

## NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

### Burkitt Lymphoma (Part 1 of 3)

The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anticancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The cancer treatment regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

REGIMEN	DOSING
<b>Induction Therapy—Low Risk</b>	
<p><b>CALGB 10002</b> (cyclophosphamide [Cytosan] and prednisone, <b>followed by</b> cycles containing ifosfamide [Ifex] or cyclophosphamide, methotrexate [MTX], leucovorin, vincristine [Oncovin], dexamethasone and either doxorubicin [Adriamycin], <b>OR</b> etoposide [Etopophos; Vepesid; VP-16], <b>OR</b> cytarabine [Cytosar-U; Ara-C] or intrathecal triple therapy (MTX, cytarabine [Cytosar-U<sup>®</sup>, Ara-C<sup>®</sup>], hydrocortisone) + <b>rituximab</b> (Rituxan)<sup>1,2</sup></p>	<p><u>Cycle 1</u>  <b>Days 1–5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV.  <b>Days 1–7:</b> Prednisone 60mg/m<sup>2</sup> orally.  <u>Cycles 2 (beginning Day 8), 4, and 6</u>  <b>Days 1–5:</b> Ifosfamide 800mg/m<sup>2</sup> IV.  <b>Day 1:</b> MTX 1.5g/m<sup>2</sup> IV (with leucovorin rescue).  <b>Day 1:</b> Vincristine 2mg IV.  <b>Days 4 and 5:</b> Cytarabine 1g/m<sup>2</sup> IV.  <b>Days 4 and 5:</b> Etoposide 80mg/m<sup>2</sup> IV.  <b>Days 1–5:</b> Dexamethasone 10mg/m<sup>2</sup> IV.  <u>Cycles 3, 5, and 7</u>  <b>Days 1–5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV.  <b>Day 1:</b> MTX 1.5g/m<sup>2</sup> IV.  <b>Day 1:</b> Vincristine 2mg IV.  <b>Days 1–5:</b> Dexamethasone 10mg/m<sup>2</sup> IV.  <b>Days 4 and 5:</b> Doxorubicin 25mg/m<sup>2</sup> IV.  <u>Cycle 2</u>  <b>Day 8:</b> Rituximab 50mg/m<sup>2</sup> IV.  <b>Days 10 and 12:</b> Rituximab 375mg/m<sup>2</sup> IV.  <u>Cycles 3–7</u>  <b>Day 8:</b> Rituximab 375mg/m<sup>2</sup> IV.                      Repeat cycles every 3 weeks.  <u>Cycles 2–7 (6 doses)</u>  <b>Day 1:</b> Triple intrathecal therapy for CNS prophylaxis.</p>
<p><b>CODOX-M (original or modified)</b> (cyclophosphamide + doxorubicin + vincristine with intrathecal MTX + cytarabine, <b>followed by</b> systemic MTX) ± <b>rituximab</b><sup>1,3</sup></p>	<p><u>Modified</u>  <b>Days 1 and 2:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV + doxorubicin 50mg/m<sup>2</sup> IV + vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg) + intrathecal MTX 12mg, <b>plus</b> cytarabine 50mg.  <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.  <b>Day 3:</b> Intrathecal cytarabine 50mg (<b>For high-risk patients only</b>).  <b>Days 3–8:</b> Administer granulocyte colony-stimulating factor (G-CSF).  <b>Day 10:</b> Vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg) + MTX 3g/m<sup>2</sup> IV.  <b>Day 11:</b> Leucovorin 200mg/m<sup>2</sup> IV, <b>followed by</b> 15mg/m<sup>2</sup> IV every 6 hrs (until MTX level &lt;0.1 x 10<sup>-6</sup> M).  <b>Day 12:</b> G-CSF restarted if ANC &lt;1,000.                      NOTE: All intrathecal therapy was mixed with 50mg of hydrocortisone. Repeat for 3 cycles.</p>
<p><b>Dose-adjusted EPOCH</b> (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + <b>intrathecal MTX + rituximab</b><sup>1,4-6</sup></p> <p>NOTE: For patients without CNS disease.</p>	<p><b>Days 1–4:</b> Etoposide 50mg/m<sup>2</sup> continuous IV + doxorubicin 10mg/m<sup>2</sup> continuous IV + vincristine 0.4mg/m<sup>2</sup> continuous IV.  <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.  <b>Days 1–5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily.  <b>Day 5:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV.  <b>Day 6:</b> G-CSF administered until ANC &gt;5 x 10<sup>9</sup>/L.                      Intrathecal MTX for 6 doses.                      Repeat for 6 cycles every 3 weeks.</p>

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## NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

### Burkitt Lymphoma (Part 2 of 3)

REGIMEN	DOSING
<b>Induction Therapy—Low Risk (continued)</b>	
<p><b>Hyper-CVAD</b> (cyclophosphamide + vincristine + doxorubicin + dexamethasone) <b>alternating with MTX + cytarabine + rituximab</b><sup>1,7,8</sup></p>	<p><b>Cycles 1, 3, 5, and 7</b>  <b>Days 1-3:</b> Cyclophosphamide 300mg/m<sup>2</sup> IV every 12 hrs + mesna 600mg/m<sup>2</sup> continuous IV.  <b>Days 4 and 11:</b> Vincristine 2mg IV.  <b>Day 4:</b> Doxorubicin 50mg/m<sup>2</sup> continuous IV.  <b>Days 1-4 and 11-14:</b> Dexamethasone 40mg IV.  <b>Cycles 1 and 3</b>  <b>Days 1 and 11:</b> Rituximab 375mg/m<sup>2</sup> IV for 8 doses.  <b>Cycles 2, 4, 6, and 8</b>  <b>Day 1:</b> MTX 1g/m<sup>2</sup> continuous IV, <b>followed by</b> leucovorin 50mg IV 12 hrs after completion of MTX, then 15mg IV every 6 hrs for 8 doses.  <b>Days 2 and 3:</b> Cytarabine 3g/m<sup>2</sup> IV every 12 hrs for 4 doses; if age ≤60 years then cytarabine 1mg/m<sup>2</sup>.  <b>Cycles 2 and 4</b>  <b>Days 2 and 8:</b> Rituximab 375mg/m<sup>2</sup> IV for 8 doses.                      Administer G-CSF daily starting 24 hrs after chemotherapy completion.                      Repeat alternating cycles every 2-3 weeks.</p>
<b>Combination Regimens—High-Risk</b>	
<p><b>CALGB 10002</b> (cyclophosphamide and prednisone, <b>followed by</b> cycles containing ifosfamide, <b>OR</b> cyclophosphamide, MTX, leucovorin, vincristine, dexamethasone and either doxorubicin, <b>OR</b> etoposide, <b>OR</b> cytarabine, <b>OR</b> intrathecal triple therapy (MTX, cytarabine, hydrocortisone) + <b>rituximab</b><sup>1,2</sup></p>	<p><b>Cycle 1</b>  <b>Days 1-5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV.  <b>Days 1-7:</b> Prednisone 60mg/m<sup>2</sup> orally.  <b>Cycles 2 (beginning Day 8), 4, and 6</b>  <b>Days 1-5:</b> Ifosfamide 800mg/m<sup>2</sup> IV.  <b>Day 1:</b> MTX 1.5g/m<sup>2</sup> IV (with leucovorin rescue).  <b>Day 1:</b> Vincristine 2mg IV.  <b>Days 4 and 5:</b> Cytarabine 1g/m<sup>2</sup> IV.  <b>Days 4 and 5:</b> Etoposide 80mg/m<sup>2</sup> IV.  <b>Days 1-5:</b> Dexamethasone 10mg/m<sup>2</sup> IV.  <b>Cycles 3, 5, and 7</b>  <b>Days 1-5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV.  <b>Day 1:</b> MTX 1.5g/m<sup>2</sup> IV.  <b>Day 1:</b> Vincristine 2mg IV.  <b>Days 1-5:</b> Dexamethasone 10mg/m<sup>2</sup> IV.  <b>Days 4 and 5:</b> Doxorubicin 25mg/m<sup>2</sup> IV.  <b>Cycle 2</b>  <b>Day 8:</b> Rituximab 50mg/m<sup>2</sup> IV.  <b>Days 10 and 12:</b> Rituximab 375mg/m<sup>2</sup> IV.  <b>Cycles 3-7</b>  <b>Day 8:</b> Rituximab 375mg/m<sup>2</sup> IV.                      Repeat cycles every 3 weeks.  <b>Cycles 2-7 (6 doses)</b>  <b>Day 1:</b> Triple intrathecal therapy for CNS prophylaxis.</p>
<p><b>CODOX-M (original or modified)</b> (cyclophosphamide + doxorubicin + vincristine, <b>plus</b> intrathecal MTX + cytarabine, <b>followed by</b> systemic MTX) <b>alternating with IVAC</b> (ifosfamide + cytarabine + etoposide) <b>and intrathecal MTX ± rituximab</b><sup>1,3,9,10</sup></p>	<p><b>CODOX-M (modified)</b>  <b>Days 1 and 2:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV.  <b>Day 1:</b> Doxorubicin 50mg/m<sup>2</sup> IV + vincristine 1.4mg/m<sup>2</sup> (max dose 2mg) + intrathecal MTX 12mg mixed with cytarabine 50mg.  <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.  <b>Day 3:</b> Intrathecal cytarabine 50mg (<b>For high-risk patients only</b>).  <b>Days 3-8:</b> Administer G-CSF.  <b>Day 10:</b> Vincristine 1.4mg/m<sup>2</sup> (max dose 2mg) + MTX 3g/m<sup>2</sup> IV.  <b>Day 11:</b> Leucovorin 200mg/m<sup>2</sup> IV, <b>followed by</b> 15mg/m<sup>2</sup> IV every 6 hrs.  <b>Day 12:</b> G-CSF restarted if ANC &lt;1,000.                      NOTE: All intrathecal therapy was mixed with 50mg of hydrocortisone.  <b>IVAC</b>  <b>Day 1:</b> Cytarabine 2g/m<sup>2</sup> IV every 12 hrs for 4 doses.  <b>Days 1-5:</b> Etoposide 60mg/m<sup>2</sup> IV + ifosfamide 1,500mg/m<sup>2</sup> IV, <b>plus</b> mesna.  <b>Day 5:</b> Intrathecal MTX 12mg, <b>followed by</b> leucovorin 24 hrs later.  <b>Day 6:</b> Administer G-CSF.                      Repeat for 4 cycles alternating between CODOX-M and IVAC regimens.</p>

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## NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Burkitt Lymphoma (Part 3 of 3)

REGIMEN	DOSING
<b>Combination Regimens—High-Risk (continued)</b>	
<p><b>Dose-adjusted EPOCH</b> (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + <b>intrathecal MTX + rituximab</b><sup>1,4-6</sup></p> <p>NOTE: For patients without CNS disease.</p>	<p><b>Days 1-4:</b> Etoposide 50mg/m<sup>2</sup> continuous IV + doxorubicin 10mg/m<sup>2</sup> continuous IV + vincristine 0.4mg/m<sup>2</sup> continuous IV.  <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.  <b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily.  <b>Day 5:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV.  <b>Day 6:</b> G-CSF administered until ANC &gt;5 x 10<sup>9</sup>/L.                      Intrathecal MTX for 6 doses.                      Repeat for 6 cycles every 3 weeks</p>
<p><b>Hyper-CVAD</b> (cyclophosphamide + vincristine + doxorubicin + dexamethasone) <b>alternating with MTX + cytarabine + rituximab</b><sup>1,7,8</sup></p>	<p><b>Cycles 1, 3, 5, and 7</b>  <b>Days 1-3:</b> Cyclophosphamide 300mg/m<sup>2</sup> IV every 12 hrs + mesna 600mg/m<sup>2</sup> continuous IV.  <b>Days 4 and 11:</b> Vincristine 2mg IV.  <b>Day 4:</b> Doxorubicin 50mg/m<sup>2</sup> continuous IV.  <b>Days 1-4 and 11-14:</b> Dexamethasone 40mg IV.  <b>Cycles 1 and 3</b>  <b>Days 1 and 11:</b> Rituximab 375mg/m<sup>2</sup> IV for 8 doses.  <b>Cycles 2, 4, 6, and 8</b>  <b>Day 1:</b> MTX 1g/m<sup>2</sup> continuous IV, <b>followed by</b> leucovorin 50mg IV 12 hrs after completion of MTX, <b>followed by</b> 15mg IV every 6 hrs for 8 doses.  <b>Days 2 and 3:</b> Cytarabine 3g/m<sup>2</sup> IV every 12 hrs for 4 doses; if age ≤60 years then cytarabine 1mg/m<sup>2</sup>.  <b>Cycles 2 and 4</b>  <b>Days 2 and 8:</b> Rituximab 375mg/m<sup>2</sup> IV for 8 doses.                      Administer G-CSF daily starting 24 hrs after chemotherapy completion.                      Repeat alternating cycles every 2-3 weeks.</p>
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