Relyvrio (sodium phenylbutyrate/taurursodiol) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Relyvrio™ (sodium phenylbutyrate-taurursodiol) Powder for oral suspension	Treatment of amyotrophic lateral sclerosis (ALS) in adults		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Amyotrophic Lateral Sclerosis (ALS)	Amyotrophic lateral sclerosis (ALS) is an idiopathic, fatal neurodegenerative disease.(2) It is characterized by loss of motor neurons in the spinal cord, brainstem, and motor cortex.(3) Age of onset is between 58-63 years for sporadic disease and 47-52 years for familial disease, with rapidly decreased incidence after 80 years. The clinical hallmark of ALS is the presence of upper and lower motor neuron (UMN and LMN) features involving brainstem and multiple spinal cord regions of innervation.(2) ALS is a rapidly progressive disease with 50% of patients dying within 30 months of symptom onset, and about 20% of patients survive between 5 years and 10 years after symptom onset. Older age at symptom onset, early respiratory muscle dysfunction, and bulbar-onset disease are associated with reduced survival, whereas limb-onset disease, younger age at presentation, and longer diagnostic delay are independent predictors of prolonged survival. Dysphagia develops in most patients, with consequent weight loss and malnutrition. Respiratory compromise eventually develops in most cases, leading to exertional dyspnea, orthopnea, hypoventilation with resultant hypercapnia, and early morning headaches. Progressive weakening of the respiratory muscles leads to respiratory failure, often precipitated by pneumonia.(2) Symptomatic treatments remain the cornerstone for management of patients with ALS. Disease modifying treatment options for ALS are limited. Riluzole is the only agent shown to have any impact on survival in ALS. The American Academy of Neurology (AAN) has recommended that riluzole be offered to slow disease progression in patients with ALS.(2) While Relyvrio has been shown to slow the functional decline in patients with ALS, a positive effect on survival was not noted.(4)
Efficacy(1)	The efficacy of Relyvrio was demonstrated in a 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study that evaluated its use in adult

	patients with ALS (Study 1; NCT03127514). For inclusion in the study, patients had to have a definite diagnosis of sporadic or familial ALS as defined by the revised El Escorial criteria, with symptom onset within the past 18 months, and a slow vital capacity (SVC) greater than 60% of predicted at screening. A total of 137 patients were randomized 2:1 to receive either Relyvrio (n=89) or placebo (n=48) for 24 weeks (Intent-to-Treat [ITT] population). Baseline disease characteristics were generally comparable between the two treatment groups; 95% were Caucasian, the median age was 57.7 years, and 68% were males. Thirty percent of patients in the Relyvrio treatment group had bulbar disease onset vs. 21% in the placebo group. On average, patients had been diagnosed with ALS six months prior to baseline with a time since onset of first symptom of approximately 13.5 months. At or prior to study entry, 71% of patients were taking riluzole and 34% were taking edaravone. The average (standard deviation) baseline ALS Functional Rating Scale Revised (ALSFRS-R) total score was 35.7 (5.8) in the Relyvrio treatment group and 36.7 (5.1) in the placebo group. Exclusion criteria included presence of tracheostomy, abnormal liver function (defined as AST and/or ALT greater than 3 times the upper limit of normal), renal insufficiency (defined as serum creatinine greater than 1.5 times the upper limit of normal), poorly controlled arterial hypertension (systolic blood pressure greater than 160 mmHg or diastolic blood pressure greater than 100 mmHg), pregnancy or breastfeeding, history of cholecystectomy, biliary disease, history of class III/IV heart failure, severe pancreatic or intestinal disorders, the presence of unstable psychiatric disease, cognitive impairment, dementia or substance abuse, and exposure at any time to any biologic under investigation for the treatment of subjects with ALS. Patients were administered the contents of one packet of Relyvrio or placebo, once daily for the first 3 weeks. After 3 weeks of treatment, the dose was increased to one packet twice daily if tolerated. The prespecified primary efficacy endpoint was a comparison of the rate of reduction in the ALSFRS-R total scores from baseline to Week 24 in the mITT population. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). Each item is scored from 0-4, with higher scores representing greater functional ability. There was a statistically significant difference in the rate of reduction in the ALSFRS-R total score from baseline to Week 24 in Relyvrio-treated patients compared to placebo-treated patients (p = 0.034).
Safety(1)	Relyvrio has no boxed warnings or contraindications.

REFERENCES

Number	Reference
1	Relyvrio prescribing information. Amylyx Pharmaceuticals Inc. September 2022.
2	Kiernan M. C., Vucic S., Cheah B. C., Turner M. R., Eisen A., Hardiman O., et al. (2011). Amyotrophic lateral sclerosis. *Lancet* 377 942–955. 10.1016/S0140-6736(10)61156-7.
3	Miller R.G., Jackson C.E., Kasarskis E.J., England J.D., Forshew D., Johnston W., Kalra S., Katz J.S., Mitsumoto H., Rosenfeld J., et al. Practice parameter update: The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review): Report of the Quality Standards Subcommittee of the American of Neurology. Neurology. 2009;73:1227–1233.
4	Paganoni S., Macklin E.A., et al. Trial of Sodium Phenylbutyrate–Taurursodiol for Amyotrophic Lateral Sclerosis. N Engl J Med 2020;383:919-30. DOI: 10.1056/NEJMoa1916945.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Relyvrio	sodium phenylbutyrate-taurursodiol powd pack	1 GM	M ; N ; O ; Y	N		03-01-2023

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Relyvrio	Sodium Phenylbutyrate-Taurursodiol Powd Pack	1 GM	56	PACKTS	28	Days				03-01-2023

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Relyvrio	sodium phenylbutyrate-taurursodiol powd pack	1 GM	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Relyvrio	Sodium Phenylbutyrate-Taurursodiol Powd Pack	1 GM	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of amyotrophic lateral sclerosis (ALS) [also known as Lou Gehrig's disease] **AND** 2. BOTH of the following: A. The patient's symptom onset was within the past 18 months **AND** B. The patient has a baseline percent predicted forced vital capacity (FVC) of 60% or greater **AND** 3. The patient does NOT have any of the following: A. Tracheostomy B. AST or ALT greater than 3 times the upper limit of normal C. Serum creatinine greater than 1.5 times the upper limit of normal D. Systolic blood pressure greater than 160 mmHg E. Diastolic blood pressure greater than 100 mmHg F. History of New York Heart Association Class III/IV heart failure G. Exposure at any time to any biologic under investigation for the treatment of ALS (off-label use or investigational) including cell therapies, gene therapies and monoclonal antibodies **AND**

Module	Clinical Criteria for Approval
	4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below. **Renewal Evaluation** **Target Agents(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization criteria **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantities above the program quantity limit for the Target Agent(s)** will be approved when the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Length of Approval:** 6 months for initial; 12 months for renewal