Radicava®
(edaravone) IV infusion 30mg/20mL

Infusion Guide

RADICAVA® (edaravone) IV infusion*

teva

*IV = intravenous.

1. Approved Indication and Mechanism of Action

RADICAVA® is indicated in adults with a diagnosis of amyotrophic lateral sclerosis (ALS) who are independent in activities of daily living with normal respiratory function and where treatment is initiated within two years of onset.

Efficacy has not been demonstrated in patients outside of this defined population

The mechanism by which RADICAVA IV infusion exerts its therapeutic effect in patients with ALS is unknown. Edaravone is a free radical scavenger to reduce oxidative stress.

2. Preparation

Preparation Method:

- Each clear glass ampoule contains 30 mg of edaravone in 20 mL concentrated injection.
- Dilute 60 mg of RADICAVA IV infusion (two ampoules) with 100 mL of 0.9% sodium chloride before each infusion.
- RADICAVA IV infusion is administered as an intravenous infusion **over a 60-minute period**

- RADICAVA IV infusion is for single use in one patient only. Discard any residue.
- To reduce microbiological hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2°-8°C for not more than 24 hours.
- Any unused medicine or waste material should be disposed of in accordance with local requirements.
- RADICAVA IV infusion is not cytotoxic.

Incompatibilities:

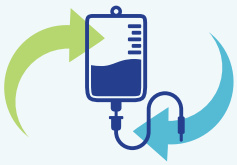
- No incompatibilities between RADICAVA IV infusion and commercially available infusion set materials have been observed.
- Other medications should not be mixed with RADICAVA or injected into the infusion bag.

It is not recommended that the RADICAVA IV infusion solution for infusion be mixed with:

- Total parenteral nutrition preparations (TPN) and/or amino acid infusions before administration and should not be administered through the same IV line as those preparations
- Infusions of potassium canreonate, or anticonvulsants including diazepam, phenytoin sodium because the solution may become cloudy.

3. Dosing Schedule

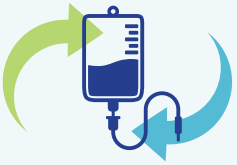
- RADICAVA IV infusion concentrated injection must be diluted before use and is for intravenous infusion only.
- RADICAVA IV infusion is administered according to the following schedule:



First Cycle

14 consecutive **days on**
14 consecutive **days off**

The first cycle includes 14 days of daily infusions, followed by a 14-day drug-free period.



Ongoing Cycles

10 out of **14 days on**
14 consecutive **days off**

Subsequent cycles consist of 10 days of infusions within a 14-day period, followed by a 14-day drug-free period.

- The following cycle is to be started at 28 days after the first dosing date of the previous cycle.

4. General Precautions

Contraindications:

RADICAVA IV infusion is contraindicated in patients with a history of hypersensitivity to edaravone or any of the excipients: Sodium bisulfite, cysteine hydrochloride monohydrate, sodium chloride, sodium hydroxide, phosphoric acid and water for injections.

Special Warnings and Precautions:

1. **Hypersensitivity reactions**

Hypersensitivity reactions (redness, wheals, and erythema multiforme) and cases of anaphylaxis (urticaria, decreased blood pressure and dyspnoea) have been reported in spontaneous post-marketing reports with edaravone.
Patients should be monitored carefully for hypersensitivity reactions. If hypersensitivity reactions occur, discontinue RADICAVA IV infusion, treat per standard of care, and monitor until the condition resolves.

2. **Sulfite allergic reactions**

RADICAVA IV infusion contains 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. Sulfite sensitivity occurs more frequently in asthmatic people.

3 **Sodium content**

Each ampoule of RADICAVA IV infusion contains 135 mg sodium chloride, 6.75 mg/mL. This should be taken into consideration by patients on a controlled sodium diet.

4 **The elderly**

Of the 184 patients with ALS who received RADICAVA IV infusion in 3 placebo-controlled clinical trials, a total of 53 patients were 65 years of age and older, including two patients 75 years of age and older. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Patients with hepatic or renal impairment:

- No dosage adjustment is required in patients with hepatic impairment and mild and moderate renal impairment (estimated glomerular filtration rate (eGFR)>30 mL/min/1.73m^2).
- The effects of severe renal impairment on the pharmacokinetics of RADICAVA IV infusion have not been studied.
- Exposure to edaravone is not expected to be significantly affected in patients with eGFR<30mL/min/1.73m^2 who do not require renal replacement therapy.
- Pharmacokinetics of RADICAVA IV infusion have not been studied in patients undergoing renal replacement therapy and use of RADICAVA IV infusion in this population is not recommended.

For more information on these precautions, please refer to the full Product Information (PI)[1]

5. Adverse Reactions

Hypersensitivity reactions and cases of anaphylaxis have been reported in spontaneous post-marketing reports with RADICAVA IV infusion.

Symptoms

- Hypersensitivity: Redness, wheals, erythema multiforme.
- Anaphylaxis: Urticaria, decreased blood pressure, dyspnoea.

Tolerability

- The safety profile has been shown in pooled randomized, placebo-controlled trials involving 184 ALS patients who received RADICAVA IV infusion 60mg in treatment cycles for 6 months.[1]

	The most frequently reported adverse events with RADICAVA IV infusion (⩾3% and greater than placebo) across three Phase III clinical studies[1]	
Adverse event	**Edaravone (N=184), n (%)**	**Placebo (N=184), n (%)**
Contusion	27 (14.7)	16 (8.7)
Gait disturbance	23 (12.5)	17 (9.2)
Headache	15 (8.2)	10 (5.4)
Eczema	12 (6.5)	4 (2.2)
Dermatitis contact	11 (6.0)	6 (3.3)
Respiratory disorder	8 (4.3)	2 (1.1)
Rash	7 (3.8)	4 (2.2)
Glucose Urine present	7 (3.8)	3 (1.6)
Upper respiratory tract inflammation	6 (3.3)	3 (1.6)

6. Observations

Excretion:

In Japanese and Caucasian healthy volunteers, edaravone was excreted mainly in the urine as its glucuronide conjugate form (70-90% of the dose). Approximately 5-10% of the dose was recovered in the urine as sulfate conjugate, and only 1% of the dose or less was recovered in the urine as unchanged form. In vitro studies suggest that the sulfate conjugate of edaravone is hydrolysed back to edaravone, which is then converted to the glucuronide conjugate in the human kidney before excretion into the urine.

The mean terminal elimination half-life of edaravone is 4.5 to 6 hours. The half-lives of its metabolites are 2 to 2.8 hour.

Observation

Observations for side effects as previously described, check for any signs/symptoms also using the Product Information[1] or Consumer Medicine Information[2].

Observe for allergic reaction, particularly if history of allergy or asthma. If hypersensitivity reactions or any other abnormality are observed, RADICAVA IV infusion administration should be discontinued, treat as per standard of care and monitor until condition resolves.

PBS Information: This product is listed on the PBS as a Section 100 item.
Refer to PBS Schedule for full authority information[3].

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

PLEASE REVIEW PRODUCT INFORMATION BEFORE PRESCRIBING. The Product Information can be accessed at https://rss.medsinfo.com.au/tb/pi.cfm?product=tbpradic or from Medical Information on 1800 AU TEVA (1800 28 8382) or by scanning the QR code.

References: 1. RADICAVA IV infusion Product Information, Australia. **2.** RADICAVA IV infusion (edaravone) Consumer Medicine Information, Australia. **3.** Pharmaceutical Benefits Scheme (PBS). Available at: https://www.pbs.gov.au/

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