Relyvrio™ (sodium phenylbutyrate/taurursodiol) – New orphan drug approval

- On September 29, 2022, the FDA announced the approval of Amylyx Pharmaceuticals' Relyvrio (sodium phenylbutyrate/taurursodiol), for the treatment of amyotrophic lateral sclerosis (ALS) in adults.

- ALS is a rapidly progressive and fatal neurodegenerative disease characterized by the death of motor neurons that results in loss of voluntary muscle control, paralysis, and eventually death typically secondary to respiratory failure. The majority of patients die within 3 years of onset of symptoms, and approximately 90% of patients with ALS die within 5 years of symptom onset.

    - Approximately 5,000 individuals in the U.S. are diagnosed with ALS annually, and approximately 20,000 Americans are currently living with the disease.

- The mechanism by which Relyvrio exerts its therapeutic effects in patients with ALS is unknown.

- The efficacy of Relyvrio was established in a randomized, double-blind, placebo-controlled study (Study 1) in 137 adult patients with ALS. 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. Patients received Relyvrio or placebo. The primary endpoint was the rate of reduction in the ALS Functional Rating Scale-Revised (ALSFRS-R) total scores from baseline to week 24 in the modified intent-to-treat population.

    - The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (total score ranges from 0 to 48, 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 (treatment difference of 2.32 points, 95% CI: 0.18, 4.47; p = 0.034).

- In a post hoc, long-term survival analysis, vital status was ascertained in 136 of 137 patients who were enrolled in Study 1. Longer median overall survival was observed in the patients originally randomized to Relyvrio compared to those originally randomized to placebo. This exploratory analysis should be interpreted cautiously given the limitations of data collected outside of a controlled study, which may be subject to confounding.

- Warnings and precautions for Relyvrio include risk in patients with enterohepatic circulation disorders, pancreatic disorders, or intestinal disorders; and use in patients sensitive to high sodium intake.

- The most common adverse reactions (at least 15% and at least 5% greater than placebo) with Relyvrio use were diarrhea, abdominal pain, nausea, and upper respiratory tract infection.

- The recommended initial dosage of Relyvrio is one packet (3 g sodium phenylbutyrate and 1 g taurursodiol) daily for the first 3 weeks. After 3 weeks, the maintenance dosage should be increased to one packet twice daily.

    - Relyvrio can be taken orally by combining one packet in 8 ounces of room temperature water. It can also be administered through a feeding tube.

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- Amylyx Pharmaceuticals plans to launch Relyvrio in the next 4 to 6 weeks. Relyvrio will be available as 3 g sodium phenylbutyrate and 1 g taurursodiol in single-dose packets for oral suspension.