Lamotrigine Orally Disintegrating Tablet

Summary

Partial-onset seizures, also known as focal seizures, start in a specific area or 'focus' in the brain. There are several subtypes of focal seizures including: focal aware seizures, focal impaired awareness seizures, focal motor seizures, focal nonmotor seizures and focal bilateral tonic-clonic seizures. The specific symptoms of a partial-onset seizure can vary widely depending on the area of the brain where the seizure originates. Focal epilepsy may be due to a focal brain pathology (due to a known syndrome or genetic cause), or be due to an unknown cause. Focal seizures can be managed with both narrow spectrum (e.g., carbamazepine, gabapentin, oxcarbazepine, phenytoin, phenobarbital, primidone, tiagabine) and broad spectrum anti-seizure medications (e.g., Briviact [brivaracetam], clobazam [Onfi], felbamate [Felbatol], lacosamide [Vimpat], levetiracetam [Keppra], valproate, zonisamide [Zonegran]) including lamotrigine (Lamictal).

Generalized tonic-clonic seizures begin with a loss of consciousness and limb stiffness (tonic phase), and move into the clonic phase as their muscles jerk and twitch. Occasionally a tonic-clonic seizure may result from a focal-onset seizure. Generalized tonic-clonic seizures are managed primarily with broad spectrum antiseizure medications.

Lennox-Gastaut syndrome (LGS) is a lifelong epileptic encephalopathy, causing chronic seizures and intellectual disability which presents in childhood. First-line management of LGS is typically valproate, however many require additional anti-seizure medications including lamotrigine (Lamictal), rufinamide (Banzel), topiramate (Topamax), clobazam (Onfi), felbamate (Felbatol), and fenfluramine (Fintepla).

Absence seizures are a form of seizures that are characterized by their frequent (multiple daily seizures) and short presentation where consciousness is impaired. They rarely present with body tone loss, and are often undiagnosed due to the subtle symptoms. Absence seizures are generally managed with ethosuximide, however second-line therapy includes lamotrigine and valproate, and less commonly topiramate, benzodiazepines, and zonisamide.

Bipolar disorder is a mental health condition characterized by symptoms of mania (elevated or irritable mood, increased activity and energy), hypomania (elevated mood, energy and activity less severe than mania episodes), or major depression (low mood, lack of interest in activities) and mania. Bipolar disorder can often be accompanied by psychotic features (e.g., delusions and hallucinations), especially in the case of mania or bipolar major depression. These episodes can impact a person's ability to function in daily life due to their severity and unpredictability. Therapy is tailored to the individual and their responses to prior therapies. First-line pharmacotherapy typically includes vaproate, divalproex (Depakote), and lithium; second-line therapies include quetiapine (Seroquel) and lamotrigine (Lamictal); third-line therapies may include antipsychotics (e.g., risperidone [Risperdal], aripiprazole [Abilify], olanzapine [Zyprexa]).

Trigeminal neuralgia is a type of neuropathic pain (stabbing, intensense, burning pain) that affects one or more branches of the trigeminal nerve of the face and head. Therapies typically include pharmacotherapy such as cabamazepine (Tegretol), oxcarbazepine (Trileptal), gabapentin (Neurontin), lamotrigine (Lamictal) or baclofen; rescue therapies, such as injectable agents (e.g., lidocaine, sumatriptan (Imitrex), phenytoin); and in rare cases, surgical interventions.

Short-lasting unilateral neuralgiform headaches attacks refers to a rare headache disorder characterized by brief, severe, and recurrent attacks of pain (burning, stabbing, or electrical in nature) on one side of the head. It is sometimes accompanied by conjunctival injection (redness of the eye) and/or tearing. In the short-term, these attacks can be managed with intravenous lidocaine; however, long-term preventative therapy can include lamotrigine (Lamictal), topiramate (Topamax), or gabapentin (Neurontin).

Lamotrigine is an oral anticonvulsant medication that has received FDA approval for its application in managing bipolar disorder, Lennox-Gastaut syndrome, focal (also known as partial-onset) seizures, and generalized tonic-clonic seizures. The precise mechanism underlying its anticonvulsant activity is not entirely understood. However, research suggests that lamotrigine may stabilize neuronal membranes by

acting on voltage-sensitive sodium channels, thereby inhibiting the release of glutamate and aspartate, two excitatory amino acids.

Lamotrigine is available in multiple oral dosage formulations: extended-release (ER) and immediate-release (IR) tablets, orally disintegrating tablets (ODTs) and chewable tablets. For members who cannot swallow a pill, lamotrigine chewable tablet is a viable alternative option to Lamotrigine ODT.

Lamotrigine carries a boxed warning for the risk of serious skin rashes, including Stevens-Johnson syndrome and toxic epidermal necrolysis. The risk of serious rash is greater in pediatrics than in adults. To prevent the development of rash, a serious potential side effect, lamotrigine requires a slow and careful dosage titration. Compared to traditional antiepileptic drugs, lamotrigine is generally less sedating and produces fewer cognitive adverse effects. Its use as a monotherapy is associated with one of the lowest teratogenicity rates, making it a preferred choice for female patients of childbearing potential.

Definitions

"Anti-epileptics" refers to medications used to treat seizures.

"Epilepsy" is a neurological disorder characterized by recurrent, unprovoked seizures. The diagnosis typically applies when a person experiences two or more seizures that occur more than 24 hours apart and are not caused by a known and reversible medical condition such as alcohol withdrawal or extremely low blood sugar.

"Bipolar Disorder" is a mental health condition marked by significant mood swings that alternate between periods of depression (low mood, lack of interest in activities) and mania (elevated or irritable mood, increased activity and energy). These episodes can impact a person's ability to function in daily life due to their severity and unpredictability.

"Lennox-Gastaut syndrome" is a rare and severe form of epilepsy that starts in childhood, characterized by multiple types of seizures and intellectual disability.

"Focal (Partial) Seizures" refers to seizures that start in, and affect, just one part of the brain. They can sometimes spread to wider areas on the same side of the brain.

"Generalized Tonic-Clonic Seizures," formerly known as grand mal seizures, involve the whole body and typically include a period of muscle rigidity (the "tonic" phase) followed by rhythmic muscle contractions (the "clonic" phase).

"Short-lasting unilateral neuralgiform headaches attacks" refers to a rare headache disorder characterized by brief, severe, and recurrent attacks of pain (burning, stabbing, or electrical in nature) on one side of the head. It is accompanied by conjunctival injection (redness of the eye) and/or tearing.

"Teratogenicity" is the capability of a drug or other substance to cause birth defects.

"Trigeminal neuralgia" is a type of neuropathic pain (stabbing, intensense, burning pain) that affects one or more branches of the trigeminal nerve of the face and head.

Medical Necessity Criteria forAuthorization

The Plan considers Lamotrigine ODT medically necessary when ALL the following criteria are met for the applicable indication listed below:

For the treatment of Seizure Disorders:

1. The member is 2 years of age or older*; AND*
2. The member has ONE (1) of the following diagnoses:
    a. Partial-onset (focal) seizures*; or*
    b. primary generalized tonic-clonic (PGTC) seizures*; or*
    c. generalized seizures of Lennox-Gastaut syndrome*; or*
    d. absence seizures*; AND*
3. The member is unable to use or has tried and failed BOTH of the following:
    a. Lamotrigine immediate-release*; and*
    b. Lamotrigine chewable tablet*; AND*
4. Lamotrigine ODT is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature*; AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

For the treatment of Bipolar Disorder:

1. The member is 12 years of age or older*; AND*
2. The member has a documented diagnosis of bipolar disorder*; AND*
3. The member is unable to use or has tried and failed BOTH of the following:
    a. Lamotrigine immediate-release*; and*
    b. Lamotrigine chewable tablet*; AND*
4. Lamotrigine ODT is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature*; AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

For other off-label uses:

1. The member is 18 years of age or older*; AND*
2. The medication is being requested for ONE (1) of the following:
    a. acute treatment of bipolar major depression*; or*
    b. prophylactic therapy to decrease severity and frequency of short-lasting unilateral neuralgiform headache attacks*; or*
    c. management of symptoms associated with trigeminal neuralgia*; AND*
3. The member is unable to use or has tried and failed BOTH of the following:
    a. Lamotrigine immediate-release*; and*
    b. Lamotrigine chewable tablet*; AND*
4. Lamotrigine ODT is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature*; AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria is met, lamotrigine ODT will be approved up to a lifetime.

Experimental or Investigational / Not Medically Necessary

Lamotrigine ODT for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

References

1. Bendtsen L, Zakrzewska JM, Abbott J, et al. European Academy of Neurology guideline on trigeminal neuralgia. Eur J Neurol. 2019;26(6):831-849. doi:10.1111/ene.13950.
2. Bobo WV, Shelton RC. Bipolar major depression in adults: Efficacy and adverse effects of antidepressants. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed July 21, 2022.
3. Cohen AS. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing. Cephalalgia. 2007;27(7):824-832. doi: 10.1111/j.1468-2982.2007.01352.x
4. Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55:475.
5. Fountoulakis KN, Yatham LN, Grunze H, et al. The CINP Guidelines on the Definition and Evidence-Based Interventions for Treatment-Resistant Bipolar Disorder. Int J Neuropsychopharmacol. 2020 Apr 23;23(4):230-256. doi: 10.1093/ijnp/pyz064.
6. Fredskild MU, Bruun CF, Vinberg M, et al. Lithium and lamotrigine for the treatment of bipolar II disorder - a systematic review and meta-analysis of randomized trials. J Affect Disord. 2025 Aug 15;383:341-353. doi: 10.1016/j.jad.2025.04.125. Epub 2025 Apr 25.
7. Glauser TA, Cnaan A, Shinnar S, et al. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy. N Engl J Med. 2010;362(9):790-799.
8. Gloss D, Pargeon K, Pack A, et al; AAN Guideline Subcommittee. Antiseizure Medication Withdrawal in Seizure-Free Patients: Practice Advisory Update Summary: Report of the AAN

Guideline Subcommittee. Neurology. 2021 Dec 7;97(23):1072-1081. doi: 10.1212/WNL.0000000000012944. PMID: 34873018.
9. Gronseth G, Cruccu G, Alksne J, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008 Oct 7;71(15):1183-90. doi: 10.1212/01.wnl.0000326598.83183.04. Epub 2008 Aug 20.
10. Grunze H, Vieta E, Goodwin GM, et al; WFSBP Task Force on Treatment Guidelines for Bipolar Disorders. The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2010 on the treatment of acute bipolar depression. World J Biol Psychiatry. 2010;11(2):81-109. doi:10.3109/15622970903555881
11. Guideline Development Panel for the Treatment of Depressive Disorders. Summary of the clinical practice guideline for the treatment of depression across three age cohorts. Am Psychol. 2022 Sep;77(6):770-780. doi: 10.1037/amp0000904. Epub 2021 Nov 29. PMID: 34843274.
12. Haenen N, Kamperman AM, Prodan A, Nolen WA, Boks MP, Wesseloo R. The efficacy of lamotrigine in bipolar disorder: A systematic review and meta-analysis. Bipolar Disord. 2024 Aug;26(5):431-441. doi: 10.1111/bdi.13452. Epub 2024 May 15.
13. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs I: Treatment of new-onset epilepsy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2018 Jul 10;91(2):74-81. doi: 10.1212/WNL.0000000000005755. Epub 2018 Jun 13. PMID: 29898971.
14. Lamictal (lamotrigine) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2025.
15. Lamictal ODT (lamotrigine) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; February 2023.
16. Lamictal XR (lamotrigine) [prescribing information]. Durham, NC: GlaxoSmithKline; January 2023.
17. May A, Leone M, Afra J, et al; EFNS Task Force. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. Eur J Neurol. 2006;13(10):1066-1077. doi: 10.1111/j.1468-1331.2006.01566.x
18. McQuaid JR, Buelt A, Capaldi V, et al. The Management of Major Depressive Disorder: Synopsis of the 2022 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline. Ann Intern Med. 2022 Oct;175(10):1440-1451. doi: 10.7326/M22-1603. Epub 2022 Sep 20. PMID: 36122380.
19. Mula M, Brodie MJ, de Toffol B, et al. ILAE clinical practice recommendations for the medical treatment of depression in adults with epilepsy. Epilepsia. 2022 Feb;63(2):316-334. doi: 10.1111/epi.17140. Epub 2021 Dec 5. PMID: 34866176.
20. O'Mahony D, Cherubini A, Guiteras AR, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 3. Eur Geriatr Med. 2023 Aug;14(4):625-632. doi: 10.1007/s41999-023-00777-y. Epub 2023 May 31. Erratum in: Eur Geriatr Med. 2023 Aug;14(4):633. doi: 10.1007/s41999-023-00812-y. PMID: 37256475; PMCID: PMC10447584.
21. Piña-Garza JE, Elterman RD, Ayala R, et al. Long-Term Tolerability and Efficacy of Lamotrigine in Infants 1 to 24 Months Old. J Child Neurol. 2008;23(8):853-861.
22. Piña-Garza JE, Levisohn P, Gucuyener K, et al. Adjunctive Lamotrigine for Partial Seizures in Patients Aged 1 to 24 Months. Neurology. 2008a;70(22, pt 2):2099-2108.
23. Schachter SC. Overview of the management of epilepsy in adults. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed June 27, 2022.

24. Selle V, Schalkwijk S, Vázquez GH, Baldessarini RJ. Treatments for acute bipolar depression: meta-analyses of placebo-controlled, monotherapy trials of anticonvulsants, lithium and antipsychotics. Pharmacopsychiatry. 2014;47(2):43-52. doi:10.1055/s-0033-1363258.
25. Taylor DM, Cornelius V, Smith L, Young AH. Comparative efficacy and acceptability of drug treatments for bipolar depression: a multiple-treatments meta-analysis. Acta Psychiatr Scand. 2014;130(6):452-469. doi:10.1111/acps.12343.
26. Wang E, Liu Y, Wang Y, et al. Comparative Safety of Antipsychotic Medications and Mood Stabilizers During Pregnancy: A Systematic Review and Network Meta-analysis of Congenital Malformations and Prenatal Outcomes. CNS Drugs. 2025 Jan;39(1):1-22. doi: 10.1007/s40263-024-01131-x. Epub 2024 Nov 11.
27. Wang S, Sun H, Wang Z, et al. Adjunctive treatment for pediatric focal epilepsy: a systematic review. Eur J Clin Pharmacol. 2025 Apr;81(4):507-523. doi: 10.1007/s00228-025-03807-9. Epub 2025 Feb 13.
28. Williams MH, Broadley SA. SUNCT and SUNA: clinical features and medical treatment. J Clin Neurosci. 2008;15(5):526-534. doi:10.1016/j.jocn.2006.09.006.
29. Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018;20(2):97-170. doi:10.1111/bdi.12609.

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