CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT R-EPOCH THERAPY FOR NON-HODGKIN'S LYMPHOMA

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
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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.

Pharmacy 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.

II. PROCEDURES

PHARMACOLOGY OVERVIEW

Doxorubicin is an anthracycline topoisomerase II inhibitor. The R-EPOCH dosing for non-Hodgkin's lymphoma may range from 10-29.8mg/m2 /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 may range from 50-149.3mg/m2/ 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/m2/day continuously on days 1-4. Vincristine is considered a NIOSH group 1 hazardous agent.

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

B. 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
    a. Patients will initiate therapy at Dose Level 1. Dose modifications and management of toxicity will be determined by the prescribing oncology team.

5. Duration: total of six cycles unless otherwise specified by ordering provider.

	Dose Levels									
Adjusted Agents	**-3**	**-2**	**-1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Doxorubicin (mg/m^2/day)	10	10	10	**10**	12	14.4	17.3	20.7	24.8	29.8
Etoposide (mg/m^2/day)	50	50	50	**50**	60	72	86.4	103.7	124.4	149.3
Cyclophosphamide (mg/m^2)	384	480	600	**750**	900	1080	1296	1555	1866	2239
Non-Adjusted Agents										
Rituximab (mg/m^2)	375	375	375	**375**	375	375	375	375	375	375
Vincristine (mg/m^2/day) (No cap)	0.4	0.4	0.4	**0.4**	0.4	0.4	0.4	0.4	0.4	0.4
Prednisone (mg/m^2 BID)	60	60	60	**60**	60	60	60	60	60	60

C. Compounding:

1. Doxorubucin, etoposide and vincristine will be compounded in a single 1000 mL NS bag. IV bag must be DEHP/PVC plastic-free. Exactamix EVA bags may be used.
2. The following concentration ranges have been studied:
    a. Doxorubicin 0.025 mg/mL-0.040 mg/mL
    b. Etoposide 0.125 mg/mL-0.20 mg/mL
    c. Vincristine 1 mcg/mL-1.6 mcg/mL

    All drugs should not exceed the upper limit of studied concentration, if possible. Etoposide is of particular concern for precipitation and should not exceed 250 mcg/mL in any case.
3. BUD = 72 hours at room temperature, protected from light.
4. Infuse 1000 mL dose via ambulatory infusion pump over 24 hours at a rate of 41.7 mL/hr.

    Please contact Management and Clinical Support Team to utilize volumes other than 1000 mL due to specific concentration, compatibility or stability concerns.

D. Supplies:

1. Syringes of normal saline and heparin (strength based on patient's access device or oncologist's orders)
2. Alcohol swabs
3. Chemo spill kit
4. Ambulatory pump
5. Batteries for pump/power pack
6. Chemotherapy precautions teaching sheet
7. Battery change procedure teaching sheet
8. Pump continuous delivery mode teaching sheet
9. Pump return box
10. Pouch for pump and bag

E. Monitoring:

1. Follow up pharmacy assessment will include:
    a. Assessment of signs and symptoms of adverse effects
    b. Reminder for patient to bring 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/m2. Obtain baseline dose from prescribing team at time of initial referral. Maintain documentation of cumulative dose on written Plan of Treatment (Appendix A, specific to UPMC).**

    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.

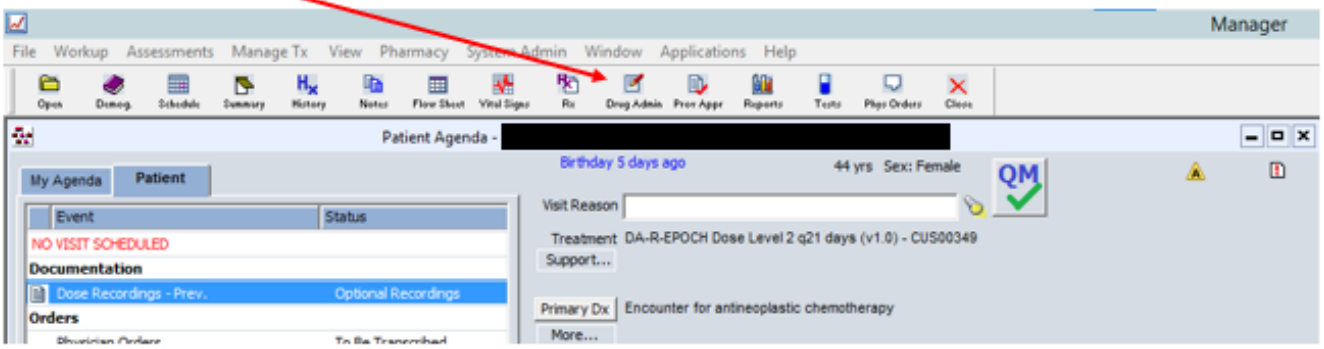
5. Vincristine: Contraindicated in patient with a demyelinating form of Charcot-Marie Tooth syndrome. For intravenous use only. May cause fetal harm. Advise patients of reproductive potential to use adequate form of contraception during therapy and 6 months after discontinuation. My cause azoospermia 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.

F. References:

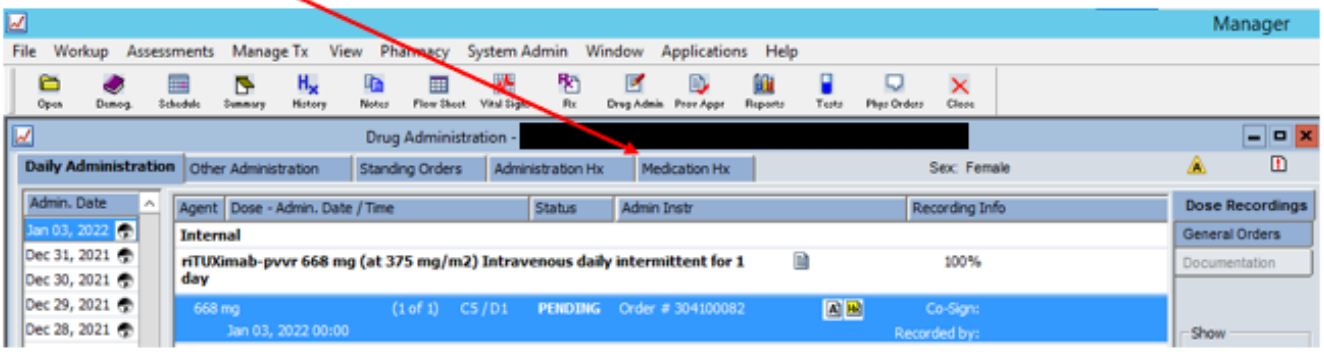
1. Wolfe JL, Thoma LA, Du C, et al: Compatibility and stability of vincristine sulfate, doxorubicin hydrochloride, and etoposide in 0.9% sodium chloride injection. Am J Health-Syst Pharm: 1999. 56: 985-9.
2. Bing Caryn, Nowobilski-Vasilios Anna et al. Extended Stability for Parenteral Drugs. Sixth Edition. 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.
5. Barlett NL, Zelenetz AD etal. Phase III randomized study of R-CHOP versus dose-adjusted EPOCH-R with molecular profiling in untreated de novo diffuse large B-cell lymphomas [study protocol].ClinicalTrials.gov. 15 February 2018, https://clinicaltrials.gov/ProvidedDocs/09/NCT00118209/Prot_SAP_000.pdf.

APPENIX A: Obtaining Cumulative Doxorubicin Dose in Aria (UPMC Only)

Select "Drug Admin"



Select "Medication Hx"



Double click on doxorubicin