Oscar Clinical Guideline: Relyvrio (Sodium Phenylbutyrate/Taurursodiol) (PG129, Ver. 2)

Relyvrio (Sodium Phenylbutyrate/Taurursodiol)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Amyotrophic lateral sclerosis (ALS) is a progressive degenerative disease of the motor neurons in the brain and spinal cord that results in the inability to initiate and control muscle movement. Most patients with ALS lose the ability to speak, eat, move, and breathe, and die from respiratory failure within 2-3 years after the onset of symptoms. Treatment of ALS primarily involves management of symptoms and palliative care.

Relyvrio is a fixed-dose combination of sodium phenylbutyrate and taurursodiol that received FDA approval in September 2022 for the treatment of ALS based on the 24-week phase 2 CENTAUR trial (ClinicalTrials.gov Identifier: NCT03127514) that showed a slowing of functional decline compared to placebo. However, in April 2024, Amylyx Pharmaceuticals announced that Relyvrio failed to meet its primary and secondary endpoints in the confirmatory phase 3 PHOENIX trial (ClinicalTrials.gov Identifier: NCT05021536). As a result, Amylyx is voluntarily withdrawing Relyvrio from the market.

Definitions

"Amyotrophic lateral sclerosis (ALS)" is a disease that affects voluntary muscle control and movement due to nerve damage to neurons (nerve cells) in the brain and spinal cord. ALS is sometimes also referred to as motor neuron disease, classic motor neuron disease, Lou Gehrig disease, or Charcot disease.

"Atrophy" is the wasting, or progressive loss of muscle mass due to reduction in the size or number of muscle cells.

"Central Nervous System (CNS)" is the brain and spinal cord.

"Dementia" is a condition in which memory and thinking are affected.

"Frontotemporal dementia" is a type of dementia caused by damage to nerve cells in certain parts of the brain. Some people with ALS may develop frontotemporal dementia, but it is not a universal symptom of the disease.

"Neurologist" is a physician who specializes in the nervous system and its disorders.

"Neurotransmitter" is a molecule that sends signals from neurons to different parts of the body (e.g., muscles).

Relyvrio (Sodium Phenylbutyrate/Taurursodiol) Efficacy Information

FDA approval of Relyvrio in September 2022 was based on results from the 24-week phase 2 CENTAUR randomized controlled trial (RCT) (ClinicalTrials.gov Identifier: NCT03127514). This study showed Relyvrio significantly slowed the rate of decline on the ALS Functional Rating Scale-Revised (ALSFRS-R) compared to placebo, but the trial did not meet its secondary endpoints. In a long-term survival analysis, Relyvrio showed a 6.5-month survival advantage over placebo.

However, the pivotal phase 3 PHOENIX RCT (ClinicalTrials.gov Identifier: NCT05021536), which was required to confirm the results of CENTAUR, showed Relyvrio failed to meet its primary endpoint of slowing decline on the ALSFRS-R compared to placebo at 48 weeks. The drug also failed to demonstrate benefit on secondary endpoints. Based on these negative results, Amylyx has decided to voluntarily withdraw marketing authorization and remove Relyvrio from the market as of April 4, 2024.

Medical Necessity Criteria for Relyvrio (Sodium Phenylbutyrate/Taurursodiol)

The negative results of the phase 3 PHOENIX trial indicate Relyvrio does not have proven clinical benefit for ALS patients. Therefore, there are no circumstances under which Relyvrio would be considered medically necessary by the Plan.

Experimental or Investigational / Not Medically Necessary

Relyvrio (sodium phenylbutyrate and taurursodiol) for any indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. The pivotal phase 3 PHOENIX RCT failed to confirm the clinical benefit of Relyvrio for the treatment of ALS that was seen in the smaller phase 2 CENTAUR trial. Amylyx has initiated a process to voluntarily withdraw marketing authorization and remove Relyvrio from the market as of April 4, 2024 based on the lack of proven efficacy. Therefore, Relyvrio does not meet the Plan's standards for medical necessity.

Appendix

Table 1: ICD-10-CM (diagnosis) Codes for Migraine and Cluster Headaches

Codes	Description
G12.21	Amyotrophic lateral sclerosis

References

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