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NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

Multiple Myeloma

Overall management of Multiple Myeloma is described in the full NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma. Visit NCCN.org to view the complete library of NCCN Guidelines®.

NCCN National Comprehensive Cancer Network®

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-o,q] Relapsed/Refractory Disease After 1–3 Prior Therapies	
Preferred Regimens *Order of regimens does not indicate comparative efficacy*	
Bortezomib-Refractory[p]	**Lenalidomide-Refractory[p]**
• **Carfilzomib/lenalidomide/dexamethasone (category 1)** • **Daratumumab/carfilzomib/dexamethasone (category 1)** • **Daratumumab/lenalidomide/dexamethasone (category 1)** • **Isatuximab-irfc/carfilzomib/dexamethasone (category 1)** • **Carfilzomib/pomalidomide/dexamethasone**	• **Daratumumab/bortezomib/dexamethasone (category 1)** • **Daratumumab/carfilzomib/dexamethasone (category 1)** • **Isatuximab-irfc/carfilzomib/dexamethasone (category 1)** • **Pomalidomide/bortezomib/dexamethasone (category 1)** • **Selinexor/bortezomib/dexamethasone (category 1)** • **Carfilzomib/pomalidomide/dexamethasone** • **Elotuzumab/pomalidomide/dexamethasone**
After one prior therapy including lenalidomide and a PI ▸ **Daratumumab/pomalidomide/dexamethasone (category 1)**	*After one prior therapy including lenalidomide and a PI* ▸ **Daratumumab/pomalidomide/dexamethasone (category 1)**
After two prior therapies including lenalidomide and a PI ▸ **Isatuximab-irfc/pomalidomide/dexamethasone (category 1)**	*After two prior therapies including lenalidomide and a PI* ▸ **Isatuximab-irfc/pomalidomide/dexamethasone (category 1)** *After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy* ▸ **Ixazomib/pomalidomide/dexamethasone**

* 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

[a] [b] 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.
[b] Supportive Care Treatment for Multiple Myeloma (MYEL-H).
[c] General Considerations for Myeloma Therapy (MYEL-F).
[d] Management of Renal Disease in Multiple Myeloma (MYEL-K).
[n] 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.
[o] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.
[p] 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.
[q] 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

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-r] Relapsed/Refractory Disease After 1–3 Prior Therapies	
Other Recommended Regimens	
• **Carfilzomib (twice weekly)/dexamethasone (category 1)** • **Elotuzumab/lenalidomide/dexamethasone (category 1)** • **Ixazomib/lenalidomide/dexamethasone (category 1)** • **Bortezomib/cyclophosphamide/dexamethasone** • **Bortezomib/lenalidomide/dexamethasone** • **Carfilzomib/cyclophosphamide/dexamethasone** • **Daratumumab/cyclophosphamide/bortezomib/dexamethasone** • **Elotuzumab/bortezomib/dexamethasone** • **Ixazomib/cyclophosphamide/dexamethasone** • **Lenalidomide/cyclophosphamide/dexamethasone**	*After two prior therapies including an IMiD and a PI and disease progression on/within 60 days of completion of last therapy* ▸ **Pomalidomide/cyclophosphamide/dexamethasone**
Useful in Certain Circumstances	
• **Bortezomib/dexamethasone (category 1)** • **Bortezomib/liposomal doxorubicin/dexamethasone (category 1)** • **Lenalidomide/dexamethasone (category 1)** • **Carfilzomib/cyclophosphamide/thalidomide/dexamethasone** • **Carfilzomib (weekly)/dexamethasone** • **Selinexor/carfilzomib/dexamethasone** • **Selinexor/daratumumab/dexamethasone** • **Venetoclax/dexamethasone ± daratumumab or PI only for t(11;14) patients**	*After two prior therapies including IMiD and a PI and with disease progression on/within 60 days of completion of last therapy* ▸ **Pomalidomide/dexamethasone (category 1)** ▸ **Ixazomib/pomalidomide/dexamethasone** ▸ **Selinexor/pomalidomide/dexamethasone** *For treatment of aggressive MM* ▸ **Dexamethasone/cyclophosphamide/etoposide/cisplatin (DCEP)** ▸ **Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE) ± bortezomib (VTD-PACE)** *After at least three prior therapies including a PI and an IMiD or are double-refractory to a PI and an IMiD* ▸ **Daratumumab**

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[d] Management of Renal Disease in Multiple Myeloma (MYEL-K).
[n] 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.
[o] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.
[q] If relapse occurs >6 months after stopping treatment, the primary regimen could be considered.
[r] Consider single-agent lenalidomide or pomalidomide for patients with steroid intolerance.

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Continued

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-o] Relapsed/Refractory Disease After 3 Prior Therapies
Preferred Regimens
After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD[s] ▸ *CAR T-cell Therapy*: ◊ **Ciltacabtagene autoleucel** ◊ **Idecabtagene vicleucel** ▸ *Bispecific Antibodies* ◊ **Elranatamab-bcmm** ◊ **Talquetamab-tgvs** ◊ **Teclistamab-cqyv**
Other Recommended Regimens
• **Bendamustine**[t] • **Bendamustine/bortezomib/dexamethasone**[t] • **Bendamustine/carfilzomib/dexamethasone**[t] • **Bendamustine/lenalidomide/dexamethasone**[t] • **High-dose or fractionated cyclophosphamide** *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* • **Selinexor/dexamethasone**
Useful in Certain Circumstances
After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD • **Belantamab mafodotin-blmf (if available through compassionate use program)**

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[b] Supportive Care Treatment for Multiple Myeloma (MYEL-H).
[c] General Considerations for Myeloma Therapy (MYEL-F).
[d] Management of Renal Disease in Multiple Myeloma (MYEL-K).
[n] 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.
[o] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.
[s] Patients can receive more than one B-cell maturation antigen (BCMA) targeted therapy, but optimal sequencing is unclear.
[t] 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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