RADICAVA ORS® (EDARAVONE) ROAD TO FDA APPROVAL

The comprehensive clinical development program for edaravone in amyotrophic lateral sclerosis (ALS) has spanned over a decade and included multiple clinical trials for the intravenous (IV) and oral formulations.

We know people with ALS and their families never give up and neither did we. Our determined researchers went to work on finding a treatment option for a disease that is not yet fully understood. Each clinical trial became an opportunity to learn more about ALS and how edaravone could benefit patients.

Company researchers demonstrated great perseverance and applied in-depth analyses to demonstrate the clinical profile of edaravone, which led to the development of an oral formulation that gives patients another administration option.

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Clinical Trial Timeline and Significant Milestones

MCI186-19 (Phase 3): Pivotal Trial of IV Edaravone (2011-2014)
Applied critical learnings from previous studies of edaravone, and prospectively demonstrated the safety and efficacy profile of the treatment in ALS patients. This clinical trial showed that RADICAVA® (edaravone) slowed the loss of physical function, as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R), by 33% compared to placebo over 6 months. These data formed the basis for the FDA approval of RADICAVA in 2017.[1]

Phase 1: Series of Clinical Pharmacology Studies Examine Oral Formulation (2019-2020)
MTP group companies completed a series of Phase 1 studies administering the oral and IV formulations of edaravone in healthy volunteers.

- Seven Phase 1 studies examining the pharmacokinetics, safety, drug-to-drug interactions, dosing, bioavailability and bioequivalence of the oral formulation in healthy individuals and ALS patients with and without a percutaneous endoscopic gastrostomy (PEG) tube/nasogastric (NG) tube.

MT-1186-A01 (Phase 3): Global Phase 3 Open-Label Safety Study (2019-2021)
A 24-week, Phase 3, open-label clinical trial in 185 patients with ALS, which showed a similar safety profile for RADICAVA ORS as the IV formulation. Fatigue was also seen in 7.6% of patients taking RADICAVA ORS.

MT-1186-A03 (Phase 3): Long-Term Safety Extension (2020-Ongoing)
An extension of study A01 continuing to evaluate oral edaravone in patients with ALS for up to 96 weeks.

New Drug Application (NDA) for Oral Edaravone Submitted in U.S. (November 2021)

FDA Accepted NDA for Oral Edaravone (January 2022)

FDA APPROVED RADICAVA ORS MAY 2022

RADICAVA and RADICAVA ORS are indicated for the treatment of amyotrophic lateral sclerosis (ALS).

RADICAVA and RADICAVA ORS are contraindicated in patients with a history of hypersensitivity to edaravone or any of the inactive ingredients of this product. Hypersensitivity reactions and anaphylactic reactions have been reported in patients treated with RADICAVA.

The most common adverse reactions (≥10%) reported in patients treated with RADICAVA were bruising (contusion) [15%], problems with walking (gait disturbance) [13%] and headache (10%). In an open label study, fatigue was also observed in 7.6% of patients receiving RADICAVA ORS.

IMPORTANT SAFETY INFORMATION

Do not receive RADICAVA (edaravone) or RADICAVA ORS (edaravone) if you are allergic to edaravone or any of the ingredients in RADICAVA and RADICAVA ORS.

Before you take RADICAVA or RADICAVA ORS, tell your healthcare provider about all of your medical conditions, including if you:

- have asthma.
- are allergic to other medicines.
- are pregnant or plan to become pregnant. It is not known if RADICAVA or RADICAVA ORS will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if RADICAVA or RADICAVA ORS passes into your breastmilk. You and your healthcare provider should decide if you will receive RADICAVA or RADICAVA ORS or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of RADICAVA and RADICAVA ORS?

RADICAVA and RADICAVA ORS may cause serious side effects, including hypersensitivity (allergic) reactions and sulfite allergic reactions.

- Hypersensitivity reactions have happened in people receiving RADICAVA or taking RADICAVA ORS and can happen after your medicine has been given.
- RADICAVA and RADICAVA ORS contain sodium bisulfite, a sulfite that may cause a type of allergic reaction that can be serious and life-threatening. Sodium bisulfite can also cause less severe asthma episodes in certain people. Sulfite sensitivity can happen more often in people who have asthma than in people who do not have asthma.
- Tell your healthcare provider right away or go to the nearest emergency room if you have any of the following symptoms: hives; swelling of the lips, tongue, or face; fainting; breathing problems; wheezing; trouble swallowing; dizziness; itching; or an asthma attack (in people with asthma).

Your healthcare provider will monitor you during treatment to watch for signs and symptoms of all the serious side effects and allergic reactions.

The most common side effects include bruising (contusion), problems walking (gait disturbance), and headache.

These are not all the possible side effects of RADICAVA or RADICAVA ORS. **Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to www.fda.gov/medwatch or Mitsubishi Tanabe Pharma America, Inc. at 1-888-292-0058.**

INDICATION

RADICAVA and RADICAVA ORS are indicated for the treatment of amyotrophic lateral sclerosis (ALS).

For more information, including full Prescribing Information, please visit www.RADICAVA.com.

Media Inquiries:
Media_MTPA@MT-Pharma-US.com

Additional Information:
For further information, visit RADICAVA.com

Mitsubishi Tanabe Pharma America

Radicava ORS (edaravone) Oral Suspension

References
1. RADICAVA and RADICAVA ORS Prescribing Information. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc.; 2022.

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