UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2021 P 2004-16
Program	Prior Authorization/Medical Necessity - Multisource Brand/Modified Release Anticonvulsants
Medication/Therapeutic Class	Multisource Brand/Modified Release Anticonvulsants – Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal XR (brand and generic), Lamictal ODT (brand and generic), Lyrica, Mysoline, Neurontin, Onfi, Sabril, Topamax, 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, 8/2019, 7/2020, 6/2021, 8/2021
Effective Date	11/1/2021; Oxford only: 11/1/2021

1. Background:

Multisource Brand Anticonvulsants
This program requires a member to try the A-rated generic prior to receiving coverage for brand Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Mysoline, Neurontin, Onfi, Sabril, 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 lamotrigine or lamotrigine chewable tablet prior to coverage of lamotrigine extended-release^ or lamotrigine orally disintegrating tablet 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 **Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Mysoline, Neurontin, Onfi, Sabril, 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) Intellectual disability
(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. **Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR,**

Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Mysoline, Neurontin, Onfi, Sabril, 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 product^ **lamotrigine orally disintegrating tablet** 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

-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) (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) Intellectual disability (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** 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 **Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Mysoline, Neurontin, Onfi, Sabril, 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)

2. The multisource brand anticonvulsant **Lyrica** will be approved based on **both** of the following criteria:

   a. **One** of the following:

      (1) Diagnosis of neuropathic pain and history of failure, contraindication, or intolerance to **two** of the following medications (Document date of trial):

         (a) gabapentin (generic Neurontin)
         (b) duloxetine (generic Cymbalta)
         (c) tricyclic antidepressant (e.g. amitriptyline)

-OR-

      (2) All other diagnoses and history of failure, contraindication or intolerance to the following: (Document the diagnosis and ensure that the diagnosis is not associated with nerve pain which would require review as neuropathic pain. [Document date of trial]).

         (a) gabapentin (generic Neurontin)

-AND-

   b. **One** of the following:

      (1) **Both** of the following:

         (a) History of greater than or equal to 4 week trial of the therapeutically equivalent generic (document date of trial)
         (b) Documented history of an inadequate response to the therapeutically equivalent generic (document inadequate response)

-OR-

      (2) 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. **Banzel, Depakote, Depakote ER, Felbatol, Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Mysoline, Neurontin, Onfi, Sabril, 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** and **lamotrigine orally disintegrating tablet** 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

-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** and **lamotrigine orally disintegrating tablet** 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 [package insert]. North Chicago, IL: AbbVie Inc; February 2021.
2. Depakote ER [package insert]. North Chicago, IL: AbbVie Inc; February 2021.
3. Keppra [package insert]. Smyrna, GA: UCB, Inc; October 2020.
4. Keppra XR [package insert]Smyrna, GA: UCB, Inc; October 2020.
5. Lamictal/Lamictal ODT [package insert]. Research Triangle Park, NC: GSK LLC; October 2020.
6. Lamictal XR [package insert]. Research Triangle Park, NC: GSK LLC; October 2020.
7. Neurontin [package insert]. New York, NY: Pfizer Inc; April 2020.
8. Trileptal [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2020.
9.
10. Topamax [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc; June 2020.
11. Zonegran [package insert]. Dublin, Ireland: Concordia Pharmaceuticals Inc; April 2020.
12. Britton JW. Antiepileptic drug withdrawal: literature review. Mayo Clin Proc. 2002;77(12):1378.
13. 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.
14. Talati R, et al. Effectiveness and Safety of Antiepileptic Medications in Patients with Epilepsy. Agency for Healthcare Research and Quality (US); December 2011.
15. Felbatol [package insert]. Sommerset, NJ: Meda Pharmaceuticals Inc; February 2018.
16. Mysoline [package insert]. Bridgewater, NJ: Bausch Health US, LLC; October 2019.
17. Lyrica [package insert]. New York, NY: Pfizer Inc; June 2020.

18. Onfi [package insert]. Deerfield, IL: Lundbeck Pharmaceuticals LLC; February 2021.
19. Onfi [package insert]. Deerfield, IL: Lundbeck Pharmaceuticals LLC; June 2018.
20. Sabril [package insert]. Deerfield, IL: Lundbeck Pharmaceuticals, LLC; February 2020.
21. Banzel [package insert]. Woodcliff Lake, NJ: Eisai Inc; April 2020.

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.
8/2019	Added Lyrica and Onfi to criteria. Updated references.
7/2020	Updated Lyrica criteria for non-seizure disorders to require trial failure of step one medications based on indication. References updated.
6/2021	Added Sabril to criteria. Updated mental retardation language to intellectual disability. Removed the typically excluded medications: Oxtellar XR, Qudexy XR, Spritam and Trokendi XR. Updated references.
8/2021	Added Banzel to criteria.