UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2018 P 2004-12
Program	Prior Authorization/Medical Necessity - Multisource Brand/Modified Release Anticonvulsants
Medication/Therapeutic Class	Multisource Brand/Modified Release Anticonvulsants – Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal XR (brand and generic), Lamictal ODT (brand and generic), Mysoline, Neurontin, Oxtellar XR*, Qudexy XR* (brand and authorized generic), Spritam*, Topamax, Trokendi XR*, Trileptal, Zonegran
P&T Approval Date	10/2013, 2/2014, 7/2014, 8/2014, 4/2015, 2/2016, 6/2016, 9/2016, 10/2017, 9/2018
Effective Date	12/1/2018; Oxford only: 12/1/2018

1. Background:

Multisource Brand Anticonvulsants
This program requires a member to try the A-rated generic prior to receiving coverage for brand Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Trileptal, Topamax, or Zonegran unless patient has a history of drug-resistant epilepsy or is at high risk of seizure recurrence.

Modified Release Products
This program requires a member to try divalproex sodium delayed release, Depakote delayed-release, generic valproic acid, Depakene formulations, Depakote sprinkles, divalproex sodium sprinkles, lamotrigine, lamotrigine chewable tablet, oxcarbazepine, topiramate, Topamax or Trileptal prior to coverage of their respective modified release formulations: lamotrigine extended-release^, lamotrigine orally disintegrating tablet, Oxtellar XR*, Qudexy XR*, Spritam*, and Trokendi XR* unless patient has a history of drug-resistant epilepsy or is at high risk of seizure recurrence.

2. Coverage Criteria[a]:

A. Epilepsy, Seizures and Status Epilepticus

1. The multisource brand anticonvulsants **Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Trileptal, Topamax, or Zonegran** will be approved based on **one** of the following criteria:

   a. **Both** of the following:

      (1) History of greater than or equal to 4 week trial of the therapeutically

equivalent generic (document date of trial)

-AND-

(2) Documented history of an inadequate response to the therapeutically equivalent generic as evidenced by **one** of the following (document inadequate response):

(a) Change in seizure frequency from baseline
(b) Breakthrough seizures not explained by medication nonadherence or significant provoking factor
(c) Status epilepticus

-OR-

b. Documented history of an intolerance to the therapeutically equivalent generic which was unable to be resolved with attempts to minimize the adverse effects where appropriate (e.g. change timing of dosing, divide daily dose out for more frequent but smaller doses)

-OR-

c. Documented history of drug-resistant epilepsy (defined as the failure of two tolerated and appropriately chosen and used anti-epileptic drug schedules [as either mono-therapy or combination therapy] to achieve sustained seizure freedom) (document names of the two medications and dates of trials)

-OR-

d. Documented history of a high risk for seizure recurrence defined as **one** or more of the following:

(1) Identifiable brain disease
(2) Mental retardation
(3) Abnormal neurologic examination
(4) Seizure onset after the first decade
(5) Multiple seizure types
(6) Poor initial response to treatment
(7) Juvenile myoclonic epilepsy
(8) Epileptiform discharges on electroencephalogram (EEG)
(9) Family history of epilepsy
(10) Hippocampal atrophy or abnormal hippocampal signal on magnetic resonance imaging (MRI)

Authorization will be issued for 12 months.

Reauthorization

1. **Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Trileptal, Topamax, or Zonegran** will be approved based on the following criterion:

    a. Documentation of positive clinical response to therapy

Reauthorization will be issued for 12 months.

2. The modified release products^ **lamotrigine orally disintegrating tablet**, **Oxtellar XR*, Qudexy XR (brand and authorized generic)*, Spritam* and Trokendi XR*** will be approved based on **one** of the following criteria:

    a. **Both** of the following:

        (1) History of greater than or equal to 4 week trial of the corresponding release products:

            (a) For **lamotrigine orally disintegrating tablet**: a trial of lamotrigine immediate-release or lamotrigine chewable tablet
            (b) For **Oxtellar XR**: a trial of either oxcarbazepine or Trileptal
            (c) For **Spritam**: a trial of levetiracetam immediate-release or levetiracetam solution
            (d) For **Qudexy XR** (brand and authorized generic) or **Trokendi XR**: a trial of either topiramate or Topamax

        -AND-

        (2) Documented history of an inadequate response to the corresponding release product as evidenced by **one** of the following (document inadequate response):

            (a) Change in seizure frequency from baseline
            (b) Breakthrough seizures not explained by medication nonadherence or significant provoking factor
            (c) Status epilepticus

    -OR-

    b. Documented history of an intolerance to the corresponding release product which is unable to be resolved with attempts to minimize the adverse effects where appropriate (e.g. change timing of dosing, divide daily dose out for more frequent but smaller doses)

-OR-

c. Documented history of drug-resistant epilepsy (defined as the failure of two tolerated and appropriately chosen and used anti-epileptic drug schedules [as either mono-therapy or combination therapy] to achieve sustained seizure freedom) (documentnames of the two medications and dates of trials)

-OR-

d. Documented history of a high risk for seizure recurrence defined as **one** or more of the following:

(1) Identifiable brain disease
(2) Mental retardation
(3) Abnormal neurologic examination
(4) Seizure onset after the first decade
(5) Multiple seizure types
(6) Poor initial response to treatment
(7) Juvenile myoclonic epilepsy
(8) Epileptiform discharges on electroencephalogram (EEG)
(9) Family history of epilepsy
(10) Hippocampal atrophy or abnormal hippocampal signal on magnetic resonance imaging (MRI)

Authorization will be issued for 12 months.

Reauthorization

1. **Lamotrigine orally disintegrating tablet**, **Oxtellar XR*, Qudexy XR (brand and authorized generic)*, Spritam* and Trokendi XR*** will be approved based on the following criterion:

   a. Documentation of positive clinical response to therapy

Reauthorization will be issued for 12 months.

B. Other Indications (e.g. mania, bipolar disorder, migraine prophylaxis, neuropathy, postherpetic neuralgia)

1. The multisource brand anticonvulsants **Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Trileptal, Topamax, or Zonegran** will be approved based on **one** of the following criteria:

a. **Both** of the following:

(1) History of greater than or equal to 4 week trial of the therapeutically equivalent generic (document date of trial)

-AND-

(2) Documented history of an inadequate response to the therapeutically equivalent generic (document inadequate response)

-OR-

b. Documented history of an intolerance to the therapeutically equivalent generic which was unable to be resolved with attempts to minimize the adverse effects where appropriate (e.g. change timing of dosing, divide daily dose out for more frequent but smaller doses)

Authorization will be issued for 12 months.

Reauthorization

1. **Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Trileptal, Topamax, or Zonegran** will be approved based on the following criterion:

   a. Documentation of positive clinical response to therapy

Reauthorization will be issued for 12 months.

2. The modified release products **lamotrigine extended-release, lamotrigine orally disintegrating tablet**, **Oxtellar XR*, Qudexy XR* (brand and authorized generic), Spritam* and Trokendi XR*** will be approved based on **one** of the following criteria:

   a. **Both** of the following:

   (1) History of greater than or equal to 4 week trial of the corresponding release products (document date of trial):

   (a) For **lamotrigine extended-release^ or orally disintegrating tablet**: a trial of lamotrigine immediate-release or lamotrigine chewable tablet
   (b) For **Oxtellar XR**: a trial of either oxcarbazepine or Trileptal
   (c) For **Spritam**: a trial of levetiracetam immediate-release or levetiracetam solution

(d) For **Qudexy XR** (brand and authorized generic) or **Trokendi XR**: a trial of either topiramate or Topamax

-AND-

(2) Documented history of an inadequate response to the corresponding release product (document inadequate response)

-OR-

b. Documented history of an intolerance to the corresponding release product which is unable to be resolved with attempts to minimize the adverse effects where appropriate (e.g. change timing of dosing, divide daily dose out for more frequent but smaller doses)

Authorization will be issued for 12 months.

Reauthorization

1. **Lamotrigine extended-release, lamotrigine orally disintegrating tablet**, **Oxtellar XR*, Qudexy XR* (brand and authorized generic), Spritam* and Trokendi XR*** will be approved based on the following criterion:

   a. Documentation of positive clinical response to therapy

Reauthorization will be issued for 12 months.

^Lamotrigine extended-release will be approved for seizure disorders

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.

* Oxtellar XR, Qudexy XR (brand and authorized generic), Spritam and Trokendi XR are typically excluded from coverage.

4. References:

1. Depakote Prescribing Information. AbbVie. North Chicago, IL. October 2017.
2. Depakote ER Prescribing Information. AbbVie. North Chicago, IL. October 2017.
3. Keppra Prescribing Information. UCB. Smyrna, GA. October 2017.

4. Keppra XR Prescribing Information. UCB. Smyrna, GA. October 2017.
5. Lamictal/Lamictal ODT Prescribing Information. GSK. Research Triangle Park, NC. May 2018.
6. Lamictal XR Prescribing Information. GSK. Research Triangle Park, NC. May 2018.
7. Neurontin Prescribing Information. Pfizer Inc. New York, NY. February 2018.
8. Oxtellar XR Prescribing Information. Supernus Pharmceuticals Inc. Rockville, MD. December 2015.
9. Qudexy XR Prescribing Information. Upsher-Smith Laboratories, Inc. Maple Grove, MN. March 2017.
10. Trileptal Prescribing Information. Novartis. East Hanover, NJ. November 2017.
11. Trokendi XR Prescribing Information. Supernus Pharmaceutical Inc. Rockville, MD. April 2017.
12. Topamax Prescribing Information. Janssen Pharmaceuticals, Inc. Titusville, NJ. June 2018.
13. Zonegran Prescribing Information. Concordia Pharmaceuticals Inc. St. Michael, Barbados. April 2016.
14. Britton JW. Antiepileptic drug withdrawal: literature review. Mayo Clin Proc. 2002;77(12):1378.
15. Kwan P, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia. 2010;51(6);1069.
16. Talati R, et al. Effectiveness and Safety of Antiepileptic Medications in Patients with Epilepsy. Agency for Healthcare Research and Quality (US); December 2011.
17. Felbatol Prescribing Information. Meda Pharmaceuticals Inc. Sommerset, NJ. July 2011.
18. Mysoline Prescribing Information. Valeant Pharmaceuticals Inc. Bridgewater, NJ. September 2012.
19. Spritam Prescribing Information. Aprecia Pharmaceuticals Company. East Windsor, NJ. February 2018.

Program	Prior Authorization/Medical Necessity - Multisource Brand/Modified Release Anticonvulsants
Change Control	
Date	Change
10/2013	New program
2/2014	Added modified release products Oxtellar XR, Stavzor and Trokendi XR to program.
7/2014	Moved Lamictal ODT from Multisource Brand section to Modified release section, as generic launch has been delayed.
8/2014	Updates to FAERS requirement to allow for submission of medical records documenting failure or intolerance to generic rather than submission of FAERS report.
4/2015	Added Qudexy XR to criteria. Moved brand Lamictal ODT to Multisource Brand section as the generic has launched.
2/2016	Added lamotrigine extended-release, Felbatol and Mysoline to

	criteria. Reduced authorization period from 5 years to 12 months.
6/2016	Stavzor removed from criteria as product was discontinued. Added Spritam to criteria. Removed FAERS requirement as an exception to requiring medical record submission. Added Maryland requirements. Added Indiana and West Virginia coverage information.
9/2016	Updated formatting.
11/2016	Administrative change. Added California coverage information.
10/2017	Removed requirement for submission of medical records. References and state mandate language updated.
9/2018	Added reauthorization criteria. Added requirement to document name of drug and trial dates or adverse event. References updated.
12/2018	Administrative change to add statement regarding use of automated processes.