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

----------INDICATIONS AND USAGE----------
QUDEXY XR is an antiepileptic drug indicated for:
- Partial Onset Seizures and Primary Generalized Tonic-Clonic Seizures - initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures (1.1)
- Lennox-Gastaut Syndrome (LGS) - adjunctive therapy in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome (1.2)

----------DOSAGE AND ADMINISTRATION----------

	Initial Dose	Titration	Recommended Dose
Monotherapy: Partial Onset or Primary Generalized Tonic-Clonic Seizures			
Adults and pediatric patients 10 years and older (2.1)	50 mg orally once daily	Increase dose weekly by increments of 50 mg for first 4 weeks then 100 mg for weeks 5 to 6	400 mg once daily
Adjunctive Therapy			
Adults with partial onset seizures or LGS (2.2)	25 mg to 50 mg orally once daily	Increase dose weekly by increments of 25 mg to 50 mg to achieve an effective dose	200 mg to 400 mg once daily
Adults with primary generalized tonic-clonic seizures (2.2)	25 mg to 50 mg orally once daily	Increase dose weekly to an effective dose by increments of 25 mg to 50 mg	400 mg once daily
Pediatric patients 2 years and older with partial onset seizures, primary generalized tonic-clonic seizures or LGS (2.2)	25 mg once at night-time (based on a range of 1 mg/kg to 3 mg/kg once daily) for first week	Increase dosage at 1 or 2 week intervals by increments of 1 mg/kg to 3 mg/kg. Dose titration should be guided by clinical outcome	5 mg/kg to 9 mg/kg once daily

Capsules may be swallowed whole or opened and sprinkled on a spoonful of soft food (2.8)

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

----------CONTRAINDICATIONS----------
In patients with metabolic acidosis taking concomitant metformin (4) (5.4)

----------WARNINGS AND PRECAUTIONS----------
- Acute myopia and secondary angle closure glaucoma: Untreated elevated intraocular pressure can lead to permanent visual loss. Discontinue QUDEXY XR if it occurs (5.1)
- Visual field defects: These have been reported independent of elevated intraocular pressure. Consider discontinuation of QUDEXY XR (5.2)
- Oligohydrosis and hyperthermia: Monitor decreased sweating and increased body temperature, especially in pediatric patients (5.3)
- Metabolic acidosis: Measure baseline and periodic measurement of serum bicarbonate. Consider dose reduction or discontinuation of QUDEXY XR if clinically appropriate (5.4)
- Suicidal behavior and ideation: Antiepileptic drugs increase the risk of suicidal behavior or ideation (5.5)
- Cognitive/neuropsychiatric: QUDEXY XR may cause cognitive dysfunction. Use caution when operating machinery including automobiles. Depression and mood problems may occur (5.6)
- Fetal toxicity: Topiramate use during pregnancy can cause cleft lip and/or palate (5.7)
- Withdrawal of AEDs: Withdrawal of QUDEXY XR should be done gradually (5.8)
- Hyperammonemia and encephalopathy: Patients with inborn errors of metabolism or reduced mitochondrial activity may have an increased risk of hyperammonemia. Measure ammonia if encephalopathic symptoms occur (5.9)
- Kidney stones: Avoid use with other carbonic anhydrase inhibitors, other drugs causing metabolic acidosis, or in patients on a ketogenic diet (5.10)
- Hypothermia: Reported with concomitant valproic acid use (5.11)

----------ADVERSE REACTIONS----------
The most common (≥ 5% more frequent than placebo or low-dose topiramate in monotherapy) adverse reactions in a controlled, clinical trial of immediate release topiramate were paresthesia, anorexia, weight decrease, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, difficulty with memory, difficulty with concentration/attention, cognitive problem, confusion, mood problems, fever, infection, and flushing (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Upsher-Smith Laboratories, Inc. at 1-855-899-9180 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------
- Oral contraceptives: Decreased contraceptive efficacy and increased breakthrough bleeding, especially at doses greater than 200 mg per day (7.1)
- Phenytoin or carbamazepine: Concomitant administration with topiramate decreased plasma concentrations of topiramate (7.2)
- Other carbonic anhydrase inhibitors: Monitor for the appearance or worsening of metabolic acidosis (7.4)
- Lithium: Monitor lithium levels when co-administered with high-dose topiramate (7.6)

----------USE IN SPECIFIC POPULATIONS----------
- Renal Impairment: (creatinine clearance less than 70 mL/min/1.73m^2), one-half of the adult dose is recommended (2.3) (8.7)
- Patients undergoing hemodialysis: Topiramate is cleared by hemodialysis. Dosage adjustment is necessary to avoid rapid drops in topiramate plasma concentration during hemodialysis (2.4) (8.8)
- Pregnancy: Increased risk of cleft lip and/or palate. Pregnancy registry available (8.1)
- Nursing mothers: Caution should be exercised when administered to a nursing mother (8.3)
- Geriatric use: Dosage adjustment may be necessary for elderly with impaired renal function (8.5)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 3/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Partial Onset Seizures and Primary Generalized Tonic-Clonic Seizures

QUDEXY XR (topiramate) extended-release capsules are indicated as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures *[see Clinical Studies (14.2, 14.3 and 14.4)]*. Safety and effectiveness in patients who were converted to monotherapy from a previous regimen of other anticonvulsant drugs have not been established in controlled trials *[see Clinical Studies (14.2)]*.

1.2 Lennox-Gastaut Syndrome

QUDEXY XR (topiramate) extended-release capsules are indicated as adjunctive therapy in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome *[see Clinical Studies (14.5)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Monotherapy Use

Adults and Pediatric Patients 10 Years and Older with Partial Onset or Primary Generalized Tonic-Clonic Seizures

The recommended dose for topiramate monotherapy in adults and pediatric patients 10 years of age and older is 400 mg orally once daily. Titrate QUDEXY XR according to the following schedule:

Week 1	50 mg once daily
Week 2	100 mg once daily
Week 3	150 mg once daily
Week 4	200 mg once daily
Week 5	300 mg once daily
Week 6	400 mg once daily

2.2 Adjunctive Therapy Use

Adults (17 Years of Age and Older) - Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome

The recommended total daily dose of QUDEXY XR as adjunctive therapy in adults with partial onset seizures or Lennox-Gastaut Syndrome is 200 mg to 400 mg orally once daily. The recommended total dose for adults with primary generalized tonic-clonic seizures is 400 mg orally once daily.

Initiate therapy at 25 mg to 50 mg once daily followed by titration to an effective dose in increments of 25 mg to 50 mg every week. Daily topiramate doses above 1,600 mg have not been studied.

In the study of primary generalized tonic-clonic seizures using topiramate, the assigned dose was reached at the end of 8 weeks *[see Clinical Studies (14.4)]*.

Pediatric Patients (Ages 2 Years to 16 Years) - Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome

The recommended total daily dose of QUDEXY XR as adjunctive therapy for pediatric patients with partial onset seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome is approximately 5 mg/kg to 9 mg/kg orally once daily. Begin titration at 25 mg once daily (based on a range of 1 mg/kg/day to 3 mg/kg/day) given nightly for the first week. Subsequently, increase the dosage at 1 or 2 week intervals by increments of 1 mg/kg to 3 mg/kg to achieve optimal clinical response. Dose titration should be guided by clinical outcome. If required, longer intervals between dose adjustments can be used.

In the study of primary generalized tonic-clonic seizures, the assigned dose of 6 mg/kg once daily was reached at the end of 8 weeks *[see Clinical Studies (14.3, 14.4 and 14.5)]*.

2.3 Dose Modifications in Patients with Renal Impairment

In patients with renal impairment (creatinine clearance less than 70 mL/min/1.73 m^2), one-half of the usual adult dose is recommended. Such patients will require a longer time to reach steady-state at each dose *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

Prior to dosing, obtain an estimated creatinine clearance (CrCl) in patients at high risk for renal insufficiency (e.g., older patients, or those with diabetes mellitus, hypertension, or autoimmune disease). CrCl can be estimated using the following equation (multiply by 0.85 for women):

$$CrCl = \frac{(140 - age) \times weight(kg)}{SerumCr(mg/dl) \times 72}$$

2.4 Dosage Modifications in Patients Undergoing Hemodialysis

Topiramate is cleared by hemodialysis at a rate that is 4 to 6 times greater than in patients with normal renal function. Accordingly, a prolonged period of dialysis may cause topiramate concentration to fall below that required to maintain an anti-seizure effect. To avoid rapid drops in topiramate plasma concentration during hemodialysis, a supplemental dose of topiramate may be required. The actual adjustment should take into account the:

- duration of dialysis period
- clearance rate of the dialysis system being used
- effective renal clearance of topiramate in the patient being dialyzed *[see Use in Specific Populations (8.8) and Clinical Pharmacology (12.3)]*.

2.5 Laboratory Testing Prior to Treatment Initiation

Measurement of baseline and periodic serum bicarbonate during QUDEXY XR treatment is recommended *[see Warnings and Precautions (5.4)]*.

2.6 Dosing Modifications in Patients Taking Phenytoin and/or Carbamazepine

The co-administration of QUDEXY XR with phenytoin may require an adjustment of the dose of phenytoin to achieve optimal clinical outcome. Addition or withdrawal of phenytoin and/or carbamazepine during adjunctive therapy with QUDEXY XR may require adjustment of the dose of QUDEXY XR *[see Drug Interactions (7.2) and Clinical Pharmacology (12.3)]*.

2.7 Monitoring for Therapeutic Blood Levels

It is not necessary to monitor topiramate plasma concentrations to optimize QUDEXY XR therapy.

2.8 Administration Instructions

QUDEXY XR capsules may be swallowed whole or may be administered by carefully opening the capsule and sprinkling the entire contents on a small amount (teaspoon) of soft food. This drug/food mixture should be swallowed immediately and not chewed or crushed. Do not store drug/food mixture for further use. QUDEXY XR can be taken without regard to meals *[see Clinical Pharmacology (12.3)]*.

DOCKET ALARM

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