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GUIDELINES FOR INTRAVENOUS EDARAVONE (RADICAVA)

Section: Nursing

Compliance: ACHC Infusion Pharmacy

ACHC Standards: N/A

URAC Standards: N/A

Policy ID: NUR255

Effective: 1/3/23

Reviewed:

Revised:

Approved by: Kathleen Patrick, President 1/3/23

I. BACKGROUND

Edaravone (Radicava) is a free radical and peroxynitrite scavenger that prevents oxidative damage to cell membranes and may contribute to inhibiting the progression of Amyotrophic lateral sclerosis (ALS). Edaravone is an intravenous therapy approved for ALS that has been shown to reduce decline in daily functioning as demonstrated by ALS Functional Rating Scale (ALSFRS) scoring. The following outlines the procedures for servicing patients in need of outpatient edaravone home infusions.

II. PATIENT ACCEPTANCE CRITERIA

- A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon dispensing pharmacy admission criteria.
- B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:
 - 1. Prescriber preference
 - 2. Allergy profile
 - 3. Age \geq 18 years
 - 4. Ability to secure contracted nursing for subsequent infusions
 - 5. Other relevant social and/or medical history
- C. Physician orders for edaravone must include:
 - 1. Drug and dose

2. Route of administration
 3. Frequency of administration
 4. Emergency medications per protocol
 5. Orders for pre-medications if applicable
 6. Line care protocol
 7. Routine lab monitoring if applicable
- D. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless more comprehensive patient-specific orders are provided by physician. See policy NUR012. (Appendix A).
- E. Patients must be enrolled in the manufacturer’s Searchlight program. Confirmation of enrollment and Searchlight number must be confirmed with the provider
1. Searchlight provides education and copay assistance for edaravone patients and will identify copay assistance or foundations to subsidize out-of-pocket costs when eligible.
 2. Onboarding IVC will collaborate with Searchlight to check coverage, obtain authorization, review copay assistance or foundation assistance, and verify patient can manage any out-of-pocket costs.
 3. A Searchlight number is needed to order

III. PHARMACOLOGY OVERVIEW

Please refer to the package insert for the most up to date guidance on this medication.

A. Indications

1. Treatment of adults with amyotrophic lateral sclerosis

B. Dosing

1. Initial treatment: 60mg daily for 14 days, followed by a 14-day drug-free period
2. Subsequent treatment: 60mg daily for 10 of 14 days, followed by a 14-day drug-free period
3. Each dosing cycle is 28 days

C. Contraindications

1. Patients with a history of hypersensitivity to edaravone or any of the inactive ingredients

D. Precautions

1. Hypersensitivity reactions (redness, wheals, and erythema multiforme) and cases of anaphylaxis (urticaria, decreased blood pressure, and dyspnea) have been reported

2. Approval from pharmacy management to dispense therapy will be obtained for patients with a history of asthma or sulfite intolerance (i.e. dried fruits, wine, sauerkraut, grape juices) or females that are pregnant, plan to become pregnant, or are breastfeeding
 - a. Edaravone 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
 - b. In animal studies, administration of edaravone resulted in adverse developmental effects. The background risk of major birth defects and miscarriage in patients with ALS is unknown

E. Adverse Reactions

1. Contusion (15%)
2. Gait Disturbance (13%)
3. Headache (10%)
4. Dermatitis (8%)
5. Eczema (7%)
6. Respiratory failure, disorder, or hypoxia (6%)
7. Glycosuria (4%)
8. Tinea infection (4%)

F. Drug Interactions

1. No drug interactions found

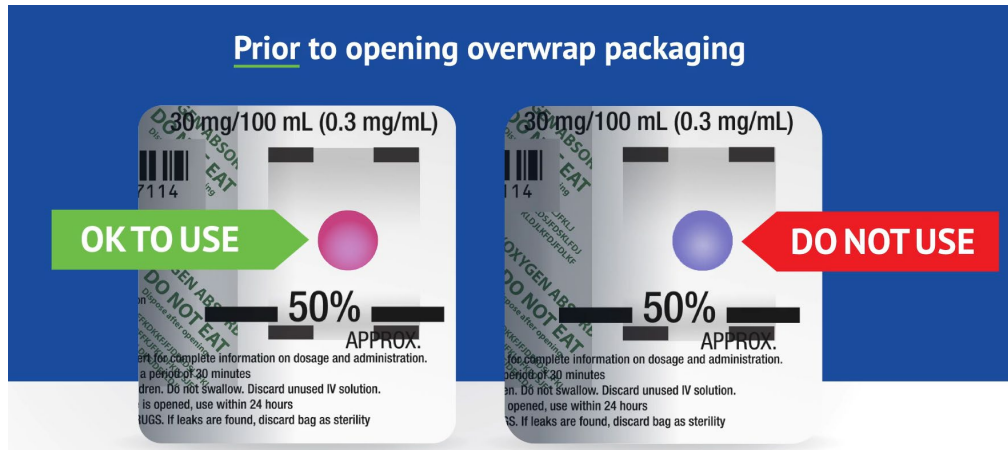
G. Pharmacokinetics

1. $V_d = 63.1L$
2. Half-life is 4.5 to 9 hours. Half-life of metabolites is 3 to 6 hours.

IV. ADMINISTRATIVE GUIDELINES

A. Site: for IV administration only

1. Do not use if oxygen indicator on overwrap has turned blue or purple before opening the package. The overwrap package contains an oxygen indicator which should be pink to reflect appropriate oxygen levels.
2. Once the overwrap is opened, use within 24 hours.



- B. Therapy Duration
 - 1. Duration of therapy is dependent on patient response and adverse reactions. Edaravone therapy is long term until disability progression or adverse reaction/hypersensitivity.
- C. Dose Adjustment
 - 1. No dose adjustment for patients with renal or hepatic impairment.

V. NURSING PROCEDURE

- A. Supplies include but are not limited to:
 - 1. Alcohol pads
 - 2. Gloves
 - 3. Tape
 - 4. Port Access Needle (Ex: 22 Gauge x 3/4" Safe step)
 - 5. IV injection cap
 - 6. Dressing Change kit
 - 7. Administration tubing
 - 8. Extension set 8"
 - 9. IV start kit for peripheral line
 - 10. IV peripheral catheter (Ex: 24 Gauge x 3/4" or 22 Gauge x 1")
 - 11. Pole mounted infusion pump
 - 12. IV pole and pole clamp
 - 13. Batteries for pump administration
- B. How Supplied
 - 1. Edaravone is supplied as a 30mg/100mL RTU polypropylene bag. Each 60mg dose (two, back-to-back 30mg/100mL infusion bags)
- C. Storage and Handling
 - 1. The RTU bag should not be used if the oxygen indicator has turned blue or purple before opening the package
 - 2. Doses will be dispensed in the manufacturer's box and stored at room temperature (up to 77° F) and protected from light
 - 3. Once the overwrap is opened, use within 24 hours
- D. Compatibility
 - 1. Other medications should not be injected into the infusion bag or mixed with edaravone. Not tested with other drugs via y-site
- E. Procedures
 - 1. Explain reasoning for visit and use of edaravone
 - 2. Done gloves
 - 3. Establish venous access prior to preparing drug product
 - 4. Counsel patient on warnings, precautions, and potential side effects
 - 5. Remove edaravone RTU bags from over wrap and inspect oxygen color indicator
 - 6. Edaravone must be infused within 24 hours of removing from over wrap
 - 7. Infuse edaravone 60 mg/200mL (two 30 mg/100mL bags) over a total of 60 minutes (30 minutes per each bag)

8. Mode of administration may be case-by-case based on patient/caregiver, nursing, or provider preference/judgment
9. Nurse to stay with patient and monitor vital signs and response to therapy 30 minutes after the infusion is complete

VI. CLINICAL MONITORING

- A. Monitor for lack of disability progression or maintained functional ability
- B. Monitor for hypersensitivity reactions and/or sulfite allergic reactions
- C. ALS Functional Rating Scale (ALS FRS)
 1. The ALSFRS will be completed at the time of onboarding and prior to subsequent edaravone cycles being dispensed
 2. Twelve standardized assessment questions (Appendix B) will be scored and trended in the patient's chart

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

- A. Radicava [package insert]. Jersey City, NJ: Mitsubishi Tanabe Pharma Corporation; 2021.
- B. Cedarbaum, JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functioning rating scale that incorporates assessments of respiratory function. *J Neurol Sci.* 1999 October 31; 169: 13-21.

APPENDIX A: ANAPHYLAXIS KIT INSTRUCTIONS

Emergency Medication after Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. Bag containing Pills (2 Acetaminophen and 2 Diphenhydramine)
2. Bag containing Alcohol Prep Pads
3. Bag labeled IM Epinephrine

All other contents will not be needed.

Open the IM Epinephrine Bag

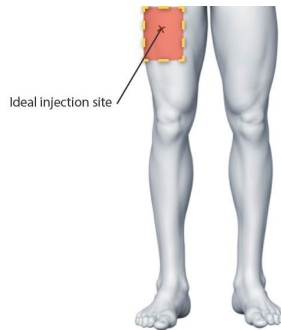
1. Remove 1 of each item
 - a. 1 -syringe
 - b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
 - c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1")
 - d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. Attach the brown filtered needle to syringe
 - a. Be careful to not touch the tip of the syringe or the needle.
2. Using an alcohol swab, wipe the neck of the epinephrine ampule.
3. Holding the ampule upright, swirl and flick the ampule until all fluid flows to the bottom chamber (the top chamber should be empty).

4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**
5. **Place the tip of the brown filter needle inside the ampule.** Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and **hold the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger.**
8. Replace the cap on the brown filter needle. Discard remainder in ampule.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

- a. 2 – Acetaminophen
- b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. Give the bag to the nurse or EMT, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

Call 911 or have someone drive you to the emergency department.

Appendix B

ALSFRS-R

<p>1. Speech 4 = Normal speech processes 3 = Detectable speech disturbances 2 = Intelligible with repeating 1 = Speech combined with nonvocal communication 0 = Loss of useful speech SCORE: _____</p> <p>2. Salivation 4 = Normal 3 = Slight but definite excess of saliva in mouth; may have nighttime drooling 2 = Moderately excessive saliva; may have minimal drooling 1 = Marked excess of saliva with some drooling 0 = Marked drooling; requires constant tissue or handkerchief SCORE: _____</p> <p>3. Swallowing 4 = Normal eating habits 3 = Early eating problems – occasional choking 2 = Dietary consistency changes 1 = Needs supplemental tube feeding 0 = NPO (exclusively parenteral or enteral feeding) SCORE: _____</p> <p>4. Handwriting 4 = Normal 3 = Slow or sloppy; all words are legible 2 = Not all words are legible 1 = Able to grip pen but unable to write 0 = Unable to grip pen SCORE: _____</p> <p>5a. Cutting Food and Handling Utensils (alternate scale for patients with gastrostomy) 4 = Normal 3 = Clumsy, but able to perform all manipulations independently 2 = Some help needed with closures and fasteners 1 = Provides minimal assistance to caregiver 0 = Unable to perform any aspect of task SCORE: _____</p> <p>5b. Cutting Food and Handling Utensils (alternate scale for patients without gastrostomy) 4 = Normal 3 = Somewhat slow and clumsy, but no help needed 2 = Can cut most foods, although clumsy and slow; some help needed 1 = Provides minimal assistance to caregivers 0 = Unable to perform any aspect of task SCORE: _____</p> <p>6. Dressing and Hygiene 4 = Normal function 3 = Independent and complete self-care with effort or decreased efficiency 2 = Intermittent assistance or substitute methods 1 = Needs attendant for self-care 0 = Total dependence SCORE: _____</p>	<p>7. Turning in Bed and Adjusting Bed Clothes 4 = Normal 3 = Somewhat slow and clumsy, but no help needed 2 = Can turn alone or adjust sheets, but with great difficulty 1 = Can initiate, but not turn or adjust sheets alone 0 = Helpless SCORE: _____</p> <p>8. Walking 4 = Normal 3 = Early ambulation difficulties 2 = Walks with assistance 1 = Nonambulatory functional movement only 0 = No purposeful leg movement SCORE: _____</p> <p>9. Climbing Stairs 4 = Normal 3 = Slow 2 = Mild unsteadiness or fatigue 1 = Needs assistance 0 = Cannot do SCORE: _____</p> <p>10. Dyspnea 4 = None 3 = Occurs when walking 2 = Occurs with one or more of the following: eating, bathing, dressing 1 = Occurs at rest, difficulty breathing when either sitting or lying 0 = Significant difficulty, considering using mechanical respiratory support SCORE: _____</p> <p>11. Orthopnea 4 = None 3 = Some difficulty sleeping at night due to shortness of breath, does not routinely use more than two pillows 2 = Needs extra pillow in order to sleep (more than two) 1 = Can only sleep sitting up 0 = Unable to sleep SCORE: _____</p> <p>12. Respiratory Insufficiency 4 = None 3 = Intermittent use of BiPAP 2 = Continuous use of BiPAP during the night 1 = Continuous use of BiPAP during the night and day 0 = Invasive mechanical ventilation by intubation or tracheostomy SCORE: _____</p> <p>TOTAL SCORE: _____</p>
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