

NCCN Clinical Practice Guidelines in Oncology  
(NCCN Guidelines®)

# Multiple Myeloma

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THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA <sup>a-d,n-o,q</sup> Relapsed/Refractory Disease After 1–3 Prior Therapies	
Preferred Regimens <i>Order of regimens does not indicate comparative efficacy</i>	
Bortezomib-Refractory <sup>P</sup>	Lenalidomide-Refractory <sup>P</sup>
<ul style="list-style-type: none"> <li>• Carfilzomib/lenalidomide/dexamethasone (category 1)</li> <li>• Daratumumab/carfilzomib/dexamethasone (category 1)</li> <li>• Daratumumab/lenalidomide/dexamethasone (category 1)</li> <li>• Isatuximab-irfc/carfilzomib/dexamethasone (category 1)</li> <li>• Carfilzomib/pomalidomide/dexamethasone</li> </ul> <p><i>After one prior therapy including lenalidomide and a PI</i></p> <ul style="list-style-type: none"> <li>▶ Daratumumab/pomalidomide/dexamethasone (category 1)</li> </ul> <p><i>After two prior therapies including lenalidomide and a PI</i></p> <ul style="list-style-type: none"> <li>▶ Isatuximab-irfc/pomalidomide/dexamethasone (category 1)</li> </ul>	<ul style="list-style-type: none"> <li>• Daratumumab/bortezomib/dexamethasone (category 1)</li> <li>• Daratumumab/carfilzomib/dexamethasone (category 1)</li> <li>• Isatuximab-irfc/carfilzomib/dexamethasone (category 1)</li> <li>• Pomalidomide/bortezomib/dexamethasone (category 1)</li> <li>• Selinexor/bortezomib/dexamethasone (category 1)</li> <li>• Carfilzomib/pomalidomide/dexamethasone</li> <li>• Elotuzumab/pomalidomide/dexamethasone</li> </ul> <p><i>After one prior therapy including lenalidomide and a PI</i></p> <ul style="list-style-type: none"> <li>▶ Daratumumab/pomalidomide/dexamethasone (category 1)</li> </ul> <p><i>After two prior therapies including lenalidomide and a PI</i></p> <ul style="list-style-type: none"> <li>▶ Isatuximab-irfc/pomalidomide/dexamethasone (category 1)</li> </ul> <p><i>After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy</i></p> <ul style="list-style-type: none"> <li>▶ Ixazomib/pomalidomide/dexamethasone</li> </ul>

\* For Other Recommended Regimens and for regimens Useful in Certain Circumstances for Relapsed/Refractory Disease After 1–3 Prior Therapies, see [MYEL-G 4 of 5](#)

<sup>a</sup> Selected, but not inclusive of all regimens. The regimens under each preference category are listed by order of NCCN Category of Evidence and Consensus alphabetically.  
<sup>b</sup> [Supportive Care Treatment for Multiple Myeloma \(MYEL-H\)](#).  
<sup>c</sup> [General Considerations for Myeloma Therapy \(MYEL-F\)](#).  
<sup>d</sup> [Management of Renal Disease in Multiple Myeloma \(MYEL-K\)](#).  
<sup>n</sup> Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior.  
<sup>o</sup> Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.  
<sup>p</sup> Regimens without anti-CD38 should be considered for those refractory to anti-CD38 antibody as long as they have not received or are refractory to other agents in the regimen.  
<sup>q</sup> If relapse occurs >6 months after stopping treatment, the primary regimen could be considered.

**Note:** All recommendations are category 2A unless otherwise indicated.  
**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

**Continued**

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THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA <sup>a-d,n-r</sup> Relapsed/Refractory Disease After 1–3 Prior Therapies	
<b>Other Recommended Regimens</b>	
<ul style="list-style-type: none"> <li>• Carfilzomib (twice weekly)/dexamethasone (category 1)</li> <li>• Elotuzumab/lenalidomide/dexamethasone (category 1)</li> <li>• Ixazomib/lenalidomide/dexamethasone (category 1)</li> <li>• Bortezomib/cyclophosphamide/dexamethasone</li> <li>• Bortezomib/lenalidomide/dexamethasone</li> <li>• Carfilzomib/cyclophosphamide/dexamethasone</li> <li>• Daratumumab/cyclophosphamide/bortezomib/dexamethasone</li> <li>• Elotuzumab/bortezomib/dexamethasone</li> <li>• Ixazomib/cyclophosphamide/dexamethasone</li> <li>• Lenalidomide/cyclophosphamide/dexamethasone</li> </ul>	<p><i>After two prior therapies including an IMiD and a PI and disease progression on/within 60 days of completion of last therapy</i></p> <ul style="list-style-type: none"> <li>▶ Pomalidomide/cyclophosphamide/dexamethasone</li> </ul>
<b>Useful in Certain Circumstances</b>	
<ul style="list-style-type: none"> <li>• Bortezomib/dexamethasone (category 1)</li> <li>• Bortezomib/liposomal doxorubicin/dexamethasone (category 1)</li> <li>• Lenalidomide/dexamethasone (category 1)</li> <li>• Carfilzomib/cyclophosphamide/thalidomide/dexamethasone</li> <li>• Carfilzomib (weekly)/dexamethasone</li> <li>• Selinexor/carfilzomib/dexamethasone</li> <li>• Selinexor/daratumumab/dexamethasone</li> <li>• Venetoclax/dexamethasone ± daratumumab or PI only for t(11;14) patients</li> </ul>	<p><i>After two prior therapies including IMiD and a PI and with disease progression on/within 60 days of completion of last therapy</i></p> <ul style="list-style-type: none"> <li>▶ Pomalidomide/dexamethasone (category 1)</li> <li>▶ Ixazomib/pomalidomide/dexamethasone</li> <li>▶ Selinexor/pomalidomide/dexamethasone</li> </ul> <p><i>For treatment of aggressive MM</i></p> <ul style="list-style-type: none"> <li>▶ Dexamethasone/cyclophosphamide/etoposide/cisplatin (DCEP)</li> <li>▶ Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE) ± bortezomib (VTD-PACE)</li> </ul> <p><i>After at least three prior therapies including a PI and an IMiD or are double-refractory to a PI and an IMiD</i></p> <ul style="list-style-type: none"> <li>▶ Daratumumab</li> </ul>

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<sup>b</sup> Supportive Care Treatment for Multiple Myeloma (MYEL-H).

<sup>c</sup> General Considerations for Myeloma Therapy (MYEL-F).

<sup>d</sup> Management of Renal Disease in Multiple Myeloma (MYEL-K).

<sup>n</sup> Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior.

<sup>o</sup> Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.

<sup>q</sup> If relapse occurs >6 months after stopping treatment, the primary regimen could be considered.

<sup>r</sup> Consider single-agent lenalidomide or pomalidomide for patients with steroid intolerance.

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THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA <sup>a-d,n-o</sup> Relapsed/Refractory Disease After 3 Prior Therapies
<b>Preferred Regimens</b>
<p>After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD<sup>s</sup></p> <ul style="list-style-type: none"> <li>▶ CAR T-cell Therapy:               <ul style="list-style-type: none"> <li>◊ Ciltacabtagene autoleucl</li> <li>◊ Idecabtagene vicleucl</li> </ul> </li> <li>▶ Bispecific Antibodies               <ul style="list-style-type: none"> <li>◊ Elranatamab-bcmm</li> <li>◊ Talquetamab-tgvs</li> <li>◊ Teclistamab-cqyv</li> </ul> </li> </ul>
<b>Other Recommended Regimens</b>
<ul style="list-style-type: none"> <li>• Bendamustine<sup>t</sup></li> <li>• Bendamustine/bortezomib/dexamethasone<sup>t</sup></li> <li>• Bendamustine/carfilzomib/dexamethasone<sup>t</sup></li> <li>• Bendamustine/lenalidomide/dexamethasone<sup>t</sup></li> <li>• High-dose or fractionated cyclophosphamide</li> </ul> <p>After at least four prior therapies and whose disease is refractory to at least two PIs, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody</p> <ul style="list-style-type: none"> <li>• Selinexor/dexamethasone</li> </ul>
<b>Useful in Certain Circumstances</b>
<p>After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD</p> <ul style="list-style-type: none"> <li>• Belantamab mafodotin-blmf (if available through compassionate use program)</li> </ul>

<sup>a</sup> Selected, but not inclusive of all regimens. The regimens under each preference category are listed by order NCCN Category of Evidence and Consensus alphabetically.

<sup>b</sup> [Supportive Care Treatment for Multiple Myeloma \(MYEL-H\)](#).

<sup>c</sup> [General Considerations for Myeloma Therapy \(MYEL-F\)](#).

<sup>d</sup> [Management of Renal Disease in Multiple Myeloma \(MYEL-K\)](#).

<sup>n</sup> Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior.

<sup>o</sup> Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.

<sup>s</sup> Patients can receive more than one B-cell maturation antigen (BCMA) targeted therapy, but optimal sequencing is unclear.

<sup>t</sup> Agents such as bendamustine can impact the ability to collect T cells for CAR T-cell therapy. See [NCCN Guideline for Management of Immunotherapy-Related Toxicities](#).

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