

# B-cell Lymphomas: Burkitt Lymphoma Treatment Regimens

**Clinical Trials:** The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

**Note:** All recommendations are category 2A unless otherwise indicated.

## ► Induction Therapy: Low-Risk Regimens — Age <60 years<sup>1,a</sup>

REGIMEN	DOSING
<b>Preferred Regimens</b>	
CODOX-M + Rituximab (modified) <sup>2,3,b,c</sup>	<p><b>Days 1-2:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV over 30 minutes daily.</p> <p><b>Days 1 and 10:</b> Vincristine 1.4mg/m<sup>2</sup> (maximum 2 mg) IV over 5-10 minutes.</p> <p><b>Day 1:</b> Doxorubicin 50mg/m<sup>2</sup> IV push.</p> <p><b>Day 10:</b> Methotrexate 3,000mg/m<sup>2</sup> IV over 4 hours.</p> <p><b>Day 11:</b> Leucovorin 200mg/m<sup>2</sup> IV over 15 minutes (starting 24 hours after initiation of methotrexate), <b>followed by:</b></p> <p>Leucovorin 15mg/m<sup>2</sup> orally <b>or</b> IV over 15 minutes every 6 hours (until methotrexate level is &lt;0.05micromol/L).</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Cytarabine 50mg intrathecally.</p> <p><b>Day 1:</b> Methotrexate 12mg intrathecally.</p> <p>Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 3 cycles.</p>
CODOX-M + Rituximab (original) <sup>3,4,b,c</sup>	<p><b>Day 1:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV over 30 minutes, <b>followed by:</b></p> <p><b>Days 2-5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV over 30 minutes daily.</p> <p><b>Days 1 and 8:</b> Vincristine 1.5mg/m<sup>2</sup> (maximum 2 mg) IV over 5-10 minutes.</p> <p><b>Day 1:</b> Doxorubicin 40mg/m<sup>2</sup> IV push.</p> <p><b>Day 10:</b> Methotrexate 1,200mg/m<sup>2</sup> IV over 1 hour, <b>followed by:</b></p> <p>Methotrexate 5,520mg/m<sup>2</sup> IV continuous infusion over 23 hours.</p> <p><b>Day 11:</b> Leucovorin 192mg/m<sup>2</sup> IV over 15 minutes (starting 36 hours after initiation of methotrexate), <b>followed by:</b></p> <p>Leucovorin 12mg/m<sup>2</sup> orally <b>or</b> IV over 15 minutes every 6 hours (until methotrexate level &lt;0.05micromol/L).</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 3:</b> Cytarabine 70mg intrathecally.</p> <p><b>Day 15:</b> Methotrexate 12mg intrathecally.</p> <p>Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 3 cycles.</p>
Dose-adjusted EPOCH+ Rituximab (CNS negative disease) <sup>5,6,c-e</sup>	<p><b>Days 1–4 (Cycle 1):</b> Etoposide 50mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Etoposide IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle), <b>concurrent with:</b></p> <p><b>Days 1-4:</b> Vincristine 0.4mg/m<sup>2</sup> IV continuous infusion over 24 hours daily <b>concurrent with:</b></p> <p><b>Days 1-4 (Cycle 1):</b> Doxorubicin 10mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Doxorubicin IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Day 5 (Cycle 1):</b> Cyclophosphamide 750mg/m<sup>2</sup> IV over 30 minutes.</p> <p><b>Day 5 (Cycles 2 and beyond):</b> Cyclophosphamide IV over 30 minutes (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 5:</b> Methotrexate 12mg intrathecally beginning with cycle 1 for 8 total doses.</p> <p>Repeat cycle every 3 weeks for 3 cycles (if interim positron emission tomography scan after 2 cycles is negative) for a minimum of 3 cycles with 1 additional cycle beyond complete response.</p>

continued

# B-cell Lymphomas: Burkitt Lymphoma Treatment Regimens

## ► Induction Therapy: Low-Risk Regimens — Age <60 years<sup>1,a</sup> (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
HyperCVAD Alternating with High-Dose Methotrexate and Cytarabine + Rituximab <sup>7b,e,f</sup>	<p><b>Cycle A</b> <b>Days 1-3:</b> Cyclophosphamide 300mg/m<sup>2</sup> IV over 3 hours every 12 hours for 6 doses. <b>Days 1-3:</b> Mesna 600mg/m<sup>2</sup> IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of cyclophosphamide and completing 12 hours after the last dose of cyclophosphamide is started. <b>Days 4 and 11:</b> Vincristine 2mg IV over 5-10 minutes. <b>Day 4:</b> Doxorubicin 50mg/m<sup>2</sup> IV continuous infusion over 24 hours. <b>Days 1-4 and 11-14:</b> Dexamethasone 40mg IV or orally daily. <b>Days 1:</b> Rituximab 375mg/m<sup>2</sup> IV. <b>Day 2:</b> Methotrexate 12 mg intrathecally. <b>Day 7:</b> Cytarabine 100 mg intrathecally. Repeat cycle every 3 weeks (earlier if count recovery occurs; minimum of 2 weeks) for 4 cycles alternating with Cycle B for a total of 8 cycles.</p> <p><b>Cycle B</b> <b>Day 1:</b> Methotrexate 200mg/m<sup>2</sup> IV over 2 hours, <b>immediately followed by:</b> Methotrexate 800mg/m<sup>2</sup> IV continuous infusion over 22 hours. <b>Day 2:</b> Leucovorin 50mg IV over 15 minutes (starting 12 hours after completion of the 22-hour methotrexate infusion), <b>followed by:</b> Leucovorin 15mg orally or IV over 15 minutes every 6 hours for at least 8 doses (until methotrexate level &lt;0.05micromol/L). <b>Days 2-3:</b> Cytarabine 3,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses. <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV. <b>Day 2:</b> Methotrexate 12mg intrathecally. <b>Day 7:</b> Cytarabine 100mg intrathecally. Repeat cycle every 3 weeks (earlier if count recovery occurs; minimum of 2 weeks) for 4 cycles alternating with Cycle A for a total of 8 cycles.</p>

## ► Induction Therapy: High-Risk Regimens — Age <60 years<sup>1,a</sup>

Preferred Regimens (High-risk patients presenting with symptomatic CNS disease should be started with the portion of the systemic therapy that contains CNS penetrating drugs.)	
CODOX-M (modified) + Rituximab Alternating with IVAC + Rituximab <sup>2,4,b,c,e,g</sup>	<p><b>Cycle A</b> <b>Days 1-2:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV over 30 minutes daily. <b>Days 1 and 10:</b> Vincristine 1.4mg/m<sup>2</sup> (maximum 2mg) IV over 5-10 minutes. <b>Day 1:</b> Doxorubicin 50mg/m<sup>2</sup> IV push. <b>Day 10:</b> Methotrexate 3,000mg/m<sup>2</sup> IV over 4 hours. <b>Day 11:</b> Leucovorin 200mg/m<sup>2</sup> IV over 15 minutes (starting 24 hours after initiation of methotrexate), <b>followed by:</b> Leucovorin 15mg/m<sup>2</sup> orally or IV over 15 minutes every 6 hours (until methotrexate level is &lt;0.05micromol/L). <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV. <b>Days 1 and 3:</b> Cytarabine 50mg intrathecally. <b>Day 1:</b> Methotrexate 12mg intrathecally. Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 2 cycles alternating with IVAC + R (Cycle B) for a total of 4 cycles.</p> <p><b>Cycle B</b> <b>Days 1-5:</b> Ifosfamide 1,500mg/m<sup>2</sup> IV over 3 hours daily. <b>Days 1-5:</b> Mesna 500mg/m<sup>2</sup> IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose). <b>Days 1-5:</b> Etoposide 60mg/m<sup>2</sup> IV over 1 hour daily <b>Days 1-2:</b> Cytarabine 2,000 mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses. <b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV. <b>Day 5:</b> Methotrexate 12mg intrathecally. Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 2 cycles alternating with CODOX-M + R (Cycle A) for a total of 4 cycles.</p>

continued

# B-cell Lymphomas: Burkitt Lymphoma Treatment Regimens

## ► Induction Therapy: High-Risk Regimens — Age <60 years<sup>1,a</sup> (continued)

REGIMEN	DOSING
Preferred Regimens (High-risk patients presenting with symptomatic CNS disease should be started with the portion of the systemic therapy that contains CNS penetrating drugs.) (continued)	
CODOX-M (original) + Rituximab Alternating with IVAC + Rituximab <sup>2-4,b,c,e,g</sup>	<p><b>Cycle A</b></p> <p><b>Day 1:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV over 30 minutes, <b>followed by:</b></p> <p><b>Days 2-5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV over 30 minutes daily.</p> <p><b>Days 1 and 8:</b> Vincristine 1.5mg/m<sup>2</sup> (maximum 2mg) IV over 5-10 minutes.</p> <p><b>Day 1:</b> Doxorubicin 40mg/m<sup>2</sup> IV push.</p> <p><b>Day 10:</b> Methotrexate 1,200mg/m<sup>2</sup> IV over 1 hour, <b>followed by:</b> Methotrexate 5,520mg/m<sup>2</sup> IV continuous infusion over 23 hours.</p> <p><b>Day 11:</b> Leucovorin 192mg/m<sup>2</sup> IV over 15 minutes starting 36 hours from the initiation of the first methotrexate infusion, <b>followed by:</b> Leucovorin 12mg/m<sup>2</sup> orally or IV over 15 minutes every 6 hours (until methotrexate level &lt;0.05 micromol/L).</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 3:</b> Cytarabine 70mg intrathecally.</p> <p><b>Day 15:</b> Methotrexate 12mg intrathecally.</p> <p>Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 2 cycles alternating with IVAC + R (Cycle B) for a total of 4 cycles.</p> <p><b>Cycle B</b></p> <p><b>Days 1-5:</b> Ifosfamide 1,500mg/m<sup>2</sup> IV over 3 hours daily.</p> <p><b>Days 1-5:</b> Mesna 500mg/m<sup>2</sup> IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose).</p> <p><b>Days 1-5:</b> Etoposide 60mg/m<sup>2</sup> IV over 1 hour daily.</p> <p><b>Days 1-2:</b> Cytarabine 2,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 5:</b> Methotrexate 12mg intrathecally.</p> <p>Repeat cycle every 4 weeks (or when post-nadir ANC is ≥1000 cells/mm<sup>3</sup>) for 2 cycles alternating with CODOX-M + R (Cycle A) for a total of 4 cycles.</p>
HyperCVAD Alternating with High-Dose Methotrexate and Cytarabine + Rituximab <sup>7,b,e,f</sup>	<p><b>Cycle A</b></p> <p><b>Days 1-3:</b> Cyclophosphamide 300mg/m<sup>2</sup> IV over 3 hours every 12 hours for 6 doses.</p> <p><b>Days 1-3:</b> Mesna 600mg/m<sup>2</sup> IV continuous infusion over 24 hours daily starting 15 minutes before the first dose of cyclophosphamide and completing 12 hours after the last dose of cyclophosphamide is started</p> <p><b>Days 4 and 11:</b> Vincristine 2mg IV over 5-10 minutes.</p> <p><b>Day 4:</b> Doxorubicin 50mg/m<sup>2</sup> IV continuous infusion over 24 hours.</p> <p><b>Days 1-4 and 11-14:</b> Dexamethasone 40mg IV or orally daily</p> <p><b>Days 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 2:</b> Methotrexate 12mg intrathecally.</p> <p><b>Day 7:</b> Cytarabine 100mg intrathecally.</p> <p>Repeat cycle every 3 weeks (earlier if count recovery occurs; minimum of 2 weeks) for 4 cycles alternating with Cycle B for a total of 8 cycles.</p> <p><b>Cycle B</b></p> <p><b>Day 1:</b> Methotrexate 200mg/m<sup>2</sup> IV over 2 hours, <b>immediately followed by:</b> Methotrexate 800mg/m<sup>2</sup> IV continuous infusion over 22 hours.</p> <p><b>Day 2:</b> Leucovorin 50mg IV over 15 minutes (starting 12 hours after completion of the 22-hour methotrexate infusion), <b>followed by:</b> Leucovorin 15mg orally or IV over 15 minutes every 6 hours for at least 8 doses (until methotrexate level &lt;0.05micromol/L).</p> <p><b>Days 2-3:</b> Cytarabine 3,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 2:</b> Methotrexate 12mg intrathecally.</p> <p><b>Day 7:</b> Cytarabine 100mg intrathecally.</p> <p>Repeat cycle every 3 weeks (earlier if count recovery occurs; minimum of 2 weeks) for 4 cycles alternating with Cycle A for a total of 8 cycles.</p>

continued

# B-cell Lymphomas: Burkitt Lymphoma Treatment Regimens

## ► Induction Therapy: High-Risk Regimens — Age <60 years<sup>1,a</sup> (continued)

REGIMEN	DOSING
<b>Other Recommended Regimens</b>	
Dose-adjusted EPOCH+ Rituximab (for high-risk patients with baseline CNS disease not able to tolerate aggressive treatments) <sup>5,6,c-e</sup>	<p><b>Days 1–4 (Cycle 1):</b> Etoposide 50mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Etoposide IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle), <b>concurrent with:</b></p> <p><b>Days 1-4:</b> Vincristine 0.4mg/m<sup>2</sup> IV continuous infusion over 24 hours daily <b>concurrent with:</b></p> <p><b>Days 1-4 (Cycle 1):</b> Doxorubicin 10mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Doxorubicin IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Day 5 (Cycle 1):</b> Cyclophosphamide 750mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Day 5 (Cycles 2 and beyond):</b> Cyclophosphamide IV over 30 minutes (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 5:</b> Methotrexate 12mg intrathecally beginning with Cycle 1 for 8 total doses.</p> <p>Repeat cycle every 3 weeks for 6 cycles.</p>

## ► Induction Therapy: Low- and High-Risk Regimens, Age ≥60 years<sup>1,a</sup>

<b>Preferred Regimen (High-risk patients presenting with symptomatic CNS disease should be started with the portion of the systemic therapy that contains CNS penetrating drugs.)</b>	
Dose-adjusted EPOCH+ Rituximab <sup>5,6,c-e</sup>	<p><b>Days 1–4 (Cycle 1):</b> Etoposide 50mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Etoposide IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle), <b>concurrent with:</b></p> <p><b>Days 1-4:</b> Vincristine 0.4mg/m<sup>2</sup> IV continuous infusion over 24 hours daily <b>concurrent with:</b></p> <p><b>Days 1-4 (Cycle 1):</b> Doxorubicin 10mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Doxorubicin IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p><b>Day 5 (Cycle 1):</b> Cyclophosphamide 750mg/m<sup>2</sup> IV over 30 minutes</p> <p><b>Day 5 (Cycles 2 and beyond):</b> Cyclophosphamide IV over 30 minutes (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV</p> <p><b>Days 1 and 5:</b> Methotrexate 12mg intrathecally beginning with Cycle 1 for 8 total doses.</p> <p>Repeat cycle every 3 weeks for 3 cycles (if interim positron emission tomography scan after 2 cycles is negative) for a minimum of 3 cycles with 1 additional cycle beyond complete response for low-risk disease or repeat cycle every 3 weeks for 6 cycles for high-risk disease.</p>

## ► Second Line Therapy<sup>1,a</sup>

<b>Other Recommended Agents</b>	
Dose-adjusted EPOCH+ Rituximab <sup>5,6,c-e</sup>	<p><b>Days 1-4 (Cycle 1):</b> Etoposide 50mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Etoposide IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle), <b>concurrent with:</b></p> <p><b>Days 1-4:</b> Vincristine 0.4mg/m<sup>2</sup> IV continuous infusion over 24 hours daily <b>concurrent with:</b></p> <p><b>Days 1-4 (Cycle 1):</b> Doxorubicin 10mg/m<sup>2</sup> IV continuous infusion over 24 hours daily, <b>followed by:</b></p> <p><b>Days 1-4 (Cycles 2 and beyond):</b> Doxorubicin IV continuous infusion over 24 hours daily (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Day 5 (Cycle 1):</b> Cyclophosphamide 750mg/m<sup>2</sup> IV over 30 minutes.</p> <p><b>Day 5 (Cycles 2 and beyond):</b> Cyclophosphamide IV over 30 minutes (dose based on absolute neutrophil count and platelet nadir measurements during the previous cycle).</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> orally twice daily.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 5:</b> Methotrexate 12mg intrathecally beginning with Cycle 1 for 8 total doses.</p> <p>Repeat cycle every 3 weeks for 6 cycles for a minimum of 3 cycles with 1 additional cycle beyond complete response.</p>

continued

# B-cell Lymphomas: Burkitt Lymphoma Treatment Regimens

## ► Second Line Therapy<sup>1,a</sup> (continued)

REGIMEN	DOSING
<b>Other Recommended Agents</b> (continued)	
RICE <sup>8,9,c,e,h</sup>	<p><b>Days 1-3:</b> Etoposide 100mg/m<sup>2</sup> IV over 1 hour daily.</p> <p><b>Day 2:</b> Ifosfamide 5,000mg/m<sup>2</sup> IV continuous infusion over 24 hours, <b>concurrent with:</b></p> <p><b>Day 2:</b> Mesna 5,000mg/m<sup>2</sup> IV continuous infusion over 24 hours.</p> <p><b>Day 2:</b> Carboplatin AUC 5 IV over 30 minutes.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 3:</b> Methotrexate 15mg intrathecally (if not previously given during first-line therapy). Repeat cycle every 2 weeks for 3 cycles.</p>
RIVAC <sup>2,3,c,e,i</sup>	<p><b>Days 1-5:</b> Ifosfamide 1,500mg/m<sup>2</sup> IV over 3 hours daily.</p> <p><b>Days 1-5:</b> Mesna 500mg/m<sup>2</sup> IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose).</p> <p><b>Days 1-5:</b> Etoposide 60mg/m<sup>2</sup> IV over 1 hour daily.</p> <p><b>Days 1-2:</b> Cytarabine 2,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses (age &lt;60 years)</p> <p><b>OR</b></p> <p>Cytarabine 1,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses (age &gt;60 years).</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 5:</b> Methotrexate 12mg intrathecally (if not previously given during first-line therapy). Repeat cycle every 4 weeks for 4 cycles.</p>
<b>Useful in certain circumstances</b>	
High-dose Cytarabine + Rituximab <sup>10,c,e</sup>	<p><b>Days 1-2:</b> Cytarabine 3,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses (age ≤60 years)</p> <p><b>OR</b></p> <p>Cytarabine 2,000mg/m<sup>2</sup> IV over 3 hours every 12 hours for 4 doses (age &gt;60 years).</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Methotrexate 12mg intrathecally (if not previously given during first-line therapy). Repeat cycle every 3 weeks for 4 cycles.</p>
RGDP <sup>11,c,e,j</sup>	<p><b>Days 1 and 8:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes.</p> <p><b>Days 1-4:</b> Dexamethasone 40mg IV or orally daily.</p> <p><b>Day 1:</b> Cisplatin 75mg/m<sup>2</sup> IV over 1 hour.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Methotrexate 12mg intrathecally (if not previously given during first-line therapy). Repeat cycle every 3 weeks for 6 cycles.</p>

<sup>a</sup> All regimens for Burkitt lymphoma include central nervous system (CNS) prophylaxis/therapy.

<sup>b</sup> CODOX-M = Cyclophosphamide, doxorubicin, vincristine with intrathecal and systemic methotrexate and cytarabine.

<sup>c</sup> The recommended infusion rate of rituximab for the first dose is 50mg/hour, increased by 50mg/hour every 30 minutes until a maximum infusion rate of 400mg/hour is reached. Rapid-infusion may be administered to patients who meet the criteria. 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.

<sup>d</sup> EPOCH = Etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin.

<sup>e</sup> Some patients may present with CNS disease at diagnosis or recurrence. If a patient has active CNS disease, modifications to this regimen may be needed including additional intrathecal therapy and/or CNS-penetrating high-dose chemotherapy. The frequency and duration of therapy are dependent on the patient's CNS disease status and risk of CNS relapse.

<sup>f</sup> HyperCVAD = Cyclophosphamide, vincristine, doxorubicin, and dexamethasone.

<sup>g</sup> IVAC + R = Ifosfamide, cytarabine, etoposide + rituximab.

<sup>h</sup> RICE = Rituximab, ifosfamide, carboplatin, etoposide.

<sup>i</sup> RIVAC = Rituximab, ifosfamide, cytarabine, etoposide.

<sup>j</sup> RGDP = Rituximab, gemcitabine, dexamethasone, cisplatin.

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## References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-cell Lymphomas V.2.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/occult.pdf](https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf). Accessed April 9, 2022.
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