HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TROKENDI XR safely and effectively. See full prescribing information for TROKENDI XR.

Trokendi XR (topiramate) extended-release capsules for oral use
Initial US Approval: 1996

----------INDICATIONS AND USAGE----------
Trokendi XR™ is an antiepileptic drug indicated for:
- Partial Onset Seizure 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 6 years of age and older with partial onset or primary generalized tonic-clonic seizures (1.1)
- Lennox-Gastaut Syndrome (LGS) - adjunctive therapy in patients 6 years of age and older with seizures associated with Lennox-Gastaut syndrome (1.2)

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

	Initial Dose	Titration	Recommended Dose
Monotherapy Therapy: 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 6 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

Swallow capsule whole and intact. Do not sprinkle on food, chew or crush (2.9)

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

----------CONTRAINDICATIONS----------
- With recent alcohol use (i.e., within 6 hours prior to and 6 hours after Trokendi XR use [(4), (5.4)]
- In patients with metabolic acidosis taking concomitant metformin [(4), (5.3)]

----------WARNINGS AND PRECAUTIONS----------
- *Acute myopia and secondary angle closure glaucoma:* Untreated elevated intraocular pressure can lead to permanent visual loss. Discontinue Trokendi XR™ if it occurs (5.1)
- *Oligohydrosis and hyperthermia:* Monitor decreased sweating and increased body temperature, especially in pediatric patients (5.2)
- *Metabolic acidosis:* Measure baseline and periodic measurement of serum bicarbonate. Consider dose reduction or discontinuation of Trokendi XR™ if clinically appropriate (5.3)
- *Suicidal behavior and ideation:* Antiepileptic drugs increase the risk of suicidal behavior or ideation (5.5)
- *Cognitive/neuropsychiatric:* Trokendi 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 Trokendi 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 hyper-ammonemia. 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 (greater than 5% more frequent than placebo or low-dose topiramate in monotherapy) adverse reactions 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 Supernus Pharmaceuticals at 1-866-398-0833- 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 (7.2)
- *Phenytoin or carbamazepine:* Concomitant administration with topiramate decreased plasma concentrations of topiramate (7.3)
- *Other carbonic anhydrase inhibitors:* Monitor for the appearance or worsening of metabolic acidosis (7.5)
- *Lithium:* Monitor lithium levels when co-administered with high-dose topiramate (7.7)

----------USE IN SPECIFIC POPULATIONS----------
- *Renal Impairment:* (creatinine clearance less than 70 mL/min/1.73m2), one-half of the adult dose is recommended (8.7)
- *Patients undergoing hemodialysis:* Topiramate is cleared by hemodialysis. Dosage adjustment is necessary to avoid rapid drops in topiramate plasma concentration during hemodialysis (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)
- *Pediatric Use:* Because the capsule must be swallowed whole, and may not be sprinkled on food, crushed or chewed, Trokendi XR™ is recommended only for children ages 6 years and older (8.4)

See *17* for PATIENT COUNSELING INFORMATION and Medication Guide

August 2013

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Partial Onset Seizure and Primary Generalized Tonic-Clonic Seizures

Trokendi 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 6 years of age and older with partial onset or primary generalized tonic-clonic seizures [*see Clinical Studies (14.2, 14.3, 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

Trokendi XR™ (topiramate) extended-release capsules are indicated as adjunctive therapy in patients 6 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 Trokendi 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 Trokendi XR™ as adjunctive therapy in adults with partial onset seizures or Lennox-Gaustaut Syndrome is 200 mg to 400 mg orally once daily 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 50mg 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 6 years to 16 Years) - Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome

The recommended total daily dose of Trokendi 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 (14.4)*].

2.3 Administration with Alcohol

Alcohol use should be completely avoided within 6 hours prior to and 6 hours after Trokendi XR™ administration [see *Warnings and Precautions (5.4)*].

2.4 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.

Prior to dosing, obtain an estimated GFR measurement in patients at high risk for renal insufficiency (e.g., older patients, or those with diabetes mellitus, hypertension, or autoimmune disease).

2.5 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.

2.6 Laboratory Testing Prior to Treatment Initiation

Measurement of baseline and periodic serum bicarbonate during Trokendi XR™ treatment is recommended [*see Warnings and Precautions (5.3)*].

2.7 Dosing Modifications in Patients Taking Phenytoin and/or Carbamazepine

The co-administration of Trokendi 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 Trokendi XR™ may require adjustment of the dose of Trokendi XR™.

2.8 Monitoring for Therapeutic Blood Levels

2.9 Administration Instructions

Trokendi XR™ can be taken without regard to meals.

Swallow capsule whole and intact. Do not sprinkle on food, chew or crush.

3 DOSAGE FORMS AND STRENGTHS

Trokendi XR™ (topiramate) extended-release capsules are available in the following strengths and colors:

25 mg: Size 2 capsules, light green opaque body/yellow opaque cap (printed "SPN" on the cap, "25" on the body)
50 mg: Size 0 capsules, light green opaque body/orange opaque cap (printed "SPN" on the cap, "50" on the body)
100 mg: Size 00 capsules, green opaque body/blue opaque cap (printed "SPN" on the cap, "100" on the body)
200 mg: Size 00 capsules, pink opaque body/blue opaque cap (printed "SPN" on the cap, "200" on the body)

4 CONTRAINDICATIONS

Trokendi XR™ is contraindicated in patients:

- With recent alcohol use (i.e., within 6 hours prior to and 6 hours after Trokendi XR™ use) *[see Warnings and Precautions (5. 4)]*
- With metabolic acidosis who are taking concomitant metformin *[see Warnings and Precautions (5.3) and Drug Interactions (7.6)]*

5 WARNINGS AND PRECAUTIONS

5.1 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. Symptoms include acute onset of decreased visual acuity and/or ocular pain. Ophthalmologic findings can include myopia, anterior chamber shallowing, ocular hyperemia (redness) and increased intraocular pressure. Mydriasis may or may not be present. This syndrome may be associated with supraciliary effusion resulting in anterior displacement of the lens and iris, with secondary angle closure glaucoma. Symptoms typically occur within 1 month of initiating topiramate therapy. In contrast to primary narrow angle glaucoma, which is rare under 40 years of age, secondary angle closure glaucoma associated with topiramate has been reported in pediatric patients as well as adults. The primary treatment to reverse symptoms is discontinuation of Trokendi XR™ as rapidly as possible, according to the judgment of the treating physician. Other measures, in conjunction with discontinuation of Trokendi XR™, may be helpful.

Elevated intraocular pressure of any etiology, if left untreated, can lead to serious sequelae including permanent vision loss.

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