Clinical Policy Title:	lamotrigine
Policy Number:	RxA.197
Drug(s) Applied:	Lamictal® XR, Lamictal® ODT
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Lamotrigine (Lamictal® XR, Lamictal® ODT) is an anticonvulsant.

Lamictal® XR is indicated for:

- Adjunctive therapy for primary generalized tonic-clonic seizures and partial onset seizures with or without secondary generalization in patients ages 13 years and older.
- Conversion to monotherapy in patients 13 years and older with partial-onset seizures who are receiving treatment with a single antiepileptic drug (AED).

Limitation(s) of use: Safety and effectiveness in patients younger than 13 years have not been established.

Lamictal® ODT is indicated for:

- Epilepsy - adjunctive therapy in patients aged 2 years and older:
  - partial-onset seizures;
  - primary generalized tonic-clonic seizures; and
  - generalized seizures of Lennox-Gastaut syndrome.
- Epilepsy - monotherapy in patients aged 16 years and older: Conversion to monotherapy in patients with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as a single AED.
- Bipolar disorder: Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy.

Limitation(s) of use: Treatment of acute manic or mixed episodes is not recommended. Effectiveness of lamotrigine in the acute treatment of mood episodes has not been established.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lamotrigine ODT (Lamictal® ODT)	Epilepsy	25 mg every other day to 500 mg once daily, in divided doses. Refer to full prescribing information for specific dosing recommendations depending upon concomitant AEDs or other concomitant medications, indication, and patient age.	500 mg/day

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lamotrigine ODT (Lamictal® ODT)	Bipolar	25 mg every other day to 400 mg once daily, in divided doses. Refer to full prescribing information for specific dosing recommendations depending upon concomitant AEDs or other concomitant medications, indication, and patient age.	400 mg /day
lamotrigine (Lamictal® XR)	Epilepsy	25 mg every other day to 600 mg PO once daily. Refer to full prescribing information for specific dosing recommendations depending upon concomitant AEDs or other concomitant medications, indication, and patient age.	600 mg/day

Dosage Forms

- Extended-release tablets: 25 mg, 50 mg, 100 mg, 200 mg, 250 mg, and 300 mg
- ODT Tablets: 25 mg, 50 mg, 100 mg, and 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. Epilepsy, Bipolar Disorder (must meet all)**:**

a. For Lamictal® XR only: Failure of immediate-release lamotrigine unless contraindicated or clinically significant adverse effects are experienced;

b. For Lamictal® ODT only: Documentation supports inability to swallow tablets or capsules or member has a documented swallowing disorder.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

II. Continued Therapy Approval

A. Epilepsy, Bipolar disorder (must meet all)**:**

a. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;

b. Member is responding positively to therapy.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AED: antiepileptic drug

FDA: Food and Drug Administration
ODT: orally disintegrating tablet
XR: extended release

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
lamotrigine immediate- release (Lamictal®)	Dosing is based on concomitant medications, indication, and patient age. Refer to full prescribing information.	In seizure disorders, individualize to the patient's age, weight, indication, concurrent medication, and clinical response. In bipolar disorder, maximum monotherapy dosage is 200 mg/day PO; 100 mg/day PO if taking valproate; 400 mg/day PO if taking enzyme-inducing drugs.

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):
  - Hypersensitivity to the drug (e.g., rash, angioedema, acute urticaria, extensive pruritus, mucosal ulceration.

- Boxed Warning(s):
  - Serious skin rashes (e.g., Stevens-Johnson Syndrome and toxic epidermal necrolysis) and/or rash-related death have been caused by lamotrigine.
  - Benign rashes

APPENDIX D: General Information

- Life-threatening serious rash and/or rash-related death: Discontinue at the first sign of rash, unless the rash is clearly not drug related.
- Fatal or life-threatening hypersensitivity reaction: Multiorgan hypersensitivity reactions, also known as drug reaction with eosinophilia and systemic symptoms, may be fatal or life threatening. Lamotrigine should be discontinued if alternate etiology for rash, fever, and/or lymphadenopathy not found.
- Cardiac rhythm and conduction abnormalities: Avoid lamotrigine in patients with certain underlying cardiac disorders or arrhythmias.
- Blood dyscrasias (e.g., neutropenia, thrombocytopenia, pancytopenia): May occur, either with or without an associated hypersensitivity syndrome. Monitor for signs of anaemia, unexpected infection, or bleeding.
- Hemophagocytic lymphohistiocytosis: Consider this diagnosis and evaluate patients immediately if they develop signs or symptoms of systemic inflammation. Discontinue lamotrigine if an alternative etiology is not established.
- Suicidal behavior and ideation: Monitor for suicidal thoughts or behaviors.
- Aseptic meningitis: Monitor for signs of meningitis.

References

1. Lamictal XR Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; October 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3e2c9a35-6a39-41d7-ad84-3c0bb8894b09&type=display. Accessed February 22, 2021.
2. Lamictal tablets, Lamictal chewable dispersible tablets, Lamictal ODT [Prescribing Information] Research Triangle Park, NC: GlaxoSmithKline; October 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d7e3572d-56fe-4727-2bb4-013ccca22678&type=display . Accessed February 22, 2021.
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4. Lamictal. American Hospital Formulary Service Drug Information. Available at: http://www.medicinescomplete.com/mc/ahfs/current/. Accessed February 22, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 22, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1) Clinical Policy title was updated. 2) Initial approval duration updated from “length of benefit” to 12 months. 3) Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4) Lines of business ‘Policy Applies to’ was updated to ‘All lines of business’. 5) References reviewed and updated.	07/2020	09/14/2020
Policy was reviewed: 1) Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 2) Appendix D was added. 3) References reviewed and updated.	02/22/2021	06/10/2021