Clinical Policy Title:	sodium phenylbutyrate and taurursodiol
Policy Number:	RxA.781
Drug(s) Applied:	Relyvrio™
Original Policy Date:	01/17/2023
Last Review Date:	01/17/2023
Line of Business Policy Applies to:	All lines of business

Background

Relyvrio™ is indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults.

Dosing Information

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

Dosage Forms

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

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. Amyotrophic Lateral Sclerosis (must meet all):

1. Diagnosis of ALS;
2. Prescribed by or in consultation with a neurologist, neuromuscular specialist or physician specializing in terms of treatment of ALS;
3. Age ≥ 18 years;
4. Dose does not exceed 6 gm sodium phenylbutyrate/2 gm taurursodiol (2 packets) per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Amyotrophic Lateral Sclerosis (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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 gm sodium phenylbutyrate/2 gm taurursodiol (2 packets) per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ALS: amyotrophic lateral sclerosis
SVC: slow vital capacity
LMN: lower motor neuron
UMN: upper motor neuron disease

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
riluzole (Rilutek®), Tiglutik®, Exservan™	50 mg orally twice daily	100 mg/day
Radicava®	60 mg intravenous once daily for 14 days followed by a 14-day drug-free period.	60 mg/day
Radicava ORS®	105 mg (5 mL) taken orally for 14 days, followed by a 14-day drug-free period.	105 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Clinical experts viewed the pivotal (CENTAUR) trial eligibility requirement of having a “definite” diagnosis of ALS per the El Escorial criteria as being too narrow, as they do not use the El Escorial criteria to diagnose patients with ALS in practice. A “misdiagnosis” of ALS is extremely uncommon.Signs of lower motor neuron (LMN) degeneration by clinical, electrophysiological or neuropathologic examination;
- The pivotal trial inclusion/exclusion criteria (symptom onset within 18 months, SVC >60%, exclusion of tracheostomy) were chosen to enroll a population that was not at risk for imminent death, in order to

detect a benefit over a very short time frame. Clinical experts felt these criteria do not represent clinically meaningful subpopulations to which coverage should be limited in real-world practice. However, it is unknown based on available data whether Relyvrio is effective in more advanced disease.

References

1. Relyvrio™ Prescribing Information. Cambridge, MA: Amylyx Pharmaceuticals; September 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216660s000lbledt.pdf. Accessed December 08, 2022.
2. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2022. Available at: http://www.clinicalkey.com. Accessed December 08, 2022.
3. IPD Analytics Rx Insights_New Drug Review_ Relyvrio™ 10.2022. Available at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q=Relyvrio. Accessed December 08, 2022.
4. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: Revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders. 2000;1(5):293-299. Available at: https://www.tandfonline.com/doi/abs/10.1080/146608200300079536. Accessed December 08, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	12/08/2022	01/17/2023