MULTIPLE MYELOMA TREATMENT REGIMENS (Part 1 of 9)

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 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 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.

General treatment note: Exposure to myelotoxic agents—including alkylating agents and nitrosoureas—should be limited to avoid compromising stem-cell reserve prior to stem-cell harvest in patients who may be candidates for transplant.[1]

Primary Therapy for Transplant Candidates[1]

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

Preferred Regimens

REGIMEN	DOSING
Bortezomib + Doxorubicin + Dexamethasone (Category 1)[2ab]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC, **plus** **Days 1–4:** Doxorubicin 9mg/m² IV push or continuous IV infusion over 24 hours daily, **plus** **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily for cycle 1, followed by dexamethasone on days 1–4 for cycles 2–4. Repeat cycle every 3 weeks for 3–4 cycles. **OR** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC, **plus** **Days 1–4:** Doxorubicin 9mg/m² IV push or continuous IV infusion over 24 hours daily, **plus** **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks for 3–4 cycles.
Bortezomib + Lenalidomide + Dexamethasone (RVD) (Category 1)[3-6abc]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–21:** Lenalidomide 25mg orally daily, **plus** **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. **OR** **Days 1, 8, and 15:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.
Bortezomib + Cyclophosphamide + Dexamethasone (BCD)[7-10ab]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1, 8, 15, and 22:** Cyclophosphamide 300mg/m²/day orally **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks for 3–4 cycles. **OR** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1, 8, and 15:** Cyclophosphamide 500mg/m²/day orally **Days 1, 8, and 15:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles. **OR** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Day 1:** Cyclophosphamide 900mg/m² IV over 60 minutes **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.

Other Regimens

Bortezomib + Dexamethasone (Category 1)[11,12abd]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC, **plus** **Days 1–4 (all cycles) and 9–12 (cycles 1 and 2):** Dexamethasone 40mg orally daily. **OR** **Days 1–2, 4–5, 8–9, and 11–12:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.
Carfilzomib + Lenalidomide + Dexamethasone (CRD)[13,14ac]	**Cycle 1:** **Days 1 and 2:** Carfilzomib 20mg/m² IV over 10 minutes **Days 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1–21:** Lenalidomide 25mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. **Cycles 2–12:** **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1–21:** Lenalidomide 25mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks. **Subsequent Cycles:** **Days 1, 2, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily **Days 1–21:** Lenalidomide 25 mg orally daily. Repeat cycle every 4 weeks through cycle 13, then continue lenalidomide and dexamethasone only thereafter.

continued

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 2 of 9)

Primary Therapy for Transplant Candidates[1] (continued)

Other Regimens (continued)

REGIMEN	DOSING
Ixazomib + Lenalidomide + Dexamethasone[15c]	**Days 1, 8, and 15:** Ixazomib 4mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily **Days 1–21:** Lenalidomide 25mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Lenalidomide + Dexamethasone (Category 1)[16-18cd]	**Days 1–21:** Lenalidomide 25mg orally daily, **plus** **Days 1, 8, 15 and 22:** Dexamethasone 40mg orally daily. **OR** **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks for 3–4 cycles. **OR** **Days 1–28:** Lenalidomide 25mg orally daily **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily. Repeat cycle every 5 weeks for 3–4 cycles.
Bortezomib + Thalidomide + Dexamethasone (Category 1)[19-22abc]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–21:** Thalidomide 50–200mg orally daily at bedtime, **plus** **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. **OR** **Days 1–4 and 9–12:** Dexamethasone 40mg orally daily. **OR** **Days 1–4 (all cycles) and 9–12 (cycles 1 and 2):** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.

Primary Therapy for Non-Transplant Candidates[1]

Preferred Regimens

Lenalidomide + Low-dose Dexamethasone (Category 1)[23,24cd]	**Days 1–21:** Lenalidomide 25mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Bortezomib + Cyclophosphamide + Dexamethasone[25ab]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1, 8, 15, and 22:** Cyclophosphamide 300mg/m²/day orally **Days 1–4, 9–12, and 17–20:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks for 3–4 cycles. **OR** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1, 8, and 15:** Cyclophosphamide 500mg/m²/day orally **Days 1, 8, and 15:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles. **OR** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Day 1:** Cyclophosphamide 900mg/m² IV over 60 minutes **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.
Bortezomib + Lenalidomide + Dexamethasone (Category 1)[26abc]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–21:** Lenalidomide 25mg orally daily, **plus** **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. **OR** **Days 1, 8, and 15:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.

Other Regimens

Bortezomib + Dexamethasone[27abd]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC, **plus** **Days 1–4 (all cycles) and 9–12 (cycles 1 and 2):** Dexamethasone 40mg orally daily. **OR** **Days 1–2, 4–5, 8–9, and 11–12:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks until maximal response, disease progression, or unacceptable toxicity.

continued

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 3 of 9)

Primary Therapy for Non-Transplant Candidates[1] (continued)

Other Regimens (continued)

REGIMEN	DOSING
Carfilzomib + Lenalidomide + Dexamethasone (Category 2B)[13ac]	**Cycle 1:** **Days 1 and 2:** Carfilzomib 20mg/m² IV over 10 minutes **Days 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1–21:** Lenalidomide 25mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. **Cycles 2–12:** **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1–21:** Lenalidomide 25mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks. **Subsequent Cycles:** **Days 1, 2, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily **Days 1–21:** Lenalidomide 25 mg orally daily. Repeat cycle every 4 weeks through cycle 13, then continue lenalidomide and dexamethasone only thereafter.
Ixazomib + Lenalidomide + Dexamethasone[15ac]	**Days 1, 8, and 15:** Ixazomib 4mg orally **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally **Days 1–21:** Lenalidomide 25mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

Maintenance Therapy[1]

Bortezomib[28ab]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC. Repeat cycle every 2 weeks for 2 years or until disease progression or unacceptable toxicity. **OR** **Days 1, 8, 15, and 22:** Bortezomib 1.6mg/m² IV push over 3–5 seconds or SC. Repeat cycle every 5 weeks for 6 months or until disease progression or unacceptable toxicity.
Lenalidomide (Category 1)[29,30c]	**Days 1–28:** Lenalidomide 10mg orally daily for 3 cycles, followed by 15mg for subsequent cycles. **OR** **Days 1–21:** Lenalidomide 10mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

Therapy for Previously Treated Multiple Myeloma[1]

Preferred Regimens

Repeat induction therapy if relapse > 6 months.

Bortezomib + Dexamethasone (Category 1)[31,32abd]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC, **plus** **Days 1–4 (all cycles) and 9–12 (cycles 1 and 2):** Dexamethasone 40mg orally daily. **OR** **Days 1–2, 4–5, 8–9, and 11–12:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.
Bortezomib + Cyclophosphamide + Dexamethasone[33,34ab]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1, 8, and 15:** Cyclophosphamide 500mg orally daily **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks until maximal response, disease progression, or unacceptable toxicity. **OR** **Cycles 1–8:** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–21:** Cyclophosphamide 50mg orally daily **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks for 8 cycles. **Subsequent Cycles:** **Days 1, 8, 15, and 22:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–35:** Cyclophosphamide 50mg orally daily **Days 1, 2, 8, 9, 15, 16, 22, and 23:** Dexamethasone 20mg orally daily. Repeat cycle every 5 weeks until maximal response, disease progression, or unacceptable toxicity.

continued

Therapy for Previously Treated Multiple Myeloma[1] (continued)

Preferred Regimens (continued)

REGIMEN	DOSING
Bortezomib + Lenalidomide + Dexamethasone[35,36abc]	**Cycles 1–8:** **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–14:** Lenalidomide 25mg orally daily, **plus** **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 40mg orally daily for cycles 1–4, followed by dexamethasone 20mg orally daily for cycles 5–8 **OR** **Days 1, 8, and 15:** Dexamethasone 20–40mg orally daily Repeat cycle every 3 weeks for 8 cycles. **Subsequent Cycles:** **Days 1 and 8:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Days 1–14:** Lenalidomide 15mg orally daily **Days 1, 2, 8, and 9:** Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks until maximal response, disease progression, or unacceptable toxicity.
Carfilzomib + Dexamethasone (Category 1)[37ad]	**Cycle 1:** **Days 1 and 2:** Carfilzomib 20mg/m² IV over 30 minutes **Days 8, 9, 15, and 16:** Carfilzomib 56mg/m² IV over 30 minutes **Days 1, 2, 8, 9, 15, 16, 22, and 23:** Dexamethasone 20mg IV or orally **Subsequent Cycles:** **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 56mg/m² IV over 30 minutes **Days 1, 2, 8, 9, 15, 16, 22, and 23:** Dexamethasone 20mg IV or orally. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Carfilzomib + Lenalidomide + Dexamethasone (Category 1)[38ac]	**Cycle 1:** **Days 1 and 2:** Carfilzomib 20mg/m² IV over 10 minutes. **Days 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1, 8, 15, and 22:** Dexamethasone 40mg IV or orally **Days 1-21:** Lenalidomide 25mg orally daily **Cycles 2–12:** **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1, 8, 15, and 22:** Dexamethasone 40mg IV or orally **Days 1-21:** Lenalidomide 25mg orally daily **Subsequent Cycles:** **Days 1, 2, 15, and 16:** Carfilzomib 27mg/m² IV over 10 minutes **Days 1, 8, 15, and 22:** Dexamethasone 40mg IV or orally **Days 1–21:** Lenalidomide 25mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Daratumumab[39,40e]	**Weeks 1–8:** Daratumumab 16mg/kg IV once weekly **Weeks 9–24:** Daratumumab 16mg/kg IV every 2 weeks **Subsequent Weeks:** Daratumumab 16mg/kg IV every 4 weeks until disease progression or unacceptable toxicity.
Daratumumab + Bortezomib + Dexamethasone (Category 1)[41ab]	**Cycles 1–3:** **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 20mg IV or orally daily (20mg weekly in patients >75 years old) **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² SC **Days 1, 8, and 15:** Daratumumab 16mg/kg IV. Repeat cycle every 3 weeks. **Cycles 4–8:** **Day 1:** Daratumumab 16mg/kg IV **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 20mg IV or orally daily (20mg weekly in patients >75 years old) **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² SC Repeat cycle every 3 weeks. **Subsequent Cycles:** **Day 1:** Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

continued

Therapy for Previously Treated Multiple Myeloma[1] (continued)

Preferred Regimens (continued)

REGIMEN	DOSING
Daratumumab + Lenalidomide + Dexamethasone (Category 1)[42c]	**Cycles 1 and 2:** **Days 1, 8, 15, and 22:** Daratumumab 16mg/kg IV + dexamethasone 40mg orally daily (20mg in patients >75 years old) **Days 1–21:** Lenalidomide 25mg orally once daily Repeat cycle every 4 weeks. **Cycles 3–6:** **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily (20mg in patients >75 years old) **Days 1 and 15:** Daratumumab 16mg/kg IV **Days 1–21:** Lenalidomide 25mg orally once daily Repeat cycle every 4 weeks. **Subsequent Cycles:** **Day 1:** Daratumumab 16mg/kg IV **Days 1–21:** Lenalidomide 25mg orally once daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily (20mg in patients >75 years old). Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Elotuzumab + Lenalidomide + Dexamethasone (Category 1)[43,44cf]	**Cycles 1 and 2:** **Days 1, 8, 15, and 22:** Elotuzumab 10mg/kg IV + dexamethasone 28mg orally between 3 and 24 hours before elotuzumab + 8mg IV between 45 and 90 minutes before elotuzumab **Days 1–21:** Lenalidomide 25mg orally daily. **Subsequent Cycles:** **Days 1 and 15:** Elotuzumab 10mg/kg IV + dexamethasone 28mg orally between 3 and 24 hours before elotuzumab + 8mg IV between 45 and 90 minutes before elotuzumab **Days 1–21:** Lenalidomide 25mg orally daily **Days 8 and 22:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Ixazomib + Lenalidomide + Dexamethasone (Category 1)[45acg]	**Days 1, 8, and 15:** Ixazomib 4mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily **Days 1–21:** Lenalidomide 25mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Lenalidomide + Dexamethasone (Category 1)[46,47cdh]	**Days 1–21:** Lenalidomide 25mg orally daily **Days 1–4 (all cycles), 9–12, and 17–20 (cycles 1–4):** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Pomalidomide + Dexamethasone (Category 1)[48-53dhi]	**Days 1–21:** Pomalidomide 4mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg (age ≤75 years) or 20mg (age >75 years) orally daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Pomalidomide + Bortezomib + Dexamethasone[54-56i]	**Days 1–21:** Pomalidomide 4mg orally daily **Days 1, 8, 15, and 22:** Bortezomib 1.3mg/m² SC or IV + dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Pomalidomide + Carfilzomib + Dexamethasone[57,58i]	**Days 1–21:** Pomalidomide 4mg orally daily **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 20 or 27mg/m² IV **Days 1, 8, 15, and 22:** Dexamethasone 40mg IV or orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Other Regimens	
Bendamustine[59,60]	**Days 1 and 2:** Bendamustine 80–150mg/m² IV over 30 minutes. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Bendamustine + Bortezomib + Dexamethasone[61]	**Days 1 and 4:** Bendamustine 70mg/m² IV **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV + dexamethasone 20mg IV or orally daily. Repeat cycle every 4 weeks for a maximum of 8 cycles, or until disease progression or unacceptable toxicity.
Bendamustine + Lenalidomide + Dexamethasone[62]	**Days 1 and 2:** Bendamustine 75mg/m² IV over 30 minutes **Days 1–21:** Lenalidomide 10mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.

continued

Therapy for Previously Treated Multiple Myeloma[1] (continued)

Other Regimens (continued)

REGIMEN	DOSING
Bortezomib + Liposomal Doxorubicin (Category 1)[63]	**Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV push over 3–5 seconds or SC **Day 4:** Pegylated liposomal doxorubicin 30mg/m² IV over 60 minutes. Repeat cycle every 3 weeks until maximal response, disease progression, or unacceptable toxicity.
Cyclophosphamide + Lenalidomide + Dexamethasone[64]	**Days 1, 8, 15, and 22:** Cyclophosphamide 500mg orally daily **Day 1–21:** Lenalidomide 25mg orally daily **Days 1–4 and 12–15:** Dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Dexamethasone + Cyclophosphamide + Etoposide + Cisplatin (DCEP)[65,66]	**Days 1–4:** Dexamethasone 40mg/m² orally daily **Days 1–4:** Cyclophosphamide 400mg/m² continuous IV infusion over 24 hours daily + etoposide 40mg/m² continuous IV infusion over 24 hours daily + cisplatin 10–15mg/m² continuous IV infusion over 24 hours daily. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide (DT-PACE)[67cj]	**Days 1–4:** Dexamethasone 40mg orally daily **Days 1–4:** Cyclophosphamide 400mg/m² continuous IV infusion over 24 hours daily + etoposide 40mg/m² continuous IV infusion over 24 hours daily + cisplatin 10mg/m² continuous IV infusion over 24 hours daily + doxorubicin 10mg/m² continuous IV infusion over 24 hours daily **Day 1–28:** Thalidomide 50–200mg orally daily at bedtime. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.
Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide + Bortezomib (VTD-PACE)[68cj]	**Induction:** **Days 1, 4, 8, and 11:** Bortezomib 1mg/m² IV push over 3–5 seconds or SC **Day 4–7:** Thalidomide 50–200mg orally daily at bedtime + dexamethasone 40mg orally daily **Days 4–7:** Cyclophosphamide 400mg/m² continuous IV infusion over 24 hours daily + etoposide 40mg/m² continuous IV infusion over 24 hours daily + cisplatin 10mg/m² continuous IV infusion over 24 hours daily + doxorubicin 10mg/m² continuous IV infusion over 24 hours daily. **Consolidation:** **Cycle 1: Beginning 6 weeks–4 months after last transplant:** **Days 1, 4, 8, and 11:** Bortezomib 1mg/m² IV push over 3–5 seconds or SC **Day 1–4:** Thalidomide 50–200mg orally daily at bedtime + dexamethasone 40mg orally daily **Days 1–4:** Cyclophosphamide 300mg/m² continuous IV infusion over 24 hours daily + etoposide 30mg/m² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m² continuous IV infusion over 24 hours daily. **Cycle 2: Beginning 2–4 months after cycle 1:** **Days 1, 4, 8, and 11:** Bortezomib 1mg/m² IV push over 3–5 seconds or SC **Day 1–4:** Thalidomide 50–200mg orally daily at bedtime + dexamethasone 40mg orally daily **Days 4–7:** Cyclophosphamide 300mg/m² continuous IV infusion over 24 hours daily + etoposide 30mg/m² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m² continuous IV infusion over 24 hours daily.
Elotuzumab + Bortezomib + Dexamethasone[69ab]	**Cycles 1 and 2:** **Days 1, 8, and 15:** Elotuzumab 10mg/kg IV + dexamethasone 8mg orally between 3 and 24 hours before elotuzumab + 8mg IV between 45 and 90 minutes before elotuzumab **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² SC **Days 2, 4, 5, 8, 9, 11:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks. **Cycles 3-8:** **Days 1 and 11:** Elotuzumab 10mg/kg IV + dexamethasone 8mg orally between 3 and 24 hours before elotuzumab + 8mg IV between 45 and 90 minutes before elotuzumab **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² SC **Days 2, 4, 5, 9, 12:** Dexamethasone 20mg orally daily. Repeat cycle every 3 weeks. **Cycles 9 and Later:** **Days 1 and 15:** Elotuzumab 10mg/kg IV + dexamethasone 8mg orally between 3 and 24 hours before elotuzumab + 8mg IV between 45 and 90 minutes before elotuzumab **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² SC **Days 1, 8, and 15:** Bortezomib 1.3mg/m² SC **Days 2, 8, 9, 16:** Dexamethasone 20mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

continued

Therapy for Previously Treated Multiple Myeloma[1] (continued)

Other Regimens (continued)

REGIMEN	DOSING
High-dose Cyclophosphamide[70]	**Days 1–4:** Cyclophosphamide 600mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles, then every 3 months until maximal response, disease progression, or unacceptable toxicity.
Ixazomib + Dexamethasone[71,72adg]	**Days 1, 8, and 15:** Ixazomib 5.5mg orally daily **Days 1, 2, 8, 9, 15, and 16:** Dexamethasone 20mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Panobinostat + Bortezomib + Dexamethasone (Category 1)[73,74abk]	**Cycles 1–8:** **Days 1, 3, 5, 8, 10, and 12:** Panobinostat 20mg orally **Days 1, 4, 8, and 11:** Bortezomib 1.3mg/m² IV **Days 1, 2, 4, 5, 8, 9, 11, and 12:** Dexamethasone 20mg orally. Repeat cycle every 3 weeks. **Cycles 9-16:** **Days 1, 3, 5, 8, 10, and 12:** Panobinostat 20mg orally **Days 1 and 8:** Bortezomib 1.3mg/m² IV **Days 1, 2, 8 and 9:** Dexamethasone 20mg orally. Repeat cycle every 3 weeks.
Panobinostat + Carfilzomib[75,76ak]	**Cycle 1:** **Days 1 and 2:** Carfilzomib 20mg/m² IV **Days 1, 3, 5, 15, 17, and 19:** Panobinostat 30mg orally daily. **Days 8, 9, 15, and 16:** Carfilzomib 45mg/m² IV. **Subsequent Cycles:** **Days 1, 2, 8, 9, 15, and 16:** Carfilzomib 45mg/m² IV **Days 1, 3, 5, 15, 17, and 19:** Panobinostat 30mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Pomalidomide + Cyclophosphamide + Dexamethasone[77,78i]	**Days 1, 8, and 15:** Cyclophosphamide 400mg orally daily **Days 1, 8, 15, and 22:** Dexamethasone 40mg (20mg for patients >75 years old) orally daily **Days 1–21:** Pomalidomide 4mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

a Recommend herpes zoster prophylaxis for patients treated with proteasome inhibitors.
b Subcutaneous bortezomib is the preferred method of administration for patients with pre-existing or high-risk peripheral neuropathy.
c Full-dose aspirin recommended with immunomodulator-based therapy. Therapeutic anticoagulation recommended for those at high risk for thrombosis.
d Triplet regimens should be used as the standard therapy for patients with multiple myeloma; however, elderly or frail patients may be treated with doublet regimens.
e Daratumumab monotherapy is indicated for the treatment of patients who have received at least 3 prior therapies, including a proteasome inhibitor and an immunomodulatory agent or who are double refractory to a proteasome inhibitor and immunomodulatory agent.
f Elotuzumab is indicated in combination with lenalidomide and dexamethasone for the treatment of patients who have received 1 to 3 prior therapies.
g Ixazomib is indicated in combination with lenalidomide and dexamethasone for the treatment of patients who have received at least 1 prior therapy.
h Consider single-agent lenalidomide or pomalidomide for steroid-intolerant individuals.
i Indicated for the treatment of patients who have received at least 2 prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy.
j Generally reserved for the treatment of aggressive multiple myeloma.
k Indicated for the treatment of patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

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