Radicava ORS® (edaravone) Oral Suspension 105mg/5mL

INDICATION

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

THE DIFFERENCE IS EXPERIENCE

[a]Based on RADICAVA ORS® and RADICAVA® IV prescriptions submitted in the US as of March 2024. Not independently verified.
[b]Data on file. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc. Based upon data through April 2024.
FDA=Food and Drug Administration; IV=intravenous.

IMPORTANT SAFETY INFORMATION

Hypersensitivity Reactions

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 (redness, wheals, and erythema multiforme) and cases of anaphylaxis (urticaria, decreased blood pressure, and dyspnea) have occurred with RADICAVA.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

RADICAVA ORS®—built on years of clinical research and development

Demonstrated efficacy and safety of RADICAVA®

2001-2016
Edaravone clinical trials in ALS commence

- A phase 2 study evaluating the efficacy and safety of 2 different concentrations of edaravone[5]
- 3 phase 3 studies evaluating the efficacy and safety of edaravone in patients with ALS[9]

2015
RADICAVA® granted orphan drug status[10]

2016
RADICAVA® submitted for FDA approval[2]

2017
RADICAVA® approved for ALS

- The only FDA-approved treatment for ALS that met its primary endpoint in a pivotal phase 3 clinical trial[8,11,12]

IMPORTANT SAFETY INFORMATION

Hypersensitivity Reactions *(continued)*
Patients should be monitored carefully for hypersensitivity reactions. If hypersensitivity reactions occur, discontinue RADICAVA or RADICAVA ORS, treat per standard of care, and monitor until the condition resolves.

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RADICAVA ORS®—built on years of clinical research and development

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Clinical studies for RADICAVA ORS®

RADICAVA ORS®—the ONLY FDA-approved oral form of edaravone

2019-2021

Pharmacokinetic studies

- A phase 1 bioequivalence and safety study conducted in healthy subjects[3,4]
- 3 phase 1 trials evaluated the pharmacokinetics of RADICAVA ORS®[13-15]

Safety study

- A 6-month, phase 3, open-label clinical trial evaluated the safety and tolerability of RADICAVA ORS® in 185 patients with ALS[3,6]

Alternate administration studies

- A phase 1 clinical trial evaluated the pharmacokinetics and safety of RADICAVA ORS® administered via PEG tube in patients with ALS[16]
- A phase 1, open-label study investigated the safety, tolerability, pharmacokinetics, and bioavailability of RADICAVA ORS® administered orally and via NG tube in healthy subjects[17]

2021

RADICAVA ORS® submitted for FDA approval[18]

2022

RADICAVA ORS® approved for ALS[8]

2024

RADICAVA ORS® recognized as a major contribution to patient care[1]

Offering an oral route of administration provides a less burdensome option vs IV administration[1]

NG=nasogastric; PEG=percutaneous endoscopic gastrostomy.

IMPORTANT SAFETY INFORMATION

Sulfite Allergic Reactions

RADICAVA and RADICAVA ORS contain sodium bisulfite, a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown but occurs more frequently in asthmatic people.

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RADICAVA ORS®—a foundation of clinical and real world experience

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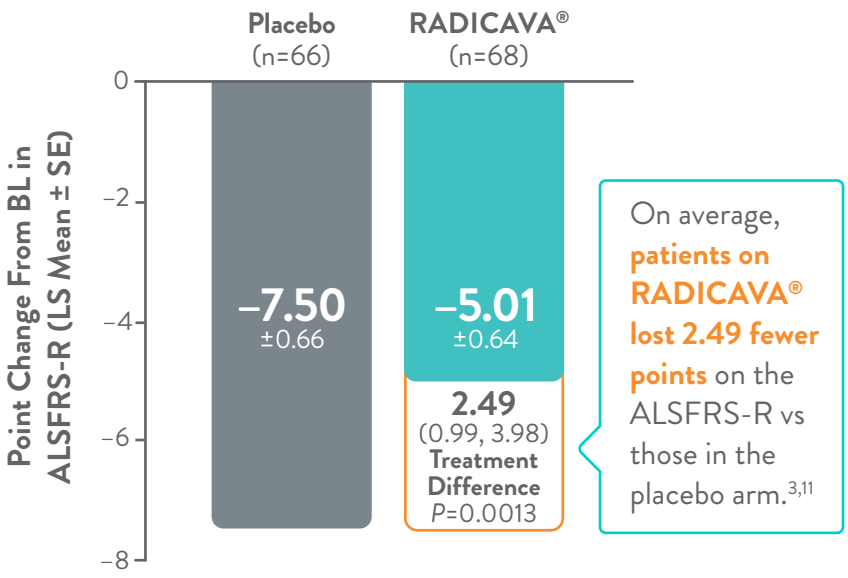
In ALS, every point matters

Losing or keeping a single point on the ALSFRS-R can have a significant impact on those living with ALS. That's why the pivotal phase 3 clinical trial of RADICAVA® was specifically designed to measure change in physical function assessed by the ALSFRS-R.[11,19]

In the clinical study, RADICAVA® showed a statistically significant difference in physical function measured by the ALSFRS-R compared with those not taking RADICAVA® at 24 weeks[11,20]

Physical Function in Daily Activities at 24 Weeks[3,11]



33% less change in ALSFRS-R scores from baseline vs placebo at 24 weeks[3,11]

- A report on a survey of 65 members of Northeast ALS Consortium (NEALS) concluded that a treatment is clinically meaningful when it results in 20% to 25% or greater change in the slope of ALSFRS-R reflecting the slowing of functional decline[20]
- Most patients in the RADICAVA® (n=63/69) and placebo (n=62/68) arms were on riluzole[2,11]

RADICAVA® was generally well tolerated[21]

The most common adverse reactions (≥10%) reported in RADICAVA®-treated patients were contusion (15%), gait disturbance (13%), and headache (10%). Fatigue was observed in 7.6% of patients receiving RADICAVA ORS®[3]

ALSFRS-R=ALS Functional Rating Scale–Revised.

IMPORTANT SAFETY INFORMATION

Adverse Reactions

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

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RADICAVA ORS®—a foundation of clinical and real world experience

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In the pivotal phase 3 study, the *P* value was calculated based on the results

It's important to note a treatment difference of 2.49 point change from baseline in ALSFRS-R (0.99, 3.98) with ***P*=0.0013 is considered statistically significant.**[11]

To put the results in context, consider what *P* values suggest and how probable the results are due to chance.[22]

Very strong statistical difference	Statistical difference	No statistical difference
***P*<0.001**	***P*≤0.05**	***P*>0.05**
That means that there is less than 1 in 1000 probability that the results are due to random chance	That means that there is less than 5% probability that the results were due to random chance	No statistical difference between groups

IMPORTANT SAFETY INFORMATION

Pregnancy
Based on animal data, RADICAVA and RADICAVA ORS may cause fetal harm.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Hear from your peers about their experiences with RADICAVA ORS® at RadicavaHCP.com

IMPORTANT SAFETY INFORMATION

To report suspected adverse reactions or product complaints, contact Mitsubishi Tanabe Pharma America, Inc., at 1-888-292-0058. You may also report suspected adverse reactions to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

References: 1. US Food and Drug Administration. Clinical superiority findings. Accessed April 11, 2024. https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/clinical-superiority-findings **2.** Data on file. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc. **3.** RADICAVA and RADICAVA ORS Prescribing Information. Jersey City, NJ: Mitsubishi Tanabe Pharma America, Inc.; 2022. **4.** Shimizu H, Nishimura Y, Shiide Y, et al. Bioequivalence study of oral suspension and intravenous formulation of edaravone in healthy adult subjects. *Clin Pharmacol Drug Dev.* 2021;10(10):1188-1197. **5.** Yoshino H, Kimura A. Investigation of the therapeutic effects of edaravone, a free radical scavenger, on amyotrophic lateral sclerosis (phase II study). *Amyotroph Lateral Scler.* 2006;7(4):241-245. **6.** ClinicalTrials.gov. Safety study of oral edaravone administered in subjects with ALS. Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04165824 **7.** Brooks BR, Heiman-Patterson T, Wiedau-Pazos M, et al. Edaravone efficacy in amyotrophic lateral sclerosis with reduced forced vital capacity: post-hoc analysis of Study 19 (MCI186-19) [clinical trial NCT01492686]. *PLoS One.* 2022;17(6):e0258614. **8.** US Food and Drug Administration. FDA approves oral form for the treatment of adults with amyotrophic lateral sclerosis (ALS). Accessed April 11, 2024. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-oral-form-treatment-adults-amyotrophic-lateral-sclerosis-als **9.** Takei K, Watanabe K, Yuki S, et al. Edaravone and its clinical development for amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Frontotemporal Degener.* 2017;18(suppl 1):5-10. **10.** US Food and Drug Administration. Orphan drug designations and approvals. Accessed May 15, 2024. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=478215 **11.** Writing Group; Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. *Lancet Neurol.* 2017;16(7):505-512. **12.** Tzeplaeff L, Wilfling S, Requardt M, et al. Current state and future directions in the therapy of ALS. *Cells.* 2023;12(11):1523. **13.** ClinicalTrials.gov. Study of oral edaravone in healthy adult males. Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04481750 **14.** ClinicalTrials.gov. Clinical pharmacology study of oral edaravone in patients with amyotrophic lateral sclerosis. Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04176224 **15.** ClinicalTrials.gov. Clinical pharmacology study of oral edaravone in healthy adult males (drug interaction study and preliminary regimen-finding study). Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04481789 **16.** ClinicalTrials.gov. Clinical pharmacology study of oral edaravone in amyotrophic lateral sclerosis patients with gastrostomy. Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04254913 **17.** ClinicalTrials.gov. Comparative bioavailability study of oral edaravone administered orally and via a nasogastric tube. Accessed April 11, 2024. https://clinicaltrials.gov/study/NCT04776135 **18.** US Food and Drug Administration. NDA 215446. Accessed May 6, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/215446Orig1s000ltr.pdf. **19.** Cedarbaum JM, Stambler N, Malta E, et al; BDNF ALS Study Group (Phase III). The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. *J Neurol Sci.* 1999;169(1-2):13-21. **20.** Castrillo-Viguera C, Grasso DL, Simpson E, et al. Clinical significance in the change of decline in ALSFRS-R. *Amyotroph Lateral Scler.* 2010;11(1-2):178-180. **21.** Genge A, Pattee GL, Sobue G, et al. Oral edaravone demonstrated a favorable safety profile in patients with amyotrophic lateral sclerosis after 48 weeks of treatment. *Muscle Nerve.* 2023;67(2):124-129. **22.** Singh P. P value, statistical significance and clinical significance. *J Clin Prev Cardiol.* 2013;2(4):202-204.

Mitsubishi Tanabe Pharma America

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