Clinical Policy: Sodium Phenylbutyrate/Taurursodiol (Relyvrio)

Reference Number: LA.PHAR.584
Effective Date: 09.29.23
Last Review Date: ~~05.01.23~~04.05.24
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Please note: This policy is for medical benefit

Description
Sodium phenylbutyrate/taurursodiol (Relyvrio™) is coformulation of the compounds sodium phenylbutyrate, a molecular chaperone, and taurursodiol, a Bax inhibitor.

FDA Approved Indication(s)
Relyvrio is indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® that Relyvrio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Amyotrophic Lateral Sclerosis (must meet all)**:**

1. Diagnosis of definite ALS per revised El Escorial diagnostic criteria (*see Appendix D)*;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Concomitant use of riluzole (at up to maximally indicated doses), unless contraindicated or clinically significant adverse effects are experienced;
5. Percent predicted slow vital capacity (SVC) > 60%;
6. Symptom onset of ≤ 18 months;
7. Member does not have presence of tracheostomy or permanent assisted ventilation;
8. Dose does not exceed 6 g sodium phenylbutyrate/2 g taurursodiol (2 packets) per day.

Approval duration: 6 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Amyotrophic Lateral Sclerosis (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no tracheostomy or permanent assisted ventilation);
3. If request is for a dose increase, new dose does not exceed 6 g sodium phenylbutyrate/2 g taurursodiol (2 packets) per day.

Approval duration: 6 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALS: amyotrophic lateral sclerosis
~~ALSFRS-F: revised ALS Functional Rating Scale~~
EMG: electromyography
FDA: Food and Drug Administration
LMN: lower motor neuron
SVC: slow vital capacity
UMN: upper motor neuron disease

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
riluzole (Rilutek®)	50 mg PO BID	100 mg/day

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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
None reported

Appendix D: General Information

- Revised El Escorial diagnostic criteria for ALS requires the presence of:
  1. Signs of lower motor neuron (LMN) degeneration by clinical, electrophysiological or neuropathologic examination,
  2. Signs of upper motor neuron (UMN) degeneration by clinical examination, and
  3. Progressive spread of signs within a region or to other regions, together with the absence of:
     a. Electrophysiological evidence of other disease processes that might explain the signs of LMN and/or UMN degenerations; and
     b. Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs.
- The definitions of ALS diagnoses provided by the revised El Escorial criteria are as follows:

Revised El Escorial criteria	
Clinically definite ALS	Clinical/electromyography (EMG) evidence of upper and lower motor neuron signs in ≥ 3 regions
Clinically probable ALS	Clinical/EMG evidence of upper and lower motor neuron signs in ≥ 2 regions, with some upper motor neuron signs rostral to lower motor neuron signs
Clinically probable lab-supported ALS	Clinical upper and lower motor neuron signs in 1 region and lower motor neuron signs in 2 regions
Clinically possible ALS	Clinical/EMG evidence of upper and lower motor neuron signs in 1 region OR Isolated upper motor neuron signs in ≥ 2 regions OR Lower motor neuron signs rostral to upper motor neuron signs

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Appendix E: Riluzole Co-administration
There is support for the co-administration of riluzole in ALS:

- The 2009 American Academy of Neurology ALS guideline for the care of the patient with ALS (reaffirmed January 2020) recommends that riluzole should be offered to slow disease progression (Level A).
- The 2020 Canadian best practice recommendations for the management of ALS state the following: riluzole has demonstrated efficacy in improving survival in ALS (level A), there is evidence that riluzole prolongs survival by a median duration of 3 months (level A), and riluzole should be started soon after the diagnosis of ALS (expert consensus).
- Additionally, approximately 71% of patients in the phase 2 CENTAUR trial were receiving concomitant riluzole.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALS	1 packet (3 g sodium phenylbutyrate and 1 g taurursodiol) daily for the first 3 weeks, followed by 1 packet twice daily thereafter	2 packets (6 g sodium phenylbutyrate and 2 g taurursodiol) per day

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VI. Product Availability

Powder for oral suspension: 3 g of sodium phenylbutyrate and 1 g of taurursodiol in single dose packet

VII. References

1. Relyvrio Prescribing Information. Cambridge, MA: Amylyx Pharmaceuticals; September 2022. Available at: https://www.~~accessdata.fda.gov/drugsatfda_docs/label/2022/216660s000lbledt~~relyvrio.com/RELYVRIO-US-Prescribing-Information.pdf. Accessed ~~September 29, 2022~~January 6, 2023.
2. Paganoni S, Macklin EA, Hendrix S, et al. Trial of sodium phenylbutyrate-taurursodiol for amyotrophic lateral sclerosis. N Engl J Med. 2020 Sep 3;383(10):919-930.
3. Paganoni S, Hendrix S, Dickson SP, et al. Long-term survival of participants in the CENTAUR trial of sodium phenylbutyrate-taurursodiol in amyotrophic lateral sclerosis. Muscle Nerve. 2021 Jan;63(1):31-39.
4. Paganoni S, Hendrix S, Dickson SP, et al. Effect of sodium phenylbutyrate/taurursodiol on tracheostomy/ventilation-free survival and hospitalisation in amyotrophic lateral sclerosis: long-term results from the CENTAUR trial. J Neurol Neurosurg Psychiatry. 2022;93(8):871-875.
5. Brooks BR, Miller RG, Swash M, et al. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000 Dec;1(5):293-9.
6. Shoesmith C, Abrahao A, Benstead T, et al. Canadian best practice recommendations for the management of amyotrophic lateral sclerosis. CMAJ. 2020 Nov;192(46):E1453-E1468.
7. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2009 Oct 13;73(15):1218-26.

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	08.28.23
Annual review; no significant changes; references reviewed and updated.	04.05.24	

Important Reminder

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CLINICAL POLICY
Sodium Phenylbutyrate/Taurursodiol

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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