National Comprehensive Cancer Network®

Chemotherapy Order Template

Diffuse Large B-Cell Lymphoma

R-CHOP (Cyclophosphamide/DOXOrubicin/ VinCRIStine/PrediSONE + Rituximab)

INDICATION:

First line

REFERENCES:

1. NCCN Guidelines® for Non-Hodgkin's Lymphomas. V.1.2016.
2. Coiffier B, et al. *N Engl J Med.* 2002;346(4):235-42.[b]

NCCN SUPPORTIVE CARE:

1. *Emetic Risk:* Day 1 High
2. *Fever Neutropenia Risk:* Intermediate

CHEMOTHERAPY REGIMEN

21-day cycle for 3 cycles with radiation therapy (Stage I-II nonbulky disease), for 6 cycles (Stage I-II bulky or nonbulky disease), or for 2 – 6 cycles (Stage III-IV disease)

- **Rituximab** 375 mg/m^2 IV on Day 1
- See *Safety Parameters and Special Instructions* for recommended infusion rate.
- See *Safety Parameters and Special Instructions* for alternative dosing information.
- **Cyclophosphamide** 750 mg/m^2 IV over 30 minutes on Day 1
- Oral hydration is strongly encouraged with cyclophosphamide; poorly hydrated patients may need supplemental IV hydration. Patients should attain combined oral and IV hydration of 2000 – 3000 mL/day on day of chemotherapy. See *Other Supportive Therapy* for example of IV hydration.
- **DOXOrubicin** 50 mg/m^2 IV Push on Day 1
- See *Safety Parameters and Special Instructions* for information on slow IV Push administration.
- **VinCRIStine** 1.4 mg/m^2 (maximum 2 mg) IV over 5 – 10 minutes on Day 1
- **PrediSONE** 100 mg PO daily on Days 1 – 5

CNS prophylaxis may be considered in select settings (4 – 6 factors according to prognostic model to assess risk of CNS disease [See NCCN Guidelines for Non-Hodgkin's Lymphomas], HIV lymphoma, testicular, or double hit lymphoma).
CNS prophylaxis is recommended (4 – 8 doses of intrathecal methotrexate and/or cytarabine, or systemic methotrexate) during the course of treatment.
Please see Order Template DBL32 (Intrathecal Cytarabine), DBL34 (Intrathecal Methotrexate), or DBL39 (High-Dose Methotrexate) for examples of CNS prophylaxis courses.

SUPPORTIVE CARE

Premedications

- Rituximab requires premedication for hypersensitivity. The recommended dosing is:
  - Diphenhydramine 12.5 – 50 mg IV/PO 30 – 60 minutes pre-rituximab
    AND
  - Acetaminophen 650 mg PO 30 – 60 minutes pre-rituximab

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Antiemetic therapy (See www.nccn.org/professionals/physician_gls/PDF/antiemesis.pdf)

Dexamethasone dose may be modified or omitted based on steroids within the chemotherapy regimen.

Scheduled prophylactic antiemetic therapy should be given for prevention of acute and delayed nausea and vomiting based on the emetic risk of the chemotherapy regimen. This may include antiemetic therapy given on the days following chemotherapy as suggested by the NCCN Guidelines for Antiemesis. For more information on emetic prophylaxis, refer to NCCN Guidelines for Antiemesis and Appendix D to the NCCN Chemotherapy Order Templates.

PRN for breakthrough: All patients should be provided with at least one medication for breakthrough emesis. Please consult the NCCN Guidelines for Antiemesis for appropriate antiemetic therapy.

Myeloid growth factor therapy (See www.nccn.org/professionals/physician_gls/PDF/myeloid_growth.pdf)

CSFs may be considered for primary prophylaxis based on FN risk of chemotherapy regimen. For more information on prophylaxis of FN, refer to NCCN Guidelines for Myeloid Growth Factors and Appendix C to the NCCN Templates.

Other Supportive Therapy

- For R-CHOP: This regimen may be associated with a risk of tumor lysis syndrome with the first cycle. Tumor lysis prophylaxis and/or treatment may be indicated. Review NCCN Guidelines for Non-Hodgkin's Lymphomas for additional information.
- For rituximab: Hepatitis B prophylaxis (entecavir or equivalent) is recommended during treatment for patients who are HBsAg+ or HBcAb+ or have an increasing HBV viral load.
- For cyclophosphamide: *Example of recommended hydration:* Sodium chloride 0.9% infused IV at a rate of 1.5 – 3 mL/kg/hour for a total of 500 mL on day of chemotherapy.
- For vinCRIStine: This agent may cause constipation. Symptoms of constipation should be assessed as clinically indicated for potential dose modification or discontinuation. Patients often require prophylaxis with a bowel regimen (eg, docusate sodium and senna) to maintain normal bowel function.
- For predniSONE: Risk of stress ulcers may occur with treatment. Consider use of a H_2 blocker or proton pump inhibitor.

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MONITORING AND HOLD PARAMETERS

- CBC with differential should be assessed as clinically indicated for potential dose modification.
- For R-CHOP: This regimen may be associated with a risk of tumor lysis syndrome in some patients. Patients at risk should be monitored for clinical presentation of tumor lysis, including laboratory abnormalities of potassium, phosphate, uric acid, and serum creatinine.
- For rituximab:
  - Hypersensitivity reaction may occur with administration. Monitor for and treat hypersensitivity reactions per institutional standard. Initiation and/or adjustment of premedications should be considered. Infusion rate changes may be warranted.
  - Risk of hepatitis B reactivation exists with therapy. Review drug package insert and NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections for monitoring and prophylaxis recommendations.
  - Risk of serious bacterial, viral, and fungal infections exists during treatment. Review drug package insert and NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections for monitoring and prophylaxis recommendations.
- For cyclophosphamide: Renal function should be monitored as clinically indicated for potential dose modification or discontinuation.
- For DOXOrubicin:
  - DOXOrubicin is an anthracycline. Cumulative anthracycline dosage should be monitored.
  - Ejection fraction should be monitored prior to initiation of treatment and as clinically indicated.
  - Liver function should be monitored prior to each cycle for potential dose modification or discontinuation.
- For vinCRIStine:
  - Liver function should be monitored as clinically indicated for potential dose modification or discontinuation.
  - Signs and symptoms of neurotoxicity should be monitored prior to each dose for potential dose modification or discontinuation.
- For predniSONE:
  - Hypertension may occur with therapy. Blood pressure should be monitored as clinically indicated for potential dose modification.
  - Serum glucose should be monitored as clinically indicated.

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SAFETY PARAMETERS AND SPECIAL INSTRUCTIONS

- For rituximab:
  - The recommended infusion rate of rituximab for the first dose is 50 mg/hr, increased by 50 mg/hr every 30 minutes until a maximum infusion rate of 400 mg/hr is reached.
  - For subsequent doses, rapid-infusion rituximab may be administered to patients meeting the following specific criteria:
    - no severe infusion-related event during the first dose
    - no clinically significant cardiovascular disease
    - lymphocyte count <5000/mm^3
  - Rapid-infusion rituximab consists of a 90-minute infusion given as
    - 20% of the total dose administered in the first 30 minutes, followed by
    - 80% of the total dose administered over the next 60 minutes
  - For patients not meeting criteria for rapid-infusion rituximab, the recommended infusion rate for subsequent doses is 100 mg/hr increased by 100 mg/hr every 30 minutes until a maximum infusion rate of 400 mg/hr is reached.
  - Infusion rates are adjusted based on patient tolerance and may be decreased in the setting of infusion-related reactions.
  - Consider modification of rituximab in first cycle. Evidence exists for split-dose rituximab or delayed administration in patients with high tumor burden.
- For cyclophosphamide: Secondary malignancies have been associated with this drug. Review drug package insert for additional information.
- For DOXOrubicin:
  - **DOXOrubicin is a vesicant.**
  - This agent is administered IV Push. The preferred IV Push method for a vesicant is administration through the side port of a freely flowing IV; alternatively, the drug can be administered via direct IV push.
  - Central venous access is recommended for administration of this agent.
  - Secondary malignancies have been associated with this drug. Review drug package insert for additional information.
- For vinCRIStine:
  - **VinCRIStine is a vesicant.**
  - VinCRIStine is for IV use only and should be administered via a minibag (e.g. 25 mL for pediatric patients and 50 mL for adults).
  - **Intrathecal Injection must be avoided and usually results in death or serious neurological damage**.
  - Central venous access is recommended for administration of this agent.
  - VinCRIStine can be safely administered in a minibag via a peripheral vein by allowing the infusion to flow via gravity. Use of infusion pumps are not recommended for peripheral administration.
- For predniSONE: Take with food.