

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Epilepsy	P&T DATE:	9/15/2020
THERAPEUTIC CLASS:	Neurologic Disorders	REVIEW HISTORY:	9/19,9/18, 2/17, 2/16
LOB AFFECTED:	Medi-Cal	(MONTH/YEAR)	

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

This coverage policy has been developed from HPSJ Coverage Criteria using the best practices guidelines as developed by the American Academy of Neurology and American Epilepsy Society.

Available Agents for Epilepsy (Current as of 7/2020)

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Avg Cost/Rx	Notes/Restriction Language
Barbiturates	Primidone (Mysoline)	50mg, 250mg	--	\$9.72	--
	Phenobarbital (Luminal)	15mg, 16.2mg, 30mg, 32.4mg, 60mg, 64.8mg, 97.2mg, 100mg, 20mg/5mL Elixir	--	\$35.48	--
Succinimides	Methsuximide (Celontin)	300mg	--	--	--
	Ethosuximide (Zarontin)	250mg, 250mg/5mL Soln	PL	\$78.64	Restricted to Neurologists
Benzodiazepines	Clobazam (Onfi)	10mg, 20mg	PL	\$113.98	Restricted to Neurologists
	Clonazepam (Klonopin)	ODT: 0.125mg, 0.25mg, 0.5mg, 1mg, 2mg Tablet: 0.5mg, 1mg, 2mg	--	\$1.52	--
Miscellaneous Anticonvulsants	Acetazolamide (Diamox)	125mg, 250mg, 500mg ER	--	\$132.18	--
	Lacosamide (Vimpat)	50mg, 10mg/mL Soln, 200mg/20mL IV Soln	PL	\$801.27	Restricted to Neurologists
	Carbamazepine (Tegretol)	200mg	--	\$70.52	--
	Oxcarbazepine (Trileptal)	150mg, 300mg, 600mg, 300mg/5mL Susp	--	\$14.79	--
	Divalproex Sodium (Depakote)	125mg DR, 250mg DR, 250mg ER, 500mg ER, 125mg sprinkle caps	--	\$20.94	--
	Valproic Acid (Depakene)	250mg, 250mg/5mL Soln	--	\$35.48	--
	Topiramate (Topamax)	15mg Sprinkle Cap, 25mg Sprinkle Cap, 25mg, 50mg, 100mg, 200mg	Sprinkle Cap: AL IR: No Limit	IR: \$4.37 Sprinkle: \$66.61	Sprinkle Capsules are restricted to members who are ≤ 12 years of age.
	Topiramate (Trokendi XR)	25mg, 50mg, 100mg, 200 mg	AL, PA, PL	\$906.95	Restricted to neurologists. Step therapy to a treatment failure of topiramate immediate release.
	Topiramate (Quedexy XR)	25mg, 50mg, 100mg, 150mg, 200mg	AL, PA, PL	\$792.42	Restricted to neurologists. Step therapy to a treatment failure of topiramate immediate release.
	Felbamate (Felbatol)	400mg, 600mg	PL	\$136.35	Restricted to Neurologists
	Gabapentin (Neurontin)	200mg, 300mg, 600mg, 800mg, 250mg/5mL Soln	--	\$6.99	--
	Phenytoin (Dilantin)	50mg, 100mg 125mg/5mL	--	\$29.25	--
	Pregabalin (Lyrica)	25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg	--	\$43.58	--
	Tiagabine (Gabitril)	2mg, 4mg, 12mg, 16mg	PL	--	Restricted to Neurologists
	Levetiracetam (Keppra)	250mg, 500mg, 750mg, 1000mg, 500mg ER, 750mg ER, 500mg/5mL Soln, 500mg/5mL IV Soln	--	IR: \$11.82 ER: \$35.15	--
Brivaracetam (Briviact)	10mg, 25mg, 50mg, 75mg, 100mg, 10 mg/mL Oral Soln, 50mg/5mL IV Soln	AL, PA, PL	Oral: \$929.86 Soln: \$1,443.52	Restricted to neurologists. Restricted to patients ≥21 years of age. Patient concurrently using at least one other antiepileptic drug. Not	

					concurrently using levetiracetam. Step therapy of levetiracetam and one other antiepileptic agent listed.
	Eslicarbazepine (Aptiom)	200mg, 400mg, 600mg, 800mg	AL, PA, PL	\$1,222.64	Restricted to neurologists. Restricted to patients ≥21 years of age. Patient concurrently using at least one other antiepileptic drug. Step therapy of two other antiepileptic agents listed.
	Perampanel (Fycompa)	2mg, 4mg, 6mg, 8mg, 10mg, 0.5mg/mL oral Soln	AL, PA, PL	Oral: \$1,156/49 Soln: --	Restricted to neurologists. Restricted to patients ≥21 years of age. Patient concurrently using at least one other antiepileptic drug. Step therapy of two other antiepileptic agents listed.
	Lamotrigine (Lamictal)	5mg Chew Tab, 25mg Chew Tab, 25mg, 100mg, 150mg, 200mg	--	IR: \$3.52 ODT: \$337.61 ER: \$215.11	--
	Zonisamide (Zonegran)	25mg, 50mg, 100mg	--	\$11.58	--

PL = Restricted to Neurologist Providers, PA = PA required. ST = Step Therapy, IR = Immediate Release, ER = Extended Release, ODT = Orally Dissolving Tablet

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

CCS Coverage Requirements for Members aged 0-20:

California Children's Services covers HPSJ members with refractory epilepsy who are concurrently on two or more epileptic medications (not including rescue medication, such as Diastat, or other benzodiazepines).

For coverage through the CCS program, members must be seen by a CCS Panelled Provider. Submit the member's most recent 6 months of records to the CCS Program for review. Fax numbers are listed below.

San Joaquin County: (209) 953-3632

Stanislaus County: (209) 558-7862

Barbiturates

Primidone (Mysoline), Phenobarbital (Luminal)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Succinimides

Methsuximide (Celontin)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Ethosuximide (Zarontin)

- Coverage Criteria:** None
- Limits:** Restricted to Neurologists
- Required Information for Approval:** PA must be submitted by a neurologist.

Benzodiazepines

Clobazam (Onfi)

- Coverage Criteria:** None
- Limits:** Restricted to Neurologists
- Required Information for Approval:** PA must be submitted by a neurologist.

Clonazepam (Klonopin)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Miscellaneous Anticonvulsants

Acetazolamide (Diamox)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Lacosamide (Vimpat)

- Coverage Criteria:** None
- Limits:** Restricted to Neurologists
- Required Information for Approval:** PA must be submitted by a neurologist.

Carbamazepine (Tegretol), Oxcarbazepine (Trileptal)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Divalproex Sodium (Depakote), Valproic Acid (Depakene)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Topiramate (Topamax)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Topiramate (Topamax) Sprinkle Capsules (15mg and 25mg)

- Coverage Criteria:** For patients ≤ 12 years of age.
- Limits:** None
- Required Information for Approval:** None

Topiramate (Trokendi XR)

- Coverage Criteria:** For patients ≥ 6 years of age. Patients must have a diagnosis of partial onset seizures and primary generalized tonic-clonic seizures or Lennox-Gastaut Syndrome. Trokendi XR is step therapy to treatment failure due to intolerance of topiramate immediate release. Must be prescribed by a neurologist.
- Limits:** Must be prescribed by a neurologist.
- Required Information for Approval:** Chart notes and pharmacy fill history documenting age of patient and treatment failure of topiramate immediate release.

Topiramate (Qudexy XR)

- Coverage Criteria:** For patients ≥ 2 years of age. Patients must have a diagnosis of partial onset seizures and primary generalized tonic-clonic seizures or Lennox-Gastaut Syndrome. Trokendi XR is step therapy to treatment failure due to intolerance of topiramate immediate release. Must be prescribed by a neurologist.
- Limits:** Must be prescribed by a neurologist.
- Required Information for Approval:** Chart notes and pharmacy fill history documenting age of patient and treatment failure of topiramate immediate release.

Felbamate (Felbatol)

- Coverage Criteria:** None
- Limits:** Restricted to Neurologists
- Required Information for Approval:** PA must be submitted by a Neurologist.

Gabapentin (Neurontin)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Phenytoin (Dilantin)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Pregabalin (Lyrica)

- Coverage Criteria:** None
- Limits:**
 - Pregabalin 25mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 50mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 75mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 100mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 150mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 200mg capsules: Limited to 90 capsules per 30 days
 - Pregabalin 225mg capsules: Limited to 60 capsules per 30 days
 - Pregabalin 300mg capsules: Limited to 60 capsules per 30 days
- Required Information for Approval:** N/A
- Other Notes:** None

Tiagabine (Gabitril)

- Coverage Criteria:** None
- Limits:** Restricted to Neurologists
- Required Information for Approval:** PA must be submitted by a Neurologist.

Lamotrigine (Lamictal)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

Brivaracetam (Briviact)

- Coverage Criteria:** For patients ≥ 21 years of age. Patients must have a diagnosis of partial onset seizures. Patient must be concurrently using at least one antiepileptic drug. Patient must not be concurrently using levetiracetam. The member should have had an insufficient response or intolerance to levetiracetam and one of the following: felbamate, gabapentin, lamotrigine, pregabalin, oxcarbazepine, topiramate, or zonisamide. Must be prescribed by a neurologist.
- Limits:** Must be prescribed by neurologists.
- Required Information for Approval:** Chart notes and pharmacy fill history of medications indicated for epilepsy.

Eslicarbazepine (Aptiom)

- Coverage Criteria:** For patients ≥ 21 years of age. Patients must have a diagnosis of partial onset seizures. Patient must be concurrently using at least one antiepileptic drug. The member should have had an insufficient response or intolerance to two of the following: levetiracetam, felbamate, gabapentin, lamotrigine, pregabalin, oxcarbazepine, topiramate, or zonisamide. Must be prescribed by a neurologist.
- Limits:** Must be prescribed by neurologists.
- Required Information for Approval:** Chart notes and pharmacy fill history of medications indicated for epilepsy.

Perampanel (Fycompa)

- Coverage Criteria:** For patients ≥ 21 years of age. Patients must have a diagnosis of partial onset seizures or primary generalized tonic-clonic seizures. Patient must be concurrently using at least one antiepileptic drug. The member should have had an insufficient response or intolerance to two other antiepileptic drugs.
- Limits:** Must be prescribed by neurologists.
- Required Information for Approval:** Chart notes and pharmacy fill history of medications indicated for epilepsy.

Vigabatrin (Sabril)

- Coverage Criteria:** PA required. Sabril is restricted for use in Infantile Spasms or Complex Partial Seizures. For Complex Partial Seizures, Sabril is reserved as adjunct therapy for patients 10 years and older with documented dose-optimized treatment failure of three formulary anti-epileptic agents for complex partial seizures including at least one of the following: carbamazepine, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, topiramate, valproic acid, divalproex sodium, zonisamide or tiagabine. Must be prescribed by a neurologist.
- Limits:**
 - Infantile Spasms:
 - Less than 2 years of age
 - Limited to 150mg/kg/day
 - Complex Partial Seizures:
 - For patients age 17 and older: Limit 3g per day
 - For patients age 10-16: Limit 2g per day
- Required Information for Approval:**
 - Documentation of visual acuity exam prior to initiation regardless of indication being requested.
 - Prescribed by neurologist.
 - For Complex Partial Seizure only:
 - Prescription fill history of previous agents used/tried.
 - Documentation of planned adjunct therapy.
- Approval Time Frame**
 - Initial approval is for 4 weeks.
 - Continuation of Therapy: Updated notes describing patient clinical course (clinical improvement of symptoms) will be required for renewal).

Zonisamide (Zonegran)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A

⊞ CLINICAL JUSTIFICATION

As can be seen from the above list of formulary anticonvulsants, many options are available to providers wishing to control seizure activity in their patients. Some agents are restricted to use by neurologists. These restrictions are in place to ensure that members are seen on a regular basis by their neurologist to ensure that standards of practice are met, and that patients receive adequate follow up. Generally, medications in this category are free of restrictions when prescribed by a neurologist. Some medications may have additional criteria due to similar efficacy as other comparators while the long-term safety is still undetermined.

REFERENCES

1. FDA news release. Sabril Approved by FDA to Treat Spasms in Infants and Epileptic Seizures. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm179855.htm>. Sabril (vigabatrin) [prescribing information]. Cincinnati, OH:Patheon; June 2016.
2. French JA, et al. A double-blind, placebo-controlled study of vigabatrin three g/day in patients with uncontrolled complex partial seizures. Vigabatrin Protocol 024 Investigative Cohort. *Neurology* 1996 Jan;46(1):54-61.
3. Dean C, et al. Dose-Response Study of Vigabatrin as add-on therapy in patients with uncontrolled complex partial seizures. *Epilepsia* 1999 Jan;40(1):74-82
4. Elterman RD, et al. Randomized trial of vigabatrin in patients with infantile spasms. *Neurology* 201 Oct;57(8):1416-1421.
5. Jason TL, et al. Clinical profile of vigabatrin as monotherapy for treatment of infantile spasms. *Neuropsychiatr Dis Treat* 2010; 6: 731–740
6. Waterhouse EJ, et al. Treatment of refractory complex partial seizures: role of vigabatrin. *Neuropsychiatr Dis Treat*. 2009; 5: 505–515
7. Appleton, Re, et al. Randomised, placebo-controlled study of vigabatrin as first-line treatment of infantile spasms. *Epilepsia*. 1999; 40.11: 1627-1633.
8. Lux, Andrew. Et al. The united kingdom infantile spasms study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. *The Lancet*. 2004; 364, 1773-1778.
9. Sergott, Andrew, et al. Evidence-based review of recommendations for visual function testing in patients treated with vigabatrin. *Neuro-Ophthalmology*. 2010, 34(1), 20-35
10. Ovation Pharmaceuticals. Sabril® (vigabatrin) Tablet and Powder for Oral Solution. For Adjunctive Treatment of Refractory Complex Partial Seizures in Adults (NDA 20-427) For Monotherapy Treatment of Infantile Spasms (NDA 22-006). Advisory Committee Briefing Document.
11. O'neal W, Hur EE, Liranso T, Patel B. Real-world assessment of treatment with extended-release topiramate (Trokendi XR) and comparison with previous immediate-release topiramate treatment. *J Comp Eff Res*. 2018;7(11):1095-1105.
12. Briviact® [package insert]. Smyrna, GA: UCB, Inc. 2016 [revised May 2018].
13. Charokopou M, Harvey R, Srivastava K, Brandt C, Borghs S. Relative performance of brivaracetam as adjunctive treatment of focal seizures in adults: a network meta-analysis. *Curr Med Res Opin*. 2019;35(8):1345-1354.
14. Bresnahan R, Panebianco M, Marson AG. Brivaracetam add-on therapy for drug-resistant epilepsy. *Cochrane Database Syst Rev*. 2019;3:CD011501.
15. Aptiom® [package insert]. Marlborough, MA: Sunovion Pharmaceuticals Inc. 2013.
16. Zhuo C, Jiang R, Li G, et al. Efficacy and tolerability of second and third generation anti-epileptic drugs in refractory epilepsy: A network meta-analysis. *Sci Rep*. 2017;7(1):2535.
17. Fycompa™ [package insert]. Woodcliff Lake, NJ: Eisai Inc. 2012.
18. Slater J, Chung S, Huynh L, et al. Efficacy of antiepileptic drugs in the adjunctive treatment of refractory partial-onset seizures: Meta-analysis of pivotal trials. *Epilepsy Res*. 2018;143:120-129.

⌘ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Potential Generics 2007 and 2008.doc	5/10/2007	Allen Shek PharmD BCPS
Update to Policy	Banzel Monograph.docx	9/24/2009	Allen Shek PharmD BCPS
Update to Policy	Formulary realignment 2-2010.xlsx	3/5/2010	Allen Shek PharmD BCPS
Update to Policy	Formulary realignment 5-11.xlsx	5/16/2011	Allen Shek PharmD BCPS
Update to Policy	Formulary realignment 09-17-2013	9/16/2013	Allen Shek PharmD BCPS
Update to Policy	HPSJ Coverage Policy - Neurologic Disorders - Epilepsy 2016-02.docx	2/16/2016	Johnathan Yeh PharmD
Update to Policy	HPSJ Coverage Policy - Neurologic Disorders - Epilepsy 2017-02.docx	2/2017	Johnathan Yeh PharmD
Update to Policy	HPSJ Coverage Policy - Neurologic Disorders - Epilepsy 2018-09.docx	9/2018	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy - Neurologic Disorders - Epilepsy 2019-09.docx	9/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy - Neurologic Disorders - Epilepsy 2020-09.docx	9/2020	Matthew Garrett, PharmD