Edaravone: Care and Management of the Patient Receiving Edaravone in the Ambulatory Setting

Site Applicability

VCH: Restricted to approved Ambulatory care sites at Richmond Hospital & Vancouver General Hospital

Practice Level

- **Physician**: Specialized Skill: Amyotrophic Lateral Sclerosis (ALS) Clinic Neurologist or a physician who has first consulted with the patient's ALS Clinic Neurologist
- **Pharmacist**: Basic Skill
- **Registered Nurse (RN)**: Basic Skill

Policy Statement

1. All Ambulatory sites must have approval from their Operational Director, Pharmacy Manager and Professional Practice Director prior to administering Edaravone to patients.
2. Prior to the first scheduled treatment:
   - The patient will obtain Edaravone supply (90 days) in accordance to the Health Canada Personal Importation Regulations.
   - The Prescriber must be an ALS Clinic Neurologist or a physician who has first consulted with the patient's ALS Clinic Neurologist.
   - The Prescriber (Most Responsible Physician (MRP) must provide:
     - Edaravone orders written on the Edaravone preprinted order (PPO)
     - A completed Assumption of risk, release and waiver of liability form for Administration of Medication acquired for Personal Use to the Ambulatory Clinic (Appendix A)
     - Other relevant history prior to the first treatment
3. Long term intravenous access will be considered to facilitate further treatment between the first course of treatment (2 weeks) and the beginning of the second course of treatment.
4. The nurse administering Edaravone must follow their College of Registered Nurses of British Columbia Practice Standard: Medication Administration and RN scope of practice: Part 4 (Section 7) Restricted activities that require an order: Administering substances, as well as the PPO: Edaravone Personal Import Medication and this CPD.

Need to Know

Edaravone supply must be arranged by the patient and obtained according to the Health Canada Personal Importation regulations prior to their first scheduled treatment as Edaravone is not available on the Canadian market and is not available through the Health Canada Special Access Program.

Edaravone is used in the treatment of ALS. The mechanism by which edaravone slows the decline of physical function in patients with ALS is unknown. Edaravone is a free radical and peroxynitrite scavenger that prevents oxidative damage to cell membranes and may contribute to inhibiting the progression of ALS (Lexi comp, 2017 as cited by Nagase, 2016).

Edaravone is for IV use only. Initial/Induction cycle: 60 mg once daily for 14 days, followed by a 14 day drug-free period. Subsequent cycles: 60 mg once daily for 10 days within a 14 day period, followed by a 14 day drug-free period.

Edaravone is administered as 60mg diluted in sodium chloride 200 mL over 60 minutes (infusion rate: ~1 mg/minute [3.33 mL/minute]). Do not mix edaravone with other medications. Hypersensitivity reactions have been reported. Edaravone contains sodium bisulfite and should NOT be administered to patients with a Sulfite allergy; **use caution in patients with asthma**. Refer to the PPO: Edaravone FOR ALS for prescriber orders and this CPD for nursing actions related to a patient experiencing symptoms of a sensitivity reaction, adverse drug reaction or if anaphylaxis is suspected.

Equipment & Supplies

- Ambulatory Clinic Documentation Record
- Edaravone infusion bag (prepared by Pharmacy (VGH) or Ambulatory Clinic Nurse (Richmond Hospital)
- IV initiation supplies and IV tubing
- BP monitor, including SpO2 monitor
- Medication to treat headache and hypersensitivity reaction per PPO is available in the area ADC

Procedure

1. The Prescriber will follow the Ambulatory Clinic scheduling process to arrange patient treatment appointments and inform patient of first treatment appointment time and location.

2. The prescriber will ensure the following documents are completed and sent to Pharmacy and the clinical unit **at least 5 days** prior to patients first scheduled appointment:
   a. The Assumption of Risk, Release and Waiver of Liability Form for Administration of Medication acquired for Personal Use Importation
   b. Allergy Form (confirming the patient does not have a Sulphite allergy)
   c. Edaravone PPO

3. The prescriber will inform the patient of their responsibility to bring an Edaravone supply to pharmacy:
   a. **Initial clinic cycle**: 5 days prior to scheduled date of first infusion the patient must bring one cycle supply of medication, e.g. a 14-day supply (28 vials) or a 10 day supply (20 vials) to the hospital pharmacy
   b. **Subsequent clinic cycles**: on the day of the last treatment of the prior cycle the patient must bring a 10-day supply (20 vials) of medication for the following maintenance cycle to the hospital pharmacy

4. Pharmacy will:
   a. Receive patient's own supply of Edaravone
   b. **VGH only**: Store Edaravone in pharmacy, and keep a patient specific drug log
   c. **Richmond only**: will keep a patient specific log and stock the Edaravone in the Automated Dispensing Cabinet used by the Clinic
   d. **Richmond only**: Enter the order into PCIS using the Edavarone PPO

5. The clinical area will process the orders on the day of the first scheduled infusion.

6. **VGH only**: When the patient arrives at the Ambulatory Clinic for treatment, the nurse assigned to the patient will inform Pharmacy that the patient has arrived in the clinic.

7. **VGH** Pharmacy will:
   a. Enter the order into PCIS using the edaravone PPO
   b. Prepare edaravone under the laminar air-flow hood using aseptic technique

8. **VGH only**: Pharmacy will dispense the Edaravone to the Ambulatory Clinic via porter unless otherwise directed by the clinical area.

9. Once the Edaravone arrives in the clinical area (VGH) or the nurse has prepared the Edaravone (Appendix B), the assigned nurse will follow the related PPO "Edaravone For ALS", this CPD: Care and management of patient receiving Edaravone in the Ambulatory setting, and review the Drug Data Sheet, Lower Mainland Pharmacy Services (Appendix C).

   Unless otherwise prescriber ordered, treatment monitoring and assessment must include:

   a. **First Infusion**: Vital signs and clinical assessment to be completed prior to infusion, and 5 minutes after the start of the infusion, then every 30 minutes (or more frequently if indicated) during the infusion and 30 minutes post infusion. If a reaction has occurred, patient MUST be assessed and monitored for 60 minutes post infusion.

   b. **Subsequent Infusions**: First Infusion: Vital signs and clinical assessment to be completed prior to infusion, and 5 minutes after the start of the infusion, then every 30 minutes (or more frequently if indicated) during the infusion and 15 minutes post infusion. If a reaction has occurred, patient MUST be assessed and monitored for 60 minutes post infusion.

   c. **For all infusions** report to the prescriber, prior to patient discharge:
      - Adverse drug events
        - Complete Health Canada Report
      - Mild hypersensitivity reactions
        - Administer medication as per PPO
      - Severe hypersensitivity reactions
        - Call a code Blue or 911 as per established clinic policy/procedure
        - Refer to site specific CPD: Code Blue Response
        - Administer medication as per PPO

10. All hypersensitivity reactions and adverse drug events must have a Safety Learning System (SLS) report completed. Additionally, all adverse drug events must be reported to Health Canada by Fax at 1-866-678-6789 on the Side Effect Reporting Form according to instructions. A copy of the report must be retained in the patient chart.

11. Prior to discharge, for all infusions, patient must meet the following clinical parameters, or return to pre-infusion baseline status (e.g. use or a walker, requirement for home O2, SpO2 92% or greater, etc.).

Discharge Criteria Table	
Clinical Parameter	**Criteria**
Level of Consciousness	Alert, no light-headedness or dizziness
Hemodynamics BP & Pulse *(consider patient's trend throughout infusion)*	Within 30% of Baseline AND asymptomatic
Respiration	No dyspnea, chest tightness, stridor, or tongue or airway swelling
Oxygen Saturation	Greater than or equal to 94% on room air
Activity	Steady gait
Skin	No rash, hives, pruritus, or swelling

12. On completion of infusion the nurse will ensure the patient meets the clinic discharge criteria (above) and provide/reinforce patient education prior to discharge, including the time of their next scheduled appointment.

13. The prescriber will make arrangements for the patient to have a long term intravenous access inserted between the first course of treatment and second course of treatment if clinically indicated.

Expected Patient/Client/Resident Outcomes

A slowing of the decline of physical function in patients with ALS.

Patient/Client/Resident Education

The **Prescriber** provides the patient education related to:

- The options available for infusion therapy care, including Hospital Medical Day/Ambulatory Care, and Home self-managed.
- The process of providing Pharmacy with the Edaravone supply and required related documentation
  - The Assumption of risk, release and waiver of liability form for Administration of Medication acquired for Personal Use Importation.
- The specific use of the drug and side effects with the patient as it relates to treatment:
  - The patient may experience headache or skin irritation. Have patient report immediately to prescriber severe dizziness, passing out, shortness of breath, bruising, difficulty walking, change in balance, or decreased urine output.
  - To report any signs of a significant reaction during infusion to the nurse (e.g., wheezing; chest tightness; fever; itching; bad cough; blue skin color; seizures; or swelling of face, lips, tongue, or throat, etc.) or if experienced following an infusion to report immediately to an Emergency Department.

The **Nurse** will provide/reinforce the patient education pre and post each treatment session as assessment indicates.

- Provide patient with the Edaravone Patient Education – Adult Medication available on Lexi Comp: https://online.lexi.com/lco/action/pcm
- Provide the patient with information on how they are to care for their IV (e.g. peripheral IV):
  - Keep it clean and dry at all times.
  - Cover it well with plastic wrap or a plastic bag when you shower or bath (do not get your IV wet).
  - Do not bump or push on your IV.
  - Tell the nurse if you have pain, redness, or swelling around your IV.
  - Do not worry if you see blood in the IV tubing, this is not unusual.
  - If your IV is accidentally removed, remove the entire bandage and then apply pressure to the area with a piece of gauze or clean tissue until the bleeding stops. The bandage and IV can be discarded in the garbage. [PHEM Resource Catalogue: EA.200.A58, Emergency Department, Antibiotic IV Therapy (2017)].

Evaluation

Ongoing patient assessment by the MRP and discussion with the family and/or patient.

Documentation

Prescriber

- VCH PPO Dec. 2017: Edaravone Personal Import Medication for the treatment of Amyotrophic Lateral Sclerosis (ALS).
- The Assumption of risk, release and waiver of liability form for Administration of Medication acquired for Personal Use Importation

Pharmacist

- PCIS for order entry
- Patient specific drug log

Assigned Nurse

- Ambulatory Clinic Treatment documentation form as per Ambulatory Clinic documentation standard. **Note:** document any unusual event or care concerns are documented in the interdisciplinary Progress Notes, including the submission of a Side Effect Reporting Form if completed.

Prescriber/Pharmacist/Nurse

- Side Effect Reporting Form

Site Specific Practices

Code Blue Response CPDs:

- Vancouver Acute: C-080: Code Blue Response
- Richmond: Code Blue: Cardiac Arrest/Respiratory Arrest

Related Documents

- Edaravone PPO: VA: VGH/UBCH/GFS and VC: BP/Purdy/GPC
- Assumption of Risk, Release and Waiver Form (Appendix A)
- Diluting Edaravone for administration in an Ambulatory Setting (Appendix B)
- Edaravone Drug Data Sheet, Lower Mainland Pharmacy Services (Appendix C)
- Edaravone PPO: Richmond
- Edaravone Drug Monograph, Lexi Comp: https://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/6485309
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Appendix A: Assumption of Risk, Release and Waiver Form

Patient Name/Identification

ASSUMPTION OF RISK, RELEASE AND WAIVER OF LIABILITY, V2, 22 11 17

Administration of Medication acquired for Personal Use Importation:

This document affects your legal rights and liabilities. Please read carefully. You may wish to seek independent legal advice in respect of this agreement.

I, _____(print name of patient) want to have the following Medication _____ (the "Medication") administered to me by health care providers at the Vancouver Coastal Health Authority ("VCH").

I understand and acknowledge that this Medication does not have Health Canada approval for sale and is not authorized for public use in Canada and that administration of this Medication is not solicited, encouraged, endorsed, or approved by VCH. I understand and acknowledge that there is no assurance from VCH that the drug is safe, efficacious, or of high quality. I further understand and acknowledge that the possible risks, side-effects, drug interactions, and other adverse effects related to the use of this Medication are unknown to VCH, its employees, agents, and physicians.

I acknowledge and understand that VCH has not sourced or provided the Medication and that I have legally acquired and personally brought the Medication into Canada from another country under the Personal Use Importation Requirements for Human Drugs [the *Food and Drugs Act* and its Regulations, and POL-0060 of Health Canada], and have stored and handled it as instructed by the manufacturer. I further understand that VCH accepts no responsibility for any costs associated with obtaining the Medication.

I acknowledge that the manufacturer's labeling, instructions, and/or directions for this Medication are not written in English or French. I further acknowledge that that while the labeling, instructions, and/or directions have been translated into English, VCH, its employees, agents and physicians, are not responsible to ensure the reliability or accuracy of the translated information.

In consideration of VCH agreeing to the administration of the Medication, I, for myself, my heirs, agents, executors, and administrators, hereby waive my right of recovery and release VCH, its employees, agents, and physicians from any and all liability, claims, costs, expenses, damages, and other relief I have or may have in the future in relation to the administration of the Medication and any damage, harm, or adverse effects that may result therefrom, including but not limited to adverse side-effects and/or drug interactions, including death.

I acknowledge that the administration of the Medication is solely at my own risk, and I personally accept all responsibility for and assume all liability for any damage, harm, or other adverse effects that I may suffer as a result of the administration of this Medication.

I acknowledge that I have been informed that I should seek my physician's approval to take this Medication. I acknowledge that I have either been given a physician's approval to take the Medication or that I have decided to take the Medication without the approval of a physician and assume all responsibility for my decision.

I understand that VCH may, in its sole discretion, stop administering the Medication to me.

I have read and understand this Assumption of Risk, Release and Waiver of Liability.

_____ _____

Signature Date

_____ _____

Witness Signature Date

Appendix B: Diluting Edaravone for Administration in an Ambulatory Setting

Alternate Name: Radicut (Japan)
NOTE: Edaravone and Radicut are compatible with NS

Supplies:

- 1 250 mL infusion bag of 0.9% Sodium Chloride (NS)
- 1 50 mL syringe
- 2 Unfiltered Blunt needle (18 gauge)
- 1 Filtered blunt needle (18 gauge)
- 2 alcohol swipes
- 1 Medication added label

Procedure:

1. Swab port of NS, let dry.
2. Using an unfiltered blunt needle attached to a 50 mL syringe remove 50 mL of NS from the infusion bag.
3. Swab port of NS, let dry.
4. Using a filtered needle attached to a 50 mL syringe withdraw Edaravone from 2 ampoules Edaravone 30 mg/20 mL for a total of 60 mg/40 mL.
5. Remove the blunt filtered needle from the syringe and attach a blunt unfiltered needle.
6. Add the 60 mg/40 mL of Edaravone to the infusion bag of NS.
7. Complete the medication added label including:
    - Date and time
    - Patient name and MRN
    - Drug name and dose added
    - Initials/signature of nurse that prepared the medication

Appendix C: Edaravone Drug Data Sheet (Lower Mainland Pharmacy Services)

VANCOUVER GENERAL HOSPITAL/UBCH/GFS
PHARMACEUTICAL SCIENCES
DRUG DATA SHEET

DRUG NAME	ALTERNATE NAME
edaravone	Radicut® (Japan)

MANUFACTURER
MITSUBISHI TANABE (Radicut) KYORIN Pharmaceuticals (generic edaravone)

STRENGTH	DOSAGE FORM
30 mg / 20 mL ampule (Room Temperature)	injectable

INDICATIONS
Slow disease progression of Amyotrophic lateral sclerosis (ALS); mechanism unknown but drug is a free radical scavenger presumed to inhibit oxidative damage to nerve cells

DOSAGE
Initial treatment cycle: 60 mg IV DAILY for 14 days, followed by a 14-day drug-free period
Subsequent treatment cycles: 60 mg IV Monday to Friday for 10 days out of 14-day periods, followed by 14-day drug-free periods

PREPARATION
Dilute 60 mg in 200 mL NS
(Remove 50ml from 250ml of NS and dilute 60mg (2 amps) of edaravone into remaining 200ml; total volume after compounding is 240ml)
Compatible with NS only
Prepare just prior to administration. Use solution as soon as possible after preparation.

ADMINISTRATION
Infuse 60 mg dose over 60 minutes.
Do not administer with any other medications or solutions
Store at room temperature and protect from light

KNOWN SIDE EFFECTS*
Less severe: Bruising and gait disturbance (most common adverse reactions reported in clinical trials), contact dermatitis/eczema/rash (1.3%), hypersensitivity reactions, dysphagia, headache, nausea/vomiting.
More severe: Renal impairment (acute renal failure (0.26%), nephrotic syndrome (0.02%)), hepatic impairment (fulminant hepatitis (0.24%), hepatic dysfunction (0.24%)), aggravated cardiac diseases (increased cholesterol/triglycerides, hypertension (0.9%)), disseminated intravascular coagulation (0.08%), thrombocytopenia (0.08%). Unknown incidence of acute lung injury and rhabdomyolysis. Increased or decreased serum potassium. Fatal outcomes have been reported in patients with infections or severe altered level of consciousness. Evaluate risk/benefit. No long term safety data exists (longest trial = 24 weeks).

SPECIAL PRECAUTIONS
- Contraindication: Hypersensitivity reaction to edaravone; Severe renal impairment (crcl<30ml/min); Sulfite allergy (edaravone contains sodium bisulfite)
- Use with caution in patients with renal impairment, dehydration, infections, hepatic impairment, cardiac diseases, severe disturbances of consciousness, elderly
- Monitor renal function (BUN, creatinine), liver function (AST, ALT, LDH, total and direct bilirubin, LDH, CK), CBC
- This drug is not available on the Canadian market and is not available through the Health Canada Special Access Programme. Medication supplies must be arranged by the patient and obtained according to the Personal Importation regulations of Health Canada
- The Assumption of risk, release and waiver liability form for Administration of Medication acquired for Personal Use Importation must be completed

Knowledge of its side effects is incomplete and may involve risks that are unknown and currently unforeseen.
***REPORT ANY ADVERSE DRUG REACTIONS TO THE PHYSICAN AND HEALTH CANADA**