CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

CLINICAL GUIDELINES FOR OUTPATIENT R-EPOCH THERAPY FOR NON-HODGKINS LYMPHOMA

Section: Nursing
Compliance: ACHC Infusion Pharmacy
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I. POLICY

R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) is a five-day continuous infusion chemotherapy regimen used to treat aggressive or high-risk lymphomas. The R-EPOCH regimen is traditionally administered in an inpatient setting but can be administered safely as an ambulatory regimen. Potential advantages of outpatient administration include reduced inpatient burden for routine chemotherapy, less exposure to resistant bacterial infections, increased patient satisfaction, and reduced cost.

Chartwell will provide the etoposide/vincristine/doxorubicin components of therapy in a 24-hour continuous infusion on days 1-4 of cycles 2-6.

While not all patients who receive the R-EPOCH regimen will be candidates for outpatient administration, it is anticipated that a significant number of patients will be appropriate candidates. The following outlines the procedure for identifying such patients and the protocol for coordination of services.

PHARMACOLOGY OVERVIEW:

Doxorubicin is an anthracycline topoisomerase II inhibitor. The R-EPOCH dosing for Non-Hodgkin's lymphoma is 10mg/m^2 / day continuously on days 1-4. Doxorubicin is considered NIOSH group 1 hazardous agent.

Etoposide is an antineoplastic agent that inhibits DNA-topoisomerase II or free radical formation resulting in DNA strand breaks. The R-EPOCH dosing for Non-Hodgkin's lymphoma is 50mg/m^2/ day continuously on days 1-4. Etoposide is considered a NIOSH group 1 hazardous agent.

Vincristine is an oncolytic vinca alkaloid that arrests replicating cells of the metaphase stage through prevention of microtubule formation in the mitotic spindle. The R-EPOCH dosing for Non-Hodgkin's lymphoma is 0.4 mg/m^2/day continuously on days 1-4. Vincristine is considered a NIOSH group 1 hazardous agent.

II. PROCEDURES

A. Patient Acceptance/Inclusion Criteria:

1. All patients referred for outpatient Doxorubicin/Etoposide/Vincristine therapy must meet clinical admission criteria. Patients who may be eligible for outpatient administration of the remaining 5 cycles will be identified by the oncologist, physician extender and/or pharmacist. Candidates for outpatient administration will demonstrate:
    a. Patient is willing to receive treatment as an outpatient
    b. Acceptable performance status at diagnosis
    c. Availability of at least one caregiver
    d. No perceived difficulty with instructions / no deficits in memory or cognition
    e. No current substance abuse. Patients with remote history of substance abuse will be evaluated on a case-by-case basis.
    f. Residence that is a reasonable distance to Cancer Center
    g. Residence that is a reasonable distance to hospital facility with ability to provide dexrazoxane in case of extravasation
    h. Reliable transportation
    i. Insurance approval for outpatient administration of chemotherapy

2. Lab work will be completed per protocol or at the discretion of outpatient oncology team or provider. In addition, the following must be completed prior to the receipt of outpatient R-EPOCH:
    a. Hepatitis B screening
    b. ECHO or MUGA
    c. Insertion of PICC line, implanted port, or other central line access

ADMINISTRATIVE GUIDELINES:

1. R-EPOCH regimen must be given through central venous access

2. Patients receiving outpatient R-EPOCH will receive their first cycle inpatient prior to starting outpatient therapy.

3. Administration: Chartwell will provide Doxorubicin/Etoposide/Vincristine chemotherapy as a three-in-one admixture. This chemotherapy regimen will be a continuous infusion over 24 hours on day 1,2,3, and 4 of the cycle, and patients will have their bag hooked up and changed out at clinic on M-F. Patients will be responsible for bringing their pump to clinic for day 1 hookup.

4. Dosing/ Compounding/and Administration rates:
    a. Doxorubicin 10mg/m2/day
    b. Etoposide 50mg/m2/day
    c. Vincristine 0.4mg/m2/day

5. Duration: Total of 6 cycles unless otherwise specified by ordering provider

COMPOUNDING:

1. Standard order template codes:
    a. EPOCH500BAG
    b. EPOCH800BAG

2. Compounding instructions are based on the patient's BSA, dose, and drug concentrations

3. Stability: In NSS at room temperature and Protect from Light for 72 hours at the following concentrations:
    a. Doxorubicin 0.025 mg/mL- 0.040mg/mL
    b. Etoposide 0.125 mg/mL- 0.20 mg/mL
    c. Vincristine 1mcg/mL- 1.6 mcg/mL

4. Room temperature and PFL for 3 days[1-2]
    a. Limited stability ranges at 96 hours room temperature. Please contact Management and Clinical Support team to utilize 96-hour stability for certain accommodations.

5. Doxorubicin, Etoposide, and Vincristine must be mixed in Exactamix EVA bags or DEHP/PVC plastic free bags as Etoposide leaches DEHP plasticizer from PVC containers and tubing.

6. Utilize total volume with **500 mL** of Normal saline (BSA from 1.2 – 1.9 at regular dosing guidelines)
    a. Doxorubicin 12-19.9 mg
    b. Etoposide 60-99.5 mg
    c. Vincristine 0.48-0.75 mg
    d. Rate= 19.8 mL/hour

7. Utilize total volume with **800 mL** of Normal saline (BSA 2.0- 3.0 at regular dosing guidelines)
    a. Doxorubicin 20-30 mg
    b. Etoposide 100-150 mg
    c. Vincristine 0.8-1.2 mg
    d. Rate= 31.7 mL/hour

    *Wouldn't anticipate seeing a BSA less than 1.4 or greater than 2.5. Please contact Management and Clinical Support team to utilize volumes other than 500mL or 800mL

8. Outpatient Treatment Cycle Schedule- See UPMC Hillman Cancer Center R-EPOCH Outpatient Policy for Cycle Regimen

PROCEDURE:

1. Supplies:
    a. Syringes of normal saline and heparin (strength based on patient's access device or oncologist's orders)
    b. Alcohol swabs
    c. Chemo spill kit
    d. CADD Prizm or Solis pump
    e. 9 Volt Duracell battery for Prizm or 4 Double A batteries for Solis
    f. Chemotherapy precautions teaching sheet
    g. CADD Prizm/Solis battery change procedure teaching sheet
    h. CADD Prizm/Solis continuous delivery mode teaching sheet
    i. Pump return box
    j. Pouch for pump and bag

MONITORING:

1. Follow up pharmacy assessment will include:
    a. Assessment of signs and symptoms of adverse effects
    b. Reminder for patient to bring CADD pump to cancer center on day 1 of cycle.

2. Patients receiving this outpatient regimen will have 24/7 access to nursing and/or pharmacy staff outside of clinic hours for any questions or pump troubleshooting.

3. Doxorubicin: *The recommended lifetime cumulative dose of Doxorubicin is 450-550mg/m^2 May cause fetal harm. Advise patients of reproductive potential to use adequate form of contraception during therapy and 6 months after discontinuation. Doxorubicin has potential to induce premature menopause in females and loss of fertility in males. Advise lactating patients to not breastfeed while receiving therapy. Counsel patients that urine may appear red 1-2 days after administration, to report any new onset of signs of infection, and to report any symptoms of heart failure. Monitor lab work and severe myelosuppression. Monitor for signs/symptoms of tumor lysis syndrome and extravasation. Side effects may include nausea, vomiting, diarrhea, mouth pain/sores, and alopecia.

4. Etoposide: May cause fetal harm. Advise patients of reproductive potential to use adequate form of contraception during therapy and 6 months after discontinuation. Etoposide has potential to induce premature menopause, infertility, and amenorrhea in females and loss of fertility in males. Advise lactating patients to not breastfeed while receiving therapy. Monitor lab work and for severe myelosuppression. Monitor for signs/symptoms of infection, nausea, vomiting, diarrhea, mouth pain/sores, alopecia, extravasation, and hypersensitivity reactions.

5. Vincristine: Contraindicated in patient with a demyelinating form of Charcot-Marie Tooth syndrome. For intravenous use only. May cause fetal harm. Advise patients of reproductive potential to use adequate form of contraception during therapy and 6 months after discontinuation. My cause azoospermia in males. Advise lactating patients to not breastfeed while receiving therapy. Monitor lab work and for severe myelosuppression. Monitor for signs/symptoms of infection, nausea, vomiting, constipation, alopecia, extravasation, neurotoxicity, and hypersensitivity reactions.

REFERENCES:

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2. Bing Caryn, Nowobilski-Vasilios Anna et al. Extended Stability for Parenteral Drugs. Sixth Edition. American Society of Health Systems Pharmacists. Pages 176-78.
3. UPMC Hillman Cancer Center R-EPOCH Outpatient Policy
4. Doxorubicin [package insert]. Lake Forest, Illinois. Hospira; 2016.