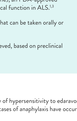
Understanding RADICAVA ORS® (edaravone)

What is RADICAVA ORS® (edaravone)?

RADICAVA ORS, the oral form of edaravone, is approved by the U.S. Food and Drug Administration (FDA) for the treatment of amyotrophic lateral sclerosis (ALS), a neurodegenerative disease that currently has no cure and can progress rapidly.[1,2]



- RADICAVA ORS offers the same drug and efficacy as RADICAVA® (edaravone), an FDA-approved intravenous (IV) treatment shown in a pivotal trial to help slow the loss of physical function in ALS.[3]
- RADICAVA ORS provides ALS patients with a flexible administration option that can be taken orally or via feeding tube, without the need for dose adjustment.[1]
- While the exact mechanism of action of edaravone in ALS is unknown, it is believed, based on preclinical studies, to reduce oxidative stress.[1,4]

Important Safety Information

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 cases of anaphylaxis have occurred with RADICAVA.

Please see additional **Important Safety Information** at the end of this document and accompanying full Prescribing Information.

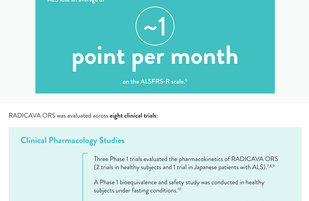
What does the data show?

The FDA approval of RADICAVA ORS was supported by several clinical studies in ALS for both the IV and oral formulations of edaravone.

In a pivotal, Phase 3 clinical trial (n=137), RADICAVA demonstrated

33% less

change in physical function in daily activities at 24 weeks vs. placebo, as measured by the **ALS Functional Rating Scale-Revised (ALSFRS-R)**, a validated rating instrument for monitoring the progression of disease in people with ALS.[3,5]



Although rates of ALS progression can vary significantly, research shows people with ALS lose an average of

~1 point per month

on the ALSFRS-R scale.[6]

RADICAVA ORS was evaluated across **eight clinical trials**:

Clinical Pharmacology Studies

Phase 1

Three Phase 1 trials evaluated the pharmacokinetics of RADICAVA ORS (2 trials in healthy subjects and 1 trial in Japanese patients with ALS).[7,8,9]

A Phase 1 bioequivalence and safety study was conducted in healthy subjects under fasting conditions.[10]

A Phase 1 clinical trial evaluated the pharmacokinetics and safety of RADICAVA ORS administered via percutaneous endoscopic gastrostomy (PEG) tube (feeding tube) in patients with ALS.[11]

A Phase 1 clinical trial evaluated the effect of food on the pharmacokinetics of RADICAVA ORS in healthy adult subjects.[12]

A Phase 1, open-label study investigated the safety, tolerability, pharmacokinetics and bioavailability of RADICAVA ORS administered orally and via a nasogastric (NG) tube in healthy subjects.[13]

Safety Study

Phase 3

A 24-week, Phase 3, open-label clinical trial evaluated the safety and tolerability of RADICAVA ORS in 185 patients with ALS.[14]

An extension of the Phase 3 safety study is continuing to evaluate RADICAVA ORS in people with ALS for up to 96-weeks.[15]

Safety Profile of RADICAVA and RADICAVA ORS

The safety profile of RADICAVA and RADICAVA ORS was derived from

500+ patients

with ALS in multiple clinical trials.[1]

RADICAVA ORS offers a similar safety profile as the IV formulation.[1]

The safety profile of RADICAVA ORS was demonstrated in a 6-month, Phase 3, open-label clinical trial in 185 patients with ALS.[1]

- In addition to contusion, gait disturbances, and headache reported with RADICAVA, fatigue was experienced in 7.6% of people receiving RADICAVA ORS.[1]

Low rate of discontinuations due to side effects

- Fewer than 6% of patients discontinued RADICAVA ORS because of side effects.[16]
- Approximately 1% of patients discontinued RADICAVA ORS due to gastrointestinal side effects (diarrhea and trouble swallowing).[16]
  - Other reasons for discontinuation (1%) included respiratory failure and muscular weakness[16]

The safety profile of RADICAVA ORS was generally consistent across age, race and gender[16,17]

- No overall differences in the safety of RADICAVA ORS were observed between geriatric patients over the age of 65 and younger patients, but greater sensitivity of some older individuals cannot be ruled out.[1]
- RADICAVA ORS has no known drug interactions and may be taken with riluzole.

RADICAVA and RADICAVA ORS are contraindicated in people with a history of hypersensitivity to edaravone or any of the inactive ingredients of this product. Hypersensitivity reactions and anaphylactic reactions have been reported.[1]

How is RADICAVA ORS administered?[1]

RADICAVA ORS should be taken on an empty stomach in the morning after overnight fasting (eight hours after a high-fat meal or four hours after a low-fat meal), and food should not be consumed for 1 hour after administration except water.[1]

- For people taking RADICAVA ORS who are unable to fast, see additional instructions in the full Prescribing Information.

Dosing schedule for RADICAVA ORS

Initial treatment cycle

14 consecutive days of treatment

14 consecutive drug-free days

Subsequent treatment cycles

10 out of **14** days of treatment

14 consecutive drug-free days

*For patients, RADICAVA ORS should be stored upright at room temperature between 68°F to 77°F and protected from light. The bottle should be discarded 15 days after opening or, if unopened, 30 days from date of shipment indicated on the carton pharmacy label.

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:
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