INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

Mitsubishi Tanabe Pharma America – oral edaravone
August 2022

Background

Mitsubishi Tanabe Pharma America (MTPA) is a wholly-owned subsidiary of Mitsubishi Tanabe Pharma Corporation (MTPC), founded in Japan in 1678. MTPC began studying an intravenous (IV) formulation (Radicava) of edaravone for ALS in 2001 and was approved for the treatment of ALS in Japan and South Korea in 2015, with subsequent approvals in Canada, Switzerland, China, Indonesia and Thailand.

Treatment with Radicava follows a regimen of initial treatment daily for 14 days, followed by a 14-day drug free period, and subsequent cycles of daily dosing for 10 of 14 days, followed by a 14-day drug free period.

During clinical development of IV Radicava, MTPA began a series of steps to determine if an oral suspension of edaravone could add to or replace the IV formulation for treatment of people living with ALS. First, bioequivalence had to be established to demonstrate that the oral edaravone could provide identical exposure as the established IV formulation. Multiple studies were performed.

The process began with a phase 1, open-label, single-dose crossover study in 42 participants, comparing 105 mg oral edaravone with 60 mg/hr IV formulation. Through comparing the pharmacokinetics (how it moves through the body) of both, it was concluded that the two formulations, at their respective doses, demonstrated equivalent exposure. This is published here.

Further, two additional phase 1 studies were performed. First, a placebo-controlled, randomized, single-blind study of increasing oral edaravone doses from 30 to 300 mg in 56 participants was completed. The second study, involving 84 participants, assessed whether oral edaravone interacted with other drugs and also examined potential pharmacokinetic differences between people of different racial backgrounds. In both cases, oral edaravone was considered safe and tolerable with no significant drug interaction effects or differences between racial backgrounds. These studies are published here.

Following bioequivalence, the next step was to undertake a large safety and tolerability trial of oral edaravone at the intended clinical dose. On December 9, 2021, MTPA announced the results of the global phase 3 clinical trial assessing safety and tolerability of oral edaravone over 24 weeks. The study enrolled 185 participants with ALS across 50 sites in the United States, Canada, Europe and Japan and included a long-term safety extension study of up to 96 weeks. No severe treatment emergent adverse events (TEAEs) were reported. It is expected that these results will be used in a regulatory submission for oral edaravone to be considered an equivalent treatment for ALS as Radicava, in the jurisdictions where it is currently approved.

On May 13, 2022, it was announced that the U.S. Food and Drug Administration (FDA) had approved RADICAVA ORS and it became available as of June 16. As of July 2022, edaravone oral suspension is also under review in Japan, Switzerland and Canada.

Simultaneously, MTPA has launched a phase 3b, multi-national, randomized, double-blind study to evaluate daily dosing of oral edaravone as compared to the current IV dosing regimen. Over 48 weeks, 380 participants either received oral edaravone once daily or for 10 days followed by an 18 day placebo suspension. This trial will evaluate a comparison of change in ALSFRS-R as the primary outcome measure and additional outcomes including slow vital capacity, quality of life (ALSAQ-40). It is set to read out in the second half of 2023.

Summary

Based on the available evidence, it is the opinion of the SAC that oral edaravone appears to be safe, tolerable and provides an equivalent drug exposure to intravenous Radicava. For those who currently access Radicava, it may provide a less burdensome alternative if approved.