Clinical Policy Title:	topiramate extended-release
Policy Number:	RxA.257
Drug(s) Applied:	Qudexy® XR, Trokendi XR®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Topiramate extended-release (Qudexy® XR, Trokendi XR®) is a sulfamate-substituted monosaccharide.
Qudexy® XR is indicated:

- As initial monotherapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures
- As adjunctive therapy in patients 2 years of age and older with partial onset or primary generalized tonic-clonic seizures or seizures associated with Lennox-Gastaut Syndrome (LGS)
- For the prophylaxis of migraine headache in patients 12 years of age and older

Trokendi XR® is indicated:

- In patients 6 years of age and older as initial monotherapy for partial onset or primary generalized tonic-clonic seizures.
- As adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures, or seizures associated with LGS.
- For patients 12 years and older for the prophylaxis of migraine headache.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
topiramate extended release (Qudexy® XR)	Monotherapy: Partial onset or primary generalized tonic-clonic seizures	Adults and pediatric patients 10 years and older: Initial: 50 mg by mouth once daily; Increase dose weekly by increments of 50 mg for the first 4 weeks then 100 mg for weeks 5 to 6 Recommended dose: 400 mg once daily Pediatric patients 2 years to 9 years: Initial: 25 mg by mouth once daily at night time for the first week; Titrate the dosage by 25 mg to 50 mg by mouth once daily each subsequent week over 5 to 7 weeks. Recommended dose: based on weight	400 mg/day (varies by weight for pediatric patients)
	Adjunctive therapy	Adults (≥ 17 years) with partial onset seizures or LGS:	

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Initial: 25 mg to 50 mg by mouth once daily; Increase dose weekly by increments of 25 mg to 50 mg to achieve an effective dose Recommended dose: 200 mg to 400 mg by mouth once daily Adults (≥ 17 years) with primary generalized tonic-clonic seizures: Initial: 25 mg to 50 mg by mouth once daily; Increase dose weekly to an effective dose by increments of 25 mg to 50 mg Recommended dose: 400 mg by mouth once daily Pediatric patients 2 to 16 years with partial onset seizures, primary generalized tonic-clonic seizures or LGS: Initial: 25 mg by mouth once daily at night time for the 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 Recommended dose: 5 mg/kg to 9 mg/kg once daily	Adults: 400 mg/day Pediatric patients 2 to 16 years old: 9 mg/kg/day
	Migraine prophylaxis	25 to 100 mg by mouth once daily	100 mg/day
topiramate extended release (Trokendi XR®)	Monotherapy: Partial onset or primary generalized tonic-clonic seizures	Adults and pediatric patients 10 years and older: Initial: 50 mg by mouth once daily; Increase dose weekly by increments of 50 mg for the first 4 weeks then 100 mg for weeks 5 to 6 Recommended dose: 400 mg once daily Pediatric patients 6 years to 9 years of age: Dosing is based on weight; 150 mg to 400 mg by mouth once daily	400 mg/day (varies by weight for pediatric patients)
	Adjunctive therapy	Adults (≥ 17 years) with partial onset seizures or LGS: 200 mg to 400 mg by mouth once daily Adults (≥ 17 years) with primary generalized tonic-clonic seizures: 400 mg by mouth once daily	Adults: 400 mg/day Pediatric patients 6 to 16 years old: 9 mg/kg/day (the total daily dose should not exceed 400 mg/day)

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Pediatric patients 6 to 16 years of age with partial onset seizures, primary generalized tonic-clonic seizures, or seizures associated with LGS: 5 mg/kg to 9 mg/kg by mouth once daily	
	Migraine prophylaxis	25 to 100 mg by mouth once daily	100 mg/day

Dosage Forms

- Topiramate extended release (Qudexy® XR): Capsule: 25 mg, 50 mg, 100 mg, 150 mg, 200 mg.
- Topiramate extended release (Trokendi XR®): Capsule: 25 mg, 50 mg, 100 mg, 200 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome (must meet all):

1. Diagnosis of partial onset seizures, primary generalized tonic-clonic seizures, or LGS;
2. One of the following (a or b):
   a. For Qudexy® XR: Age ≥ 2 years;
   b. For Trokendi XR®: Age ≥ 6 years;
3. Failure of immediate - release topiramate at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed:
   a. Monotherapy for adults and pediatric members ≥ 10 years old: 400 mg per day;
   b. Monotherapy for members 2 to 9 years of age if request is for Qudexy XR or 6 to 9 years of age if request is for Trokendi XR:
      i. Weight 11 kg or less: 250 mg per day;
      ii. Weight between 12 to 22 kg: 300 mg per day;
      iii. Weight between 23 to 38 kg: 350 mg per day;
      iv. Weight greater than 38 kg: 400 mg per day;
   c. Adjunctive therapy for members ≥ 17 years of age: 400 mg per day;
   d. Adjunctive therapy for members ≤ 16 years of age: 9 mg per kg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Migraine Prophylaxis (must meet all):

1. Prescribed for prophylaxis of migraine headache;
2. Age ≥ 12 years;
3. Failure of immediate- release topiramate at up to maximally indicated doses, unless contraindicated or

clinically significant adverse effects are experienced;
4. Dose does not exceed 100 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or LennoxGastaut Syndrome (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Qudexy® XR or Trokendi XR® for partial seizures, primary generalized tonic-clonic seizures, or LGS and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed:
   a. Monotherapy for adults and pediatric members ≥10 years old: 400 mg per day;
   b. Monotherapy for members 2 to 9 years of age if request is for Qudexy XR or 6 to 9 years of age if request is for Trokendi XR:
      i. Weight 11 kg or less: 250 mg per day;
      ii. Weight between 12 to 22 kg: 300 mg per day;
      iii. Weight between 23 to 38 kg: 350 mg per day;
      iv. Weight greater than 38 kg: 400 mg per day;
   c. Adjunctive therapy for members ≥ 17 years of age: 400 mg per day;
   d. Adjunctive therapy for members ≤ 16 years of age: 9 mg per kg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Migraine Prophylaxis (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 100 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
LGS: Lennox-Gastaut syndrome

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
topiramate, immediate release (Topamax®)	Initial dose, titration, and recommended maintenance dose varies by indication and age group	100 to 400 mg/day based on age and indication

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Qudexy® XR: None.
  - Trokendi XR®: Patients with recent alcohol use (i.e., within 6 hours prior to and 6 hours after Trokendi XR ®use)

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Qudexy® XR and Trokendi XR® taken once a day provides steady state plasma levels comparable to immediate release topiramate taken every 12 hours, when administered at the same total 200 mg daily dose.

References

1. Trokendi XR® Prescribing Information. Winchester, KY: Catalent Pharma Solutions; November 2020. Available at: https://www.trokendixr.com/. Accessed February 25, 2021.
2. Qudexy® XR Prescribing Information. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; February 2020. Available at: https://qudexyxr.com/. Accessed February 25, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/ Accessed February 25, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy Established	01/2020	02/07/2020
Policy was reviewed: 1) Policy description table updated 2) Dosing Regimen was updated to replace “QD” with "once daily" 3) Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Qudexy XR or Trokendi XR for partial seizures, primary generalized tonic-clonic seizures, or LGS and has received this medication for at least 30 days” 4) Initial therapy and continued therapy approval duration Added Medicaid 5) References were updated.	07/02/2020	09/14/2020
Policy was reviewed: 1) Dosing Information abbreviated form PO changed to "by mouth".	02/25/2021	06/10/2021

2) Therapeutic Alternative verbiage changed. 3) References were updated. 4) Updated the language of I.A.4.b and II.A.3.b to specific age criteria for Trokendi XR and Qudexy XR		