Effective Date 3/15/2024
Next Review Date 3/15/2025
Coverage Policy Number IP0048

Rufinamide

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following rufinamide products:

- **Banzel®** tablets and oral suspension
- rufinamide tablets and oral suspension

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Rufinamide products are considered medically necessary when ONE of the following is met:

1. **Lennox-Gastaut Syndrome.** Individual meets **ALL** of the following criteria:
   A. Age 1 year or older

B. Has tried and/or is concomitantly receiving at least **TWO** other antiepileptic drugs
C. Medication is prescribed by, or in consultation with, neurologist
D. Non-Covered Product Criteria is met, refer to below table

2. **Treatment-Refractory Seizures/Epilepsy.** Individual meets **ALL** of the following criteria:
   A. Age 1 year or older
   B. Has tried and/or is concomitantly receiving at least **TWO** other antiepileptic drugs
   C. Medication is prescribed by, or in consultation with, neurologist
   D. Non-Covered Product Criteria is met, refer to below table

Employer Group Plans Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Banzel (rufinamide oral suspension)	Documentation of trial of **rufinamide oral suspension** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction.
Banzel (rufinamide tablets)	Documentation of trial of **rufinamide tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of rufinamide products is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

Background

OVERVIEW
Rufinamide is indicated for adjunctive treatment of **seizures associated with Lennox-Gastaut syndrome** (LGS) in patients ≥ 1 year of age.[1]

Although rufinamide is only FDA-approved for use in LGS, clinical trial data indicate the drug may also be beneficial as adjunctive treatment of refractory focal epilepsy.[2] A review of six clinical trials found that rufinamide when used as an add-on treatment was effective in reducing seizure frequency in patients with drug-resistant focal epilepsy.

Disease Overview
LGS is a severe epileptic and developmental encephalopathy associated with a high rate of morbidity and mortality.[3,4] LGS most often begins between 3 years and 5 years of age and comprises approximately 3% to 4%

of childhood epilepsies.[3-6] Affected children experience several different types of seizures, most commonly atonic seizures (sudden loss of muscle tone and limpness, also called drop seizures) and tonic seizures (increased muscle tone and muscle stiffness).[3,6] The three main forms of treatment of LGS are antiseizure medications (ASMs), dietary therapy (typically the ketogenic diet), and device/surgery (e.g., vagus nerve stimulation, corpus callosotomy).[6] None of the therapies are effective in all cases of LGS and the disorder has proven particularly resistant to most therapeutic options. The choice of treatment should take into consideration the patient's age and other associated conditions.

Guidelines/Recommendations

Lennox-Gastaut syndrome: Currently, the FDA-approved drugs for this condition are Epidiolex® (cannabidiol oral solution), felbamate, lamotrigine, rufinamide, topiramate, and clobazam.[7] Despite the lack of level I or level II evidence, valproic acid remains a mainstay in treatment.[5,6,8] If valproic acid does not provide adequate seizure control, which is almost always the case, lamotrigine should be added as the first adjunctive therapy.[4] If the combination regimen of valproic acid and lamotrigine does not provide adequate control, then rufinamide should be initiated and either valproic acid or lamotrigine should be discontinued. If seizure control is still not achieved, the next adjunctive therapies to consider are topiramate, clobazam, and felbamate. There is limited evidence for the use of levetiracetam, zonisamide, and Fycompa® (perampanel tablets and oral suspension). Where possible, no more than two ASMs should be used concomitantly; use of multiple ASMs raise the risk of side effects and/or drug-drug interactions.

References

1. Banzel tablets and oral suspension [prescribing information]. Woodcliff Lake, NJ: Eisai; November 2019.
2. Brigo F, Jones K, Eltze C, et al. Anti-seizure medications for Lennox-Gastaut syndrome. *Cochrane Database Syst Rev*. 2021;4(4):CD003277.
3. Sirven JI, Shafer PO. Epilepsy Foundation – Lennox-Gastaut Syndrome. Updated February 2020. Available at: https://www.epilepsy.com/learn/types-epilepsy-syndromes/lennox-gastaut-syndrome-lgs. Accessed on September 14, 2023.
4. Cross JH, Auvin S, Falip M, et al. Expert opinion on the management of Lennox-Gastaut syndrome: treatment algorithms and practical considerations. *Front Neurol*. 2017;8:505.
5. Ostendorf AP, Ng YT. Treatment-resistant Lennox-Gastaut syndrome: therapeutic trends, challenges, and future directions. *Neuropsych Dis Treatment*. 2017;13:1131-1140.
6. Wheless JW. National Organization for Rare Diseases (NORD) – Lennox-Gastaut syndrome. Available at: https://rarediseases.org/rare-diseases/lennox-gastaut-syndrome/. Accessed on September 14, 2023.
7. Lennox-Gastaut Syndrome Foundation – Lennox-Gastaut Syndrome. Updated August 2022. Available at: https://www.lgsfoundation.org/about-lgs-2/how-is-lgs-treated/. Accessed on September 14, 2023.
8. Cherian KA. Lennox-Gastaut syndrome treatment & management. Updated August 6, 2020. Available at: https://emedicine.medscape.com/article/1176735-treatment. Accessed on September 14, 2023.