Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

**Description:**

Qudexy XR (topiramate) extended-release capsules are indicated as initial monotherapy in patients 2 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 (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); and is indicated as adjunctive therapy in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome.

Trokenidi XR (topiramate) extended-release capsules are indicated in patients 6 years of age and older as initial monotherapy for partial onset or primary generalized tonic-clonic seizures (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); and as adjunctive therapy in patients 6 years of age and older with partial onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome.
BCBSAZ covers Topiramate Capsule ER with applicable quantity level limits without precertification. Qudexy™ XR and Trokendi XR™ require precertification and approval is based on medical necessity and failure of Topiramate Capsule ER.

**Definitions:**

**Drug related events:**

- **Ineffective / failure**
  
  Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

  A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

**Adverse Drug Event:** Allergic reaction / Hypersensitivity / Intolerance

Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual’s outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

- **Allergic reaction / hypersensitivity** – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

  If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

- **Intolerance** – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

**Contraindication**

Use of a drug that is not recommended by the manufacturer or FDA labelling
Use of any drug in the face of a contraindication is outside of the FDA and manufacturer's labelled recommendation and is considered investigational or experimental.

Non-adherence
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record.

Precertification:
Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Criteria:
See “Resources” section for FDA-approved dosage.

- Precertification for Qudexy XR and Trokendi XR requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

Criteria for Qudexy XR:
- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Qudexy XR is considered medically necessary with medical record documentation of ALL of the following:
  1. Individual is 2 years of age or older
  2. Medical record documentation of a confirmed diagnosis of ONE of the following:
     - Partial onset seizure, as initial monotherapy or adjunctive therapy
     - Primary generalized tonic-clonic seizure, as initial monotherapy or adjunctive therapy
     - Seizures associated with Lennox-Gastaut syndrome, as adjunctive therapy
3. Individual is unable to use Topiramate Capsule ER due to **ONE** of the following:
   - Experienced a significant intolerant reaction to Topiramate Capsule ER that has been identified
   - Experienced an allergic or hypersensitivity reaction to Topiramate Capsule ER that has been identified
   - Has a contraindication to Topiramate Capsule ER that has been identified

4. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Serum bicarbonate
   - Pregnancy test in a woman of child bearing potential, unless using effective contraception

5. Absence of **ALL** of the following contraindications:
   - Metabolic acidosis when used simultaneously with Metformin

6. Absence of **ALL** of the following exclusions:
   - Pregnancy in a woman of child bearing potential, unless on adequate contraception
   - Simultaneous use with other carbonic anhydrase inhibitors [acetazolamide, dichlorphenamide (Daranide, Keveyis), zonisamide]
   - Simultaneous use with other drugs that cause metabolic acidosis
   - Simultaneous use with a ketogenic diet

**Criteria for Trokendi XR:**

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Trokendi XR is considered **medically necessary** with medical record documentation of **ALL** of the following:

1. Medical record documentation of **ONE** of the following diagnosis:
   - Individual who is 6 years of age or older with partial onset or primary generalized tonic-clonic seizures, as initial monotherapy
   - Individual who is 6 years of age or older with partial onset or primary generalized tonic-clonic seizures, as adjunctive therapy
   - Individual who is 6 years or age or older with seizures associated with Lennox-Gastaut syndrome, as adjunctive therapy

2. Individual is unable to use Topiramate Capsule ER due to **ONE** of the following:
   - Experienced a significant intolerant reaction to Topiramate Capsule ER that has been identified
   - Experienced an allergic or hypersensitivity reaction to Topiramate Capsule ER that has been identified
   - Has a contraindication to Topiramate Capsule ER that has been identified

3. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Serum bicarbonate
   - Pregnancy test in a woman of child bearing potential, unless using effective contraception
4. Absence of **ALL** of the following contraindications:
   - Metabolic acidosis when used simultaneously with Metformin
   - Recent alcohol use (6 hours before and after)

5. Absence of **ALL** of the following exclusions:
   - Pregnancy in a woman of child bearing potential, unless on adequate contraception
   - Simultaneous use with other carbonic anhydrase inhibitors [acetazolamide, dichlorphenamide (Daranide, Keveyis), zonisamide]
   - Simultaneous use with other drugs that cause metabolic acidosis
   - Simultaneous use with a ketogenic diet

- Qudexy XR and Trokendi XR for all other indications not previously listed is considered **experimental or investigational** based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

**Resources:**


QUDEXY™ XR (topiramate) extended-release capsule
TROKENDI™ XR (topiramate) extended-release capsule (cont.)

Qudexy™ XR, FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qudexy XR is an antiepileptic drug indicated for:</td>
<td></td>
</tr>
<tr>
<td>- 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</td>
<td></td>
</tr>
<tr>
<td>- Lennox-Gastaut Syndrome (LGS) -adjunctive therapy in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial Dose</th>
<th>Titration</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy: Partial Onset or Primary Generalized Tonic-Clonic Seizures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults and pediatric patients 10 years and older</td>
<td>50 mg orally once daily</td>
<td>Increase dose weekly by increments of 50 mg for first 4 weeks then 100 mg for weeks 5 to 6</td>
<td>400 mg once daily</td>
</tr>
<tr>
<td>Pediatric patients 2 to less than 10 years of age</td>
<td>25 mg orally once daily</td>
<td>Increase dose weekly by 25-50 mg once daily over 5 to 7 weeks</td>
<td>250 mg to 400 mg once daily, maximum dose is based on weight</td>
</tr>
</tbody>
</table>

| Adjunctive Therapy                                                         |              |           |                 |
| Adults with partial onset seizures or LGS                                  | 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                      | 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 | 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.
**QUDEXY™ XR (topiramate) extended-release capsule**
**TROKENDI™ XR (topiramate) extended-release capsule** (cont.)

**Tro肯迪 XR™**, FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tro肯迪 XR™ is an antiepileptic drug indicated for:</td>
<td>Initial Dose</td>
</tr>
<tr>
<td>- 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</td>
<td>Adults and pediatric patients 10 years and older</td>
</tr>
<tr>
<td>- Lennox-Gastaut Syndrome (LGS) - adjunctive therapy in patients 6 years of age and older with seizures associated with Lennox-Gastaut syndrome</td>
<td>Pediatric patients 6 to less than 10 years of age</td>
</tr>
</tbody>
</table>

### Adjunctive Therapy

| Adults with partial onset seizures or LGS | 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 | 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 | 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.