Original Effective Date: 02/25/2023
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Last P&T Approval/Version: 01/25/2023
Next Review Due By: 01/2024
Policy Number: C24678-A

Relyvrio (sodium phenylbutyrate/taurursodiol)

PRODUCTS AFFECTED

Relyvrio (sodium phenylbutyrate/taurursodiol)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Amyotrophic lateral sclerosis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

A. AMYOTROPHIC LATERAL SCLEROSIS (ALS):
   1. Documented diagnosis of ALS
      AND
   2. Documentation of less than or equal to 18 months since ALS symptom onset
      AND
   3. Documentation member does not have tracheostomy or permanent assisted ventilation

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:
   1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
      AND
   2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   3. Documentation member is not dependent on invasive ventilation or tracheostomy

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 6 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified neurologist experienced in the management/treatment of amyotrophic lateral sclerosis (ALS) [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
1 packet twice daily (60 packets per 30 days)
NOTE: initial titration is 1 packet once daily for 3 weeks

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
ALS Agent Combinations

FDA-APPROVED USES:
indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Amyotrophic lateral sclerosis (ALS) is a rare, fatal, progressive neurodegenerative disorder that affects upper and lower motor neurons. A loss of motor neurons in the brain and spinal cord initially leads to focal weakness, with muscle weakness spreading over time. Most patients die of respiratory failure within 2 to 5 years of onset.

An estimated 24,800 patients are living with ALS in the United States. Currently, there are no treatments that stop or significantly slow the progression of ALS; therefore, the management of ALS is largely supportive, including symptomatic treatment, nutritional support, and respiratory management. Relyvrio is the third FDA-approved therapy for ALS, following riluzole and Mitsubishi Tanabe's Radicava (edaravone) and Radicava ORS (oral suspension). The current FDA-approved therapies for ALS only modestly slow progression of disease.

Relyvrio (sodium phenylbutyrate/taurursodiol) is an oral, fixed-dose combination therapy that is thought to target endoplasmic reticulum stress and mitochondrial dysfunction for the treatment of ALS. The FDA approval was supported by data from the phase 2 CENTAUR trial, a double-blind, placebo-controlled, parallel-group study that evaluated Relyvrio in adult patients with ALS (N=137) and the CENTAUR open-label extension (OLE) study. Patients were randomly assigned to receive Relyvrio (n=89) or placebo (n=48) for 24 weeks (intent-to-treat [ITT] population); baseline disease characteristics were reported to be comparable between the 2 groups.

The primary endpoint of the study was a comparison of the rate of reduction in the ALS Functional Rating Scale-Revised (ALSFRS-R) total scores from baseline to week 24 in the mITT population. Results showed a statistically significant difference in the rate of reduction in the ALSFRS-R total score from baseline to week 24 in the Relyvrio group compared with the placebo group (treatment difference, 2.32 points [95% CI, 0.18-4.47]; P =.034).

The CENTAUR-OLE trial was a single-arm, open-label extension study in which participants completing the 6-month randomized phase (the CENTAUR trial) were eligible to receive Relyvrio for up to 30 months (132 weeks). Overall, 66% of participants originally randomized in the CENTAUR trial enrolled in the OLE, which included 56 participants (64%) from the Relyvrio arm and 34 participants (71%) from the placebo arm. The post-hoc, long-term, intention-to-treat (ITT) survival analysis showed a difference in median survival of 4.8 months in the group originally randomized to Relyvrio compared to those originally randomized to placebo (23.5 months and 18.7 months, respectively; HR, 0.64; 95% CI, 0.42–0.995, P = 0.0475)

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Relyvrio (sodium phenylbutyrate/taurursodiol)are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Relyvrio (sodium phenylbutyrate/taurursodiol) include: no current FDA label contraindications.

OTHER SPECIAL CONSIDERATIONS:

Relyvrio will be available through limited distribution. The drug is available at select specialty pharmacies: CVS Specialty, Accredo, and Optum Specialty Pharmacy

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Relyvrio PACK 3-1GM

REFERENCES

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6. Paganoni S, et al. Effect of sodium phenylbutyrate/taurursodiol on tracheostomy/ventilation-free survival and hospitalization in amyotrophic lateral sclerosis: long-term results from the CENTAUR trial [published online ahead of print, May 16, 2022].
7. J Neurol Neurosurg Psychiatry. 2022;93(8):871–875. doi:10.1136/jnnp-2022-329024 Paganoni S, et al. Long-term survival of participants in the CENTAUR trial of sodium phenylbutyrate-taurursodiol in amyotrophic lateral sclerosis. Muscle Nerve. 2021;63(1):31–39. doi:10.1002/mus.27091
8. Paganoni S, et al. Trial of sodium phenylbutyrate-taurursodiol for amyotrophic lateral sclerosis. N Engl J Med. 2020;383(10):919–930. doi:10.1056/NEJMoa1916945
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10. Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well-defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2017;16(7):505–512. doi:10.1016/S1474- 4422(17)30115-1

SUMMARY OF REVIEW/REVISIONS	DATE
NEW Development	Q1 2023