HODGKIN LYMPHOMA TREATMENT REGIMENS (Part 1 of 5)

Clinical Trials: The National Comprehensive Cancer Network 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 health care 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 provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become 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 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.

Classical Hodgkin Lymphoma[1]

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

Primary Treatment

Stage IA, IIA Favorable (No Bulky Disease, <3 Sites of Disease, ESR <50, and No E-lesions)

REGIMEN	DOSING
Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD) (Category 1)[2-5]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles followed by radiation therapy.
ABVD (Preference to treat with chemotherapy alone)[2-5]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 3 cycles.
ABVD (Preference to treat with combined modality therapy)[2-5]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles.
Doxorubicin + Vinblastine + Mechlorethamine + Etoposide + Vincristine + Bleomycin + Prednisone (Stanford V)[6-9]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes **Day 1:** Mechlorethamine 6mg/m² IV push **Days 8 and 22:** Vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes + bleomycin 5units/m² IV push **Days 15 and 16:** Etoposide 60mg/m² IV over 60 minutes **Days 1–28:** Prednisone 40mg/m² orally every other day. Taper prednisone dose by 10mg every other day beginning Day 15 of Cycle 2. Repeat cycle every 4 week for 2 cycles followed by radiation therapy, optimally within 3 weeks of chemotherapy completion.

Stage I–II Unfavorable (Bulky or Non-bulky Disease)

Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD)(Category 1 for Bulky Disease)[2-5]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Bulky or non-bulky disease: Repeat cycle every 4 weeks for 4-6 cycles total of ABVD or 4 cycles of AVD with or without subsequent radiation therapy (category 1 for bulky disease); or, for select patients younger than 60 years, repeat for 2 cycles, following 2 cycles of escalated BEACOPP, with or without subsequent radiation therapy.
Doxorubicin + Vinblastine + Mechlorethamine + Etoposide + Vincristine + Bleomycin + Prednisone (Stanford V)[6-9]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes **Day 1:** Mechlorethamine 6mg/m² IV push **Days 8 and 22:** Vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes + bleomycin 5units/m² IV push **Days 15 and 16:** Etoposide 60mg/m² IV over 60 minutes **Days 1–28:** Prednisone 40mg/m² orally every other day. Taper prednisone dose by 10mg every other day beginning Day 15 of Cycle 3. Repeat cycle every 4 weeks for 3 cycles with or without subsequent radiation therapy.
Bleomycin + Etoposide + Doxorubicin + Cyclophosphamide + Vincristine + Procarbazine + Prednisone (Escalated BEACOPP) (In selected patients if IPS≥4, age <60)[10,11]	**Day 1:** Cyclophosphamide 1,250mg/m² IV over 60 minutes + doxorubicin 35mg/m² IV push **Days 1–3:** Etoposide 200mg/m² IV over 2 hours **Days 1–7:** Procarbazine 100mg/m² orally. **Day 8:** Vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes + bleomycin 10units/m² IV push. **Days 1–14:** Prednisone 40mg/m² orally daily. Repeat cycle every 3 weeks for 2 cycles followed by ABVD for 2 cycles and then by radiation therapy.

continued

HODGKIN LYMPHOMA TREATMENT REGIMENS (Part 2 of 5)

Classical Hodgkin Lymphoma[1] (continued)

Primary Treatment (continued)

Stage III–IV

REGIMEN	DOSING
Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD)[2-5]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles followed by 4 cycles of AVD or 4 cycles of escalated BEACOPP, cycles with or without subsequent radiation.
Doxorubicin + Vinblastine + Mechlorethamine + Etoposide + Vincristine + Bleomycin + Prednisone (Stanford V) (In selected patients if IPS ≤3)[6-9]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes **Day 1:** Mechlorethamine 6mg/m² IV push **Days 8 and 22:** Vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes + bleomycin 5units/m² IV push **Days 15 and 16:** Etoposide 60mg/m² IV over 60 minutes **Days 1–28:** Prednisone 40mg/m² orally every other day. Taper prednisone dose by 10mg every other day beginning Day 15 of Cycle 3. Repeat cycle every 4 weeks for 3 cycles with or without subsequent radiation therapy.
Bleomycin + Etoposide + Doxorubicin + Cyclophosphamide + Vincristine + Procarbazine + Prednisone (Escalated BEACOPP) (In selected patients if IPS≥4, age <60)[10,11]	**Day 1:** Cyclophosphamide 1,250mg/m² IV over 60 minutes + doxorubicin 35mg/m² IV push **Days 1–3:** Etoposide 200mg/m² IV over 2 hours **Days 1–7:** Procarbazine 100mg/m² orally daily. **Day 8:** Vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes + bleomycin 10units/m² IV push. **Days 1–14:** Prednisone 40mg/m² orally daily. Repeat cycle in selected patients (IPS≥4, aged <60 years) every 3 weeks for 6 cycles, with or without subsequent radiation therapy.
Brentuximab Vedotin + Doxorubicin + Vinblastine + Dacarbazine (BV + AVD)[12] **(Category 2B)(Category 2A in select patients if IPS>4, bleomycin contraindicated, no known neuropathy)**	**Days 1 and 15:** Brentuximab vedotin 1.2mg/kg IV over 30 minutes + doxorubicin 25mg/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for up to 2 cycles.

Second-line Systemic Therapy Options[1]

Note: No data have established the superiority of any of the subsequent chemotherapy options, and NCCN guidelines recommend an individualized approach.

Brentuximab vedotin[22] **(Alone or in combination with the second-line regimens below)**	**Day 1:** Brentuximab 1.8mg/kg (maximum 180mg) IV over 30 minutes; for patients with hepatic impairment: 1.2mg/kg (up to 120mg). Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
Dexamethasone + Cytarabine + Cisplatin (DHAP)[23,24]	**Days 1–4:** Dexamethasone 40mg orally or IV daily **Day 1:** Cisplatin 100mg/m² IV continuous infusion over 24 hours **Day 2:** Cytarabine 2,000mg/m² IV over 3 hours every 12 hours. Repeat cycle every 3 to 4 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Etoposide + Methylprednisolone + Cytarabine + Cisplatin (ESHAP)[25–27]	**Days 1–4:** Etoposide 40mg/m² IV over 60 minutes + methylprednisolone 500mg IV over 15 minutes + cisplatin 25mg/m² continuous IV infusion over 24 hours **Day 5:** Cytarabine 2,000mg/m² IV over 3 hours. Repeat cycle every 3–4 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Gemcitabine + Bendamustine + Vinorelbine (BeGEV)[28]	**Day 1:** Vinorelbine 20mg/m² IV **Days 1 and 4:** Gemcitabine 800mg/m² IV **Days 2 and 3:** Bendamustine 90mg/m² IV. Repeat cycle every 3 weeks for 4 cycles.
Gemcitabine + Vinorelbine + Pegylated liposomal doxorubicin (GVD)[29]	**For transplant-naive patients:** **Days 1 and 8:** Gemcitabine 1,000mg/m² IV over 30 minutes + vinorelbine 20mg/m² IV over 5–10 minutes + pegylated liposomal doxorubicin 15mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates). **For post-transplant patients:** **Days 1 and 8:** Gemcitabine 800mg/m² IV over 30 minutes + vinorelbine 15mg/m² IV over 5–10 minutes + pegylated liposomal doxorubicin 10mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).

continued

HODGKIN LYMPHOMA TREATMENT REGIMENS (Part 3 of 5)

Classical Hodgkin Lymphoma[1] (continued)

Second-line Systemic Therapy Options[1] (continued)

REGIMEN	DOSING
Ifosfamide + Carboplatin + Etoposide (ICE)[30,31]	**Days 1–3:** Etoposide 100mg/m² IV over 60 minutes **Day 2:** Carboplatin AUC 5mg•min/mL (max 800mg) IV + ifosfamide 5,000mg/m² IV + mesna 5,000mg/m² IV administered concurrently as a continuous infusion over 24 hours. Repeat cycle every 2–3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Ifosfamide + Gemcitabine + Vinorelbine (IGEV)[32]	**Days 1–4:** Ifosfamide 200mg/m² IV over 2 hours plus mesna 2,600mg/m² IV **Days 1 and 4:** Gemcitabine 800mg/m² IV over 30 minutes **Day 1:** Vinorelbine 20mg/m² IV over 5–10 minutes **Days 1–4:** Prednisone 100mg PO daily. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Subsequent Systemic Therapy Options	
Bendamustine[33]	**Days 1 and 2:** Bendamustine 70–120mg/m² IV over 30 minutes. Repeat cycle every 4 weeks until maximal response or unacceptable toxicity.
Cyclophosphamide + Vincristine + Procarbazine + Prednisone (C-MOPP) (Category 2B)[1]	**Day 1:** Cyclophosphamide 650mg/m² IV over 30 minutes + vincristine 1.4mg/m² (maximum 2mg) IV **Days 1–7:** Procarbazine 100mg/m² orally daily **Days 1–14:** Prednisone 40mg/m² orally daily. Repeat cycle every 4 weeks for 4–8 cycles. **OR** **Days 1 and 8:** Cyclophosphamide 500mg/m² IV over 30 minutes + vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes **Days 1–14:** Procarbazine 100mg/m² orally daily. **Days 1–3 and 8–10:** Prednisone 40mg/m² orally daily. Repeat cycle every 4 weeks for 4–8 cycles.
Everolimus[34]	Everolimus 10mg orally daily until disease progression or unacceptable toxicity.
Gemcitabine + Carboplatin + Dexamethasone (GCD)[35,36]	**Days 1 and 8:** Gemcitabine 1000mg/m² IV over 30 minutes **Day 1:** Carboplatin AUC 5mg•min/mL (maximum 800mg) IV over 60 minutes **Days 1–4:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Lenalidomide[37]	**Days 1–21:** Lenalidomide 25mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Carmustine + Cytarabine + Etoposide + Melphalan (Mini-BEAM)[39,40]	**Day 1:** Carmustine 60mg/m² IV over 2 hours **Days 2–5:** Etoposide 75mg/m² IV over 60 minutes daily + cytarabine 100mg/m² IV over 3 hours every 12 hours **Day 6:** Melphalan 30mg/m² IV over 15 minutes. Repeat cycle every 4–6 weeks for 2–4 cycles.
Mitoxantrone + Ifosfamide + Mesna + Etoposide (MINE)[38]	**Days 1–3:** Mesna 1.33 g/m² IV daily, and 500 mg PO daily 4 hours after each IV dose plus ifosfamide 1.33 g/m² IV daily, given concurrently with mesna, for 3 days. **Day 1:** Mitoxantrone 8mg/m² IV over 30 minutes. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Nivolumab[41,42,a]	Nivolumab 3mg/kg IV every 2 weeks until disease progression or unacceptable toxicity.
Pembrolizumab[43,a]	Pembrolizumab 10mg/kg IV every 2 weeks until disease progression or unacceptable toxicity.
Maintenance Therapy	
Brentuximab vedotin[44]	**Day 1:** Brentuximab 1.8mg/kg (maximum 180mg) IV over 30 minutes. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity for a maximum of 1 year after HDT/SCR (if primary refractory disease or relapse occurred <12 months after primary therapy).

Nodular Lymphocyte-Predominant Hodgkin Lymphoma[1]

Primary Treatment

Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD) ± Rituximab[13,14]	**Days 1 and 15:** Doxorubicin 25mg/m² IV push + bleomycin 10units/m² IV push + vinblastine 6mg/m² IV over 5–10 minutes + dacarbazine 375mg/m² IV over 60 minutes, **±** **Day 1:** Rituximab 375mg/m² IV for all cycles. **OR** **Days 1, 8, 15, and 22:** Rituximab 375mg/m² IV for cycle 1 only. Repeat cycle every 4 weeks for 3-4 cycles with subsequent radiation or 6-8 cycles without subsequent radiation.

continued

HODGKIN LYMPHOMA TREATMENT REGIMENS (Part 4 of 5)

Nodular Lymphocyte-Predominant Hodgkin Lymphoma[1] (continued)

Primary Treatment (continued)

REGIMEN	DOSING
Cyclophosphamide + Doxorubicin + Vincristine + Prednisone (CHOP) ± Rituximab[15]	**Day 1:** Cyclophosphamide 750mg/m² over 60 minutes + doxorubicin 50mg/m² IV push + vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes **Days 1–5:** Prednisone 100mg orally daily, **±** **Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 3 weeks for 3-4 cycles with subsequent radiation or 6-8 cycles without subsequent radiation.
Cyclophosphamide + Vincristine + Prednisone (CVP) ± Rituximab[16]	**Day 1:** Cyclophosphamide 750mg/m² OR 1,000mg/m² over 60 minutes + vincristine 1.4mg/m² (maximum 2mg) IV over 5–10 minutes **Days 1–5:** Prednisone 100mg orally daily, **±** **Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 3 weeks for 3-4 cycles with subsequent radiation or 6 cycles without subsequent radiation.
Rituximab[17–21]	**Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 7 days for 4 weeks with or without maintenance rituximab (375mg/m² IV once weekly for 4 weeks every 6 months for up to 2 years).

Second-line Systemic Therapy Options[1]

Dexamethasone + Cytarabine + Cisplatin (DHAP)[15,16]	**Days 1–4:** Dexamethasone 40mg orally or IV daily **Day 1:** Cisplatin 100mg/m² IV continuous infusion over 24 hours **Day 2:** Cytarabine 2,000mg/m² IV over 3 hours every 12 hours. Repeat cycle every 3 to 4 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Etoposide + Methylprednisolone + Cytarabine + Cisplatin (ESHAP)[17,18]	**Days 1–4:** Etoposide 40mg/m² IV over 60 minutes + methylprednisolone 500mg IV over 15 minutes + cisplatin 25mg/m² continuous IV infusion over 24 hours **Day 5:** Cytarabine 2,000mg/m² IV over 3 hours. Repeat cycle every 3–4 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Ifosfamide + Carboplatin + Etoposide (ICE)[16,21]	**Days 1–3:** Etoposide 100mg/m² IV over 60 minutes **Day 2:** Carboplatin AUC 5mg•min/mL (max 800mg) IV + ifosfamide 5,000mg/m² IV + mesna 5,000mg/m² IV administered concurrently as a continuous infusion over 24 hours. Repeat cycle every 2–3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).
Ifosfamide + Gemcitabine + Vinorelbine (IGEV)[22]	**Days 1–4:** Ifosfamide 200mg/m² IV over 2 hours plus mesna 2,600mg/m² IV **Days 1 and 4:** Gemcitabine 800mg/m² IV over 30 minutes **Day 1:** Vinorelbine 20mg/m² IV over 5–10 minutes **Days 1–4:** Prednisone 100mg PO daily. Repeat cycle every 3 weeks for 2–4 cycles (transplant candidates) or 4–8 cycles (nontransplant candidates).

a Checkpoint inhibitors (CPI) are commonly recommended for patients with refractory CHL who are transplant-ineligible based on comorbidity or failure of first salvage chemotherapy, and any patient who has relapsed after autologous HSCT+brentuximab vedotin. Nivolumab or pembrolizumab can be administered to patients post-allogeneic transplant; there is limited data regarding the use of CPI following allogeneic transplantation. Caution is advised due to increased risk of GVHD (graft-versus-host disease) and other immunological complications.

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(Revised 4/2018)