NATIONAL PBM BULLETIN

January 10, 2018

DEPARTMENT OF VETERANS AFFAIRS
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICATION SAFETY (VA MedSAFE)

Alerts are based on the clinical evidence available at the time of publication. Recommendations are intended to assist practitioners in providing consistent, safe, high quality, and cost effective drug therapy. They are not intended to interfere with clinical judgment. When using dated material, the clinician should consider new clinical information, as available and applicable.

Edaravone (Radicava®) and Potential for Leaking from Valve Site

I. ISSUE

VA medical centers (VAMCs) have reported multiple instances of product package failure involving edaravone (Radicava®) bags due to leaking at the valve site.

II. BACKGROUND

Edaravone (Radicava®) is indicated for the treatment of amyotrophic lateral sclerosis (ALS). Edaravone (Radicava®) should be given as a 60 mg dose administered with 2 consecutive 30 mg IV infusion bags over a total of 60 minutes (infusion rate approximately 1 mg per minute). For the first cycle, edaravone (Radicava®) is infused for 14 days, followed by a 14-day drug-free period. Subsequent cycles are infused for 10 days within a 14-day period, followed by a 14-day drug-free period. Edaravone (Radicava®) is supplied as a 30 mg/100 mL (0.3 mg/mL) solution for intravenous infusion in single-dose polypropylene bags (2 bags per carton). Each bag is overwrapped with polyvinyl alcohol (PVA) secondary packaging containing an oxygen absorber and oxygen indicator to minimize oxygen degradation.

III. DISCUSSION

In October 2017, one VAMC experienced incidents with edaravone (Radicava®) where the bag leaked from the spike adaptor site. This facility reported having to send a replacement dose to 4 patients because "one bag is leaking". The leaking occurred even after extensive consultation on how to spike the bag and supervised practice at the infusion clinic.

Additionally, last November 2017, another VAMC received a leaking bag in its overwrap from the supplier, which was found prior to dispensing, leaving only 1 bag available (a partial dose) in the carton. Subsequent to this finding, two additional bags failed at the site of use by a patient later in the month and again in December. Both bags were returned to the facility and replaced from the facility's stock. A nurse educator provided by the manufacturer was dispatched to the Veteran's home after the first leak was reported.

Other sites within the VA have also expressed similar experiences with the use of edaravone (Radicava) where the bag leaked from the valve site. Such product failure may result in an interruption of therapy and suboptimal symptom management. Awareness of proper technique to prepare the infusion bag for administration may help to prevent any occurrences of leaking where physical product defect is not an issue. VA is attempting to work with the manufacturer to address the valve leakage issue and obtain replacement product.

IV. RECOMMENDATIONS

- The manufacturer recommends adhering to the following instructions (available at: https://www.radicava.com/assets/dist/pdfs/radicava-preparing-the-infusion-bag.pdf) to help prevent damage to the stopper and avoid leakage of medication while preparing the infusion bag:

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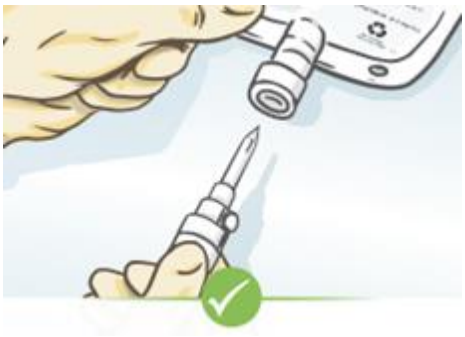
Edaravone (Radicava®) and Potential for Leaking from Valve Site

(continued from page 1)



Hold or position the bag horizontally as you align spike with center of stopper.

Carefully insert spike **straight into center of stopper** without twisting. Only spike ONCE, not multiple times.

Be careful **not** to insert spike into stopper **at an angle**.

- Facilities should document any product failure with the use of edaravone (Radicava®) and retain any leaking product.
- Any product defect with the use of edaravone (Radicava®) should also be reported, as appropriate, to the VA ADERS program, to the manufacturer, and to FDA MedWatch (1-800-FDA-1088, fax 1-800- FDA-0178, online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch- online.htm, or by mail).
- Providers should continue to report any adverse reactions with the use of edaravone (Radicava®) by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800- FDA-0178, online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch- online.htm, or by mail).

V. REFERENCES

1. Internal data.
2. Radicava® (edaravone) [package insert]. Jersey City, NJ: MT Pharma America, Inc., a US subsidiary of Mitsubishi Tanabe Pharma Corporation; May 2017.
3. Administering Radicava®: Preparing the Infusion Bag. Available at: https://www.radicava.com/assets/dist/pdfs/radicava-preparing-the-infusion-bag.pdf. (Accessed January 2, 2018).

ACTIONS

- ***Facility Director*** *(or physician designee): Forward this document to the Facility Chief of Staff (COS).*
- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers and health care staff (e.g.,* ***primary care providers, neurology staff, and pharmacy staff, including contract providers, etc****.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*