

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 1 of 9)

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.

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 The following selected regimens for Myeloma Therapy are not inclusive of all regimens.

Herpes zoster prophylaxis for patients treated with proteasome inhibitors or daratumumab.

Subcutaneous bortezomib is the preferred method of administration.

Full-dose aspirin recommended with immunomodulator-based therapy. Therapeutic anticoagulation recommended for those at high risk for thrombosis.

Primary Therapy for Transplant Candidates^{1,a}

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

Preferred Regimens

REGIMEN	DOSING
Bortezomib + Lenalidomide + Dexamethasone (RVD) (Category 1) ³⁻⁶	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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. OR Days 1, 8, and 15: Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.
Bortezomib + Cyclophosphamide + Dexamethasone (BCD) ^{7-10,b}	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² IV push over 3–5 seconds or SC Days 1, 8, 15, and 22: Cyclophosphamide 300mg/m ² /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/m ² IV push over 3–5 seconds or SC Days 1, 8, and 15: Cyclophosphamide 500mg/m ² /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/m ² IV push over 3–5 seconds or SC Day 1: Cyclophosphamide 900mg/m ² 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 Recommended Regimens

Bortezomib + Doxorubicin + Dexamethasone (Category 1) ²	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² IV push over 3–5 seconds or SC, plus Days 1–4: Doxorubicin 9mg/m ² 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/m ² IV push over 3–5 seconds or SC, plus Days 1–4: Doxorubicin 9mg/m ² 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.
Carfilzomib + Lenalidomide + Dexamethasone (CRD) ^{13,14}	Cycle 1: Days 1 and 2: Carfilzomib 20mg/m ² IV over 10 minutes Days 8, 9, 15, and 16: Carfilzomib 27mg/m ² 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/m ² 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/m ² 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,a} (continued)

Other Recommended Regimens (continued)

REGIMEN	DOSING
Ixazomib + Lenalidomide + Dexamethasone (Category 2B)¹⁵	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.
Useful in Certain Circumstances	
Bortezomib + Dexamethasone (Category 1)^{11,12,c}	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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 + Thalidomide + Dexamethasone (Category 1)^{19,22}	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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.
Lenalidomide + Dexamethasone (Category 1)^{16–18,c}	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.

Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide + Bortezomib (VTD-PACE)⁶⁸	Induction: Days 1, 4, 8, and 11: Bortezomib 1mg/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 40mg/m ² continuous IV infusion over 24 hours daily + cisplatin 10mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 10mg/m ² 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/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 30mg/m ² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m ² continuous IV infusion over 24 hours daily. Cycle 2: Beginning 2–4 months after cycle 1: Days 1, 4, 8, and 11: Bortezomib 1mg/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 30mg/m ² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m ² continuous IV infusion over 24 hours daily.
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Primary Therapy for Non-Transplant Candidates^{1,a}

Preferred Regimens

Lenalidomide + Low-dose Dexamethasone (Category 1)^{23,24,c}	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.
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MULTIPLE MYELOMA TREATMENT REGIMENS (Part 3 of 9)

Primary Therapy for Non-Transplant Candidates^{1-a} (continued)

Preferred Regimens (continued)

REGIMEN	DOSING
Bortezomib + Cyclophosphamide + Dexamethasone^{25,b}	<p>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.</p> <p style="text-align: center;">OR</p> <p>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.</p> <p style="text-align: center;">OR</p> <p>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.</p>
Bortezomib + Lenalidomide + Dexamethasone (Category 1)²⁶	<p>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.</p> <p style="text-align: center;">OR</p> <p>Days 1, 8, and 15: Dexamethasone 40mg orally daily. Repeat cycle every 3 weeks for 3–4 cycles.</p>

Other Recommended Regimens

Carfilzomib + Lenalidomide + Dexamethasone¹³	<p>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</p> <p>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</p> <p>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.</p>
Ixazomib + Lenalidomide + Dexamethasone¹⁵	<p>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.</p>

Carfilzomib/Cyclophosphamide/Dexamethasone^{1,k}

Useful in Certain Circumstances

Bortezomib + Dexamethasone^{27,c}	<p>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.</p> <p style="text-align: center;">OR</p> <p>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.</p>
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Maintenance Therapy⁴

Preferred Regimens

Lenalidomide (Category 1)^{29,30}	<p>Days 1–28: Lenalidomide 10mg orally daily for 3 cycles, followed by 15mg for subsequent cycles.</p> <p style="text-align: center;">OR</p> <p>Days 1–21: Lenalidomide 10mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.</p>
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Other Recommended Regimens

Bortezomib²⁸	<p>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.</p> <p style="text-align: center;">OR</p> <p>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.</p>
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MULTIPLE MYELOMA TREATMENT REGIMENS (Part 4 of 9)

Therapy for Previously Treated Multiple Myeloma^{1,a}

Preferred Regimens

REGIMEN	DOSING
<p>Repeat primary induction therapy if relapse at >6 months. Consideration for appropriate regimen is based on the context of clinical relapse.</p>	
<p>Bortezomib + Lenalidomide + Dexamethasone^{35,36}</p>	<p>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.</p>
<p>Carfilzomib + Dexamethasone (Category 1)^{37,c}</p>	<p>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.</p>
<p>Carfilzomib + Lenalidomide + Dexamethasone (Category 1)³⁸</p>	<p>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.</p>
<p>Daratumumab + Bortezomib + Dexamethasone (Category 1)⁴¹</p>	<p>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.</p>
<p>Daratumumab + Lenalidomide + Dexamethasone (Category 1)⁴²</p>	<p>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.</p>

continued

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 5 of 9)

Therapy for Previously Treated Multiple Myeloma¹⁻⁴ (continued)

Preferred Regimens (continued)

REGIMEN	DOSING
Elotuzumab + Lenalidomide + Dexamethasone (Category 1) ^{43,44,e}	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) ^{45,f}	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.

Other Recommended Regimens

Bortezomib + Dexamethasone (Category 1) ^{31,32,c}	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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 ^{33,34}	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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/m ² 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/m ² 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.
Daratumumab ^{39,40,d}	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.
Lenalidomide + Dexamethasone (Category 1) ^{46,47,c,g}	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.
Bendamustine + Bortezomib + Dexamethasone ⁶¹	Days 1 and 4: Bendamustine 70mg/m ² IV Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² IV + dexamethasone 20mg IV or orally daily. Repeat cycle every 4 weeks for a max
Bendamustine + Lenalidomide + Dexamethasone ⁶²	Days 1 and 2: Bendamustine 75mg/m ² 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.
Pomalidomide + Dexamethasone (Category 1) ^{48-53,c,g,h}	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 ^{54-56,h}	Days 1-21: Pomalidomide 4mg orally daily Days 1, 8, 15, and 22: Bortezomib 1.3mg/m ² SC or IV + dexamethasone 40mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Pomalidomide + Carfilzomib + Dexamethasone ^{57,58,h}	Days 1-21: Pomalidomide 4mg orally daily Days 1, 2, 8, 9, 15, and 16: Carfilzomib 20 or 27mg/m ² IV Days 1, 8, 15, and 22: Dexamethasone 40mg IV or orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.

continued

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 6 of 9)

Therapy for Previously Treated Multiple Myeloma^{1,a} (continued)

Other Recommended Regimens (continued)

REGIMEN	DOSING
Bortezomib + Liposomal Doxorubicin (Category 1) ⁶³	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² IV push over 3–5 seconds or SC Day 4: Pegylated liposomal doxorubicin 30mg/m ² 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.
Elotuzumab + Bortezomib + Dexamethasone ^{69,e}	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/m ² 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/m ² 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, 8, and 15: Bortezomib 1.3mg/m ² SC Days 2, 8, 9, 16: Dexamethasone 20mg orally daily. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Ixazomib + Dexamethasone ^{71,72,c,f}	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) ^{73,74,j}	Cycles 1–8: Days 1, 3, 5, 8, 10, and 12: Panobinostat 20mg orally Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² 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/m ² IV Days 1, 2, 8 and 9: Dexamethasone 20mg orally. Repeat cycle every 3 weeks.
Panobinostat + Carfilzomib ^{75,76,c,j}	Cycle 1: Days 1 and 2: Carfilzomib 20mg/m ² IV Days 1, 3, 5, 15, 17, and 19: Panobinostat 30mg orally daily. Days 8, 9, 15, and 16: Carfilzomib 45mg/m ² IV. Subsequent Cycles: Days 1, 2, 8, 9, 15, and 16: Carfilzomib 45mg/m ² 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 ^{77,78,h}	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.
Bortezomib/Liposomal Doxorubicin/Dexamethasone (Category 1) ^{1,k}	
Carfilzomib/Cyclophosphamide/Dexamethasone ^{1,k}	
Carfilzomib (weekly)/Dexamethasone ^{1,c,k}	
Daratumumab/Pomalidomide/Dexamethasone ^{1,h,k}	
Ixazomib/Pomalidomide/Dexamethasone ^{1,h,k}	
Panobinostat/Lenalidomide/Dexamethasone ^{1,i,k}	
Useful in Certain Circumstances	
Bendamustine ^{59,60}	Days 1 and 2: Bendamustine 80–150mg/m ² IV over 30 minutes. Repeat cycle every 4 weeks until maximal response, disease progression, or unacceptable toxicity.

continued

MULTIPLE MYELOMA TREATMENT REGIMENS (Part 7 of 9)

Therapy for Previously Treated Multiple Myeloma^{1,a} (continued)

Useful in Certain Circumstances (continued)

REGIMEN	DOSING
Dexamethasone + Cyclophosphamide + Etoposide + Cisplatin (DCEP) ^{65,66}	Days 1–4: Dexamethasone 40mg/m ² orally daily Days 1–4: Cyclophosphamide 400mg/m ² continuous IV infusion over 24 hours daily + etoposide 40mg/m ² continuous IV infusion over 24 hours daily + cisplatin 10–15mg/m ² 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) ^{67,j}	Days 1–4: Dexamethasone 40mg orally daily Days 1–4: Cyclophosphamide 400mg/m ² continuous IV infusion over 24 hours daily + etoposide 40mg/m ² continuous IV infusion over 24 hours daily + cisplatin 10mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 10mg/m ² 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) ^{68,i}	Induction: Days 1, 4, 8, and 11: Bortezomib 1mg/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 40mg/m ² continuous IV infusion over 24 hours daily + cisplatin 10mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 10mg/m ² 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/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 30mg/m ² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m ² continuous IV infusion over 24 hours daily. Cycle 2: Beginning 2–4 months after cycle 1: Days 1, 4, 8, and 11: Bortezomib 1mg/m ² 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/m ² continuous IV infusion over 24 hours daily + etoposide 30mg/m ² continuous IV infusion over 24 hours daily + cisplatin 7.5mg/m ² continuous IV infusion over 24 hours daily + doxorubicin 7.5mg/m ² continuous IV infusion over 24 hours daily.
High-dose Cyclophosphamide ⁷⁰	Days 1–4: Cyclophosphamide 600mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles, then every 3 months until maximal response, disease progression, or unacceptable toxicity.

a Assess for response after each cycle.

b Preferred initial treatment in patients with acute renal insufficiency. Consider switching to bortezomib/lenalidomide/dexamethasone after renal function improves.

c 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.

d 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.

e Elotuzumab is indicated in combination with lenalidomide and dexamethasone for the treatment of patients who have received 1 to 3 prior therapies.

f Ixazomib is indicated in combination with lenalidomide and dexamethasone for the treatment of patients who have received at least 1 prior therapy.

g Consider single-agent lenalidomide or pomalidomide for steroid-intolerant individuals.

h 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.

i Generally reserved for the treatment of aggressive multiple myeloma.

j Indicated for the treatment of patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

k References and specific dosing guidance from the NCCN's Guideline Panel will be included in the next Guideline update.

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