

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

Burkitt Lymphoma (Part 1 of 3)

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 NCCN 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 National Comprehensive Cancer Network 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.

Induction Therapy—Low Risk^{1*}

Note: All recommendations are Category 2A unless otherwise indicated.

REGIMEN	DOSING
CALGB 10002²	<p>Cycle 1: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Cyclophosphamide 200mg/m² IV Days 1–7: Prednisone 60mg/m² orally.</p> <p>Cycles 2 (beginning Day 8), 4, and 6: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Ifosfamide 800mg/m² IV + dexamethasone 10mg/m² IV Day 1: Methotrexate 1.5g/m² IV (with leucovorin rescue) + vincristine 2mg IV Days 4 and 5: Cytarabine 1g/m² IV + etoposide 80mg/m² IV Day 8: Rituximab 50mg/m² IV for cycle 2, then 375mg/m² IV for cycles 4 and 6 Days 10 and 12 (Cycle 2 only): Rituximab 375mg/m² IV.</p> <p>Cycles 3, 5, and 7: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Cyclophosphamide 200mg/m² IV + dexamethasone 10mg/m² IV Day 1: Methotrexate 1.5g/m² IV + vincristine 2mg IV Days 4 and 5: Doxorubicin 25mg/m² IV Day 8: Rituximab 375mg/m² IV. Deliver cycles every 21 days.</p>
CODOX-M (original or modified) (cyclophosphamide + doxorubicin + vincristine with intrathecal MTX + cytarabine, followed by systemic MTX and cytarabine) ± rituximab³	<p>Day 1: Cyclophosphamide 800mg/m² IV + doxorubicin 40mg/m² IV Days 2–5: Cyclophosphamide 200mg/m²/day IV Days 1 and 3: Cytarabine 70mg intrathecally Days 1 and 8: Vincristine 1.5mg/m² IV Day 10: Methotrexate 1,200mg/m² IV over 1 hour, then 240mg/m²/hour continuous IV infusion for the next 23 hours Day 11: Leucovorin 192mg/m² IV 36 hours after initiation of MTX, followed by leucovorin 12mg/m² IV every 6 hours until MTX level <5 × 10⁻⁸ M Day 13: G-CSF 5µg/kg SC daily beginning 24 hours after initiation of leucovorin until absolute granulocyte count ≥1 × 10⁹/L Day 15: Methotrexate 12mg intrathecally Day 16: Leucovorin 15mg orally given 24 hours after intrathecal MTX, ± Day 1: Rituximab 375mg/m² IV. Repeat cycle every 21 days for 3 cycles.</p>
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + intrathecal MTX + rituximab^{4-6†}	<p>Day 1: Rituximab 375mg/m² IV Days 1–4: Etoposide 50mg/m² continuous IV infusion + doxorubicin 10mg/m² continuous IV infusion + vincristine 0.4mg/m² continuous IV infusion Days 1–5: Prednisone 60mg/m² orally twice daily. Day 5: Cyclophosphamide 750mg/m² IV Day 6: G-CSF 300µg administered until ANC >5,000cells/µL Days 1 and 5 (Cycles 3–6): Methotrexate 12mg intrathecally. Repeat cycle every 3 weeks for 6 cycles.</p>
HyperCVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone alternating with high-dose methotrexate and cytarabine)^{7,8}	<p>Cycles 1, 3, 5, and 7—HyperCVAD Days 1–3: Cyclophosphamide 300mg/m² IV every 12 hours for 6 doses + mesna 600mg/m² continuous IV infusion Days 4 and 11: Vincristine 2mg IV Day 4: Doxorubicin 50mg/m² IV Days 1–4 and Days 11–14: Dexamethasone 40mg IV daily Days 1 and 11 (Cycles 1 and 3 only): Rituximab 375mg/m² IV.</p> <p>Cycles 2, 4, 6, 8—High-dose MTX and Cytarabine Day 1: MTX 1g/m² IV over 24 hours Days 2 and 3: Cytarabine 3g/m² IV every 12 hours for 4 doses Days 2 and 8 (Cycles 2 and 4): Rituximab 375mg/m² IV. Repeat every 3 weeks for 8 cycles.</p>

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

Burkitt Lymphoma (Part 2 of 3)

Combination Regimens—High-Risk^{1*}

REGIMEN	DOSING
CALGB 10002²	<p>Cycle 1: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Cyclophosphamide 200mg/m² IV Days 1–7: Prednisone 60mg/m² orally.</p> <p>Cycles 2 (beginning Day 8), 4, and 6: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Ifosfamide 800mg/m² IV + dexamethasone 10mg/m² IV Day 1: Methotrexate 1.5g/m² IV (with leucovorin rescue) + vincristine 2mg IV Days 4 and 5: Cytarabine 1g/m² IV + etoposide 80mg/m² IV Day 8: Rituximab 50mg/m² IV for cycle 2, then 375mg/m² IV for cycles 4 and 6 Days 10 and 12 (Cycle 2 only): Rituximab 375mg/m² IV.</p> <p>Cycles 3, 5, and 7: Day 1: Triple intrathecal therapy for CNS prophylaxis Days 1–5: Cyclophosphamide 200mg/m² IV + dexamethasone 10mg/m² IV Day 1: Methotrexate 1.5g/m² IV + vincristine 2mg IV Days 4 and 5: Doxorubicin 25mg/m² IV Day 8: Rituximab 375mg/m² IV. Deliver cycles every 21 days.</p>
CODOX-M (original or modified) (cyclophosphamide + doxorubicin + vincristine, plus intrathecal MTX + cytarabine, followed by systemic MTX) alternating with IVAC (ifosfamide + cytarabine + etoposide) and intrathecal MTX ± rituximab^{3,9,10}	<p>Day 1: Cyclophosphamide 800mg/m² IV + doxorubicin 40mg/m² IV Days 2–5: Cyclophosphamide 200mg/m²/day IV Days 1 and 3: Cytarabine 70mg intrathecally Days 1 and 8: Vincristine 1.5mg/m² IV Day 10: Methotrexate 1,200mg/m² IV over 1 hour, then 240mg/m²/hour continuous IV infusion for the next 23 hours Day 11: Leucovorin 192mg/m² IV 36 hours after initiation of MTX, followed by leucovorin 12mg/m² IV every 6 hours until MTX level <5 × 10⁻⁸ M Day 13: G-CSF 5µg/kg SC daily beginning 24 hours after initiation of leucovorin until absolute granulocyte count ≥1 × 10⁹/L Day 15: Methotrexate 12mg intrathecally Day 16: Leucovorin 15mg orally given 24 hours after intrathecal MTX, ± Day 1: Rituximab 375mg/m² IV.</p> <p>Alternate Cycles With: Day 1: Cytarabine 2g/m² IV every 12 hours for 4 doses. Days 1–5: Etoposide 60mg/m² IV + ifosfamide 1,500mg/m² IV, plus mesna 360mg/m² Day 5: Methotrexate 12mg intrathecally Day 6: Leucovorin 15mg orally 24 hours after intrathecal MTX Day 7: G-CSF 5µg/kg SC daily until absolute granulocyte count ≥1 × 10⁹/L, ± Day 1: Rituximab 375 mg/m² IV. Repeat for 4 cycles alternating between CODOX-M and IVAC regimens.</p>
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + intrathecal MTX + rituximab^{4,6†}	<p>Day 1: Rituximab 375mg/m² IV Days 1–4: Etoposide 50mg/m² continuous IV infusion + doxorubicin 10mg/m² continuous IV infusion + vincristine 0.4mg/m² continuous IV infusion Days 1–5: Prednisone 60mg/m² orally twice daily Day 5: Cyclophosphamide 750mg/m² IV Day 6: G-CSF 300µg administered until ANC >5,000cells/µL Days 1 and 5 (Cycles 3–6): Methotrexate 12mg intrathecally. Repeat cycle every 3 weeks for 6 cycles.</p>
HyperCVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab^{7,8}	<p>Cycles 1, 3, 5, and 7—HyperCVAD Days 1–3: Cyclophosphamide 300mg/m² IV every 12 hours for 6 doses + mesna 600mg/m² continuous IV infusion Days 4 and 11: Vincristine 2mg IV Day 4: Doxorubicin 50mg/m² IV Days 1–4 and Days 11–14: Dexamethasone 40mg IV daily Days 1 and 11 (Cycles 1 and 3 only): Rituximab 375mg/m² IV</p> <p>Cycles 2, 4, 6, 8—High-dose MTX and Cytarabine Day 1: MTX 1g/m² IV over 24 hours Days 2 and 3: Cytarabine 3g/m² IV every 12 hours for 4 doses Days 2 and 8 (Cycles 2 and 4): Rituximab 375mg/m² IV. Repeat every 3 weeks for 8 cycles.</p>

continued

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

Second Line Therapy^{1*}

REGIMEN	DOSING
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + intrathecal MTX + rituximab^{4-6†}	<p>Day 1: Rituximab 375mg/m² IV</p> <p>Days 1-4: Etoposide 50mg/m² continuous IV infusion + doxorubicin 10mg/m² continuous IV infusion + vincristine 0.4mg/m² continuous IV infusion</p> <p>Days 1-5: Prednisone 60mg/m² orally twice daily</p> <p>Day 5: Cyclophosphamide 750mg/m² IV</p> <p>Day 6: G-CSF 300µg administered until ANC >5,000cells/µL</p> <p>Days 1 and 5 (Cycles 3-6): Methotrexate 12mg intrathecally. Repeat cycle every 3 weeks for 6 cycles.</p>
RICE (rituximab + ifosfamide + carboplatin + etoposide)¹¹	<p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 2: Ifosfamide 5,000mg/m² and Mesna 5,000mg/m² IV + carboplatin AUC 5 mg • min/ mL (maximum 800mg) IV</p> <p>Day 1-3: Etoposide 100mg/m² IV. Repeat cycle every 3 weeks.</p>
RIVAC (rituximab + ifosfamide + cytarabine + etoposide)¹⁰	<p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 1: Cytarabine 2g/m² IV every 12 hours for 4 doses</p> <p>Days 1-5: Etoposide 60mg/m² IV + ifosfamide 1,500mg/m² IV, plus mesna 360mg/m²</p> <p>Day 5: Methotrexate 12mg intrathecally</p> <p>Day 6: Leucovorin 15mg orally 24 hours after intrathecal MTX</p> <p>Day 7: G-CSF 5µg/kg SC daily until absolute granulocyte count ≥1 × 10⁹/L. Repeat cycle every 3 weeks.</p>
RGDP (rituximab + gemcitabine + dexamethasone + cisplatin)¹²	<p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 1 and 8: Gemcitabine 1,000mg/m² IV</p> <p>Day 1-3: Cisplatin 25mg/m² IV</p> <p>Day 1-4: Dexamethasone 40mg IV. Repeat cycle every 3 weeks.</p>
HDAC¹³	<p>Days 1, 3, and 5: High-dose cytarabine 3g/m² IV every 12 hours. Repeat for 4 cycles.</p>

* All regimens for Burkitt lymphoma include CNS prophylaxis/therapy.

† For patients without CNS disease

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