

Multiple Myeloma 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 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.

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

► Primary Therapy for Transplant Candidates¹

REGIMEN	DOSING
Preferred Regimens	
Bortezomib + Cyclophosphamide + Dexamethasone ^{2,55,a}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally once daily Days 1-4,9-12,17-20: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 3-4 cycles.</p> <p>OR</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,8,15: Cyclophosphamide 500mg/m² orally once daily Days 1,8,15: Dexamethasone 40mg orally once daily. Repeat cycle every 3 weeks for 3-4 cycles.</p> <p>OR</p> <p>Days 1,8,15,22: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally once daily Days 1-4,9-12,17-20 (Cycles 1-2): Dexamethasone 40mg orally once daily followed by: Day 1,8,15,22 (Cycles 3 and 4): Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 3-4 cycles.</p>
Bortezomib + Lenalidomide + Dexamethasone (Category 1) ^{2,5-8}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-14: Lenalidomide 25mg orally once daily Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily OR Days 1,8,15: Dexamethasone 40mg orally once daily. Repeat cycle every 3 weeks for 3-4 cycles.</p>
Other Recommended Regimens	
Carfilzomib + Lenalidomide + Dexamethasone ^{6,9,11,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10-30 minutes daily, followed by: Days 8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally or IV daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1-2;8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22 (Cycles 2-4): Dexamethasone 40mg orally or IV daily followed by: Days 1,8,15,22 (Cycles 5-8): Dexamethasone 20mg orally or IV daily. Repeat cycle every 4 weeks for 7 cycles beginning with Cycle 2.</p> <p>OR</p> <p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10-30 minutes daily, followed by: Days 8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily Days 1-2: Lenalidomide 25mg orally once daily Days 1-2;8-9;15-16;22-23: Dexamethasone 20mg orally or IV once daily, Administer for one 4-week cycle (Cycle 1), followed by: Days 1-2;8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily. Days 1-21: Lenalidomide 25mg orally once daily Days 1-2;8-9;15-16;22-23 (Cycles 2-4): Dexamethasone 20mg orally or IV once daily, followed by: Days 1-2;8-9;15-16;22-23 (Cycles 5-8): Dexamethasone 10mg orally or IV once daily. Repeat cycle every 4 weeks for 7 cycles beginning with cycle 7.</p>

continued

Multiple Myeloma Treatment Regimens

► Primary Therapy for Transplant Candidates¹ (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
Daratumumab + Lenalidomide + Bortezomib + Dexamethasone ^{2,6,12,13,d}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-14: Lenalidomide 25mg orally once daily Days 1-2;8-9;15-16: Dexamethasone 20mg orally once daily Days 1,8,15: Daratumumab 16mg/kg IV. Repeat cycle every 3 weeks for 4 cycles (Cycles 1-4), followed by: Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-14: Lenalidomide 25mg orally once daily Days 1-2;8-9;15-16: Dexamethasone 20mg orally once daily Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 3 weeks for 2 cycles (Cycles 5-6), followed by maintenance therapy with: Days 1-21 (Cycles 7-9): Lenalidomide 10mg orally once daily, followed by: Days 1-21 (Cycle 10): Lenalidomide 15mg orally once daily Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks beginning with cycle 7, OR maintenance therapy with: Day 1: Daratumumab 16mg/kg IV, with: Days 1-21 (Cycles 7-9): Lenalidomide 10mg orally once daily, followed by: Days 1-21 (Cycle 10 and beyond): Lenalidomide 15mg orally once daily. Repeat cycle every 4 weeks (beginning with Cycle 7).</p>
Ixazomib + Lenalidomide + Dexamethasone (Category 2B) ^{6,14,16}	<p>Days 1,8,15: Ixazomib 4mg orally once daily Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 3-4 cycles.</p>
Useful in Certain Circumstances	
Bortezomib + Doxorubicin + Dexamethasone ^{2,17,18}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-4: Doxorubicin 9mg/m² IV push OR Days 1-4: Doxorubicin 9mg/m² continuous infusion over 24 hours Days 1-4,8,11,15-18: Dexamethasone 40mg orally once daily (Cycle 1), followed by: Days 1-4: Dexamethasone 40mg orally once daily (beginning with Cycle 2). Repeat cycle every 3 weeks for 3-4 cycles. OR Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-4: Doxorubicin 9mg/m² IV push OR Days 1-4: Doxorubicin 9mg/m² IV continuous infusion over 24 hours Days 1-4,9-12,17-20: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 3-4 cycles.</p>
Bortezomib + Thalidomide + Dexamethasone (Category 1) ^{2,19,23}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-21: Thalidomide 50-200mg (usual dose range) orally once daily at bedtime Days 1-2,4-5,8-9,11-12: Dexamethasone 40mg orally once daily OR Days 1-4,9-12: Dexamethasone 40mg orally once daily. Repeat cycle every 3 weeks for 3-4 cycles.</p>
Carfilzomib + Cyclophosphamide + Dexamethasone ^{9,24,b,c,e}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10 minutes, followed by: Days 8-9,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1,8,15,22: Dexamethasone 40mg orally or IV once daily. Administer for one 4-week cycle, followed by: Days 1-2,8-9,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes daily Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 7 cycles (Cycles 2-8), followed by maintenance therapy with: Days 1-2,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes. Repeat cycle every 4 weeks (beginning with Cycle 9).</p>
Cyclophosphamide + Lenalidomide + Dexamethasone ^{2,6,24,25}	<p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks until decision to pursue HCT.</p>

continued

Multiple Myeloma Treatment Regimens

► Primary Therapy for Transplant Candidates¹ (continued)

REGIMEN	DOSING
Useful in Certain Circumstances (continued)	
Daratumumab + Bortezomib + Thalidomide + Dexamethasone ^{2,12,19,25,d}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-28: Thalidomide 100mg orally once daily</p> <p>Days 1-2,8-9,15-16,22-23: Dexamethasone 40mg orally or IV daily</p> <p>Days 1,8,15,22: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2, induction pre-transplant), followed by:</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-28: Thalidomide 100mg orally once daily</p> <p>Days 1-2: Dexamethasone 40mg orally or IV daily, followed by:</p> <p>Days 8-9,15-16: Dexamethasone 20mg orally or IV daily</p> <p>Days 1,15: 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 3-4, induction, pre-transplant), followed by:</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-28: Thalidomide 100mg orally once daily</p> <p>Days 1-2,8-9,15-16: Dexamethasone 20mg orally or IV daily</p> <p>Days 1,15: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 5-6, consolidation, post-transplant).</p>
Daratumumab + Cyclophosphamide + Bortezomib + Dexamethasone ^{2,12,28,d}	<p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1-2: Dexamethasone 20mg IV daily, followed by:</p> <p>Days 8,15,22: Dexamethasone 40mg IV daily</p> <p>Days 1-2: Daratumumab 8mg/kg IV daily, followed by:</p> <p>Days 8,15,22: Daratumumab 16mg/kg IV daily.</p> <p>Administer for one 4-week cycle (Cycle 1), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg IV or orally daily</p> <p>Days 1,8,15,22: Daratumumab 16mg/kg IV.</p> <p>Administer for one 4-week cycle (Cycle 2), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40 mg IV or orally daily</p> <p>Days 1,15: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg IV or orally daily</p> <p>Day 1: Daratumumab 16mg/kg.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 7-8), followed by maintenance therapy (beginning approximately 90 days post-transplant) with:</p> <p>Day 1: Dexamethasone 12mg IV or orally daily</p> <p>Day 1: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for a maximum of 12 cycles.</p>
Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide + Bortezomib (VTD-PACE) ^{2,19,29-31,f,g}	<p>Days 1,4,8,11: Bortezomib 1mg/m² subcutaneous</p> <p>Days 1-4: Thalidomide 100-200mg orally once daily at bedtime, followed by:</p> <p>Day 5 and beyond: Thalidomide 50-100mg orally once daily at bedtime</p> <p>Days 1-4: Dexamethasone 40mg orally once daily</p> <p>Days 1-4: Cisplatin 10mg/m² IV continuous infusion over 24 hours daily</p> <p>Days 1-4: Doxorubicin 10mg/m² IV continuous infusion over 24 hours daily</p> <p>Days 1-4: Cyclophosphamide 400mg/m² IV continuous infusion over 24 hours daily</p> <p>Days 1-4: Etoposide 40mg/m² IV continuous infusion over 24 hours daily.</p> <p>Repeat cycle every 4- to 6-weeks for 4 cycles.</p>
Ixazomib + Cyclophosphamide + Dexamethasone ^{14,32,333,e}	<p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally once daily</p> <p>Days 1,8,15: Ixazomib 4mg orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Maintenance Therapy for Transplant Candidates¹

REGIMEN	DOSING
Preferred Regimens	
Lenalidomide (Category 1) ^{6,34-36,h}	<p>Days 1-28 (Cycles 1-3): Lenalidomide 10mg orally once daily, followed by: Days 1-28 (Cycle 4 and beyond): Lenalidomide 15mg orally once daily. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1-21: Lenalidomide 10mg orally once daily. Repeat cycle every 4 weeks.</p>
Other Recommended Regimens	
Bortezomib ^{2,38,39}	<p>Day 1: Bortezomib 1.3mg/m² subcutaneous. Repeat cycle every 2 weeks for up to 2 years.</p> <p>OR</p> <p>Days 1,8,15,22: Bortezomib 1.6mg/m² subcutaneous. Repeat cycle every 5 weeks for up to 6 months.</p>
Ixazomib (Category 1) ^{14,40}	<p>Days 1,8,15 (Cycles 1-4): Ixazomib 3mg orally once daily. Repeat cycle every 4 weeks for 4 cycles, followed by: Days 1,8,15 (Cycle 5 and beyond): Ixazomib 4mg orally once daily. Repeat cycle every 4 weeks for a maximum of 2 years.</p>
Useful in Certain Circumstances	
Bortezomib + Lenalidomide ^{2,6,41}	<p>Days 1,8,15,22: Bortezomib 1.3mg/m² subcutaneous Days 1-21: Lenalidomide 10mg orally once daily. Repeat cycle every 4 weeks for 3 years, followed by: Days 1-28: Lenalidomide 10mg orally once daily. Repeat cycle every 4 weeks.</p>

► Primary Therapy for Non-Transplant Candidates¹

Preferred Regimens	
Bortezomib + Cyclophosphamide + Dexamethasone ^{2-5,a}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally once daily Days 1-4,9-12,17-20: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,8,15: Cyclophosphamide 500mg/m² orally once daily Days 1,8,15: Dexamethasone 40mg orally once daily. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Days 1,8,15,22: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally once daily Days 1-4,9-12,17-20 (Cycles 1-2): Dexamethasone 40mg orally once daily followed by: Day 1,8,15,22 (Cycle 3 and beyond): Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p>
Bortezomib + Lenalidomide + Dexamethasone (Category 1) ^{2,5-8}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-14: Lenalidomide 25mg orally once daily Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily OR Days 1,8,15: Dexamethasone 40mg orally once daily. Repeat cycle every 3 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Primary Therapy for Non-Transplant Candidates¹ (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
Daratumumab + Lenalidomide + Dexamethasone (Category 1) ^{5,12,42,43,d}	<p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1-2,8-9,15-16,22-23: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR</p> <p>Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily</p> <p>Days 1,8,15,22: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by:</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1-2,15-16: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR</p> <p>Days 8,22: Dexamethasone (age ≤75 years) 40mg orally OR</p> <p>Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily</p> <p>Days 1,15: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by:</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1-2: Dexamethasone (age ≤75 years) 20mg IV or orally once daily</p> <p>Days 8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR</p> <p>Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily.</p> <p>Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>
Lenalidomide + Low-Dose Dexamethasone (Category 1) ^{6,44,45,i}	<p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>
Other Recommended Regimens	
Carfilzomib + Lenalidomide + Dexamethasone ^{6,9-11,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10-30 minutes daily, followed by:</p> <p>Days 8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally or IV daily.</p> <p>Administer for one 4-week cycle (Cycle 1), followed by:</p> <p>Days 1-2;8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1,8,15,22 (Cycles 2-4): Dexamethasone 40mg orally or IV daily followed by:</p> <p>Days 1,8,15,22 (Cycles 5-8): Dexamethasone 20mg orally or IV daily.</p> <p>Repeat cycle every 4 weeks for 7 cycles beginning with Cycle 2.</p> <p>OR</p> <p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10-30 minutes daily, followed by:</p> <p>Days 8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily</p> <p>Days 1-2: Lenalidomide 25mg orally once daily</p> <p>Days 1-2;8-9;15-16;22-23: Dexamethasone 20mg orally or IV once daily.</p> <p>Administer for one 4-week cycle (Cycle 1), followed by:</p> <p>Days 1-2;8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 10-30 minutes daily.</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1-2;8-9;15-16;22-23 (Cycles 2-4): Dexamethasone 20mg orally or IV once daily, followed by:</p> <p>Days 1-2;8-9;15-16;22-23 (Cycles 5-8): Dexamethasone 10mg orally or IV once daily.</p> <p>Repeat cycle every 4 weeks for 7 cycles beginning with cycle 7.</p>
Daratumumab + Bortezomib + Melphalan + Prednisone (Category 1) ^{2,12,46,a,d}	<p>Days 1,4,8,11,22,25,29,32: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-4: Melphalan 9mg/m² orally once daily</p> <p>Days 2-4: Prednisone 60mg/m² orally once daily</p> <p>Days 1,8,15,22,29,36: Daratumumab 16mg/kg IV.</p> <p>Administer for one 6-week cycle (Cycle 1), followed by:</p> <p>Days 1,8,22,29: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-4: Melphalan 9mg/m² orally once daily</p> <p>Days 2-4: Prednisone 60mg/m² orally</p> <p>Days 1,22: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 6 weeks for 8 cycles (Cycles 2-9), followed by:</p> <p>Day 1: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks (Cycle 10 and beyond).</p>

continued

Multiple Myeloma Treatment Regimens

► Primary Therapy for Non-Transplant Candidates¹ (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
Daratumumab + Cyclophosphamide + Bortezomib + Dexamethasone ^{2,12,28,a,d}	<p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1-2: Dexamethasone 20mg IV daily, followed by:</p> <p>Days 8,15,22: Dexamethasone 40mg IV daily</p> <p>Days 1-2: Daratumumab 8mg/kg IV daily, followed by:</p> <p>Days 8,15,22: Daratumumab 16mg/kg IV daily.</p> <p>Administer for one 4-week cycle (Cycle 1), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg IV or orally daily</p> <p>Days 1,8,15,22: Daratumumab 16mg/kg IV.</p> <p>Administer for one 4-week cycle (Cycle 2), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40 mg IV or orally daily</p> <p>Days 1,15: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by:</p> <p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous</p> <p>Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg IV or orally daily</p> <p>Day 1: Daratumumab 16mg/kg.</p> <p>Repeat cycle every 4 weeks for 2 cycles (Cycles 7-8), followed by maintenance therapy with:</p> <p>Day 1: Dexamethasone 12mg IV or orally daily</p> <p>Day 1: Daratumumab 16mg/kg IV.</p> <p>Repeat cycle every 4 weeks for a maximum of 12 cycles.</p>
Ixazomib + Lenalidomide + Dexamethasone ^{6,14-16}	<p>Days 1,8,15: Ixazomib 4mg orally once daily</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1,8,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>
Useful in Certain Circumstances	
Bortezomib + Dexamethasone ^{2,39}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-2,4-5,8-9,11-12 (Cycles 1-4): Dexamethasone 20mg orally daily, followed by:</p> <p>Days 1-2,4-5 (Cycles 5 and beyond): Dexamethasone 20mg orally daily.</p> <p>Repeat cycle every 3 weeks for a maximum of 12 cycles.</p>
Carfilzomib + Cyclophosphamide + Dexamethasone ^{9,26,a-c,e}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10 minutes, followed by:</p> <p>Days 8-9,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes</p> <p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally or IV once daily.</p> <p>Administer for one 4-week cycle, followed by:</p> <p>Days 1-2,8-9,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes daily</p> <p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks for 7 cycles (Cycles 2-8), followed by maintenance therapy with:</p> <p>Days 1-2,15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks (beginning with Cycle 9).</p>
Cyclophosphamide + Lenalidomide + Dexamethasone ^{6,25,47}	<p>Days 1,8,15 (Cycles 1-12 only): Cyclophosphamide 300mg/m² orally once daily</p> <p>Days 1-21: Lenalidomide 25mg orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>

► Maintenance Therapy for Non-Transplant Candidates¹

Preferred Regimens	
Lenalidomide (Category 1) ^{6,34-37}	<p>Days 1-28 (Cycles 1-3): Lenalidomide 10mg orally once daily, followed by:</p> <p>Days 1-28 (Cycle 4 and beyond): Lenalidomide 15mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1-21: Lenalidomide 10mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Maintenance Therapy for Non-Transplant Candidates¹ (continued)

REGIMEN	DOSING
Other Recommended Regimens	
Bortezomib ^{2,38,39}	<p>Day 1: Bortezomib 1.3mg/m² subcutaneous. Repeat cycle every 2 weeks for up to 2 years.</p> <p>OR</p> <p>Days 1,8,15,22: Bortezomib 1.6mg/m² subcutaneous. Repeat cycle every 5 weeks for up to 6 months.</p>
Useful in Certain Circumstances	
Bortezomib + Lenalidomide ^{2,6,41}	<p>Days 1,8,15,22: Bortezomib 1.3mg/m² subcutaneous Days 1-21: Lenalidomide 10mg orally once daily. Repeat cycle every 4 weeks for 3 years, followed by: Days 1-28: Lenalidomide 10mg orally once daily. Repeat cycle every 4 weeks.</p>

► Therapy for Previously Treated Multiple Myeloma^{1,i,k}

Preferred Regimens	
Bortezomib + Lenalidomide + Dexamethasone ^{2,6,48,49}	<p>Days 1,4,8,11: Bortezomib 1-1.3mg/m² subcutaneous Days 1-14: Lenalidomide 15-25mg orally once daily Days 1-2,4-5,8-9,11-12: Dexamethasone 40 mg orally once daily (Cycles 1-4), followed by: Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily (Cycles 5-8). Repeat cycle every 3 weeks for a maximum of 8 cycles, followed by: Days 1,8: Bortezomib 1-1.3mg/m² subcutaneous Days 1-14: Lenalidomide 15mg orally once daily Days 1-2,8-9: Dexamethasone 10mg orally once daily. Repeat cycle every 3 weeks (Cycle 9 and beyond).</p>
Carfilzomib + Lenalidomide + Dexamethasone (Category 1) ^{6,9,50,b,c,l}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10 minutes, followed by: Days 8-9,15-16: Carfilzomib 27mg/m² (max 59.4mg) IV over 10 minutes Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Administer for one 28-day cycle (Cycle 1), followed by: Days 1-2,8-9,15-16: Carfilzomib 27mg/m² (max 59.4mg) IV over 10 minutes Days 1-21: Lenalidomide 25mg orally daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 11 cycles (Cycles 2-12), followed by: Days 1-2,15-16: Carfilzomib 27mg/m² (max 59.4mg) IV over 10 minutes Days 1-21: Lenalidomide 25mg orally daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks for 6 cycles (Cycles 13-18), followed by: Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks (Cycles 19 and beyond).</p>
Daratumumab + Bortezomib + Dexamethasone (Category 1) ^{2,12,51,d,f}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-2,4-5,8-9,11-12: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 1,4,8,11: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,8,15: 16mg/kg IV. Repeat cycle every 3 weeks for 3 cycles (Cycles 1-3), followed by: Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-2,4-5,8-9,11-12: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 1,4,8,11: Dexamethasone (age >75 years) 20mg IV or orally once daily. Repeat cycle every 3 weeks for 5 cycles (Cycles 4-8), followed by: Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks (Cycle 9 and beyond).</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,i,k} (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
Daratumumab + Carfilzomib + Dexamethasone (Category 1) ^{9,12,52,b-d}	<p>Day 1: Carfilzomib 20mg/m² (max 44mg) IV over 30 minutes, followed by: Days 8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1-2,8-9,15-16,22-23: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,8,15,22: Daratumumab 16mg/kg IV. Administer for one 4-week cycle (Cycle 1), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1-2,8-9,15-16,22-23: Dexamethasone (age ≤75 years) 20 mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20 mg IV or orally once daily Days 1,8,15,22: Daratumumab 16mg/kg IV. Administer for one 4-week cycle (Cycle 2), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1-2,15-16: Dexamethasone (age ≤75 years) 20mg IV or orally once daily Days 8,22: Dexamethasone (≤75 years) 40mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1-2: Dexamethasone (age ≤75 years) 20mg IV or orally once daily Days 8,15,22: Dexamethasone (age ≤75 years) 40mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>
Daratumumab + Lenalidomide + Dexamethasone (Category 1) ^{6,12,42,43,d}	<p>Days 1-21: Lenalidomide 25mg orally once daily Days 1-2,8-9,15-16,22-23: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,8,15,22: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by: Days 1-21: Lenalidomide 25mg orally once daily Days 1-2,15-16: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 8,22: Dexamethasone (age ≤75 years) 40mg orally OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by: Days 1-21: Lenalidomide 25mg orally once daily Days 1-2: Dexamethasone (age ≤75 years) 20mg IV or orally once daily Days 8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily. Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>
Isatuximab-irfc + Pomalidomide + Dexamethasone (Category 1) ^{53-56,m}	<p>Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age <75 years) 40mg orally once daily or IV OR Days 1,8,15,22: Dexamethasone (age ≥75 years) 20mg orally once daily or IV Days 1,8,15,22: Isatuximab-irfc 10mg/kg IV. Administer for one 4-week cycle (Cycle 1), followed by: Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age <75 years) 40mg orally once daily or IV OR Days 1,8,15,22: Dexamethasone (age ≥75 years) 20mg orally once daily or IV Days 1,15: Isatuximab-irfc 10mg/kg IV. Repeat cycle every 4 weeks (Cycle 2 and beyond).</p>
Ixazomib + Lenalidomide + Dexamethasone (Category 1) ^{6,14-16,l}	<p>Days 1,8,15: Ixazomib 4mg orally once daily Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p>
Ixazomib + Pomalidomide + Dexamethasone ^{52,54,57,58}	<p>Days 1,8,15: Ixazomib 4mg orally once daily Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age ≤75 years) 40 mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg orally once daily. Repeat cycle every 4 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,i,k} (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
Pomalidomide + Bortezomib + Dexamethasone (Category 1) ^{54,59,60}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-14: Pomalidomide 4mg orally once daily</p> <p>Days 1-2,4-5,8-9,11-12: Dexamethasone (age ≤75 years) 20mg orally once daily OR</p> <p>Days 1-2,4-5,8-9,11-12: Dexamethasone (age >75 years) 10mg orally once daily.</p> <p>Repeat cycle every 3 weeks for 8 cycles (Cycles 1-8), followed by:</p> <p>Days 1,8: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-14: Pomalidomide 4mg orally once daily</p> <p>Days 1-2,8-9: Dexamethasone (age ≤75 years) 20mg orally once daily OR</p> <p>Days 1-2,8-9: Dexamethasone (age >75 years) 10mg orally once daily.</p> <p>Repeat cycle every 3 weeks (Cycle 9 and beyond).</p>
Other Recommended Regimens	
Belantamab Mafodotin-blmf ^{61,62,o}	<p>Day 1: Belantamab Mafodotin-blmf 2.5mg/kg IV over 30 minutes.</p> <p>Repeat cycle every 3 weeks.</p>
Bendamustine + Bortezomib + Dexamethasone ^{2,63,64}	<p>Days 1,4: Bendamustine 70mg/m² IV over 10-60 minutes</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1,4,8,11: Dexamethasone 20mg orally once daily.</p> <p>Repeat cycle every 4 weeks for 8 cycles or until disease progression.</p>
Bendamustine + Lenalidomide + Dexamethasone ⁶⁵	<p>Days 1-2: Bendamustine 75mg/m² IV over 10-60 minutes</p> <p>Days 1-21: Lenalidomide 10mg orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks.</p>
Bortezomib + Cyclophosphamide + Dexamethasone ^{2,66,67}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-2,4-5,8-9,11-12: Dexamethasone 40mg orally once daily</p> <p>Days 1,8,15: Cyclophosphamide 500mg orally once daily.</p> <p>Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily</p> <p>Days 1,8,15: Cyclophosphamide 50mg orally once daily.</p> <p>Days 1-21: Cyclophosphamide 50mg orally once daily.</p> <p>Repeat cycle every 3 weeks for 8 cycles, followed by:</p> <p>Days 1,8,15,22: Bortezomib 1.3mg/m² subcutaneous</p> <p>Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily</p> <p>Days 1-35: Cyclophosphamide 50mg orally once daily.</p> <p>Repeat cycle every 5 weeks.</p>
Bortezomib + Liposomal Doxorubicin + Dexamethasone (Category 1) ^{2,68}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous</p> <p>Day 4: Liposomal Doxorubicin 30mg/m² IV</p> <p>Days 1-4: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 3 weeks for 8 cycles, followed by:</p> <p>Days 1,8,15,22,29: Bortezomib 1.3mg/m² subcutaneous</p> <p>Day 1-4: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 5 weeks.</p>
Carfilzomib + Cyclophosphamide + Dexamethasone ^{69,70,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10 minutes, followed by:</p> <p>Days 8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 30 minutes</p> <p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily</p> <p>Day 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Administer for one 4-week cycle (Cycle 1), followed by:</p> <p>Days 1-2;8-9;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 30 minutes</p> <p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily</p> <p>Days 1,8,15,22: Dexamethasone 40mg orally once daily.</p> <p>Repeat cycle every 4 weeks for 8 cycles (Cycles 2-9), followed by maintenance therapy with:</p> <p>Days 1-2;15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 30 minutes.</p> <p>Repeat cycle every 4 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,i,k} (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
Carfilzomib (twice weekly) + Dexamethasone (Category 1) ^{9,71,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 30 minutes daily, followed by: Days 8-9;15-16: Carfilzomib 56mg/m² (max 123.2mg) IV over 30 minutes daily Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily. Administer for one 4-week cycle, followed by: Days 1-2,8-9,15-16: Carfilzomib 56mg/m² IV (max 123.2 mg) IV over 30 minutes daily Days 1-2;8-9;15-16;22-23: Dexamethasone 20mg orally once daily. Repeat cycle every 4 weeks.</p>
Cyclophosphamide + Lenalidomide + Dexamethasone ^{6,72}	<p>Days 1,8,15,21: Cyclophosphamide 500mg orally once daily Days 1-21: Lenalidomide 25mg orally once daily Days 1-4,12-15: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p>
Daratumumab + Cyclophosphamide + Bortezomib + Dexamethasone ^{2,12,28,d}	<p>Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily Days 1-2: Dexamethasone 20mg IV daily, followed by: Days 8,15,22: Dexamethasone 40mg IV daily Days 1-2: Daratumumab 8mg/kg IV daily, followed by: Days 8,15,22: Daratumumab 16mg/kg IV daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily Days 1,8,15,22: Dexamethasone 40mg IV or orally daily Days 1,8,15,22: Daratumumab 16mg/kg IV. Administer for one 4-week cycle (Cycle 2), followed by: Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily Days 1,8,15,22: Dexamethasone 40 mg IV or orally daily Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by: Days 1,8,15: Bortezomib 1.5mg/m² subcutaneous Days 1,8,15,22: Cyclophosphamide 300mg/m² orally daily Days 1,8,15,22: Dexamethasone 40mg IV or orally daily Day 1: Daratumumab 16mg/kg. Repeat cycle every 4 weeks for 2 cycles (Cycles 7-8), followed by maintenance therapy with: Day 1: Dexamethasone 12mg IV or orally daily Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for a maximum of 12 cycles.</p>
Daratumumab + Pomalidomide + Dexamethasone ^{12,54,73,d}	<p>Days 1-21: Pomalidomide 4mg orally once daily Days 1-2,8-9,15-16,22-23: Dexamethasone (age ≤75 years) 20mg IV or orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,8,15,22: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by: Days 1-21: Pomalidomide 4mg orally once daily Days 1-2,15-16: Dexamethasone (age ≤75 years) 20mg IV or orally once daily Days 8,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycle 3-6), followed by: Days 1-21: Pomalidomide 4mg orally once daily Days 1-2: Dexamethasone (age ≤75 years) 20mg IV or orally once daily Days 8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg IV or orally once daily. Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,j,k} (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
Elotuzumab + Bortezomib + Dexamethasone ^{2,74,75}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,8,15: Dexamethasone 8mg orally once daily AND 8mg IV prior to Elotuzumab Days 4,11: Dexamethasone 20mg orally once daily Days 1,8,15: Elotuzumab 10mg/kg IV. Repeat cycle every 3 weeks for 2 cycles (Cycles 1-2), followed by: Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,11: Dexamethasone 8mg orally once daily AND 8mg IV prior to Elotuzumab Days 4,8: Dexamethasone 20mg orally once daily Days 1,11: Elotuzumab 10mg/kg IV. Repeat cycle every 3 weeks for 6 cycles (Cycles 3-8), followed by: Days 1,8,15: Bortezomib 1.3mg/m² subcutaneous Days 1,15: Dexamethasone 8mg orally once daily AND 8mg IV prior to elotuzumab Day 8: Dexamethasone 20mg orally once daily Days 1,15: Elotuzumab 10mg/kg IV. Repeat cycle every 4 weeks (Cycle 9 and beyond).</p>
Elotuzumab + Lenalidomide + Dexamethasone (Category 1) ^{6,74,76,77i}	<p>Days 1-21: Lenalidomide 25mg orally once daily Days 1,8,15,22: Dexamethasone 28mg orally AND 8mg IV prior to Elotuzumab Days 1,8,15,22: Elotuzumab 10mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by: Days 1-21: Lenalidomide 25mg orally once daily Days 1,15: Dexamethasone 28mg orally once daily AND 8mg IV prior to Elotuzumab Days 8,22: Dexamethasone 40mg orally once daily Days 1,15: Elotuzumab 10mg/kg IV. Repeat cycle every 4 weeks (Cycle 3 and beyond).</p>
Elotuzumab + Pomalidomide + Dexamethasone ^{54,74,78,p}	<p>Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg orally once daily Days 1,8,15,22: Elotuzumab 10mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by: Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily Days 1,8,15,22: Dexamethasone (age >75 years) 20mg orally once daily Day 1: Elotuzumab 20mg/kg IV. Repeat every 4 weeks (Cycle 3 and beyond).</p>
Idecabtagene Vicleuce ^l ^{79,o}	See NCCN Multiple Myeloma Guidelines ¹
Isatuximab-ifrc + Carfilzomib + Dexamethasone ^{9,53,b,c}	See NCCN Multiple Myeloma Guidelines ¹
Ixazomib + Cyclophosphamide + Dexamethasone ^{14,32,33}	<p>Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1,8,15: Ixazomib 4mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p>
Melphalan Flufenamide + Dexamethasone ^{80-83,q}	<p>Day 1: Melphalan Flufenamide 40mg IV over 30 minutes Days 1,8,15,22: Dexamethasone (age <75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age ≥ 75 years) 20mg orally once daily. Repeat cycle every 4 weeks.</p>
Panobinostat + Bortezomib + Dexamethasone (Category 1) ^{2,84,85}	<p>Day 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1,3,5,8,10,12: Panobinostat 20mg orally once daily Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily. Repeat cycle every 3 weeks for 8 cycles (Cycles 1-8), followed by: Days 1,8,22,29: Bortezomib 1.3mg/m² subcutaneous Days 1,3,5,8,10,12,22,24,26,29,31,33: Panobinostat 20mg orally once daily Days 1-2,8-9,22-23,29-30: Dexamethasone 20mg orally once daily. Repeat cycle every 6 weeks (Cycle 9 and beyond).</p>
Pomalidomide ⁿ + Cyclophosphamide + Dexamethasone ^{54,86}	<p>Days 1,8,15: Cyclophosphamide 400mg orally once daily Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,i,k} (continued)

REGIMEN	DOSING
Other Recommended Regimens (continued)	
Pomalidomide ⁿ + Carfilzomib + Dexamethasone ^{e,9,54,87,88,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 10 minutes, followed by: Days 8-9,15-16: Carfilzomib 27mg/m² (max 59.4mg) IV over 10 minutes Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone 40mg IV or orally once daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1-2,8-9,15-16: Carfilzomib 27mg/m² IV over 10 minutes Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone 40mg IV or orally once daily. Repeat cycle every 4 weeks for 5 cycles (Cycles 2-6), followed by: Days 1-2,15-16: Carfilzomib 27mg/m² IV over 10 minutes Days 1-21: Pomalidomide 4mg IV or orally once daily Days 1,15: Dexamethasone 40mg IV or orally once daily. Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>
Selinexor + Bortezomib + Dexamethasone (once weekly) (Category 1) ^{2,89,90}	<p>Days 1,8,15,22: Bortezomib 1.3mg/m² subcutaneous Days 1-2,8-9,15-16,22-23,29-30: Dexamethasone 20mg orally once daily Days 1,8,15,22,29: Selinexor 100mg orally once daily. Repeat cycle every 5 weeks.</p>
Useful in Certain Circumstances	
Bendamustine ^{91,92}	<p>Days 1-2: Bendamustine 80-150mg/m² IV over 10-60 minutes (based on dose and product selection). Repeat cycle every 4 weeks.</p>
Bortezomib + Dexamethasone (Category 1) ^{2,93-95}	<p>Days 1,4,8,11: Bortezomib 1.3mg/m² subcutaneous Days 1-2,4-5,8-9,11-12: Dexamethasone 20mg orally once daily. Repeat cycle every 3 weeks.</p>
Carfilzomib + Cyclophosphamide + Thalidomide + Dexamethasone ^{9,19,96,97,b,c}	<p>Days 1-2: Carfilzomib 20mg/m² (max 44mg) IV over 30 minutes, followed by: Days 8-9,15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 30 minutes Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1-28: Thalidomide 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1-2,8-9,15-16: Carfilzomib 36mg/m² (max 79.2mg) IV over 30 minutes Days 1,8,15: Cyclophosphamide 300mg/m² orally Days 1-28: Thalidomide 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks (Cycle 2 and beyond). OR Day 1: Carfilzomib 20mg/m² (max 44mg) IV over 30 minutes, followed by: Days 8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1-28: Thalidomide 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1,8,15: Cyclophosphamide 300mg/m² orally once daily Days 1-28: Thalidomide 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks (Cycle 2 and beyond).</p>
Carfilzomib (weekly) + Dexamethasone ^{9,98,99,b,c}	<p>Day 1: Carfilzomib 20mg/m² (max 44mg) IV over 30 minutes, followed by: Days 8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1,8,15,22: Dexamethasone 40mg IV or orally once daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1,8,15,22: Dexamethasone 40mg IV or orally once daily. Repeat cycle every 4 weeks for 7 cycles (Cycles 2-8), followed by: Days 1,8,15: Carfilzomib 70mg/m² (max 154mg) IV over 30 minutes Days 1,8,15: Dexamethasone 40mg IV or orally once daily. Repeat cycle every 4 weeks (beginning with Cycle 9).</p>

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,j,k} (continued)

REGIMEN	DOSING
Useful in Certain Circumstances (continued)	
Daratumumab ^{12,100,ft}	Days 1,8,15,22: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1 and 2), followed by: Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by: Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks (Cycle 7 and beyond).
Dexamethasone + Cyclophosphamide + Etoposide + Cisplatin (DCEP) ^{101,102,f,g}	Days 1-4: Dexamethasone 40mg orally once daily Days 1-4: Cyclophosphamide 400mg/m ² IV continuous infusion over 24 hours Days 1-4: Etoposide 40mg/m ² IV continuous infusion over 24 hours Days 1-4: Cisplatin 10-15mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 4 weeks.
Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide (DT-PACE) ^{2,19,103-105,f,g,l}	Days 1-4: Dexamethasone 40mg orally once daily Days 1-28: Thalidomide 50-200mg orally once daily at bedtime Days 1-4: Cisplatin 10mg/m ² IV continuous infusion over 24 hours Days 1-4: Doxorubicin 10mg/m ² IV continuous infusion over 24 hours Days 1-4: Cyclophosphamide 400mg/m ² IV continuous infusion over 24 hours Days 1-4: Etoposide 40mg/m ² IV continuous infusion over 24 hours. Repeat cycle every 4 weeks.
Dexamethasone + Thalidomide + Cisplatin + Doxorubicin + Cyclophosphamide + Etoposide + Bortezomib (VTD-PACE) ^{2,19,29,31,f,g}	Days 1,4,8,11: Bortezomib 1mg/m ² subcutaneous Days 1-4: Thalidomide 100-200mg orally once daily at bedtime, followed by: Day 5 and beyond: Thalidomide 50-100mg orally once daily at bedtime Days 1-4: Dexamethasone 40mg orally once daily Days 1-4: Cisplatin 10mg/m ² IV continuous infusion over 24 hours daily Days 1-4: Doxorubicin 10mg/m ² IV continuous infusion over 24 hours daily Days 1-4: Cyclophosphamide 400mg/m ² IV continuous infusion over 24 hours daily Days 1-4: Etoposide 40mg/m ² IV continuous infusion over 24 hours daily. Repeat cycle every 4- to 6-weeks.
High-Dose Cyclophosphamide ¹⁰⁶	Days 1-4: Cyclophosphamide 600mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks for 2 cycles, followed by every 3-month cycle.
Ixazomib + Dexamethasone ^{14,107}	Days 1,8,15: Ixazomib 4mg orally once daily Days 1-2,8-9,15-16: Dexamethasone 20mg orally once daily. Repeat cycle every 4 weeks.
Lenalidomide + Dexamethasone (Category 1) ^{6,108, 109,r}	Days 1-21: Lenalidomide 25mg orally once daily Days 1-4,9-12,17-20: Dexamethasone 40mg orally once daily (Cycles 1-4), followed by: Days 1-4: Dexamethasone 40mg orally once daily (Cycle 5 and beyond). Repeat cycle every 4 weeks.
Panobinostat ^s + Carfilzomib ^{9,110,b,c}	Days 1-2: Carfilzomib 20mg/m ² (max 44mg) IV over 10-30 minutes, followed by: Days 8-9,15-16: Carfilzomib 45mg/m ² (max 99mg) IV over 10-30 minutes. Days 1,3,5,15,17,19: Panobinostat 20mg orally once daily. Administer for one 4-week cycle (Cycle 1), followed by: Days 1-2,8-9,15-16: Carfilzomib 45mg/m ² (max 99mg) IV over 10-30 minutes Days 1,3,5,15,17,19: Panobinostat 20mg orally once daily. Repeat cycle every 4 weeks (Cycle 2 and beyond).
Panobinostat ^s + Lenalidomide + Dexamethasone ^{6,111}	Days 1-21: Lenalidomide 25mg orally once daily Days 1,3,5,15,17,19: Panobinostat 20mg orally once daily Days 1,8,15: Dexamethasone 40mg orally once daily. Repeat cycle every 4 weeks.
Pomalidomide ⁿ + Dexamethasone (Category 1) ^{52,112-114,r}	Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Dexamethasone (age ≤75 years) 40mg orally once daily OR Days 1,8,15,22: Dexamethasone (age >75 years) 20mg orally once daily. Repeat cycle every 4 weeks.

continued

Multiple Myeloma Treatment Regimens

► Therapy for Previously Treated Multiple Myeloma^{1,j,k} (continued)

REGIMEN	DOSING
Useful in Certain Circumstances (continued)	
Selinexor + Daratumumab + Dexamethasone ^{87,115}	<p>Days 1,8,15,22: Selinexor 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily or IV OR Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily or IV Days 1,8,15,22: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 2 cycles (Cycles 1-2), followed by: Days 1,8,15,22: Selinexor 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily or IV OR Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily or IV Days 1,15: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks for 4 cycles (Cycles 3-6), followed by: Days 1,8,15,22: Selinexor 100mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily or IV OR Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily or IV Day 1: Daratumumab 16mg/kg IV. Repeat cycle every 4 weeks (Cycle 7 and beyond).</p>
Selinexor + Dexamethasone ^{89,116,117u}	<p>Days 1,3,8,10,15,17,22,24: Selinexor 80mg orally once daily Days 1,3,8,10,15,17,22,24: Dexamethasone 20mg orally once daily. Repeat cycle every 4 weeks.</p>
Selinexor + Pomalidomideⁿ + Dexamethasone ^{89,118}	<p>Days 1-21: Pomalidomide 4mg orally once daily Days 1,8,15,22: Selinexor 60mg orally once daily Days 1,8,15,22: Dexamethasone 40mg orally once daily or IV OR Days 1-2,8-9,15-16,22-23: Dexamethasone 20mg orally once daily or IV. Repeat cycle every 4 weeks.</p>
Venetoclax + Dexamethasone (only for t(11;14) patients) ^{119,120}	<p>Days 1-21: Venetoclax 800mg orally once daily Days 1,8,15: Dexamethasone (age <75 years) 40mg orally once daily OR Days 1,8,15: Dexamethasone (age ≥75 years) 20mg orally once daily. Repeat cycle every 3 weeks.</p>

- ^a Preferred primarily as initial treatment in patients with acute renal insufficiency or those who have no access to bortezomib/lenalidomide/dexamethasone. Consider switching to bortezomib/lenalidomide/dexamethasone after renal function improved.
- ^b Hydration is recommended pre- and post-administration of carfilzomib.
- ^c Carfilzomib can potentially cause cardiac and pulmonary toxicity, especially in elderly patients.
- ^d Includes both daratumumab for intravenous infusion and daratumumab and hyaluronidase-fihj for subcutaneous injection. Daratumumab and hyaluronidase-fihj for subcutaneous injection have different dosing and administration instructions compared to daratumumab for intravenous infusion.
- ^e Treatment option for patients with renal insufficiency and/or peripheral neuropathy.
- ^f Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.
- ^g Generally reserved for the treatment of aggressive multiple myeloma.
- ^h There appears to be an increased risk for secondary cancers, especially with lenalidomide maintenance following transplant. The risks and benefits of maintenance therapy vs. secondary cancers should be discussed with patients.
- ⁱ Continuously until progression. Benboubker L, Dimopoulos MA, Dispenzieri A, et al. Lenalidomide and dexamethasone in transplant-ineligible patients with myeloma. *N Engl J Med.* 2014;371:906-917.
- ^j Consideration for appropriate regimen is based on the context of clinical relapse.
- ^k If a regimen in this section was used as a primary induction therapy and relapse is >6 mo, the same regimen may be repeated.
- ^l Clinical trials with these regimens primarily included patients who were lenalidomide-naïve or with lenalidomide-sensitive multiple myeloma.
- ^m Indicated for patients who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor.
- ⁿ Indicated for the treatment of patients who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression within 60 days of completion of the last therapy.
- ^o Indicated for patients who have received at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.
- ^p Indicated for the treatment of patients who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor.
- ^q Indicated for those who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.
- ^r Consider single-agent lenalidomide or pomalidomide for patients with steroid intolerance.
- ^s Indicated for the treatment of patients who have received at least two prior therapies, including bortezomib and an immunomodulatory agent.
- ^t Indicated for the treatment of patients who have received at least three prior therapies, including a proteasome inhibitor and an immunomodulatory agent or who are double refractory to a proteasome inhibitor and an immunomodulatory agent.
- ^u Indicated for patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

continued

Multiple Myeloma Treatment Regimens

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Multiple Myeloma V.7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 5, 2021.
2. Bortezomib (Velcade) [package insert]. Cambridge, MA: Millennial Pharmaceuticals, Inc.; April 2019.
3. Reeder CB, Reece DE, Kukreti V, et al. Once- versus twice-weekly bortezomib induction therapy with CyBORd in newly diagnosed multiple myeloma. *Blood*. 2010;115:3416-3417.
4. Reeder CB, Reece DE, Kukreti V, et al. Cyclophosphamide, bortezomib and dexamethasone induction for newly diagnosed multiple myeloma: high response rates in a phase II clinical trial. *Leukemia*. 2009;23:1337-1341.
5. Kumar S, Flinn I, Richardson PC, et al. Randomized, multicenter, phase 2 study (EVOLUTION) of combinations of bortezomib, dexamethasone, and lenalidomide in previously untreated multiple myeloma. *Blood*. 2012;119:4375-4382.
6. Lenalidomide (Revlimid) [package insert]. Summit, NJ: Celgene Corp.; October 2019.
7. Richardson PG, Weller E, Lonial S, et al. Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma. *Blood*. 2010;116:679-686.
8. Roussel M, Lauwers-Cances V, Robillard N, et al. Front-line transplantation program with lenalidomide, bortezomib, and dexamethasone combination as induction and consolidation followed by lenalidomide maintenance in patients with multiple myeloma: a phase II study by the Intergroupe Francophone du Myelome. *J Clin Oncol*. 2014;32:2712-2717.
9. Carfilzomib (Kymprolis) [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; March 2021.
10. Korde N, Roschewski M, Zingone A, et al. Treatment with carfilzomib-lenalidomide-dexamethasone with lenalidomide extension in patients with smoldering or newly diagnosed multiple myeloma. *JAMA Oncol*. 2015;1:746-754.
11. Jakubowiak A, Dytfield D, Griffith KA, et al. A phase 1/2 study of carfilzomib in combination with lenalidomide and low-dose dexamethasone as a frontline treatment for multiple myeloma. *Blood*. 2012;120:1801-1802.
12. Daratumumab (Darzalex) [package insert]. Horsham, PA: Janssen Biotech, Inc.; March 2021.
13. Voorhees PM, Kaufman JL, Laubach J, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*. 2020;136:936-945.
14. Ixazomib (Ninlaro) [package insert]. Cambridge, MA: Millennial Pharmaceuticals, Inc.; March 2021.
15. Kumar SK, Berdeja JG, Niesvizky R, et al. Safety and tolerability of ixazomib, and oral proteasome inhibitor, in combination with lenalidomide and dexamethasone in patients with previously untreated multiple myeloma: an open-label phase 1/2 study. *Lancet Oncol*. 2014; 15:1503-1512.
16. Moreau P, Masszi T, Grzasko N, et al. Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. 2016;374:1621-1634.
17. Popat R, Okervee HE, Hallam S, et al. Bortezomib, doxorubicin and dexamethasone (PAD) front-line treatment of multiple myeloma: updated results after long-term follow-up. *Br J Haematol*. 2008;141:512-516.
18. Sonneveld P, Schmidt-Wold IGH, van der Holt B, et al. Bortezomib induction and maintenance treatment in patients with newly diagnosed multiple myeloma: results of the randomized phase III HOVON-65/GMMG-HD4 trial. *J Clin Oncol*. 2012;30:2946-2955.
19. Thalidomide (Thalomid) [package insert]. Summit, NJ: Celgene Corp.; February 2021.
20. Kaufman JL, Nooka A, Vrana M, et al. Bortezomib, thalidomide, and dexamethasone as induction therapy for patients with symptomatic multiple myeloma: a retrospective study. *Cancer*. 2020;116:3143-3151.
21. Cavo M, Taccetti P, Patriarca F, et al. Bortezomib with thalidomide plus dexamethasone compared with thalidomide plus dexamethasone as induction therapy before, and consolidation therapy after, double autologous stem-cell transplantation in newly diagnosed multiple myeloma: a randomized phase 3 study. *Lancet*. 2010;376:2075-2085.
22. Moreau P, Avet-Loiseau H, Facon T, et al. Bortezomib plus dexamethasone versus reduced-dose bortezomib, thalidomide plus dexamethasone as induction treatment before autologous stem cell transplantation in newly diagnosed multiple myeloma. *Blood*. 2011;118:5752-5758.
23. Rosinol L, Oriol A, Teruel AI, et al. Superiority of bortezomib, thalidomide, and dexamethasone (VTD) as induction pretransplantation therapy in multiple myeloma: a randomized phase 3 PETHEMA/GEM study. *Blood*. 2012;120:1589-1596.
24. Kahn ML, Reeder CB, Kumar SK, et al. A comparison of lenalidomide/dexamethasone versus cyclophosphamide/lenalidomide/dexamethasone versus cyclophosphamide/bortezomib/dexamethasone in newly diagnosed multiple myeloma. *Br J Haematol*. 2012;156:326-333.
25. Kumar SK, Lacy MQ, Hayman SR, et al. Lenalidomide, cyclophosphamide and dexamethasone (CRd) for newly diagnosed multiple myeloma: results from a phase 2 trial. *Am J Hematol*. 2011;86:640-645.
26. Boccia RV, Bessudo A, Agajanian R, et al. A multicenter, open-label, phase 1b study of carfilzomib, cyclophosphamide, and dexamethasone in newly diagnosed multiple myeloma patients (CHAMPION-2). *Clin Lymphoma Myeloma Leuk*. 2017;17:433-437.
27. Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before or after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomized, open-label, phase 3 study. *Lancet*. 2019;394:29-34.
28. Yimer H, Melear J, Faber, et al. Daratumumab, bortezomib, cyclophosphamide and dexamethasone in newly diagnosed and relapsed multiple myeloma: LYRA study. *Br J Haematol*. 185:492-502.
29. Griffin PT, Ho VQ, Fulp W, et al. A comparison of salvage infusional chemotherapy regimens for recurrent/refractory multiple myeloma. *Cancer*. 2015;121:3622-3630.
30. Buda G, Orciuolo E, Galimberti S, et al. VDT-PACE as salvage therapy for heavily pretreated MM patients [abstract]. *Blood*. 2013;122:5377.
31. Lakshman A, Singh PP, Rajkumar SV, et al. Efficacy of VDT PACE-like regimens in treatment of relapsed/refractory multiple myeloma. *Am J Hematol*. 2018; 93:179-186.
32. Kumar SK, Buadi FK, LaPlant B, et al. Phase 1/2 trial of ixazomib, cyclophosphamide and dexamethasone in patients with previously untreated symptomatic multiple myeloma. *Blood Cancer J*. 2018;8:70.
33. Kumar SK, Grzasko N, Delimpasi S, et al. Phase 2 study of all-oral ixazomib, cyclophosphamide and low-dose dexamethasone for relapsed/refractory multiple myeloma. *Br J Haematol*. 2019;184:536-546.
34. McCarthy PL, Owzar K, Hofmeister CC, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. *N Engl J Med*. 2012;366:1770-1781.
35. Attal M, Lauwers-Cances V, Marit G, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. *N Engl J Med*. 2012;366:1782-1791.
36. Palumbo A, Hajek R, Delforge M, et al. Continuous lenalidomide treatment for newly diagnosed multiple myeloma. *N Engl J Med*. 2012;366:1759-1769.
37. Kneppers E, van der Holt B, Kersten M-J, et al. Lenalidomide maintenance after nonmyeloablative allogeneic stem cell transplantation in multiple myeloma is not feasible: results of the HOVON 76 trial. *Blood*. 2011;118:2413-2419.
38. Sonneveld P, Schmidt-Wolf ICH, van der Holt B, et al. Bortezomib induction and maintenance treatment in patients with newly diagnose multiple myeloma: results of the randomized phase III HOVON-65/GMMG-HD4 trial. *J Clin Oncol*. 2012;30: 2946-2955.
39. Niesvizky R, Flinn IW, Rifkin RM, et al. Community-based phase IIIB trial of three UPFRONT bortezomib-based myeloma regimens. *J Clin Oncol*. 2015;33:3921-3929.
40. Dimopoulos MA, Gay F, Schjesvold F, et al. Oral ixazomib maintenance following autologous stem cell transplantation (TOURMALINE-MM3): a double-blind, randomized, placebo-controlled phase 3 trial. *Lancet*. 2019;393:253-264.
41. Nooka AK, Kaufman JL, Muppidi S, et al. Consolidation and maintenance therapy with lenalidomide, bortezomib, and dexamethasone (RVD) in high-risk myeloma patients. *Leukemia*. 2014;28:690-693.
42. Facon T, Kumar S, Plesner T, et al. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*. 2019;380:2104-2115.
43. Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. 2016;375:1319-1331.
44. Rajkumar SV, Jacobus S, Callander NS, et al. Lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone as initial therapy for newly diagnosed multiple myeloma: an open-label randomized controlled trial. *Lancet Oncol*. 2010;11:29-37.
45. Benboubker L, Dimopoulos MA, Dispenzieri A, et al. Lenalidomide and dexamethasone in transplant-ineligible patients with myeloma. *N Engl J Med*. 2014;371:906-917.
46. Mateos M-V, Dimopoulos MA, Cavo M, et al. Daratumumab plus bortezomib, melphalan, and prednisone for untreated myeloma. *N Engl J Med*. 2018;378:518-528.
47. Khan ML, Reeder CB, Kumar SK, et al. A comparison of lenalidomide/dexamethasone versus cyclophosphamide/lenalidomide/dexamethasone versus cyclophosphamide/bortezomib/dexamethasone in newly diagnosed multiple myeloma. *Br J Haematol*. 2012;156:326-333.

continued

Multiple Myeloma Treatment Regimens

References (continued)

48. Richardson PG, Xie W, Jagannath S, et al. A phase 2 trial of lenalidomide, bortezomib, and dexamethasone in patients with relapsed and relapsed/refractory myeloma. *Blood*. 2014;123:1461-1469.
49. Richardson PG, Weller E, Jagannath S, et al. Multicenter, phase I, dose-escalation trial of lenalidomide plus bortezomib for relapsed and relapsed/refractory multiple myeloma. *J Clin Oncol*. 2009;27:5713-5719.
50. Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med*. 2015;372:142-152.
51. Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, bortezomib, and dexamethasone for multiple myeloma. *N Engl J Med*. 2016;375:754-766.
52. Chari A, Martinez-Lopez J, Mateos M-V, et al. Daratumumab plus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma. *Blood*. 2019;134:421-431.
53. Isatuximab-ifrc (Sarclisa) [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC; March 2021.
54. Pomalidomide (Pomalyst) [package insert]. Summit, NJ: Celgene Corp.; December 2020.
55. Attal M, Richardson PG, Rajkumar SV, et al. Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomized, multicentre, open-label, phase 3 study. *Lancet*. 2019;394:2096-2107.
56. Dimopoulos MA, Leleu X, Moreau P, et al. Isatuximab plus pomalidomide and dexamethasone in relapsed/refractory multiple myeloma patients with renal impairment: ICARIA-MM subgroup analysis. *Leukemia*. 2021;35:562-572.
57. Voorhees PM, Mulkey F, Hassoun H, et al. Alliance A061202, a phase I/II study of pomalidomide, dexamethasone and ixazomib versus pomalidomide and dexamethasone for patients with multiple myeloma refractory to lenalidomide and proteasome inhibitor based therapy: phase I results [abstract]. *Blood*. 2015;126:375.
58. Krishnan AY, Kapoor P, Palmer J, et al. A phase I/II study of ixazomib (Ic) pomalidomide (POM) dexamethasone (DEX) in relapsed refractory (R/R) multiple myeloma: Initial results [abstract]. *J Clin Oncol*. 2016;34(15_suppl):8008.
59. Richardson PG, Oriol A, Beksac M, et al. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISM): a randomized, open-label, phase 3 trial. *Lancet Oncol*. 2019;20:781-784.
60. Richardson PG, Hofmeister CC, Rajc NS, et al. Pomalidomide, bortezomib and low-dose dexamethasone in lenalidomide-refractory and proteasome inhibitor-exposed myeloma. *Leukemia*. 2017;31:2695-2701.
61. Belantamab mafodotin-blmf (Blenrep) [package insert]. Research Triangle Park, NC: GlaxoSmithKline; August 2020.
62. Lonial S, Lee HC, Badros A, et al. Belantamab mafodotin for relapsed multiple myeloma (DREAMM-2): a two-arm, randomized, open-label, phase 2 study. *Lancet Oncol*. 2020;21:207-221.
63. Ludwig H, Kasparu H, Leitgeb C, et al. Bendamustine-bortezomib-dexamethasone is an active and well-tolerated regimen in patients with relapsed or refractory multiple myeloma. *Blood*. 2014;123:985-991.
64. Offidani M, Corvatta I, Maracci I, et al. Efficacy and tolerability of bendamustine, bortezomib, and dexamethasone in patients with relapsed-refractory multiple myeloma: a phase II study. *Blood Cancer J*. 2013;3:e162.
65. Lentzsch S, O'Sullivan A, Kennedy RC, et al. Combination of bendamustine, lenalidomide, and dexamethasone (BLD) in patients with relapsed or refractory multiple myeloma is feasible and highly effective: results of phase 1/2 open-label, dose escalation study. *Blood*. 2021;119:4603-4613.
66. Davies FE, Wu P, Jenner M, et al. The combination of cyclophosphamide, velcade, and dexamethasone induces high response rates with comparable toxicity to velcade alone and velcade plus dexamethasone. *Haematologica*. 2007;92:1149-1150.
67. Kropff M, Bisping G, Schuck E, et al. Bortezomib in combination with intermediate-dose dexamethasone and continuous low-dose oral cyclophosphamide for relapsed multiple myeloma. *Br J Haematol*. 2007;138:330-337.
68. Orlowski RZ, Nagler A, Sonneveld P, et al. Randomized phase III study of pegylated liposomal doxorubicin plus bortezomib compared with bortezomib alone in relapsed or refractory multiple myeloma: combination therapy improves time to progression. *J Clin Oncol*. 2007;25:3892-3901.
69. Bringhen S, Petrucci MT, Larocca A, et al. Carfilzomib, cyclophosphamide, and dexamethasone in patients with newly diagnosed multiple myeloma: a multicenter, phase 2 study. *Blood*. 2014;124:63-69.
70. Yong K, Hlnsley S, Auner HW, et al. Carfilzomib, cyclophosphamide and 70 (KCD) versus bortezomib, cyclophosphamide and dexamethasone (VCD) for treatment of first relapse or primary refractory multiple myeloma (MM): first final analysis of the phase 2 Muk Five Study [abstract]. *Blood*. 2017;130(Suppl_1):835.
71. Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomized, phase 3, open-label, multicentre study. *Lancet Oncol*. 2016;17:27-38.
72. Morgan GJ, Schey SA, Wu P, et al. Lenalidomide (Revlimid), in combination with cyclophosphamide and dexamethasone (RCD), is an effective and tolerated regimen for myeloma patients. *Br J Haematol*. 2007;137:268-269.
73. Chari A, Sivannasankha A, Fay JW, et al. Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma. *Blood*. 2017;130:974-981.
74. Elotuzumab (Empliciti) [package insert]. Princeton, NJ: Bristol Myers Squibb Company; October 2019.
75. Jakubowski A, Offidani M, Pegourie B, et al. Randomized phase 2 study: elotuzumab plus bortezomib/dexamethasone vs bortezomib/dexamethasone for relapsed/refractory MM. *Blood*. 2016;127:2833-2840.
76. Lonial S, Dimopoulos M, Palumbo A, et al. Elotuzumab therapy for relapsed or refractory multiple myeloma. *N Engl J Med*. 2015;373:621-631.
77. Lonial S, Vij R, Harousseau J-L, et al. Elotuzumab in combination with lenalidomide and low-dose dexamethasone in relapsed or refractory multiple myeloma. *J Clin Oncol*. 2012;30:1953-1959.
78. Dimopoulos MA, Dytfield D, Grosicki S, et al. Elotuzumab plus pomalidomide and dexamethasone for multiple myeloma. *N Engl J Med*. 2018;379:1811-1822.
79. Idecabtagene vicleucel (Abecma) [package insert]. Summit, NJ: Celgene Corp.; March 2021.
80. Melphalan Flufenamide (Pepaxto). [package insert]. Waltham, MA: Oncoceptides Inc.; February 2021.
81. Mateos M-V, Blade J, Brinthen S, et al. Melfluden: a peptide-drug conjugate for the treatment of multiple myeloma. *J Clin Med*. 2020;27:3120.
82. Mateos M-V, Oriol A, Larocca A, et al. HORIZON (OP-106): An exploratory analysis of time-to-next treatment (TTNT) in patients (pts) with relapsed/refractory multiple myeloma (RRMM) who received melphalan plus dexamethasone (dex) [abstract]. *J Clin Oncol*. 2020;38(15_suppl):e20570.
83. Schjesvold F, Robak P, Pour L, et al. OCEAN: a randomized phase III study of melflufen + dexamethasone to treat relapsed refractory multiple myeloma. *Future Oncol*. 2020;16:631-634.
84. San-Miguel JF, Hungria VTM, Yoon S-S, et al. Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma: a multicentre, randomized, double-blind phase 3 trial. *Lancet Oncol*. 2014;15:1195-1206.
85. Richardson PG, Scholtsman RL, Alsina M, et al. PANORAMA 2: Panobinostat in combination with bortezomib and dexamethasone in patients with relapsed and bortezomib-refractory myeloma. *Blood*. 2013;122:2331-2337.
86. Baz RC, Martin 3rd TG, Lin H-Y, et al. Randomized multicenter phase 2 study of pomalidomide, cyclophosphamide, and dexamethasone in relapsed refractory myeloma. *Blood*. 2016;127:2561-2568.
87. Shah JJ, Stadtmayer EA, Abonour R, et al. Carfilzomib, pomalidomide, and dexamethasone for relapsed or refractory myeloma. *Blood*. 2015;126:2284-2290.
88. Rosenbaum CA, Stephens LA, Kukreti V, et al. Phase 1/2 study of carfilzomib, pomalidomide, and dexamethasone (KpD) in patients (Pts) with relapsed/refractory multiple myeloma (RRMM): A Multiple Myeloma Research Consortium multicenter study [abstract]. *J Clin Oncol*. 2016;34(suppl):8007.
89. Selinexor (Xpovio) [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; April 2021.
90. Grosicki S, Simonova M, Spicka I, et al. Once-per-week Selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomized, open-label, phase 3 trial. *Lancet*. 2020;393:1563-1573.
91. Knop S, Straka C, Haen M, et al. The efficacy and toxicity of bendamustine in recurrent multiple myeloma after high-dose chemotherapy. *Haematologica*. 2005;90:1287-1288.
92. Michael M, Bruns I, Bolke E, et al. Bendamustine in patients with relapsed or refractory multiple myeloma. *Eur J Med Res*. 2010;15:13-19.
93. Mikhael JR, Belch AR, Prince HM, et al. High response rate to bortezomib with or without dexamethasone in patients with relapsed or refractory multiple myeloma: results of a global phase 3b expanded access program. *Br J Haematol*. 2009;144:169-175.

continued

Multiple Myeloma Treatment Regimens

References (continued)

94. Jagannath S, Barlogie B, Berenson J, et al. A phase 2 study of two doses of bortezomib in relapsed or refractory myeloma. *Br J Haematol*. 2004;127:165-172.
95. Jagannath S, Richardson PG, Barlogie B, et al. Bortezomib in combination with dexamethasone for the treatment of patients with relapsed and/or refractory multiple myeloma with less than optimal response to bortezomib alone. *Haematologica*. 2006;9:929-934.
96. Mikhael JR, Reeder CB, Libby EN, et al. Phase Ib/II trial of CYKLONE (cyclophosphamide, carfilzomib, thalidomide and dexamethasone) for newly diagnosed myeloma. *Br J Haematol*. 2015;169:219-227.
97. Mikhael JR, Reeder CB, Libby EN, et al. A phase I/II trial of cyclophosphamide, carfilzomib, thalidomide and dexamethasone (CYCLONE) in patients with newly diagnosed multiple myeloma: final results of MTD expansion cohort [abstract]. *Blood*. 2013;122:3179.
98. Berenson JR, Carmell A, Bessudo A, et al. CHAMPION-1: a phase 1/2 study of once-weekly carfilzomib and dexamethasone for relapsed or refractory multiple myeloma. *Blood*. 2016;127:3360-3368.
99. Moreau P, Mateos M-V, Berenson JR, et al. Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of the randomized, phase 3 study. *Lancet Oncol*. 2018;19:953-964.
100. Lonial S, Weiss BM, Usmani SZ, et al. Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRUS): and open-label, randomized, phase 2 trial. *Lancet*. 2016;387:1551-1560.
101. Lazzarino M, Corso A, Barbarano I, et al. DCEP (dexamethasone, cyclophosphamide, etoposide, and cisplatin) is an effective regimen for peripheral blood stem cell collection in multiple myeloma. *Bone Marrow Transplant*. 2001;28:835-839.
102. Dadaricidou M, Papanicolaou X, Maltese D, et al. Dexamethasone, cyclophosphamide, etoposide and cisplatin (DCEP) for relapsed or refractory multiple myeloma patients. *J BUON*. 2007;12:41-44.
103. Lee C-K, Barlogie B, Munshi N, et al. DTPACE: an effective, novel combination chemotherapy with thalidomide for previously treated patients with myeloma. *J Clin Oncol*. 2003;21:2732-2739.
104. Gerrie AS, Mikhael JR, Cheng L, et al. D(T)PACE as salvage therapy for aggressive or refractory multiple myeloma. *Br J Haematol*. 2013;161:802-810.
105. Srikanth M, Davies FE, Wu P, et al. Survival and outcome of blastoid variant myeloma following treatment with the novel thalidomide containing regime DT-PACE. *Eur J Haematol*. 2008;81:431-436.
106. Lenhard Jr. RE, Oken MM, Barnes JM, et al. High-dose cyclophosphamide: an effective treatment for advanced refractory multiple myeloma. *Cancer*. 1984;53:1456-1460.
107. Kumar SK, Laplant BR, Reeder CB, et al. Randomized phase 2 trial of two different doses of ixazomib in patients with relapsed multiple myeloma not refractory to bortezomib [abstract]. *Blood*. 2015;126:3050.
108. Weber DM, Chen C, Niesvizky R, et al. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. *N Engl J Med*. 2007;357:2133-2142.
109. Dimopoulos M, Spencer A, Attal M, et al. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. *N Engl J Med*. 2007;357:2123-2132.
110. Berdeja JG, Hart LL, Mace JR, et al. Phase I/II study of the combination of panobinostat and 6in patients with relapsed/refractory multiple myeloma. *Haematologica*. 2015;100:670-676.
111. Chari A, Cho HJ, Dhadwai A, et al. A phase 2 study of Panobinostat with lenalidomide and weekly dexamethasone in myeloma. *Blood Adv*. 2017;1:1575-1583.
112. San Miguel J, Weisel K, Moreau P, et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomized, open-label, phase 3 trial. *Lancet Oncol*. 2013;14:1055-1066.
113. Dimopoulos MA, Palumbo A, Corradini P, et al. Safety and efficacy of pomalidomide plus low-dose dexamethasone in STRATUS (MM-010): a phase 3b study in refractory multiple myeloma. *Blood*. 2016;128:497-503.
114. Dimopoulos MA, Palumbo A, Weisel K, et al. Safety and efficacy in the Stratus (MM-010) trial, a single-arm phase 3b study evaluating pomalidomide + low-dose dexamethasone in patients with refractory or relapsed and refractory multiple myeloma [abstract]. *Blood*. 2014;124:80.
115. Gasparetto C, Lentzsch S, Schiller G, et al. Selinexor, daratumumab, and dexamethasone in patients with relapsed or refractory multiple myeloma. *Eur J Haematol*. 2021;2:56-65.
116. Chari A, Vogl DT, Gavriatopoulou M, et al. Oral Selinexor-dexamethasone for triple-class refractory multiple myeloma. *N Engl J Med*. 2019;381:727-738.
117. Vogl DT, Dingli D, Cornell RF, et al. Selective inhibitor of nuclear export with oral selinexor for treatment of relapsed or refractory multiple myeloma. *J Clin Oncol*. 2018;36:859-866.
118. Chen CI, Bahlis N, Gasparetto C, et al. Selinexor, pomalidomide, and dexamethasone (SPd) in patients with relapsed or refractory multiple myeloma. *Blood*. 2019;134(suppl_1):141.
119. Venetoclax (Venclexta) [package insert]. North Chicago, IL: AbbVie Inc.; November 2020.
120. Kaufman JL, Gasparetto C, Schjesvold FH, et al. Phase I/II study evaluating the safety and efficacy of venetoclax in combination with dexamethasone as targeted therapy for patients with t(11;14) relapsed/refractory multiple myeloma [abstract]. *Blood*. 2019;134(suppl_1):926.

(Revised 5/2021; NCCN Multiple Myeloma Cancer Guidelines 7.2021.) © 2021 by Haymarket Media, Inc.