Approval of new ALS drug comes with controversy

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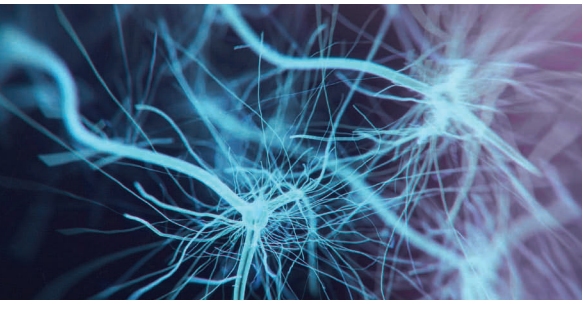
After 5 years with no breakthroughs for patients living with amyotrophic lateral sclerosis (ALS), FDA has approved a new oral treatment called Relyvrio from Amylyx Pharmaceuticals. This new medication is approved for the treatment of ALS in adults; however, the decision was made despite controversy surrounding the safety and efficacy of the drug.

Independent advisors to FDA voted and recommended against FDA approval in March 2022 due to an insufficient amount of evidence showing effectiveness from a single clinical trial with only 137 patients.



In September 2022, the group revoted and recommended that the drug be approved after additional analyses were submitted by Amylyx. Although uncertainties remain, the lack of effective treatment options for such a severe disease swayed the opinions of the panel.

Amylyx officials have vowed to remove Relyvrio from the market if a larger, 600-participant study fails to show effectiveness once completed late next year or in early 2024.

Recommended dosage and how it works

Relyvrio is packaged as a powder that needs to be mixed with 8 oz of room temperature water and stirred vigorously prior to administration. The recommended dosage is 1 packet (3 g sodium phenylbutyrate and 1 g taurursodiol) administered orally or via feeding tube daily for the first 3 weeks of therapy. After this initiation period, the dose should be increased to 1 packet twice daily.

Relyvrio is a combination of sodium phenylbutyrate and taurursodiol. The mechanism by which Relyvrio works as treatment for ALS is unknown. Sodium phenylbutyrate is used to treat individuals with urea cycle disorders and works by enhancing a pathway that removes nitrogen through the kidneys. It is hypothesized that it may also have an effect on misfolded proteins, which could explain the impact on progression of ALS. Taurursodiol is a bile acid that may interfere with apoptosis. It is speculated that the combination of these mechanisms could explain Relyvrio's effectiveness.

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Drug interactions

Relyvrio should not be taken with bile acid sequestering agents as this may interfere with the absorption of the taurursodiol component of the medication. Additionally, use of strong inhibitors of the bile salt export pump should be avoided. If concomitant use is medically necessary, serum transaminases and bilirubin should be monitored.

Aluminum-based antacids may interfere with the absorption of taurursodiol and should be avoided if other acid-lowering agents are available. The use of probenecid with Relyvrio should be avoided. Phenylbutyrate is a pan-histone deacetylase (HDAC) inhibitor and use of other HDAC inhibitors should not be used concomitantly with Relyvrio. Avoid use of Relyvrio with inhibitors of OATP1B3, as Relyvrio has been identified as a substrate of OATP1B3 during in vitro studies.

Clinical trial highlights

The clinical trial used to demonstrate the efficacy of Relyvrio was a 24-week, multicenter, randomized, double-blinded, placebo-controlled, parallel group study of 137 adult participants with ALS. The participants were randomized to either receive Relyvrio or placebo for 24 weeks. The primary endpoint was a comparison of the rate of reduction in the ALSFRS-R total scores from baseline to week 24.

Study investigators found a statistically significant difference in the rate of reduction in the ALSFRS-R total score from baseline to week 24 in patients treated with Relyvrio compared to patients treated with placebo.

Adverse effects and contraindications

There are currently no contraindications for treatment with Relyvrio. The most common adverse reactions are diarrhea, abdominal pain, nausea, and upper respiratory tract infection.

In patients with enterohepatic circulation disorders, pancreatic disorders, intestinal disorders, or another disorder that interferes with bile acid circulation, consulting with a specialist should be considered. These conditions may lead to decreased absorption of Relyvrio. These patients should be monitored for new or worsening diarrhea.

Additionally, Relyvrio has a high sodium content and sodium levels should be monitored in patients sensitive to salt intake.

Patient counseling

Patients should be advised on how to mix Relyvrio packets with water prior to administration. The dose must be taken within an hour after mixing.

Any unused Relyvrio should be discarded after one hour. Relyvrio should be taken before a snack or meal. ■