is added to pioglitazone therapy or pioglitazone is added to Qudexy XR therapy, careful attention should be given to the routine monitoring of patients for adequate control of their diabetic disease state.
- Amitriptyline: Some patients may experience a large increase in amitriptyline concentration in the presence of Qudexy XR and any adjustments in amitriptyline dose should be made according to the patient's clinical response and not on the basis of plasma levels.

ADVERSE REACTIONS

- Epilepsy: The most common adverse reactions in adult and pediatric controlled, clinical trials of immediate-release topiramate were: paresthesia, anorexia, weight loss, speech disorders and related speech problems, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, and fever.
- Migraine: The most common adverse reactions at recommended doses in adult and adolescent controlled, clinical trials were: paresthesia, anorexia, weight loss, difficulty with memory, taste perversion, diarrhea, hypoesthesia, nausea, abdominal pain and upper respiratory tract infection.
- Qudexy XR has been studied in a randomized, placebo-controlled, phase 3 clinical study in 249 adult patients with a history of partial-onset seizures with or without secondary generalization. See the ADVERSE REACTIONS section of the Qudexy XR full prescribing information for adverse reaction rates from this clinical trial.
- The most serious adverse reactions are listed above in the WARNINGS AND PRECAUTIONS section.

This safety information is not comprehensive. Please refer to the full Prescribing Information for Qudexy XR and Medication Guide. You can also visit www.upsher-smith.com or call 1-888-650-3789.

You are encouraged to report suspected adverse reactions to Upsher-Smith Laboratories, LLC at 1-855-899-9180 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

Qudexy is a registered trademark of Upsher-Smith Laboratories, LLC.

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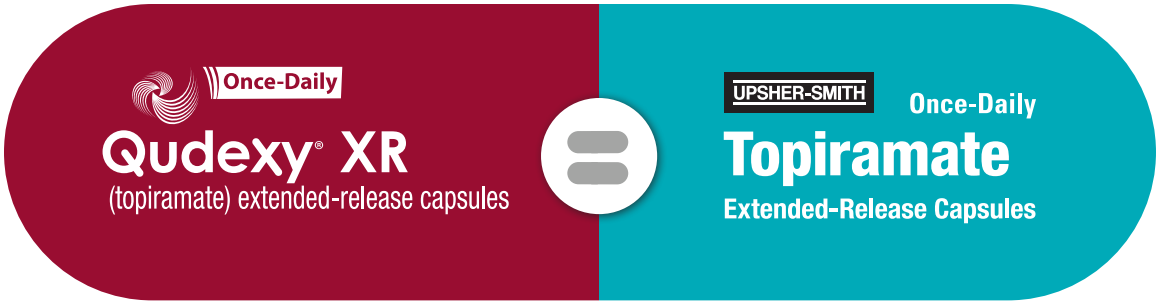

Learn more about Qudexy® XR and its authorized generic, Topiramate Extended-Release Capsules, at **hcp.QudexyXR.com**

Please see complete Important Safety Information on pages 14–15 and accompanying full Prescribing Information.

REFERENCES
1. Data on file. Maple Grove, MN: Upsher-Smith Laboratories, LLC: 2019.
2. Qudexy® XR [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: February 2019.

UPSHER-SMITH
Partners in Health Since 1919

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use QUDEXY XR safely and effectively. See full prescribing information for QUDEXY XR.

QUDEXY™ XR (topiramate) extended-release capsules, for oral use
Initial U.S. Approval: 1996

——— RECENT MAJOR CHANGES ———
Indications and Usage (1.1, 1.3) 02/2019
Dosage and Administration (2.2) 02/2019
Contraindications (4) 02/2019
Warnings and Precautions (5.4, 5.7, 5.8, 5.15) 02/2019

——— INDICATIONS AND USAGE ———
QUDEXY XR is indicated for:
- Epilepsy: initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years of age and older (1.1); adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut Syndrome in patients 2 years of age and older (1.2)
- Prophylaxis of migraine in patients 12 years of age and older (1.3)

——— DOSAGE AND ADMINISTRATION ———
- Qudexy XR initial dose, titration, and recommended maintenance dose varies by indication and age group. See Full Prescribing Information for recommended dosages and dosing considerations in patients with renal impairment, geriatric patients, patients undergoing hemodialysis (2.1, 2.2, 2.3, 2.4, 2.5, 2.6)
- Capsules may be swallowed whole or opened and sprinkled on a spoonful of soft food (2.6).

——— DOSAGE FORMS AND STRENGTHS ———
Extended-release capsules: 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg (3)

——— CONTRAINDICATIONS ———
None (4)

——— WARNINGS AND PRECAUTIONS ———
- Acute myopia and secondary angle closure glaucoma: Monitor and treat promptly; permanent visual loss. Discontinue QUDEXY XR as soon as possible (5.1)
- Visual field defects: Consider discontinuation of QUDEXY XR (5.2)
- Hyperchloremic, non-anion gap, metabolic acidosis (i.e., decreased serum bicarbonate below the normal reference range in the absence of chronic respiratory alkalosis). This condition may result in kidney stone formation and/or osteopenia, which may be severe. Monitor baseline and periodic serum bicarbonat

Patients who experienced 3 to 12 migraine headaches over the 4 weeks in the baseline phase were randomized to either topiramate 50 mg/day, 100 mg/day, 200 mg/day (twice the recommended daily dosage for migraine prophylaxis), or placebo and treated for a total of 26 weeks (8-week titration period and 18-week maintenance period). Treatment was initiated at 25 mg/day for one week, and then the daily dosage was increased by 25 mg increments each week until reaching the assigned target dose or maximum tolerated dose (administered twice daily).

Effectiveness of treatment was assessed by the reduction in migraine headache frequency, as measured by the change in 4-week migraine rate (according to migraines classified by IHS criteria) from the baseline phase to double-blind treatment period in each immediate-release topiramate treatment group compared to placebo in the Intent-To-Treat (ITT) population.

In Study 11, a total of 469 patients (416 females, 53 males), ranging in age from 13 to 70 years, were randomized and provided efficacy data. Two hundred sixty-five patients completed the entire 26-week double-blind phase. The median average daily dosages were 48 mg/day, 88 mg/day, and 132 mg/day in the target dose groups of topiramate 50, 100, and 200 mg/day, respectively.

The mean migraine headache frequency rate at baseline was approximately 5.5 migraine headaches per 28 days and was similar across treatment groups. The change in the mean 4-week migraine headache frequency from baseline to the double-blind phase was −1.3, −2.1, and −2.2 in the immediate-release topiramate 50, 100, and 200 mg/day groups, respectively, versus −0.8 in the placebo group (see Figure 3). The treatment differences between the immediate-release topiramate 100 and 200 mg/day groups versus placebo were similar and statistically significant (p<0.001 for both comparisons).

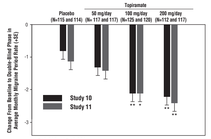
In Study 12, a total of 468 patients (406 females, 62 males), ranging in age from 12 to 65 years, were randomized and provided efficacy data. Two hundred fifty-five patients completed the entire 26-week double-blind phase. The median average daily dosages were 47 mg/day, 86 mg/day, and 150 mg/day in the target dose groups of immediate-release topiramate 50, 100, and 200 mg/day, respectively.

The mean migraine headache frequency rate at baseline was approximately 5.5 migraine headaches per 28 days and was similar across treatment groups. The change in the mean 4-week migraine headache period frequency from baseline to the double-blind phase was −1.4, −2.1, and −2.4 in the immediate-release topiramate 50, 100, and 200 mg/day groups, respectively, versus −1.1 in the placebo group (see Figure 3). The differences between the immediate-release topiramate 100 and 200 mg/day groups versus placebo were similar and statistically significant (p=0.008 and p <0.001, respectively).

In both studies, there were no apparent differences in treatment effect within age or gender subgroups. Because most patients were Caucasian, there were insufficient numbers of patients from different races to make a meaningful comparison of race.

For patients withdrawing from immediate-release topiramate, daily dosages were decreased in weekly intervals by 25 to 50 mg/day.

Figure 3: Reduction in 4-Week Migraine Headache Frequency (Studies 11 and 12 for Adults and Adolescents)



*** p<0.010, ** p <0.001**

Pediatric Patients 12 to 17 Years of Age

The effectiveness of immediate-release topiramate as prophylaxis for migraine headache in pediatric patients 12 to 17 years of age was established in a multicenter, randomized, double-blind, parallel-group trial (Study 13). The study enrolled 103 patients (40 male, 63 female) 12 to 17 years of age with episodic migraine headaches with or without aura. Patient selection was based on IHS criteria for migraines (using proposed revisions to the 1988 IHS pediatric migraine criteria [IHS-R criteria]).

Patients who experienced 3 to 12 migraine attacks (according to migraines classified by patient reported diaries) and ≤14 headache days (migraine and non-migraine) during the 4-week prospective baseline period were randomized to either immediate-release topiramate 50 mg/day, 100 mg/day, or placebo and treated for a total of 16 weeks (4-week titration period followed by a 12-week maintenance period). Treatment was initiated at 25 mg/day for one week, and then the daily dosage was increased by 25 mg increments each week until reaching the assigned target dose or maximum tolerated dose (administered twice daily). Approximately 80% or more patients in each treatment group completed the study. The median average daily dosages were 45 and 79 mg/day in the target dose groups of immediate-release topiramate 50 and 100 mg/day, respectively.

Effectiveness of treatment was assessed by comparing each immediate-release topiramate treatment group to placebo (ITT population) for the percent reduction from baseline to the last 12 weeks of the double-blind phase in the monthly migraine attack rate (primary endpoint). The percent reduction from baseline to the last 12 weeks of the double-blind phase in average monthly migraine attack rate is shown in Table 15. The 100 mg immediate-release topiramate dose produced a statistically significant treatment difference relative to placebo of 28% reduction from baseline in the monthly migraine attack rate.

The mean reduction from baseline to the last 12 weeks of the double-blind phase in average monthly attack rate, a key secondary efficacy endpoint in Study 3 (and the primary efficacy endpoint in Studies 1 and 2, of adults) was 3.0 for 100 mg immediate-release topiramate dose and 1.7 for placebo. This 1.3 treatment difference in mean reduction from baseline of monthly migraine rate was statistically significant (p = 0.0087).

Table 15: Percent Reduction from Baseline to the Last 12 Weeks of Double-Blind Phase in Average Monthly Attack Rate: Study 13 (Intent-to-Treat Analysis Set)

Category	Placebo (N=33)	Topiramate 50 mg/day (N=35)	Topiramate 100 mg/day (N=35)
Baseline			
Median	3.6	4.0	4.0
Last 12 Weeks of Double-Blind Phase			
Median	2.3	2.3	1.0
Percent Reduction (%)			
Median	44.4	44.6	72.2
P-value versus Placebo[a,b]		0.7875	0.0164[c]

[a]P-values (two-sided) for comparisons relative to placebo are generated by applying an ANCOVA model on ranks that includes subject's stratified age at baseline, treatment group, and analysis center as factors and monthly migraine attack rate during baseline period as a covariate.

[b]P-values for the dose groups are the adjusted p-value according to the Hochberg multiple comparison procedure.

[c]Indicates p-value is < 0.05 (two-sided).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

QUDEXY® XR (topiramate) extended-release capsules contain beads of topiramate in a capsule and are available in the following strengths and colors:

25 mg: light pink and grey capsules, printed with "UPSHER-SMITH" on the cap in black ink and "25 mg" on the body in black ink. 25 mg capsules are available in the following package configurations:

- Bottle of 30 count with desiccant (NDC 0245-1071-30)
- Bottle of 90 count with desiccant (NDC 0245-1071-90)

50 mg: golden yellow and grey capsules, printed with "UPSHER-SMITH" on the cap in black ink and "50 mg" on the body in black ink. 50 mg capsules are available in the following package configurations:

- Bottle of 30 count with desiccant (NDC 0245-1072-30)
- Bottle of 90 count with desiccant (NDC 0245-1072-90)

100 mg: reddish brown and grey capsules, printed with "UPSHER-SMITH" on the cap in black ink and "100 mg" on the body in black ink. 100 mg capsules are available in the following package configurations:

- Bottle of 30 count with desiccant (NDC 0245-1074-30)
- Bottle of 90 count with desiccant (NDC 0245-1074-90)

150 mg: pale yellow and grey capsules, printed with "UPSHER-SMITH" on the cap in black ink and "150 mg" on the body in black ink. 150 mg capsules are available in the following package configurations:

- Bottle of 30 count with desiccant (NDC 0245-1075-30)
- Bottle of 90 count with desiccant (NDC 0245-1075-90)

200 mg: brown and grey capsules, printed with "UPSHER-SMITH" on the cap in white ink and "200 mg" on the body in black ink. 200 mg capsules are available in the following package configurations:

- Bottle of 30 count with desiccant (NDC 0245-1073-30)
- Bottle of 90 count with desiccant (NDC 0245-1073-90)

16.2 Storage and Handling

QUDEXY XR (topiramate) extended-release capsules should be stored in a tightly closed container at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature]. Protect from moisture.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide).

Administration Instructions

Counsel patients to swallow QUDEXY XR capsules whole or carefully open and sprinkle the entire contents on a spoonful of soft food. This drug/food mixture should be swallowed immediately and not chewed. Do not store drug/food mixture for future use *[see Dosage and Administration (2.6)]*.

Eye Disorders

Advise patients taking QUDEXY XR to seek immediate medical attention if they experience blurred vision, visual disturbances or periorbital pain *[see Warnings and Precautions (5.1 and 5.2)]*.

Oligohydrosis and Hyperthermia

Closely monitor QUDEXY XR-treated patients, especially pediatric patients, for evidence of decreased sweating and increased body temperature, especially in hot weather. Counsel patients to contact their healthcare professionals immediately if they develop a high or persistent fever, or decreased sweating *[see Warnings and Precautions (5.3)]*.

Metabolic Acidosis

Warn patients about the potential significant risk for metabolic acidosis that may be asymptomatic and may be associated with adverse effects on kidney (e.g., kidney stones, nephrocalcinosis), bones (e.g., osteoporosis, osteomalacia, and/or rickets in children), and growth (e.g., growth delay/retardation) in pediatric patients, and on the fetus *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1, 8.4)]*.

Suicidal Behavior and Ideation

Counsel patients, their caregivers, and families that AEDs, including QUDEXY XR, may increase the risk of suicidal thoughts and behavior and they should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior or the emergence of suicidal thoughts, behavior or thoughts about self-harm. Instruct patients to immediately report behaviors of concern to their healthcare providers *[see Warnings and Precautions (5.5)]*.

Interference With Cognitive and Motor Performance

Warn patients about the potential for somnolence, dizziness, confusion, difficulty concentrating, visual effects, and advise patients not to drive or operate machinery until they have gained sufficient experience on QUDEXY XR to gauge whether it adversely affects their mental performance, motor performance, and/or vision *[see Warnings and Precautions (5.6)]*.

Even when taking QUDEXY XR, or other anticonvulsants, some patients with epilepsy will continue to have unpredictable seizures. Therefore, advise all patients taking QUDEXY XR for epilepsy to exercise appropriate caution when engaging in any activities where loss of consciousness could result in serious danger to themselves or those around them (including swimming, driving a car, climbing in high places, etc.). Some patients with refractory epilepsy will need to avoid such activities altogether. Discuss the appropriate level of caution with patients, before patients with epilepsy engage in such activities.

Fetal Toxicity

Inform pregnant women and women of childbearing potential that use of QUDEXY XR during pregnancy can cause fetal harm, including an increased risk for cleft lip and/or cleft palate (oral clefts), which occur early in pregnancy before many women know they are pregnant. Also inform patients that infants exposed to topiramate monotherapy *in utero* may be born small for their gestational age. There may also be risks to the fetus from chronic metabolic acidosis with use of QUDEXY XR during pregnancy *[see Warnings and Precautions (5.4, 5.7), Use in Specific Populations (8.1)]*.

When appropriate, counsel pregnant women and women of childbearing potential about alternative therapeutic options. Advise women of childbearing potential who are not planning a pregnancy to use effective contraception while using QUDEXY XR, keeping in mind that there is a potential for decreased contraceptive efficacy when using estrogen-containing birth control with topiramate *[see Drug Interactions (7.4)]*.

Encourage pregnant women using QUDEXY XR to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The registry is collecting information about the safety of antiepileptic drugs during pregnancy *[see Use in Specific Populations (8.1)]*.

Hyperammonemia and Encephalopathy

Warn patients about the possible development of hyperammonemia with or without encephalopathy. Although hyperammonemia may be asymptomatic, clinical symptoms of hyperammonemic encephalopathy often include acute alterations in level of consciousness and/ or cognitive function with lethargy and/or vomiting. This hyperammonemia and encephalopathy can develop with topiramate treatment alone or with topiramate treatment with concomitant valproic acid (VPA). Instruct patients to contact their physician if they develop unexplained lethargy, vomiting, or changes in mental status *[see Warnings and Precautions (5.8)]*.

Kidney Stones

Instruct patients, particularly those with predisposing factors, to maintain an adequate fluid intake in order to minimize the risk of kidney stone formation *[see Warnings and Precautions (5.10)]*.

Hypothermia

Counsel patients that QUDEXY XR can cause a reduction in body temperature, which can lead to alterations in mental status. If they note such changes, they should call their health care professional and measure their body temperature. Patients taking concomitant valproic acid should be specifically counseled on this potential adverse reaction *[see Warnings and Precautions (5.11)]*.

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Maple Grove, MN 55369

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MEDICATION GUIDE
QUDEXY® XR (cue-DEKS-ee ex-arr) (topiramate) Extended-Release Capsules

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

QUDEXY XR may cause eye problems. Serious eye problems include:

- any sudden decrease in vision with or without eye pain and redness,
- a blockage of fluid in the eye causing increased pressure in the eye (secondary angle closure glaucoma).

These eye problems can lead to permanent loss of vision if not treated. You should call your healthcare provider right away if you have any new eye symptoms, including any new problems with your vision.

QUDEXY XR may cause decreased sweating and increased body temperature (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. If you have a high fever, a fever that does not go away, or decreased sweating develops, call your healthcare provider right away.

QUDEXY XR can increase the level of acid in your blood (metabolic acidosis). 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 possibly harm your baby if you are pregnant. Metabolic acidosis can happen with or without symptoms. Sometimes people with metabolic acidosis will:

- feel tired
- not feel hungry (loss of appetite)
- feel changes in heartbeat
- have trouble thinking clearly

Your healthcare provider should do a blood test to measure the level of acid in your blood before and during your treatment with QUDEXY XR.

If you are pregnant, you should talk to your healthcare provider about whether you have metabolic acidosis.

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 healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

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

Do not stop QUDEXY XR without first talking to a healthcare provider.

- Stopping QUDEXY XR suddenly can cause serious problems.
- Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

How can I watch for early symptoms of suicidal thoughts and actions?

- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled.
- Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

QUDEXY XR can harm your unborn baby.

- 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.
- Cleft lip and cleft palate may happen even in children born to women who are not taking any medicines and do not have other risk factors.
- There may be other medicines to treat your condition that have a lower chance of birth defects.
- All women of childbearing age should talk to their healthcare providers about using other possible treatments instead of QUDEXY XR. If the decision is made to use QUDEXY XR, you should use effective birth control (contraception) unless you are planning to become pregnant. You should talk to your healthcare provider about the best kind of birth control to use while you are taking QUDEXY XR.
- Tell your healthcare provider right away if you become pregnant while taking QUDEXY XR. You and your healthcare provider should decide if you will continue to take QUDEXY XR while you are pregnant.
- If you take QUDEXY XR during pregnancy, your baby may be smaller than expected at birth. The long term effects of this are not known. Talk to your healthcare provider if you have any questions about this risk during pregnancy.
- Metabolic acidosis may have harmful effects on your baby. Talk to your healthcare provider if QUDEXY XR has caused metabolic acidosis during your pregnancy.
- Pregnancy Registry: If you become pregnant while taking QUDEXY XR, talk to your healthcare provider about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of QUDEXY XR and other antiepileptic drugs during pregnancy.

What is QUDEXY XR?

QUDEXY XR is a prescription medicine used:

- to treat certain types of seizures (partial-onset seizures and primary generalized tonic-clonic seizures) in adults and children 2 years of age and older.
- 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 of age and older.
- to prevent migraine headaches in adults and adolescents 12 years of age and older.

What should I tell my healthcare provider before taking QUDEXY XR?

Before taking QUDEXY XR, tell your healthcare provider about all of your medical conditions, including if you:

- have or 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
- are breastfeeding or plan to breastfeed. QUDEXY XR passes into breast milk. Breastfed babies may be sleepy or have diarrhea. It is not known if the QUDEXY XR that passes into breast milk can cause other serious harm to your baby. Talk to your healthcare provider about the best way to feed your baby if you take QUDEXY XR.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. QUDEXY XR and other medicines may affect each other causing side effects.

Especially tell your healthcare provider if you take:

- Valproic acid (such as DEPAKENE® or DEPAKOTE®)
- any medicines that impair or decrease your thinking, concentration, or muscle coordination
- birth control pills. QUDEXY XR may make your birth control pills less effective. Tell your healthcare provider if your menstrual bleeding changes while you are taking birth control pills and QUDEXY XR.

Ask your healthcare provider if you are not sure if your medicine is listed above.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine. Do not start a new medicine without talking with your healthcare provider.

How should I take QUDEXY XR?

- Take QUDEXY XR exactly as your healthcare provider tells you to.
- Your healthcare provider may change your dose. **Do not** change your dose without talking to your healthcare provider.
- QUDEXY XR capsules may be swallowed 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.
  - Do not crush or chew QUDEXY XR before swallowing.
- Drink plenty fluids during the day. This may help prevent kidney stones while taking QUDEXY XR.
- If you take too much QUDEXY XR, call your healthcare provider right away or go to the nearest emergency room.
- QUDEXY XR can be taken before, during, or after a meal.
- If you miss a single dose of QUDEXY XR, take it as soon as you can. If you have missed more than one dose, you should call your healthcare provider for advice.
- Do not stop taking QUDEXY XR without talking to your healthcare provider. Stopping QUDEXY XR suddenly may cause serious problems. If you have epilepsy and you stop taking QUDEXY XR suddenly, you may have seizures that do not stop. Your healthcare provider will tell you how to stop taking QUDEXY XR slowly.
- Your healthcare provider may do blood tests while you take QUDEXY XR.

What should I avoid while taking QUDEXY XR?

- You should not drink alcohol while taking QUDEXY XR. QUDEXY XR and alcohol can effect each other causing side effects such as sleepiness and dizziness.
- Do not drive a car or operate machinery until you know how QUDEXY XR affects you. QUDEXY XR can slow your thinking and motor skills and may affect vision.

What are the possible side effects of QUDEXY XR?

QUDEXY XR may cause serious side effects, including:

See "What is the most important information I should know about QUDEXY XR?"

- **High blood ammonia levels**. High ammonia in the blood can affect your mental activities, slow your alertness, make you feel tired, or cause vomiting. This has happened when QUDEXY XR is taken with a medicine called valproic acid (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 can cause a drop in body temperature to less than 95°F, or can cause tiredness, confusion, or coma.
- **Effects on thinking and alertness.** QUDEXY XR may affect how you think, and cause confusion, 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 healthcare provider right away if you have any of the symptoms above.

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
- decreased feeling or sensitivity, especially in the skin
- slow reactions
- difficulty with memory
- fever
- abnormal vision
- diarrhea
- pain in the abdomen

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of QUDEXY XR. 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.

You may also report side effects to Upsher-Smith Laboratories, LLC at 1-855-899-9180.

How should I store QUDEXY XR?

- Store QUDEXY XR capsules at room temperature between 68° to 77°F (20° to 25°C).
- Keep QUDEXY XR in a tightly closed container.
- Keep QUDEXY XR dry and away from moisture.
- **Keep QUDEXY XR and all medicines out of the reach of children.**

General information about the safe and effective use of QUDEXY XR.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use QUDEXY XR for a condition for which it was not prescribed. Do not give QUDEXY XR to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about QUDEXY XR that is written for health professionals.

What are the ingredients in QUDEXY XR?

Active ingredient: topiramate

Inactive ingredients: microcrystalline cellulose, hypromellose 2910, ethylcellulose, diethyl phthalate, titanium dioxide, black iron oxide, red iron oxide and/or yellow iron oxide, black pharmaceutical ink, and white pharmaceutical ink (200 mg only).

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This product may be covered by one or more U.S. patent(s). See www.uslpatents.com.

For more information, go to www.upsher-smith.com or call UPSHER-SMITH LABORATORIES, LLC at 1-888-650-3789.

This Medication Guide has been approved by the U.S. Food and Drug Administration

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