AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Multiple Myeloma

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: Multiple myeloma (**MM**) is a malignancy of clonal plasma cells in the bone marrow that secrete an abnormal monoclonal immunoglobulin (**M-protein**), crowd out normal hematopoiesis, and drive **end-organ damage**.[1] Virtually all MM is preceded by **monoclonal gammopathy of undetermined significance (MGUS**; prevalence approximately **5% in adults >50** and ~**9% in those >85**)[2,3] which transitions through **smoldering multiple myeloma** (**SMM**) to active disease at roughly **1% per year**.[2] Active disease is defined by the **IMWG SLiM-CRAB criteria**:[4,5] ≥10% clonal bone marrow plasma cells (or biopsy-proven plasmacytoma) **plus** at least one myeloma-defining event = hyper calcemia, renal insufficiency, anemia, bone lesions, ≥60% clonal plasma cells, involved:uninvolved sFLC ratio ≥100, or >1 focal MRI lesion ≥5 mm.

ICD-10 Codes:

Status must be re-evaluated and re-coded at every encounter. **C90.00** multiple myeloma, **not having achieved remission** (active, newly diagnosed, refractory). **C90.01** multiple myeloma, **in remission** (documented sCR/CR/VGPR/PR per IMWG response criteria; on maintenance still counts as active C90.01). **C90.02** multiple myeloma, **in relapse** (previously treated, documented biochemical or clinical progression). **D47.2** monoclonal gammopathy/MGUS (precursor; no HCC mapping). **Z85.79,** personal history of other malignant neoplasms of lymphoid/hematopoietic tissue, is **inappropriate while patient is on maintenance lenalidomide, under active surveillance, or has any documented residual disease**; MM is **largely incurable** and "history of" should be used **only** when the patient is truly off all therapy and oncology surveillance.[1] CRAB manifestations must be coded separately and linked to the myeloma: **D63.0** anemia in neoplastic disease, **N08** glomerular disorders in diseases classified elsewhere (myeloma cast nephropathy), **E83.52** hypercalcemia, **M84.5xx** pathological fracture in neoplastic disease.

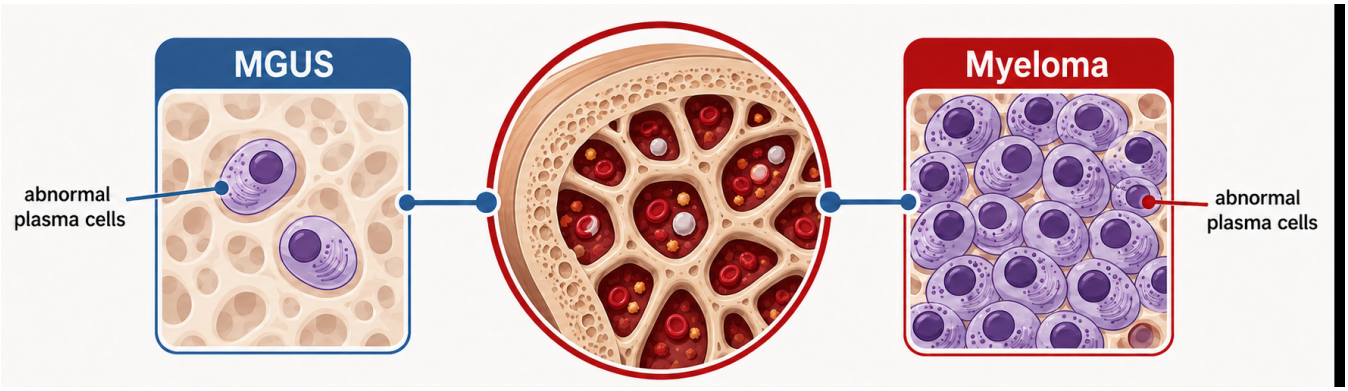
Prevalence and Burden: Approximately **36,000 new MM cases** and **12,540 deaths** are estimated in the US annually;[6] MM accounts for roughly **10% of hematologic malignancies** and **1.8% of all new cancer diagnoses**.[7] Median age at diagnosis is **69 years**;[1] MM is fundamentally a **Medicare-population disease**.[2] Black adults are diagnosed at approximately **14 per 100,000 vs 6.1 per 100,000 in White adults**, with earlier onset and more severe presentation.[1] MM carries the **highest 6-month total cost of care of any cancer in the CMS Enhancing Oncology Model: $94,518 per 6-month episode (60% above the all-cancer average of $59,220)** and 85% of cost driven by systemic therapy (44% Part B injectable; 41% Part D oral) and only 5% from inpatient utilization.[8] Median first-year out-of-pocket cost for lenalidomide maintenance reaches **$5,623 without Low-Income Subsidy vs $6 with LIS**, and LIS receipt is associated with **32% higher probability of receiving IMiDs** in adults aged 75–84.[9]

CLINICAL PEARL: THE MGUS → SMOLDERING → MM CONTINUUM

Monoclonal gammopathy of undetermined significance (MGUS) progresses to **smoldering myeloma (SMM)** or **MM** at roughly **1% per year**.[1,2] SMM progresses to active MM at approximately **10% per year** for the first 5 years, then the rate declines.[1,2] The key inflection point (and the trigger for treatment) is the development of **any SLiM-CRAB criterion** (Sixty percent bone marrow plasma cells, Light chain ratio ≥100, MRI >1 focal lesion, hyperCalcemia, Renal insufficiency, Anemia, Bone lesions), which reclassifies a patient from smoldering to **active MM requiring therapy**.[3,7]

The clinical takeaway: MGUS and SMM are **monitored, not treated**; monitoring must be systematic, because the window between smoldering progression and end-organ damage is where **early intervention preserves the most function**.

How is MGUS Different From Multiple Myeloma



In healthy bone marrow, plasma cells help fight infection. **In MGUS**, a small number of abnormal plasma cells appear but cause no symptoms or organ damage — it requires **monitoring, not treatment**. **In multiple myeloma**, abnormal plasma cells multiply uncontrollably, crowding out healthy cells and damaging bones, kidneys, and blood counts. MGUS progresses to myeloma at about 1% per year, which is why **regular lab monitoring matters**.

HCC/RAF V28 Mapping

ICD-10 CODE[10]	HCC CATEGORY[11]	RAF (CNA)*[12]	DOCUMENTATION REQUIREMENT[4,5]
C90.00: MM, not having achieved remission	**HCC 19** Myelodysplastic Syndromes, **Multiple Myeloma**, and Other Cancers	1.798	Document active/newly diagnosed myeloma or on-treatment status without remission; specify "**active myeloma**," "**on treatment, not in remission**," or equivalent language

ICD-10 CODE[10]	HCC CATEGORY[11]	RAF (CNA)*[12]	DOCUMENTATION REQUIREMENT[4,5]
C90.01: MM, in remission	**HCC 19** Myelodysplastic Syndromes, **Multiple Myeloma**, and Other Cancers	1.798	Document **IMWG response category** (sCR, CR, VGPR, or PR); patients on maintenance therapy or active surveillance **retain C90.01**; do **NOT** use Z85.79
C90.02: MM, in relapse	**HCC 19** Myelodysplastic Syndromes, **Multiple Myeloma**, and Other Cancers	1.798	Document **IMWG-defined progression** or biochemical relapse in a previously treated patient; update from C90.00 when relapse is confirmed
D47.2: MGUS	No HCC	—	**Precursor state**; document monoclonal **protein type** and **risk stratification**; **~1%/yr** progression to MM; high-risk MGUS reaches **~58%** progression at 20 years[2,3,13]
Z85.79: Personal history of LHC malignancy	No HCC	—	Use only when truly off all MM therapy with no residual disease or active surveillance; **exceedingly rare** given MM is largely incurable[1,4]
D63.0: Anemia in neoplastic disease	No HCC	—	Must explicitly link: "**anemia due to multiple myeloma**;" code **C90.0x** as underlying condition
N08: Glomerular disorders in diseases classified elsewhere	No HCC	—	Use for **myeloma cast nephropathy**; code **C90.0x** first as underlying condition; pair with appropriate **N18.x** CKD stage for kidney disease mapping
E83.52: Hypercalcemia	No HCC	—	Document "**hypercalcemia secondary to multiple myeloma**;" symptomatic or calcium **>14 mg/dL** is an **oncologic emergency** requiring urgent management[1,5]
M84.551A M84.552A M84.553A M84.559A Pathological fracture in neoplastic disease	**HCC 402** Hip Fracture/ Dislocation	0.467	**Specify**: anatomic site, laterality, and 7th-character encounter type (A/D/S); do not use osteoporosis codes (**M81.x**) = pathophysiology is distinct;[5] **ONLY** femur and hip fractures map to **HCC 402**

ICD-10 CODE[10]	HCC CATEGORY[11]	RAF (CNA)*[12]	DOCUMENTATION REQUIREMENT[4,5]

ABBREVIATIONS: ICD-10 = International Classification of Diseases, 10th Revision; HCC = hierarchical condition category; RAF = risk adjustment factor; CNA = community, non-dual, aged; MM = multiple myeloma; IMWG = International Myeloma Working Group; sCR = stringent complete response; CR = complete response; VGPR = very good partial response; PR = partial response; MGUS = monoclonal gammopathy of undetermined significance; LHC = lymphoid/hematopoietic; CKD = chronic kidney disease; CMS = Centers for Medicare & Medicaid Services; V28 = CMS-HCC model version 28 *RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model;[11] values vary across patient populations based on eligibility and care setting

Risk-Adjusted Care Resources per Patient/Year[11,12]

Risk-adjusted care resource allocation — MA base rate (~$10,402.34) × RAF coefficient

MULTIPLE MYELOMA	MULTIPLE MYELOMA + HIP/FEMUR FRACTURE
~$18.7K	**~$23.6K+**
HCC 19 · RAF 1.798	HCC 19 + HCC 402 · RAF 2.265 +chemo costs

RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model; values vary across patient populations based on eligibility and care setting

Annual risk value illustrative at base rate ~$10,402/year; actual plan payment varies by county and contract year.

AAVBC PERSPECTIVE

***From the AAVBC's perspective**, value-based care in multiple myeloma demands that primary care recognize **symptom patterns over isolated lab values:** persistent back pain paired with anemia, or back pain with elevated creatinine, in an adult over 50 warrants the **full diagnostic trio** (SPEP + serum free light chain (sFLC) + serum immunofixation (sIFE)) regardless of total protein or SPEP result.[4,14] **A normal SPEP alone is insufficient to exclude the diagnosis**, as it misses light-chain-only and oligosecretory disease, which together account for a meaningful proportion of cases.[1,7]*

*Treatment selection for older adults with high-risk cytogenetics and frailty should be guided by **geriatric assessment and functional status**, not chronological age, because dose-modified regimens and novel combinations can be effective and tolerable when appropriately selected. Treatment goals in this population should be **defined through shared decision-making**; prioritizing functional independence and symptom control is clinically appropriate and supported by both NCCN v5.2026 and the ASCO-OH 2026 Living Guideline.[5,15]*

***AAVBC emphasizes that** primary care is uniquely positioned to close the myeloma diagnostic gap by **maintaining a high index of suspicion** for symptom constellations, **ordering the complete diagnostic trio** rather than SPEP alone, and **ensuring that treatment decisions incorporate**: functional status, comorbidity burden, cytogenetic risk, and patient goals alongside disease biology.*

2 RECOGNITION AND DIAGNOSIS

Diagnostic Tests Covered Under Medicare Part B (older adults, at-risk population)

TEST	FREQUENCY	CPT CODE	CLINICAL INDICATION
Serum protein electrophoresis (SPEP)	**At workup**; **every 1-3 months** during monitoring	84165	Component of diagnostic trio; **SPEP alone is insufficient**: **~1–3% of cases are non-secretory** (no detectable M-protein on SPEP or SIFE) and require sFLC **plus** bone marrow biopsy/imaging to diagnose[1,3,5]
Serum immunofixation electrophoresis (SIFE)	**Concurrent** with SPEP	86334	Component of diagnostic trio = identifies and types the monoclonal immunoglobulin; **abnormal SIFE** can exist with **negative SPEP**[1,3,5]
Serum free light chain (sFLC) assay	**Concurrent** with SPEP and SIFE	83883	Component of diagnostic trio; **sFLC ratio ≥100** with involved **FLC ≥100 mg/L**[4] → abnormal in approximately **60–82% of non-secretory MM patients**[14]
Urine protein electrophoresis (UPEP) + urine immunofixation (UIFE)†	**At workup**; per oncology thereafter	84166 (UPEP) 86335 (UIFE)	Detects **Bence Jones proteinuria** (urinary monoclonal light chains); supports light chain–only disease detection[5]
Bone marrow biopsy with flow cytometry and FISH	**At diagnosis**	38221 85097 88271 – 88275	**Required** for diagnosis: **≥10%** clonal plasma cells; FISH detects **high-risk cytogenetics** (del(17p), t(4;14), t(14;16), 1q gain) for R-ISS/R2-ISS staging[1,4]
Whole-body low-dose CT or PET/CT or whole-body MRI‡	**At diagnosis**; with new symptoms	78816	Detects lytic bone disease (present in **79% at diagnosis**) and extramedullary disease;[1,5] Skeletal radiography (bone survey) alone is **insufficient** → modern imaging is the standard[1]
Beta-2 microglobulin + serum albumin + LDH	**At diagnosis**	82232 82040 83615	Required to assign **R-ISS stage** (Stage I 5-yr OS 82%; Stage II 62%; Stage III 40%)[16]

TEST	FREQUENCY	CPT CODE	CLINICAL INDICATION

ABBREVIATIONS: SPEP = serum protein electrophoresis; SIFE = serum immunofixation electrophoresis; sFLC = serum free light chain; FLC = free light chain; MM = multiple myeloma; UPEP = urine protein electrophoresis; UIFE = urine immunofixation electrophoresis; FISH = fluorescence in situ hybridization; R-ISS = Revised International Staging System; R2-ISS = Second Revision of the International Staging System; CT = computed tomography; PET = positron emission tomography; MRI = magnetic resonance imaging; LDH = lactate dehydrogenase; OS = overall survival; B2M = beta-2 microglobulin; CPT = Current Procedural Terminology; CMS = Centers for Medicare & Medicaid Services; MAC = Medicare Administrative Contractor; NCD = National Coverage Determination
† UPEP/UIFE: Ideally performed on a 24-hour urine collection specimen
‡ PET/CT coverage per CMS NCD 220.6; whole-body MRI coverage may vary by MAC

CLINICAL PEARL: MULTIPLE MYELOMA SCREENING & DETECTION

There are currently **no USPSTF-recommended or Medicare-covered population screening programs** for multiple myeloma or MGUS. The practical diagnostic gap is therefore **case-finding in primary care**: any adult over 50 with unexplained anemia, persistent bone pain, or rising creatinine warrants the **diagnostic trio** (SPEP + sFLC + sIFE) at the same visit, **not SPEP alone**.

CLINICAL PEARL: WHEN MONOCLONAL PROTEIN BECOMES ACTIVE MYELOMA

A monoclonal protein alone is **not myeloma**;[2,5] it becomes active (**treatment-requiring**) multiple myeloma when **clonal marrow plasma cells ≥10%** plus **≥1 CRAB criterion is present**: **C**alcium >11 mg/dL, **R**enal insufficiency (CrCl <40 mL/min), **A**nemia (Hgb <10 g/dL), or **B**one lytic lesions. If **any CRAB feature** accompanies a monoclonal protein, refer to hematology-oncology; do **not** monitor as MGUS.[5]

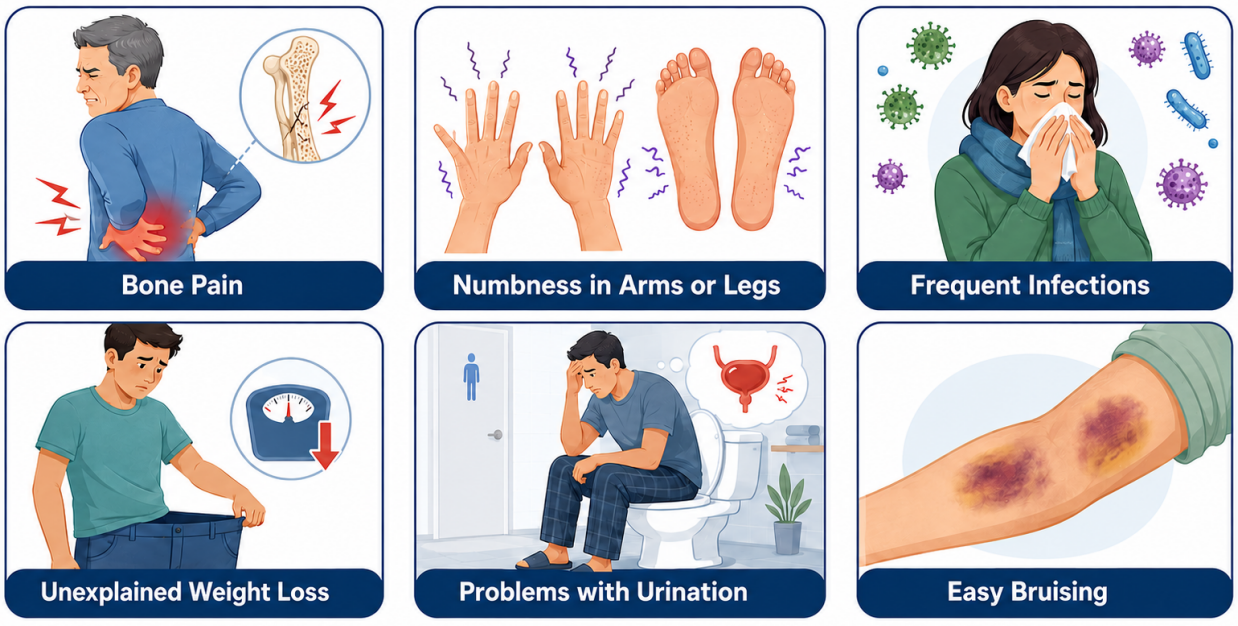
Subtle Early Signs in Older Adults (>65)

SIGN/SYMPTOM	CLINICAL SIGNIFICANCE
Persistent back pain or rib pain in adult >50 without clear musculoskeletal explanation	**Most common presenting symptom**;[1] attributing it to "aging" or degenerative disease is the leading cause of **3–6 month diagnostic delay** in primary care → think myeloma sooner[6]
Unexplained anemia (Hgb <10 g/dL or >2 g/dL below LLN) in adult >50	**CRAB-A criterion**; order the diagnostic trio (SPEP + sFLC + sIFE) at the same visit as iron studies and B12/folate[1,4]
New or rising creatinine/ unexplained renal insufficiency in adult >50	**CRAB-R criterion**; >30% of MM patients have renal impairment at diagnosis from light chain cast nephropathy; order sFLC and SPEP/ sIFE concurrently with nephrology workup[5]

SIGN/SYMPTOM	CLINICAL SIGNIFICANCE
Hypercalcemia (corrected serum calcium >11 mg/dL or >1 mg/dL above ULN)	**CRAB-C criterion**; driven by osteoclast activation; severe (>14 mg/dL) or symptomatic hypercalcemia is a **red-flag emergency**
New osteolytic lesion or pathological fracture without adequate trauma	**CRAB-B criterion**; 79% have lytic lesions at diagnosis; **do not** code as primary osteoporosis = pathophysiology different, DEXA **not informative** for MM bone disease[1]
Recurrent or atypical infections (especially encapsulated organisms)	MM-related **humoral immunodeficiency** from suppression of normal immunoglobulins; infection is the **leading cause of morbidity and mortality** in MM[1]
"Reassuring" normal SPEP but persistent CRAB-like symptoms	SPEP alone **misses** non-secretory MM (**1–3%**) and light-chain–only MM (**15–20%**);[1] sFLC and sIFE **are required**;[17] suspicion persists despite negative labs → **refer** for bone marrow biopsy and advanced imaging[1,5]

ABBREVIATIONS: Hgb = hemoglobin; LLN = lower limit of normal; CRAB = calcium/renal/anemia/bone; SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; MM = multiple myeloma; ULN = upper limit of normal; DEXA = dual-energy X-ray absorptiometry

Symptoms of Multiple Myeloma Risk



Geriatric Risk Factors

FACTOR	RISK SIGNAL	CLINICAL ACTION[5]
Frailty (not chronological age) as treatment driver	**IMWG Frailty Index 3-yr OS**: Fit 91%, Intermediate 77%, Frail 47%; [18] simplified frailty scale (age + ECOG PS + CCI) has **89%** sensitivity and can reduce unnecessary geriatric assessments by **40–45%**[19]	Assess and document frailty at oncology initiation and each transition of care; **tailor therapy intensity to frailty**, not age alone
Renal impairment at presentation	**>30%** have renal impairment at diagnosis and **>2%** require dialysis; [20] lenalidomide requires **dose adjustment by CrCl** (25 mg ≥60, 10 mg 30–59, 15 mg q48h 30, 5 mg on dialysis)*	Check CrCl at diagnosis **and** every visit; **reconcile lenalidomide dose** with renal function; coordinate with nephrology when eGFR <60
Polypharmacy and dexamethasone toxicity	**Dexamethasone** drives hyperglycemia, HTN, insomnia, cataracts;* dose reduction after 6–9 months does not impact PFS/OS[21]	Medication reconciliation **every visit**; document dexamethasone taper plan with oncology; monitor glucose closely in diabetic patients
Peripheral neuropathy from proteasome inhibitors	Bortezomib-induced PN in up to 62%; grade ≥3 uncommon with once-weekly subcutaneous dosing*[22]	Screen for neuropathy **every visit**; report symptoms early to oncology; **favor once-weekly SC dosing** in patients with pre-existing neuropathy
9-fold elevated VTE risk	Highest in **first 6 months post-diagnosis**;[5] IMiD therapy increases risk **up to 28%** without prophylaxis[23]	**All patients** on IMiDs require VTE prophylaxis (ASA, LMWH, DOAC, or warfarin);[5,24] reassess thrombotic/bleeding risk **every visit**
SDoH and treatment access barriers in MA	Black patients **lower odds of treatment initiation** within 90 days (OR 0.865);[25] dual-eligible/LIS OR 0.696; socioeconomic disadvantage associated with shorter OS (HR 1.75)	Screen SDoH **every visit**; enroll eligible patients in LIS/Extra Help and **manufacturer assistance programs**; leverage MA supplemental benefits (NEMT, meals, OTC)

ABBREVIATIONS: IMWG = International Myeloma Working Group; OS = overall survival; ECOG PS = Eastern Cooperative Oncology Group Performance Status; CCI = Charlson Comorbidity Index; CrCl = creatinine clearance; eGFR = estimated glomerular filtration rate; HTN = hypertension; PFS = progression-free survival; PN = peripheral neuropathy; SC = subcutaneous; VTE = venous thromboembolism; IMiD = immunomodulatory drug; ASA = aspirin; LMWH = low-molecular-weight heparin; DOAC = direct oral anticoagulant; SDoH = social determinants of health; MA = Medicare Advantage; OR = odds ratio; LIS = low-income subsidy; HR = hazard ratio; NEMT = nonemergency medical transportation; OTC = over-the-counter

***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Diagnostic Thresholds

CATEGORY	TEST/ MARKER	DIAGNOSIS CRITERION[1,15,19,20]	NOTES[1,15,19,20]
Diagnosis	**IMWG SLiM-CRAB**	**≥10% clonal marrow plasma cells + ≥1 myeloma-defining event**: **C**alcium >11, **R**enal (CrCl 40), **A**nemia (Hgb 10), **B**one (≥1 lytic lesion), OR any **SLiM** biomarker (≥60% plasma cells, sFLC ratio ≥100, >1 focal MRI lesion)	Diagnostic standard; SLiM biomarkers carry ~80% 2-yr progression risk and reclassified 10–15% of formerly "**smoldering**" patients as active disease
PCP Screening	**Diagnostic Trio**	SPEP + sFLC + sIFE **ordered together**; abnormal result → hematology referral for marrow biopsy + imaging	**SPEP alone misses cases**; sFLC is abnormal in 60–82% of non-secretory MM; sIFE detects monoclonal proteins SPEP cannot
Prognosis	**ISS**	β2-microglobulin and albumin → **Stage I/II/III**	Foundational; **median OS** 62/44/29 months by stage
	R-ISS (2015)	ISS + high-risk FISH (del(17p), t(4;14), t(14;16)) + LDH	Current NCCN/ASCO standard; [5,15] 5-yr OS 82%/62%/40% by stage
	R2-ISS (2022)	Additive score: ISS stage + del(17p) + t(4;14) + 1q gain + LDH → 4 risk groups	**Finer stratification** of the large **R-ISS intermediate group**; adopted in NCCN v5.2026[5]
Fitness	**IMWG Frailty Index**	Age + Charlson + ADL + IADL → Fit/Intermediate/Frail	**Guides frailty-adapted Rx**; 3-yr OS 91%/77%/47%; recommended by NCCN[5,26]
	Simplified Frailty Scale	Age + ECOG PS + Charlson → Fit vs Frail	Clinic-friendly screen (sensitivity 89%, specificity 65%); can reduce unnecessary geriatric assessments by ~40%

ABBREVIATIONS: IMWG = International Myeloma Working Group; SLiM = sixty percent/light-chain ratio/MRI focal lesion; CrCl = creatinine clearance; Hgb = hemoglobin; sFLC = serum free light chain; MRI = magnetic resonance imaging; SPEP = serum protein electrophoresis; sIFE = serum immunofixation electrophoresis; MM = multiple myeloma; ISS = International Staging System; OS = overall survival; R-ISS = Revised International Staging System; FISH = fluorescence in situ hybridization; LDH = lactate dehydrogenase; NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology; R2-ISS = Second Revision of the ISS; ADL = activities of daily living; IADL = instrumental activities of daily living; Rx = treatment; ECOG PS = Eastern Cooperative Oncology Group Performance Status; PCP = primary care physician

CLINICAL PEARL - CLUES TO DIG DEEPER

- **Persistent back or rib pain in an adult >50 without clear musculoskeletal explanation →** order the diagnostic trio (SPEP + sFLC + sIFE) at the same visit**,** not just imaging[6]
- **Unexplained anemia + new or rising creatinine + bone pain in an adult >50 → CRAB triad until proven otherwise**; initiate the full myeloma workup (CBC, calcium, creatinine, SPEP, sFLC, sIFE, β2-microglobulin) and refer to hematology within 1–2 weeks[1,6]
- **Hypercalcemia with confusion, polyuria, nausea, or cardiac arrhythmias → symptomatic hypercalcemia is a red flag:** confirm corrected calcium, hydrate aggressively, transfer to ED if calcium >14 mg/dL or unstable vitals[27]
- **"Normal" SPEP but high clinical suspicion** → non-secretory MM (1–3%) and light-chain–only disease (15–20%) require sFLC and sIFE plus bone marrow biopsy; do not prematurely stop the workup at a negative SPEP[5,15]

Common Oversights

OVERSIGHT/SHORTCUT	WHY IT MATTERS — WHAT TO DO INSTEAD[1,15,19,20]
Missing non-secretory or light-chain–only MM by relying on SPEP alone	Non-secretory disease (1–3%), light-chain–only MM (15–20%), and rare subtypes (IgD, IgE) may have **negative or low-level SPEP**; diagnostic trio (SPEP + sFLC + sIFE) = **minimum workup**; bone marrow biopsy and advanced imaging are required when suspicion remains high despite negative labs
Not suspecting MM when older patients present with unexplained anemia, bone pain, or recurrent infection	Symptoms are commonly misattributed to “normal aging”;[19] suspect MM when **normocytic anemia is unexplained**, calcium is elevated, creatinine rises without clear cause, vertebral pain persists, or infections recur
Treating MM bone disease as osteoporosis	MM bone lesions are **osteolytic and pathophysiologically distinct** from osteoporotic bone loss; DEXA **does not detect them**; whole-body low-dose CT or PET-CT is the imaging standard; bisphosphonate or denosumab use here is for skeletal-related event prevention in active MM, not osteoporosis management
Missing renal injury as an MM presentation	Light-chain cast nephropathy, light-chain deposition, hypercalcemia, and amyloid **all cause renal dysfunction in MM**; unexplained AKI or progressive CKD in an older patient warrants urinary protein electrophoresis and sFLC

OVERSIGHT/SHORTCUT	WHY IT MATTERS — WHAT TO DO INSTEAD[1,15,19,20]
Underrecognizing hypercalcemia in older patients	Symptoms (fatigue, confusion, constipation, polyuria, weakness) are often vague and attributed to other conditions; **serum calcium above 10.5 mg/dL** in a patient with anemia or bone pain warrants further workup
Missing VTE prophylaxis on IMiD-based regimens	Lenalidomide, pomalidomide, and thalidomide carry **substantial VTE risk**, especially with concurrent dexamethasone;***** aspirin (low risk) or DOAC/LMWH/warfarin (intermediate or high risk) prophylaxis = standard
Missing infection-prevention measures during induction and maintenance	**MM impairs humoral immunity**;[1,7] encapsulated organisms (pneumococcus, *H. influenzae*) and herpes zoster reactivation are common; pneumococcal, influenza, COVID-19, and zoster vaccination, plus acyclovir or valacyclovir during proteasome-inhibitor therapy, are standard
Treating MM as a static "history of cancer" clinically	**MM is a chronic active disease even on maintenance**; annual review **should document**: current disease status, current therapy with last administered date, monitoring labs (SPEP/sFLC/sIFE cadence), CRAB-related complications, and the ongoing management plan

ABBREVIATIONS: MM = multiple myeloma; SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; DEXA = dual-energy X-ray absorptiometry; CT = computed tomography; PET = positron emission tomography; AKI = acute kidney injury; CKD = chronic kidney disease; VTE = venous thromboembolism; IMiD = immunomodulatory drug; DOAC = direct oral anticoagulant; LMWH = low-molecular-weight heparin; CRAB = calcium/renal/anemia/bone
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Comorbidity Screening

CONDITION	PREVALENCE IN THIS POPULATION	SCREENING AND CLINICAL ACTION
Chronic kidney disease and myeloma cast nephropathy	**>30% of MM patients have renal impairment at diagnosis, >2% requiring dialysis**;[20] pre-existing CKD predicts later-stage diagnosis and higher mortality	Creatinine and eGFR **at every visit**; dose-adjust lenalidomide; denosumab over bisphosphonates if CrCl 30; avoid nephrotoxins
VTE	**9-fold elevated VTE risk** vs general population;[28] IMiDs increase risk **up to 28% without prophylaxis**	**All IMiD patients require VTE prophylaxis** (ASA, DOAC, or LMWH); assess bleeding/renal risk; coordinate agent selection with oncology
Infection	Leading cause of MM morbidity/mortality;[4,15] **highest risk in first 3 months** and during relapsed/refractory therapy	Acyclovir/valacyclovir mandatory with PI or anti-CD38 Rx; optimize PCV20, influenza, COVID-19, RZV vaccines (responses may be blunted)

CONDITION	PREVALENCE IN THIS POPULATION	SCREENING AND CLINICAL ACTION
Bone disease/ fractures	Osteolytic disease in **79% at diagnosis**; **40–50% experience a skeletal-related event**	Bone-targeting therapy (bisphosphonate or denosumab) ≥2 years; **orthopedic referral** for pathologic fracture; vertebroplasty for symptomatic compression fractures
Cardiovascular disease	Carfilzomib carries **cardiac risk**;* dexamethasone contributes to HTN, hyperglycemia, fluid retention	Baseline NT-proBNP + echo before carfilzomib;* monitor BP and glucose on dexamethasone; **cardiology referral** as needed
Polypharmacy/ DDIs	MM **polypharmacy high**;[1] bortezomib levels rise with CYP3A4 inhibitors;* daratumumab causes false-positive indirect Coombs	Med reconciliation **every visit**; alert blood bank to daratumumab before transfusion/ surgery; coordinate with oncology pharmacy
Anemia of malignancy	Hgb 10 g/dL is one **CRAB-A criterion**;[4] persistent anemia requires evaluation for disease activity, treatment toxicity, and nutritional deficiency	**CBC every visit**; iron studies, B12, folate, retic count as indicated; coordinate transfusion or ESA with oncology

ABBREVIATIONS: MM = multiple myeloma; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; CrCl = creatinine clearance; VTE = venous thromboembolism; IMiD = immunomodulatory drug; ASA = aspirin; DOAC = direct oral anticoagulant; LMWH = low-molecular-weight heparin; PI = proteasome inhibitor; CD38 = cluster of differentiation 38; Rx = treatment; PCV20 = pneumococcal 20-valent conjugate vaccine; RZV = recombinant zoster vaccine; HTN = hypertension; NT-proBNP = N-terminal pro–B-type natriuretic peptide; BP = blood pressure; DDI = drug-drug interaction; CYP3A4 = cytochrome P450 3A4; Hgb = hemoglobin; CRAB = calcium/renal/anemia/bone; CBC = complete blood count; ESA = erythropoiesis-stimulating agent
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Staging/Severity Matrix

SEVERITY	DEFINING CRITERIA	ACTION REQUIRED
MGUS (precursor)[2,3,17]	M-protein <3 g/dL **and** clonal plasma cells <10% **and** no MDE; ~3-5% prevalence >50, **~10%** >80; **~1%/yr** progression; high-risk (all three Mayo risk factors) reaches 58% at 20 yr[2]	**Risk-stratified monitoring only** = no treatment;[2,3] **low-risk**: labs at 6 mo, then q2–3 yr; **intermediate/high-risk**: hematology referral, bone marrow biopsy, imaging, closer intervals

SEVERITY	DEFINING CRITERIA	ACTION REQUIRED
Smoldering multiple myeloma (SMM)	M-protein ≥3 g/dL or clonal plasma cells 10–60% **without** MDE;[4,5] risk-stratified into low/ intermediate/high	**Standard**: Active monitoring per shared decision-making; **High-risk SMM**: per ASCO-OH 2026, **daratumumab for up to 36 months** is a conditional option based on **AQUILA trial** (~22 percentage-point PFS advantage at 5 yr;[15,29] OS benefit; grade 3–4 AEs in 36%)
Active MM, R-ISS Stage I (5-yr OS 82%)	β2-microglobulin **<3.5** + albumin **≥3.5** + **standard cytogenetics** + **normal LDH**	Fit, non-frail, age <80: quadruplet **Dara-VRd or Isa-VRd** (Category 1); transplant eligibility assessed separately.[19,30] Frail or ≥80: VRd-lite, dose-adjusted DRd, or Rd doublet with dexamethasone de-escalation[19,31]
Active MM, R-ISS Stage II (5-yr OS 62%)	Neither Stage I nor Stage III = **defined by exclusion**; majority of patients fall here (~62%)[16]	Treatment per frailty;[5,18,19] R2-ISS provides **finer stratification** within this group
Active MM, R-ISS Stage III (5-yr OS 40%)	β2-microglobulin **≥5.5 AND high-risk cytogenetics OR elevated LDH**	**Highest-risk**; consider clinical trial; full quadruplet if fit; carefully tailored regimen if frail; [5,18,19] emphasize palliative care comanagement early[5,26,30]
Relapsed/ refractory disease	IMWG biochemical or clinical relapse criteria **after prior therapy**	Triplet from non–cross-resistant classes; bispecific antibodies and **CAR T-cell therapy** for multiply relapsed disease per NCCN v5.2026;[5] re-transplant **only if first remission >4–5 yr**

ABBREVIATIONS: MGUS = monoclonal gammopathy of undetermined significance; MDE = myeloma-defining event; SMM = smoldering multiple myeloma; ASCO-OH = American Society of Clinical Oncology–Ontario Health; PFS = progression-free survival; OS = overall survival; AE = adverse event; MM = multiple myeloma; R-ISS = Revised International Staging System; LDH = lactate dehydrogenase; Dara-VRd = daratumumab/bortezomib/lenalidomide/ dexamethasone; Isa-VRd = isatuximab/bortezomib/lenalidomide/dexamethasone; VRd = bortezomib/lenalidomide/ dexamethasone; DRd = daratumumab/lenalidomide/dexamethasone; Rd = lenalidomide/dexamethasone; R2-ISS = Second Revision of the ISS; IMWG = International Myeloma Working Group; NCCN = National Comprehensive Cancer Network; CAR T = chimeric antigen receptor T-cell

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

These emergency conditions require **same-day ED transfer** or **emergent specialist consultation** for patients with known or suspected **multiple myeloma**:[27]

- **Spinal cord compression** (new back pain with neurologic deficits)
  - → Emergent **MRI entire spine**; dexamethasone 10 mg IV bolus then 4 mg q6h (**do not wait for MRI**); urgent radiation oncology/neurosurgery consultation
  - × Deficits present >48 hours are frequently **irreversible**
- **Symptomatic hypercalcemia** (calcium >14 mg/dL or confusion, arrhythmias)
  - → **Aggressive IV hydration**; IV zoledronic acid (preferred);[1] calcitonin for rapid initial reduction; dexamethasone 40 mg daily[1]
  - × **Fatal** cardiac arrhythmias and coma **without emergent correction**
- **Hyperviscosity syndrome** (spontaneous mucosal/retinal bleeding, neurologic deficits)
  - → Emergent plasmapheresis; avoid packed RBC transfusion before pheresis (worsens viscosity)
- **Febrile neutropenia (ANC <500 + temp ≥38.3°C)**
  - → Blood cultures × 2 and empiric broad-spectrum antibiotics within 60 minutes of triage
  - × Mortality rises sharply with **each hour** of antibiotic delay
- **Acute renal failure with suspected cast nephropathy** (rapidly rising creatinine, **Bence Jones proteinuria**)
  - → **Aggressive IV hydration** (goal UOP 100–150 mL/h); discontinue all nephrotoxic agents;[1] urgent nephrology/hematology consultation
  - × Can progress to **dialysis dependence** within days if light chain reduction is delayed
- **Massive DVT or pulmonary embolism on IMiD therapy**
  - → Therapeutic anticoagulation (DOACs or LMWH preferred first-line);[24] for massive PE with hemodynamic instability, **consider thrombolysis**
  - × MM carries **9-fold elevated VTE risk**;[28] IMiDs without prophylaxis increase incidence up to 28%

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

Expedited workup required; **do not defer to routine follow-up**:

- **Pathological or impending fracture of a long bone**
  - → Same-day orthopedic consultation for stabilization; **do not wait** for oncology appointment
- **New neurologic symptoms in known myeloma** (confusion, cranial nerve palsies, gait instability)
  - → Urgent brain/spine MRI with contrast within 24–72 hours; dexamethasone if vasogenic edema suspected
- **Acute worsening of peripheral neuropathy on bortezomib** (new motor weakness or rapid Grade escalation)[22] → **Hold bortezomib immediately**;* contact oncology within 24–48 hours for dose reduction or switch to SC weekly;[22] Grade 3/4 neuropathy drops from 28% to 8% with once-weekly dosing[31]
  - × Continued dosing through worsening neuropathy **risks irreversible deficits**
- **Rising creatinine (>1.5× baseline) without other explanation**
  - → Check serum free light chains and urine for Bence Jones protein within 48 hours; **hold nephrotoxic agents**; aggressive hydration

***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

3 MEAT DOCUMENTATION ESSENTIALS

Multiple myeloma documentation must capture a disease that is often invisible to the patient but never truly dormant. The most frequent pitfalls include charting active disease as "**history of**" (**Z85.79**) while the patient is still on maintenance therapy, **omitting CRAB-related comorbidities** (anemia, renal disease, bone disease) that are actively co-managed, and **failing to document the rationale** for ongoing monthly monitoring in a patient who "feels fine." When documentation drifts, so does risk adjustment, care coordination, and the safety net that catches silent biochemical relapse before it becomes symptomatic. The MEAT framework below ties each element into **appropriate clinical action**:

*A 78-year-old with IgG kappa multiple myeloma (**R-ISS Stage II**) diagnosed 2 years ago, now on **lenalidomide 10 mg maintenance** (renally adjusted, CrCl 48). VGPR sustained per oncology (28-APR-2026). Reports stable energy, **no new bone pain**, full adherence → asks whether monthly labs **are still needed** since she "feels back to normal."*

MONITOR: "ECOG 1. Weight 64.5 kg, stable. No new bone pain, fevers, bleeding, or neurologic symptoms. Medications: lenalidomide 10 mg days 1–21/28; aspirin 81 mg (VTE prophylaxis); acyclovir 400 mg BID; zoledronic acid q3 mo (last 10-APR-2026); metformin 500 mg BID. Full adherence. Last oncology 28-APR-2026: VGPR sustained."

EVALUATE: "Spine nontender; gait steady; no petechiae or zoster. Distal vibratory loss bilateral feet (pre-existing diabetic, no progression). Labs (12-MAY-2026): Hgb 11.2 (stable); ANC 2.4; platelets 168; calcium 9.7; creatinine 1.4 (CrCl 48, stable CKD 3a). **M-spike 0.4 g/dL** (from 2.1 at dx); **sFLC ratio 1.8**; **sIFE positive IgG kappa** → consistent with **VGPR**. A1c 6.8%. WB low-dose CT (03/2025): stable lytic lesions T7/L2, no new lesions."

ASSESS: "Multiple myeloma, IgG kappa, R-ISS II, VGPR on maintenance = **C90.01**. Active disease requiring ongoing management; **not Z85.79**. Associated: anemia in neoplastic disease (**D63.0**), stable; CKD 3a (**N18.31**); MM bone disease, stable lytic lesions (**Z79.83**); T2DM (**E11.9**), controlled; distal sensory neuropathy (**G62.9**), stable."

TREAT: "Continue lenalidomide maintenance with **monthly labs** (CBC, CMP, SPEP, sFLC, sIFE) = counseled that monitoring **prevents silent relapse from becoming symptomatic**. Continue VTE prophylaxis, acyclovir, zoledronic acid (next 10-JUL-2026; check Cr before each dose; dental coordination). Immunizations current (PCV20, RZV complete; influenza due 09/2026). Avoid nephrotoxic agents. **Red-flag education provided**. Follow-up 3 months. ACP documented."

Clinical Documentation Elements

- **Document current disease status with status-specific code:** Every note must specify **active (C90.00)/in remission on maintenance (C90.01)/in relapse (C90.02)** = mirror the most recent oncology assessment. "Multiple myeloma" without status **defaults to C90.00** and creates downstream **specificity audit risk** even though same HCC mapping[11,12]
- **Never use Z85.79 while on maintenance or under surveillance**. Patients on lenalidomide maintenance, under oncologic surveillance, or with documented residual disease **retain active C90.0x** coding. "History of" is appropriate **only when** truly off all therapy and oncology surveillance → exceedingly rare in MM.[1,6] Z85.79 **forfeits HCC 19** entirely
- **Code CRAB manifestations separately and link to MM:**[1,18,19] Anemia (**D63.0**), renal failure/cast nephropathy (**N08** + appropriate N18.x), hypercalcemia (**E83.52**), pathological fracture (**M84.5xx** with site/laterality/encounter character) = each **individually coded and linked** to C90.0x in the note ("anemia due to multiple myeloma," "myeloma cast nephropathy"). Failure to link forfeits comorbidity HCC mapping
- **Document current therapy with drug, dose, route, schedule, and last administered date:** "Lenalidomide 10 mg PO days 1–21 of 28-day cycle, renally adjusted for CrCl 48; aspirin 81 mg daily for VTE prophylaxis; zoledronic acid 4 mg IV q3 mo, last dose 10-APR-2026; acyclovir 400 mg BID antiviral prophylaxis" = supports prior authorization, anchors MEAT, and demonstrates **ongoing management**
- **Document oncology comanagement and most recent response assessment:** Note the date of the most recent oncology visit, the documented **IMWG response category** (sCR/CR/VGPR/ PR/SD/PD), and the **current monitoring cadence** (SPEP/sFLC/sIFE/CBC/CMP). This anchors C90.01 **in remission** rather than C90.00 by default[5]
- **Document frailty status and treatment-intensity rationale in older adults:**[5,15,18,19] For patients ≥65, document **IMWG Frailty Index** or simplified frailty score (fit/intermediate/

frail), and the clinical rationale for the chosen treatment intensity (full quadruplet, VRd-lite, dose-adjusted DRd, Rd doublet, dexamethasone-sparing regimen).[5,19] **ASCO-OH 2026** mandates geriatric-assessment–guided management for all patients ≥65 on systemic therapy[15,32]

- **Document SDoH and financial stewardship interventions:** Screen for food, transportation, housing, and financial barriers; document LIS/Extra Help enrollment status and any active patient assistance program referrals. SDoH burden drives **treatment abandonment in MM**; LIS receipt is associated with **32% higher** probability of receiving IMiDs in adults aged 75–84[9,25]

Reframing Common Documentation Shortcuts

INSTEAD OF…	DOCUMENT…[1,4,6,20]
"Multiple myeloma" (no status)	"**Multiple myeloma, IgG kappa, R-ISS Stage II, currently in very good partial response on lenalidomide maintenance = C90.01**; last oncology assessment 28-APR-2026; sustained VGPR; monthly monitoring labs continued."
"History of multiple myeloma"	When the patient is on maintenance, under oncology surveillance, or has residual disease: "**Multiple myeloma, in remission on maintenance (C90.01)**"; **never Z85.79**
"On chemo for myeloma"	**Specific agents, doses, and rationale**: "Lenalidomide 10 mg PO days 1–21 of 28-day cycle (renally adjusted for CrCl 48); aspirin 81 mg daily for VTE prophylaxis on IMiD; zoledronic acid 4 mg IV q3 mo (last dose 10-APR-2026); acyclovir 400 mg BID for antiviral prophylaxis."
"Anemia, mild"	"**Anemia in neoplastic disease (D63.0) secondary to multiple myeloma (C90.01)**, Hgb 11.2, stable, asymptomatic, no transfusion or ESA needed."
"Myeloma in remission"	"**Multiple myeloma in remission (C90.01)**, IgG kappa, VGPR per IMWG criteria sustained × 14 months; M-spike 0.4 g/dL (down from 2.1 at diagnosis); sFLC ratio 1.8; bone marrow 02/2024 with 8% plasma cells; on lenalidomide 10 mg maintenance."
"Bone pain, possibly myeloma"	"**Multiple myeloma bone disease, stable lytic lesions T7 and L2** on whole-body low-dose CT 03-MAR-2025; no new lesions; no impending fracture; on zoledronic acid 4 mg IV q3 mo; pain controlled with scheduled acetaminophen; **avoid NSAIDs (renal)**."
"Patient feels fine, no need to monitor"	"Counseled patient that **clinical stability on maintenance reflects therapy working, not disease being cured**; monthly SPEP/sFLC/sIFE/CBC/CMP labs **continued** to detect biochemical relapse **before** symptomatic progression; next labs 09-JUN-2026."

INSTEAD OF…	DOCUMENT…[1,4,6,20]

ABBREVIATIONS: R-ISS = Revised International Staging System; VGPR = very good partial response; PO = by mouth; CrCl = creatinine clearance; VTE = venous thromboembolism; IMiD = immunomodulatory drug; IV = intravenous; BID = twice daily; ESA = erythropoiesis-stimulating agent; Hgb = hemoglobin; IMWG = International Myeloma Working Group; sFLC = serum free light chain; CT = computed tomography; NSAIDs = nonsteroidal anti-inflammatory drugs; SPEP = serum protein electrophoresis; sIFE = serum immunofixation electrophoresis; CBC = complete blood count; CMP = comprehensive metabolic panel

DOCUMENTATION IS COMPREHENSIVE CODING

Every active multiple myeloma encounter should document *the diagnosis with immunoglobulin subtype (IgG/IgA/IgD/light chain only), light chain restriction (kappa/lambda), risk stratification (R-ISS stage, cytogenetics), IMWG response status (CR/VGPR/PR/progressive disease), current treatment regimen and cycle, and CRAB-related comorbidities (anemia D63.0, CKD N18.x, bone disease M80–M84 series, hypercalcemia E83.52) → each coded* ***separately*** *and* ***linked to the myeloma*** *in the note. Z85.79 applies* ***only*** *after all therapy including maintenance has been completed and oncology has confirmed no further treatment or surveillance is planned;* ***premature transition eliminates HCC 19 mapping entirely****. In CMS-HCC V28, C90.00, C90.01, and C90.02* ***all map to HCC 19*** *(Myelodysplastic Syndromes, Multiple Myeloma, and Other Cancers); accurate coding ensures the documented complexity of care matches the resources required to manage these patients.*

4 TREATMENT AND REFERRAL QUICK GUIDE

Myeloma does not use anatomic TNM staging.[5] Staging is purely prognostic and rests on two parallel assessments: **disease biology** (R-ISS staging and cytogenetic risk) and **patient fitness** (transplant eligibility and frailty). For the PCP, this means the question is never simply "what stage?" but rather "**how aggressive is the disease, and how much therapy can this patient tolerate?**"

Treatment is anchored to the **NCCN Multiple Myeloma Guidelines v5.2026**, the **ASCO–Ontario Health Living Guideline 2026**, and the **NCCN Older Adult Oncology Guidelines 2026**.[5,15,26] In the Medicare population, therapy selection begins with frailty assessment, **not** regimen names. The **IMWG Frailty Index** is the validated stratification tool; importantly, frailty is dynamic: fitness may improve with effective therapy (allowing intensification), or toxicity may require de-escalation.

MM remains largely incurable. The clinical goal is the **deepest sustainable response that protects functional independence and quality of life**, not maximum response at any toxicity cost.

Therapy Escalation Criteria

TRIGGER	ACTION*
Adult >50 with new bone pain, unexplained anemia, or rising creatinine	**Order the diagnostic trio (SPEP + sFLC + sIFE) at the same visit** plus CBC, calcium, creatinine, β2-microglobulin, and skeletal imaging (low-dose whole-body CT, PET/CT, or whole-body MRI);[1,4,15] hematology referral within 1–2 weeks; expedited if hypercalcemia, severe anemia, renal injury, or impending fracture
MGUS: low-risk	**Risk-stratified monitoring only**:[3,17] labs at 6 months, then every 2–3 years (or with new symptoms); no bone marrow biopsy or imaging needed; no therapy
MGUS: intermediate or high-risk	Hematology referral; bone marrow biopsy; baseline bone imaging; **closer monitoring intervals** per oncology[2,13,17]
Smoldering MM: high-risk	**Per ASCO-OH 2026**,[32] **daratumumab for up to 36 months is a conditional option** based on **AQUILA trial** (~22 percentage-point PFS advantage at 5 yr; OS benefit; grade 3–4 AEs in 36%) = shared decision-making with oncology required;[29] otherwise active monitoring[5]
Active MM, fit, transplant-eligible, age <80	**Quadruplet Dara-VRd or Isa-VRd (Category 1)**;[5,33] transplant eligibility assessed separately; **PCP role**: comorbidity comanagement, infection prophylaxis, VTE prophylaxis, vaccination optimization, SDoH support
Active MM, transplant-ineligible, fit/ intermediate-fit	**Preferred: DRd (daratumumab/lenalidomide/dexamethasone) (Category 1) or quadruplet Dara-VRd/Isa-VRd**;[5,34] VRd is an alternative Category 1 option;[5] **PCP role**: monitor for adherence, neuropathy, dexamethasone toxicity (hyperglycemia, hypertension), and IMiD VTE
Active MM, frail or age ≥80	**VRd-lite** (lenalidomide 15 mg days 1–21; bortezomib 1.3 mg/m^2 weekly SC; dexamethasone 20 mg on bortezomib days; 35-day cycles) = **ORR 86%**, median PFS 35.1 months in transplant-ineligible patients (median age 73);[5] alternatively dose-adjusted DRd, or Rd doublet (Category 1) for very frail patients;[5] **IFM2017-03 trial** supports dexamethasone-sparing daratumumab + lenalidomide as superior to lenalidomide + dexamethasone in frail NDMM without increased infection risk[35]
Relapsed/refractory disease	Triplet therapy from non–cross-resistant classes;[5] **T-cell redirecting therapies (bispecific antibodies, CAR T-cell therapy) for multiply relapsed disease** per NCCN v5.2026;[5] re-transplant only if first remission lasted >4–5 years[5,15]
Spinal cord compression, symptomatic hypercalcemia, hyperviscosity, febrile neutropenia, acute renal failure	**Immediate ED transfer**;[27] **spinal cord compression**: emergency MRI, high-dose dexamethasone, emergent radiation or surgical decompression;[27] **hypercalcemia** >14 mg/dL or symptomatic: aggressive IV hydration, IV zoledronic acid, calcitonin, dexamethasone;[5] **hyperviscosity**: emergent plasmapheresis;[5] **febrile neutropenia**: **immediate** empiric broad-spectrum antibiotics[36]

TRIGGER	ACTION*

ABBREVIATIONS: SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; CBC = complete blood count; CT = computed tomography; PET = positron emission tomography; MRI = magnetic resonance imaging; MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma; ASCO-OH = American Society of Clinical Oncology–Ontario Health; PFS = progression-free survival; OS = overall survival; AE = adverse event; Dara-VRd = daratumumab/bortezomib/lenalidomide/dexamethasone; Isa-VRd = isatuximab/bortezomib/lenalidomide/dexamethasone; PCP = primary care provider; VTE = venous thromboembolism; SDoH = social determinants of health; DRd = daratumumab/lenalidomide/dexamethasone; VRd = bortezomib/lenalidomide/dexamethasone; IMiD = immunomodulatory drug; SC = subcutaneous; ORR = overall response rate; Rd = lenalidomide/dexamethasone; NDMM = newly diagnosed multiple myeloma; NCCN = National Comprehensive Cancer Network; CAR T = chimeric antigen receptor T-cell; ED = emergency department; IV = intravenous ***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

NCCN v5.2026/ASCO-OH 2026/NCCN Older Adult Oncology 2026 Aligned Recommendations

CATEGORY	RECOMMENDED AGENT/ APPROACH	NOTES
Frailty assessment (foundational)	**IMWG Frailty Index** (age + CCI + ADL + IADL → Fit/Intermediate-fit/ Frail) at oncology initiation and major transitions;[37] **simplified frailty scale** (age + ECOG PS + CCI) for busy-clinic screening[38]	Required by NCCN v5.2026 for **all older adults**;[5] ASCO-OH 2026 mandates geriatric-assessment–guided management for **all patients ≥65** receiving systemic therapy[15]
First-line therapy (fit, non-frail, age <80)	**Dara-VRd or Isa-VRd (Category 1)** quadruplet; transplant eligibility **assessed separately**[5]	Preferred regimens per NCCN v5.2026;[5] deepest responses with most durable PFS in fit patients; **PCP role**: vaccination, VTE prophylaxis, infection prophylaxis, SDoH support[5,26,36]
First-line therapy (transplant-ineligible, fit/ intermediate)	**DRd (Category 1)** or **Dara-VRd/ Isa-VRd** quadruplet; **VRd** is an alternative Category 1 option	**PCP role**: monitor adherence, neuropathy, dexamethasone toxicity (hyperglycemia, hypertension, insomnia), IMiD-related VTE
First-line therapy (frail or age ≥80)	**VRd-lite** (lenalidomide 15 mg days 1–21; bortezomib 1.3 mg/m^2 weekly SC; dexamethasone 20 mg on bortezomib days; 35-day cycles); **dose-adjusted DRd**; **Rd doublet (Category 1)** for very frail; **dexamethasone-sparing** regimens preferred[5]	**REST trial** (median age 77, 31% >80, 45% IMWG-frail):[39] dexamethasone-sparing Isa-VRd **tolerable in frail patients** with high relative dose intensities; **IFM2017-03** supports Dara-Rd without dexamethasone for frail NDMM[40]

CATEGORY	RECOMMENDED AGENT/ APPROACH	NOTES
Dexamethasone de-escalation	Reduce after 6–9 months or earlier as toxicity develops;[15] **stopping after 9 months did not impact PFS or OS** in multiple studies and reduced toxicity (cataracts, bone loss, hyperglycemia)[15,21]	ASCO-OH 2026 **explicitly supports** dexamethasone **reduction or discontinuation** after induction;[15] PCP should coordinate with oncology on taper[5]
Bortezomib dosing in older adults	**Once-weekly SC**	**Once-weekly SC** is the standard in older adults;[5] reduces peripheral neuropathy and clinic burden[22]
Bone-targeting therapy	**Bisphosphonate** (zoledronic acid 4 mg IV q3–4 weeks) **or denosumab** (120 mg SC q4 weeks) **for at least 2 years**;*[5] **denosumab preferred when CrCl <30** (monitor for severe hypocalcemia)	**All patients with active MM** should receive bone-targeting therapy;[5] coordinate with dental and oncology before invasive dental procedure; monitor creatinine before each zoledronic acid dose*[5]
VTE prophylaxis on IMiDs	**All patients on lenalidomide or pomalidomide require VTE prophylaxis**:[5] aspirin (low-risk), LMWH (high-risk), DOAC, or warfarin based on patient-specific risk	MM has **9-fold** elevated baseline VTE risk; [6] IMiD therapy raises risk **up to 28%** without prophylaxis;[23] coordinate agent selection with oncology and pharmacy
Antiviral prophylaxis	**Acyclovir 400 mg BID or valacyclovir 500 mg daily mandatory** for proteasome inhibitor (bortezomib, carfilzomib, ixazomib) and anti-CD38 (daratumumab, isatuximab) therapy*[5,36]	**Reduces herpes zoster reactivation risk**;[41] continue throughout therapy and for ≥3 months after completion per oncology[5]
Maintenance therapy	**Lenalidomide** typically 10-15 mg PO daily (renally adjusted) for transplant-eligible and most transplant-ineligible patients post-induction[5,15]	Median first-year OOP **$5,623 without LIS vs $6 with LIS**;[9] LIS enrollment is a **high-leverage VBC intervention**
T-cell redirecting therapies (relapsed/ refractory)	**Bispecific antibodies and CAR T-cell therapy** per NCCN v5.2026 = specialist-managed;[5] **PCP role** is comorbidity comanagement, infection surveillance (CRS, ICANS recognition), and care coordination	**Refer at relapse**; coordinate with cellular therapy program; document infection prophylaxis and emergency contact plan in the chart

CATEGORY	RECOMMENDED AGENT/ APPROACH	NOTES

ABBREVIATIONS: IMWG = International Myeloma Working Group; CCI = Charlson Comorbidity Index; ADL = activities of daily living; IADL = instrumental activities of daily living; ECOG PS = Eastern Cooperative Oncology Group Performance Status; NCCN = National Comprehensive Cancer Network; ASCO-OH = American Society of Clinical Oncology–Ontario Health; Dara-VRd = daratumumab/bortezomib/lenalidomide/dexamethasone; Isa-VRd = isatuximab/bortezomib/lenalidomide/dexamethasone; PFS = progression-free survival; PCP = primary care provider; VTE = venous thromboembolism; SDoH = social determinants of health; DRd = daratumumab/lenalidomide/dexamethasone; VRd = bortezomib/lenalidomide/dexamethasone; IMiD = immunomodulatory drug; SC = subcutaneous; Rd = lenalidomide/dexamethasone; NDMM = newly diagnosed multiple myeloma; Dara-Rd = daratumumab/lenalidomide/dexamethasone (without dexamethasone loading); OS = overall survival; IV = intravenous; CrCl = creatinine clearance; MM = multiple myeloma; LMWH = low-molecular-weight heparin; DOAC = direct oral anticoagulant; BID = twice daily; CD38 = cluster of differentiation 38; PO = by mouth; OOP = out-of-pocket; LIS = low-income subsidy; VBC = value-based care; CAR T = chimeric antigen receptor T-cell; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity syndrome
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Non-Pharmacologic Treatment and Lifestyle Modification

INTERVENTION	TARGET/RECOMMENDATION	NOTES
Bone health and falls prevention	Weight-bearing activity **as tolerated**;[19] home safety assessment; orthopedic referral for symptomatic vertebral compression fractures (consider vertebroplasty/kyphoplasty); calcium 1200 mg + vitamin D 800–1000 IU **daily**[42]	Counsel patients on activity restrictions per oncology if impending fracture; **avoid high-impact activity with known lytic lesions**; integrate physical therapy for safe mobility
Symptom diary and adherence support	Daily log of bone pain, fatigue, fever, infection signs, neuropathy, and lenalidomide cycle days; pill organizer; pharmacy auto-refill; **patient assistance program enrollment**	Supports **timely flare/relapse recognition**;[15] reduces lenalidomide abandonment;[9] documents adherence for prior authorization
Mediterranean-style diet and weight management	Plant-rich, low ultra-processed foods; protein adequate for sarcopenia prevention; weight maintenance counseling for MGUS patients (**obesity is the strongest modifiable risk factor**: BMI ≥25 **PAF 27.1%** for MGUS-to-MM progression)[43]	Weight loss **may** slow MGUS-to-MM progression in obese MGUS patients
Exercise	150 min/wk moderate aerobic + 2×/wk resistance training as tolerated; tailor to frailty and bone disease	Maintains lean muscle mass and bone density;[44] supports treatment tolerance; **reduces VTE risk**

INTERVENTION	TARGET/RECOMMENDATION	NOTES
Smoking cessation and limited alcohol	**Behavioral counseling** + nicotine replacement or varenicline as appropriate;[45] ≤1 drink/day women, ≤2 men	Although smoking and alcohol are **not consistently associated** with MM risk, both increase infection risk and worsen overall outcomes in older oncology patients[26,36]
Caregiver education and advance care planning	**Document advance care plan early**, especially for patients ≥80 or frail;[30,32] identify primary caregiver; teach red-flag recognition; document **goals-of-care discussion**	ASCO-OH 2026 explicitly states that quality of life should be assessed **at each visit** and should influence **treatment intensity and duration**[15]

ABBREVIATIONS: IU = international units; MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma; BMI = body mass index; PAF = population attributable fraction; VTE = venous thromboembolism; ASCO-OH = American Society of Clinical Oncology–Ontario Health

Medication Safety and Dose Adjustments

DRUG/CLASS	INTERACTION/ CONTRAINDICATION	CLINICAL ACTION[1,5,15,23]
Lenalidomide/ pomalidomide (IMiDs) + thrombosis risk	**Elevated VTE risk**, especially with concurrent dexamethasone, EPO, or estrogen	Mandatory VTE prophylaxis; agent selection by IMPEDE/SAVED score;[15] reassess VTE and bleeding risk **every visit**
Lenalidomide/ pomalidomide + renal impairment	**Renally cleared**; dose adjustment by CrCl required to avoid cytopenias or under-treatment*	Verify CrCl **every visit**; confirm dose matches renal function; coordinate adjustments with oncology
Bortezomib (proteasome inhibitor) + CYP3A4 inhibitors/ peripheral neuropathy	Cumulative peripheral neuropathy; strong CYP3A4 inhibitors (azoles, clarithromycin) raise levels*	Screen for neuropathy **every visit**; **flag CYP3A4 inhibitors** at med reconciliation
Daratumumab/ isatuximab (anti-CD38) + blood-bank interference	False-positive indirect Coombs; **interferes with crossmatching**	**Alert blood bank** before any transfusion or surgery; document anti-CD38 therapy prominently in med list
Bisphosphonates (zoledronic acid)/ denosumab + renal monitoring and ONJ	Bisphosphonates **nephrotoxic**; denosumab risks hypocalcemia; both carry ONJ risk*[5]	Monitor renal function **before each bisphosphonate dose**;[5] dental clearance before initiation; denosumab preferred **if CrCl <30**[46]

DRUG/CLASS	INTERACTION/ CONTRAINDICATION	CLINICAL ACTION[1,5,15,23]
High-dose dexamethasone + hyperglycemia/ hypertension fluid retention/cataracts/ bone loss/insomnia/ adrenal suppression	Hyperglycemia, hypertension, insomnia, cataracts, bone loss;* de-escalation after response **does not compromise PFS/OS**[21]	Monitor glucose and BP; coordinate taper with oncology; counsel on mood/sleep effects[5]
Carfilzomib (proteasome inhibitor) + cardiac toxicity	Heart failure, hypertension, arrhythmia risk;*[47] higher in pre-existing cardiac disease	Baseline cardiac assessment before initiation;[15] monitor for **new dyspnea/edema**; cardiology comanagement as needed
Proteasome inhibitors and anti-CD38 antibodies + antiviral prophylaxis	Clinically significant VZV reactivation without antiviral prophylaxis	Antiviral prophylaxis mandatory throughout therapy and ≥3 months after;[5,36,41] verify adherence every visit
Live vaccines (zoster ZVL, MMR, varicella, yellow fever) on active MM therapy	Disseminated infection risk in immunocompromised patients[36]	Contraindicated; use inactivated alternatives (RZV, inactivated influenza);[5,36] coordinate timing with oncology

ABBREVIATIONS: IMiD = immunomodulatory drug; VTE = venous thromboembolism; EPO = erythropoietin; CrCl = creatinine clearance; CYP3A4 = cytochrome P450 3A4; CD38 = cluster of differentiation 38; ONJ = osteonecrosis of the jaw; PFS = progression-free survival; OS = overall survival; BP = blood pressure; VZV = varicella-zoster virus; MM = multiple myeloma; ZVL = zoster vaccine live; MMR = measles-mumps-rubella vaccine; RZV = recombinant zoster vaccine.
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

When to Refer

CRITERION[5,27]	SPECIALIST	URGENCY[5,27]
Suspected new MM (CRAB triad in adult >50 + abnormal SPEP/sFLC/ sIFE)	Hematology/oncology	**URGENT** (1–2 weeks); **IMMEDIATE** if hypercalcemia, severe anemia, renal failure, or impending fracture
Suspected spinal cord compression (back pain + neurologic deficits)	ED + neurosurgery + radiation oncology	**IMMEDIATE**: emergency MRI, high-dose dexamethasone; do not delay for outpatient workup
Symptomatic hypercalcemia, hyperviscosity, febrile neutropenia, acute renal failure	ED + hematology	**IMMEDIATE** transfer

CRITERION[5,27]	SPECIALIST	URGENCY[5,27]
Pathological fracture or impending fracture of long bone	Orthopedic surgery + radiation oncology	**URGENT** (same-day/next-day)
Rising M-protein or sFLC suggesting biochemical relapse	Treating oncologist	**EXPEDITED** (within 1–2 days of result)
Symptomatic vertebral compression fracture	Interventional radiology or spine surgery (vertebroplasty/ kyphoplasty)	**URGENT** (1–2 weeks) for pain control
Worsening peripheral neuropathy on proteasome inhibitor	Treating oncologist for dose modification	**EXPEDITED** (within days)
Multiply relapsed disease and candidate for bispecific antibody or CAR T-cell therapy	Cellular therapy program (academic center)	Per oncology referral
Suspected MGUS-to-MM progression (rising M-protein, new symptoms)	Hematology	**URGENT** (1–2 weeks)
Palliative care referral	Palliative medicine	**ROUTINE at any point** for symptom management; **MANDATORY** at refractory disease or frail/age ≥80 per NCCN[5,26,30]
SDoH-driven access barriers (transportation, food, financial)	Social work + community health worker	**ROUTINE**: at diagnosis and at any change in barrier status

ABBREVIATIONS: CRAB = Calcium/Renal/Anemia/Bone; SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; MM = multiple myeloma; ED = emergency department; MRI = magnetic resonance imaging; CAR T = chimeric antigen receptor T-cell; MGUS = monoclonal gammopathy of undetermined significance; NCCN = National Comprehensive Cancer Network; SDoH = social determinants of health

Follow-Up Timing

STAGE/CATEGORY	FREQUENCY[2,3,5]	LABS TO MONITOR[3,5,17]
Newly diagnosed MM during induction	Per oncology (typically **every cycle**); PCP **every 1–2 months** for comorbidity comanagement	CBC, CMP (calcium, creatinine), SPEP, sFLC, sIFE; toxicity screen (neuropathy, neutropenia, infection); VTE prophylaxis and **medication reconciliation review**

STAGE/CATEGORY	FREQUENCY[2,3,5]	LABS TO MONITOR[3,5,17]
Active MM on maintenance therapy (e.g., lenalidomide)	Oncology **every 1–3 months**; PCP **every 3 months**	CBC, CMP, SPEP, sFLC, sIFE per oncology; glucose/BP monitoring **if on dexamethasone**; neuropathy and infection screen; annual C90.0x reconfirmation
MM in deep remission (sustained CR/VGPR for ≥1–2 yr)	Oncology **every 3 months**; PCP **every 3–6 months**	Monitoring labs per oncology; imaging annually or per oncology; **maintain active C90.01 coding while on maintenance**
MGUS: low-risk	PCP: labs at **6 months**, then **every 2–3 years** (or with new symptoms)	CBC, calcium, creatinine, SPEP, sFLC; bone marrow biopsy/imaging **only if clinical change**
MGUS: intermediate/ high-risk	Hematology **every 6–12 months**	Per hematology = typically labs every 6 months; bone marrow biopsy and imaging at baseline
Smoldering MM: high-risk on daratumumab (AQUILA-aligned)	Observe **every 3–6 months** (category 1)	CBC, creatinine, calcium, SPEP, SIFE, sFLC; imaging annually; bone marrow biopsy **as clinically indicated**
On bisphosphonate/ denosumab	Per oncology (**monthly** during treatment for up to 36 months)	Monthly monitoring per protocol; **PCP role**: comorbidity comanagement, infection prophylaxis, SDoH support
SDoH and financial review	**Before each dose**	Creatinine before zoledronic acid; calcium/vitamin D before denosumab; dental status review **every 6–12 months**

ABBREVIATIONS: MM = multiple myeloma; PCP = primary care provider; CBC = complete blood count; CMP = comprehensive metabolic panel; SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; VTE = venous thromboembolism; BP = blood pressure; CR = complete response; VGPR = very good partial response; MGUS = monoclonal gammopathy of undetermined significance; SDoH = social determinants of health

Comorbidity Management

COMORBIDITY	APPROACH[5,6,15]	CAUTION[5,6,15]
CKD (N18.x)—>30% at diagnosis[15]	Dose-adjust lenalidomide by CrCl; **denosumab preferred** over bisphosphonates **if CrCl <30**; avoid NSAIDs and unprepped contrast	Nephrology comanagement for eGFR <45 or rapid decline

COMORBIDITY	APPROACH[5,6,15]	CAUTION[5,6,15]
VTE: 9x baseline risk[1]	**Mandatory IMiD VTE prophylaxis**: aspirin (low-risk), LMWH/DOAC/warfarin (high-risk); reassess every visit	**Balance bleeding risk**;[23] coordinate agent selection with oncology; urgent duplex/CTPA if symptomatic
Infection: leading cause of MM death[48]	Acyclovir/valacyclovir **mandatory with PI** or anti-CD38 Rx; **optimize PCV20, influenza, RZV, COVID-19 vaccines**; empiric antibiotics for febrile neutropenia	**Highest risk**: in first 3 months and relapsed/refractory phase; vaccine responses may be **blunted**
Bone disease (M84.5xx): 79% lytic at diagnosis[1]	Bisphosphonate or denosumab ≥2 years; **plan around invasive dental procedures**; orthopedic referral for pathological fracture	DEXA not informative; MM bone disease is **pathophysiologically distinct**
Peripheral neuropathy: up to 62% on PI[22]	**Once-weekly SC bortezomib standard** (grade ≥2 neuropathy 10% vs 27% twice-weekly IV); early dose modification	Screen every visit; especially relevant with **pre-existing diabetic neuropathy**
Cardiovascular disease[47]	Baseline NT-proBNP and echo **before carfilzomib**;* monitor BP/glucose on dexamethasone	Cardiology comanagement **as needed**; report new dyspnea, edema, or arrhythmia
Type 2 diabetes (E11.x): worsened by dexamethasone[21,49]	**Tighten glucose monitoring** during induction; dexamethasone de-escalation after response reduces hyperglycemia[35]	Document A1c trend **during and after** steroid courses
Polypharmacy/ DDIs	Med reconciliation **every visit**; alert blood bank to daratumumab (false-positive Coombs); CYP3A4 interaction audit for bortezomib*	Pharmacist consult when available; identify high-risk combinations early
SDoH/financial burden[9]	**LIS/Extra Help enrollment**; manufacturer PAP for lenalidomide/ pomalidomide; MA supplemental benefits; food/transportation screening	OOP for lenalidomide **$5,623/yr without LIS vs $6 with LIS**;[9] disadvantaged-area residence HR 1.75 for shorter OS
Frailty/functional decline[19,37]	**IMWG Frailty Index** at initiation and transitions; **GA-guided management** for all ≥65 on systemic therapy; reassess every 3–6 months	Coordinate palliative care for symptom management and goals-of-care in frail or relapsed disease

COMORBIDITY	APPROACH[5,6,15]	CAUTION[5,6,15]

ABBREVIATIONS: CKD = chronic kidney disease; CrCl = creatinine clearance; NSAID = non-steroidal anti-inflammatory drug; eGFR = estimated glomerular filtration rate; MM = multiple myeloma; VTE = venous thromboembolism; IMiD = immunomodulatory drug; LMWH = low-molecular-weight heparin; DOAC = direct oral anticoagulant; CTPA = computed tomographic pulmonary angiography; PI = proteasome inhibitor; CD38 = cluster of differentiation 38; PCV = pneumococcal conjugate vaccine; RZV = recombinant zoster vaccine; DEXA = dual-energy X-ray absorptiometry; SC = subcutaneous; IV = intravenous; NT-proBNP = N-terminal pro–B-type natriuretic peptide; BP = blood pressure; CYP3A4 = cytochrome P450 3A4; DDI = drug-drug interaction; SDoH = social determinants of health; LIS = low-income subsidy; PAP = patient assistance program; MA = Medicare Advantage; OOP = out-of-pocket; HR = hazard ratio; OS = overall survival; IMWG = International Myeloma Working Group; GA = geriatric assessment
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Patient Education and Adherence

AAVBC PERSPECTIVE

***From the AAVBC's perspective**, patient education is not ancillary to MM care: it is a **core value-based intervention**. Informed patients adhere more consistently, recognize complications earlier, and engage in shared decision-making that aligns treatment intensity with their goals. **Three high-leverage messages** anchor effective MM education in primary care:*

*(**1**) "**Feeling fine**" on maintenance **reflects the therapy working**, not the disease being cured.[5,15] MM is largely incurable; monthly monitoring (SPEP, sFLC, sIFE, CBC, CMP) is what allows **biochemical relapse to be detected before symptomatic progression**.*

*(**2**) **Report red-flag symptoms immediately** = new severe back pain (especially with leg weakness, numbness, or bowel/bladder change), severe headache or confusion, fever ≥100.4°F, mucosal bleeding, sudden shortness of breath or leg swelling.*

*(**3**) **Adherence and prophylaxis matter**.[36] Lenalidomide on its prescribed cycle; aspirin (or other VTE prophylaxis) daily; antiviral prophylaxis daily when on proteasome inhibitor or anti-CD38 therapy; bone-targeting therapy on schedule; vaccinations updated.*

***AAVBC emphasizes** that cost barriers are among the most common and most modifiable **drivers of non-adherence and treatment abandonment in MM**. Out-of-pocket cost for lenalidomide can exceed **$5,000/year without subsidy**.[9] Primary care is uniquely positioned to close this gap by **proactively screening for financial toxicity** at every visit and connecting patients to LIS/Extra Help, state pharmacy assistance programs, and manufacturer patient assistance programs before adherence breaks down.[9]*

Quality Metrics Tie-In

No MM-specific HEDIS or MIPS measures are currently active in MY2026, but MM intersects multiple quality measurement domains **simultaneously**: depression screening (PHQ-9), geriatric safety (fall risk, high-risk medications, medication reconciliation), care transitions (post-hospitalization follow-up), and goals-of-care documentation (advance care planning). The disease's combination of chronic pain, treatment-related neuropathy, polypharmacy (IMiDs, proteasome

inhibitors, bisphosphonates, antivirals, VTE prophylaxis, steroids), immunosuppression-driven hospitalizations, and high psychological distress means that cross-cutting national measures apply **across the entire care trajectory** and can anchor quality reporting for any PCP managing an MM patient in a value-based program.

MEASURE	STANDARD	APPLICABILITY TO MULTIPLE MYELOMA[1,16,50]
HEDIS COA: Care for Older Adults-Medication Review	**Denominator**: MA enrollees ≥66, continuously enrolled **Numerator**: 4 sub-measures documented annually: (**1**) functional status assessment, (**2**) medication review, (**3**) pain assessment, (**4**) advance care planning; **Exclusions**: hospice, ESRD	**Polypharmacy is common in MM**: lenalidomide, bortezomib, dexamethasone, bisphosphonates, antivirals, VTE prophylaxis, and comorbidity medications (e.g., metformin, antihypertensives) create high interaction risk; **documented medication review should reconcile** CYP3A4 substrates, QTc-prolonging agents, and nephrotoxic drugs against fluctuating renal function
HEDIS COA: Care for Older Adults-Functional Status Assessment	**Denominator**: enrollees ≥66 **Numerator**: functional status assessment documented annually **Exclusions**: hospice, ESRD	ECOG performance status and IMWG Frailty Score **directly satisfy this sub-measure**; document at every visit to track functional trajectory and guide treatment intensity (frail → dose-reduced regimens)
HEDIS TRC: Transitions of Care Patient	**Denominator:** enrollees ≥18 with inpatient discharge; **Numerator:** 4 sub-measures within 30 days: (**1**) notification of inpatient admission, (**2**) receipt of discharge information, (**3**) patient engagement after discharge, (**4**) medication reconciliation post-discharge; **Exclusions:** hospice	**MM patients have high hospitalization rates driven by:** infections (7x bacterial, 10x viral risk vs. general population), febrile neutropenia, hypercalcemia, renal failure, and pathologic fractures; medication reconciliation post-discharge is critical given polypharmacy and fluctuating renal dosing

MEASURE	STANDARD	APPLICABILITY TO MULTIPLE MYELOMA[1,16,50]
HEDIS DMS-E: Utilization of the PHQ-9 to Monitor Depression Symptoms for Adolescents and Adults	**Denominator:** enrollees ≥12 with diagnosis of major depression or dysthymia AND elevated PHQ-9 ≥10 **Numerator:** follow-up PHQ-9 documented within 4–8 months of index elevated score **Exclusions:** hospice	Depression prevalence in MM is **23–30%**; over 56% screen positive for anxiety and/or depression at diagnosis; pain, fatigue, steroid use, and incurability awareness are independent risk factors = PHQ-9 at **every visit** with follow-up plan if positive
HEDIS ACP: Advance Care Planning	**Denominator:** enrollees ≥66 **Numerator:** advance care plan or surrogate decision-maker documented, **OR** documentation that ACP was discussed but patient declined **Exclusions:** hospice	MM remains incurable, yet **only 30.6% of patients acknowledge terminal illness** despite 84.7% reporting their oncologist informed them; ACP should begin **at diagnosis**, not end-of-life; billable as CPT 99497/99498 during AWV with no copay
HEDIS PCR: Plan All-Cause Readmission	**Denominator:** enrollees ≥18 with acute inpatient discharge **Numerator:** unplanned readmission within 30 days (lower is better) **Exclusions:** planned readmissions (maintenance chemotherapy, transplant), hospice, psychiatric	Hematologic malignancies have **2.26x higher** readmission odds vs. solid tumors; MM hospitalization drivers include infection (pneumonia, sepsis), AKI, hypercalcemia, and treatment toxicity; PCP post-discharge follow-up within 7 days reduces readmission risk

ABBREVIATIONS: HEDIS = Healthcare Effectiveness Data and Information Set; COA = Care for Older Adults; MA = Medicare Advantage; ESRD = end-stage renal disease; MM = multiple myeloma; VTE = venous thromboembolism; CYP3A4 = cytochrome P450 3A4; QTc = corrected QT interval; ECOG = Eastern Cooperative Oncology Group; IMWG = International Myeloma Working Group; TRC = Transitions of Care; PHQ-9 = Patient Health Questionnaire-9; DMS-E = Depression Monitoring and Follow-Up; ACP = advance care planning; CPT = Current Procedural Terminology; AWV = Annual Wellness Visit; PCR = plan all-cause readmissions; AKI = acute kidney injury; PCP = primary care provider; GAD-7 = Generalized Anxiety Disorder 7-item scale; IMiD = immunomodulatory drug; PI = proteasome inhibitor; PCV = pneumococcal conjugate vaccine; RZV = recombinant zoster vaccine; SDoH = social determinants of health

5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

- **Status-specific C90.0x at every encounter: C90.00** active/not in remission; **C90.01** in remission (including on maintenance with documented response); **C90.02** in relapse. Mirror the most recent oncology assessment. Defaulting to C90.00 regardless of status = **most common coding error**
- **Never use Z85.79 while patient is on maintenance or under surveillance;** exceptionally rare scenario where Z85.79 applies given MM is largely incurable and Z85.79 **forfeits HCC 19 entirely**.[1,12] Patients on lenalidomide maintenance, under oncologic surveillance, or with any documented residual disease retain **active C90.0x coding**
- **CRAB manifestations coded separately and linked to MM: D63.0** anemia in neoplastic disease (link in note: "anemia due to multiple myeloma"); **N08** glomerular disorders in diseases classified elsewhere (myeloma cast nephropathy; **code C90.0x first**); **E83.52** hypercalcemia ("hypercalcemia secondary to multiple myeloma"); **M84.5xx** pathological fracture in neoplastic disease with site/laterality/7th-character encounter (A initial, D subsequent, S sequela). Add **N18.x** for CKD stage with linkage where causal[20]
- **Do not use M81.x (osteoporosis) for MM bone disease: MM bone disease is pathophysiologically distinct from osteoporosis** and is not informed by DEXA.[42] Code **M84.5xx** for pathological fracture with site and laterality; document underlying lytic lesion location separately
- **MGUS and SMM coding distinctions: D47.2** monoclonal gammopathy/MGUS (precursor; no HCC mapping); **SMM does not have a unique ICD-10 code** → code **D47.2** with documentation specifying smoldering myeloma per IMWG criteria.[2,4,15] Risk-stratified monitoring without progression keeps **D47.2**; progression to MM triggers **C90.0x** with appropriate status modifier

Annual Clinical Review and Confirmation

- **Annual reconfirmation and visit modality:** MM must be reassessed **once per calendar year** via **in-person or synchronous audio-video encounter** to support HCC 19 mapping. Telephone-only encounters and asynchronous portal messages **do not** satisfy MEAT for **HCC 19**; **physical exam** (skeletal exam, neuropathy screen, lymph nodes, pallor, oropharynx for thrush, gait) requires **in-person assessment at least annually** for active disease

- **Status reconfirmation at every annual visit:** Document **current disease status** (active/in remission/in relapse), **current therapy** with drug/dose/route/schedule/last administered date, **most recent IMWG response category** (sCR/CR/VGPR/PR/SD/PD), and **monitoring cadence**. "Stable on lenalidomide" without objective data does not satisfy MEAT = include M-spike, sFLC ratio, CBC, CMP values with dates
- **Update status code as disease evolves:** A patient who progresses from **C90.00** active to **C90.01** in remission, or from **C90.01** to **C90.02** in relapse, should have the code updated at the visit **when the status change is confirmed by oncology**. Coding the wrong status creates **downstream specificity audit risk**
- **Reconfirm CRAB comorbidities and CKD stage annually: D63.0**, **N08**, **E83.52**, **M84.5xx**, and **N18.x** by stage should be reviewed and recoded as currently active or resolved at each annual visit. Resolution of anemia or hypercalcemia means the comorbidity is no longer coded; persistent CKD stays as the current stage
- **Frailty status and treatment-intensity rationale:** For patients ≥65 on systemic therapy, document **IMWG Frailty Index** or simplified frailty score at oncology initiation and at each major transition; document the **clinical rationale** for chosen treatment intensity (full quadruplet vs VRd-lite vs dose-adjusted DRd vs Rd doublet vs dexamethasone-sparing). ASCO-OH 2026 mandates **GA-guided management** for all patients ≥65[15]
- **SDoH and financial review at least annually:** Document LIS/Extra Help enrollment status, state pharmacy assistance program enrollment, manufacturer patient assistance program for lenalidomide/pomalidomide, transportation and food security, and advance care planning documentation. SDoH burden drives treatment abandonment and shorter OS in MM[9]
- **Avoid rollover**: **Do not** copy last year's MM note forward **without updating**: disease status (C90.00/01/02), current therapy and IMWG response category with objective labs (M-spike, sFLC ratio, CBC, CMP with dates), CRAB comorbidity status (active vs resolved), CKD stage, frailty score, vaccination status, bone-targeting therapy adherence, and **goals-of-care conversations**. Clinical context in MM **shifts with each treatment line and must be reassessed at each visit**

Good Documentation is Comprehensive Coding

EHR SHORTCUT/ RISK	PREFERRED DOCUMENTATION LANGUAGE
"Multiple myeloma"	"**Multiple myeloma, IgG kappa, R-ISS Stage II at diagnosis, currently in very good partial response on lenalidomide 10 mg maintenance — C90.01**; last oncology assessment 28-APR-2026; sustained VGPR; monthly SPEP/ sFLC/sIFE labs continued; VTE prophylaxis with aspirin 81 mg; acyclovir 400 mg BID antiviral prophylaxis; zoledronic acid 4 mg IV q3 mo."

EHR SHORTCUT/ RISK	PREFERRED DOCUMENTATION LANGUAGE
"History of multiple myeloma"	When patient is on maintenance, under surveillance, or has residual disease: "**Multiple myeloma, in remission on maintenance (C90.01)**, IgG kappa, sustained VGPR per IMWG criteria × 14 months on lenalidomide 10 mg daily; monthly monitoring labs continued; oncology comanagement maintained." **Z85.79 forfeits HCC 19**
"Anemia, mild"	"Anemia in neoplastic disease (**D63.0**) secondary to multiple myeloma (**C90.01**), Hgb 11.2 stable, asymptomatic, no transfusion or ESA needed; iron studies normal; B12 and folate replete."
"On chemo for myeloma"	"**Lenalidomide 10 mg PO** days 1–21 of 28-day cycle (**renally adjusted** for CrCl 48); aspirin 81 mg daily for VTE prophylaxis on IMiD; acyclovir 400 mg BID antiviral prophylaxis; zoledronic acid 4 mg IV q3 mo (last dose 10-APR-2026); pre-medications and infusion schedule per oncology."
"Stable"	"**M-spike 0.4 g/dL** (down from 2.1 at diagnosis; consistent with VGPR); **sFLC ratio 1.8** (involved kappa 22 mg/L, uninvolved lambda 12 mg/L); **sIFE positive IgG kappa** (consistent with VGPR); **CBC and CMP** stable; last bone marrow 02/2024 with 8% plasma cells; **no new bone pain**; ECOG PS 1; weight stable."
"Bone pain, possibly myeloma"	"**Multiple myeloma bone disease; stable lytic lesions T7 and L2** on whole-body low-dose CT 03-MAR-2025; no new lesions; no impending fracture per radiology; on zoledronic acid 4 mg IV q3 mo; pain controlled with scheduled acetaminophen; NSAIDs avoided (renal); orthopedic referral threshold reviewed with patient."
"Renal insufficiency"	"**Chronic kidney disease, stage 3a (N18.31)**, **eGFR 48 stable**, prior myeloma cast nephropathy at diagnosis with subsequent improvement; lenalidomide dose-adjusted for CrCl per current renal function; nephrotoxic agents (NSAIDs, contrast without prep) avoided; nephrology comanagement maintained."

ABBREVIATIONS: EHR = electronic health record; R-ISS = Revised International Staging System; VGPR = very good partial response; SPEP = serum protein electrophoresis; sFLC = serum free light chain; sIFE = serum immunofixation electrophoresis; VTE = venous thromboembolism; BID = twice daily; IV = intravenous; IMWG = International Myeloma Working Group; HCC = hierarchical condition category; ESA = erythropoiesis-stimulating agent; CrCl = creatinine clearance; IMiD = immunomodulatory drug; ECOG PS = Eastern Cooperative Oncology Group Performance Status; CBC = complete blood count; CMP = comprehensive metabolic panel; CT = computed tomography; NSAID = non-steroidal anti-inflammatory drug; eGFR = estimated glomerular filtration rate

EHR Workflow Tips

- **[EHR TIP — Smartphrase]** Build a **.mmvisit dot phrase** that auto-populates **C90.0x** with 6th-character status, current therapy (drug/dose/route/last date), IMWG response, monitoring labs with dates (SPEP, sFLC, sIFE, CBC, CMP, β2-microglobulin), CRAB comorbidities, frailty status, and vaccination/prophylaxis status. Companion .mmmeat block: **Monitor** (M-spike trend, sFLC ratio, CBC, CMP, symptoms); **Evaluate** (PE, labs, imaging, bone marrow); **Assess** (C90.0x with IMWG response, frailty, CRAB, trajectory); **Treat** (regimen details, dex taper,

vaccinations, SDoH, follow-up). Reduces unspecified coding and supports MEAT in a single paste

- **[EHR TIP — Alert]** Worklist filter "**Multiple Myeloma Active**" surfaces patients with **C90.0x** (6th character 0/1) or **Z51.11** encounter in 12 months plus myeloma on problem list. I**MiD VTE prophylaxis**: BPA fires when lenalidomide/pomalidomide is active without anticoagulation documented. **Anti-CD38 blood-bank alert**: BPA fires when daratumumab/isatuximab is active during transfusion order entry for false-positive Coombs interference
- **[EHR TIP — Best Practice] Problem list:** "Multiple myeloma, IgG kappa, ISS II, partial remission on VRd cycle 6," **not** "myeloma." Update 6th character at every reassessment. Code CRAB comorbidities individually (D63.0, N08, E83.52, M84.5xx, N18.x). **Flag Z85.79 persisting** while active myeloma therapy is on the med list → likely miscoded
- **[EHR TIP — Order Set]** "**MM Annual Workup**": CBC, CMP, SPEP, sFLC, sIFE, β2-microglobulin, LDH, 25-OH vitamin D, skeletal imaging review, vaccination check, ACP prompt. "**MM Diagnostic Trio**" case-finding set: SPEP + sFLC + sIFE, CBC, CMP, β2-microglobulin, low-dose whole-body CT = triggered for adults >50 with unexplained anemia, rising creatinine, or persistent bone pain. New-diagnosis add-on includes heme/onc referral template, palliative care consult, and LIS/Extra Help check
- **[EHR TIP — Auto-prompt] Annual diagnosis confirmation:** BPA fires when active **C90.0x has no MEAT encounter in 11 months**; secondary filter flags **Z85.79 with active IMiD prescription** in 90 days. **Treatment triggers**: G-8 ≤14 fires geriatric oncology referral; neuropathy ≥grade 2 fires dose-modification alert; IMiD initiation fires VTE prophylaxis order and REMS verification; bone-targeting agent >12 months fires ONJ dental referral. One-click referral auto-populates ISS stage, IMWG response, regimen, and labs

Brief Case Examples

SUCCESS: COMPREHENSIVE DOCUMENTATION

SCENARIO

A 78-year-old woman with **IgG kappa multiple myeloma** (R-ISS Stage II, diagnosed 02/2024), **IMWG intermediate-fit**, in VGPR on lenalidomide 10 mg maintenance (**renally adjusted**, CrCl 48). Co-managed with oncology and nephrology. Presents for routine follow-up; mild fatigue, no new bone pain or infections.

Documentation: "Multiple myeloma, IgG kappa, R-ISS Stage II, in VGPR on lenalidomide maintenance: **C90.01**. Last oncology assessment 28-APR-2026: sustained VGPR × 14 months; M-spike 0.4 g/dL (from 2.1); sFLC ratio 1.8; bone marrow 02/2024 with 8% plasma cells. Therapy: lenalidomide 10 mg PO days 1–21/28 (renal-adjusted CrCl 48); **aspirin 81 mg daily** (IMiD VTE prophylaxis); acyclovir 400 mg BID; zoledronic acid 4 mg IV q3 mo (last 10-APR-2026); calcium 1200 mg + vitamin D 1000 IU daily. Anemia in neoplastic disease (**D63.0**), Hgb 11.2 stable. CKD stage 3a (**N18.31**), eGFR 48 stable, prior cast nephropathy improved. Stable lytic lesions T7/L2 on WBLDCT 03-MAR-2025, no impending fracture. PCV20 11/2024, RZV complete, influenza due 09/2026. IMWG intermediate-fit; **VRd-lite induction per frailty**. LIS enrolled. ACP on file, goals unchanged. Assessment: MM in sustained VGPR = continue maintenance per oncology (Dr.

[Name]); CKD stable on nephrology co-management; bone disease stable. Follow-up 3 months; annual reconfirmation at next AWV. Return sooner for new bone pain, fever ≥38.0°C, or unexplained fatigue."

Outcome: HCC 19 confirmed with **C90.01** and IMWG response; full therapy **with prophylaxis** (VTE, antiviral, bone-targeting); CRAB comorbidities coded and linked (**D63.0**, **N18.31**); frailty and treatment-intensity rationale **documented**; SDoH (LIS) and vaccinations addressed; reconfirmation plan named. **Every MEAT element present**: labs with trends and dates, imaging with findings, therapy with dose/route/schedule, frailty assessment, coded diagnoses, follow-up with return criteria.

PITFALL: INSUFFICIENT DOCUMENTATION

Documentation as written: "History of multiple myeloma, asymptomatic. On chemotherapy. Continue current plan. Anemia improved. RTC 6 months. **Z85.79**." Same patient on active lenalidomide maintenance, but coded as "**history of**" without myeloma subtype, IMWG response, regimen details, lab values, CKD stage, bone disease status, prophylaxis, frailty, or vaccinations.

Consequence: Z85.79 on an active-maintenance patient **eliminates HCC 19 entirely** = inappropriate while on lenalidomide with monthly monitoring. **D63.0 linkage forfeited**, **N18.31** not coded, bone disease and prophylaxis **undocumented**. "On chemotherapy" without regimen/dose/cycle and "anemia improved" without values **fail MEAT on every element**. Understates complexity and impairs PCP–oncology–nephrology continuity.

RAF Impact: Z85.79 = zero HCC value. **HCC 19** forfeited, repeating annually. Additional HCC mapping for **D63.0** and **N18.31** also lost.

Fix: "Multiple myeloma, **IgG kappa**, in VGPR on lenalidomide 10 mg maintenance (**renal-adjusted CrCl 48**): **C90.01**; sustained VGPR × 14 months; M-spike 0.4 g/dL, sFLC ratio 1.8. **Aspirin 81 mg** (VTE) + acyclovir 400 mg BID + zoledronic acid q3 mo (last [date]); calcium/vitamin D daily. **D63.0** secondary to MM, Hgb 11.2 stable. **N18.31**, eGFR 48 stable. Stable lytic lesions T7/L2. PCV20/RZV complete; influenza due 09/2026. LIS enrolled. **IMWG intermediate-fit**. ACP reviewed, unchanged. Continue maintenance per oncology; nephrology co-management. Follow-up 3 months; return sooner for bone pain, fever, or fatigue." Coding after fix: **C90.01** (→ **HCC 19**, RAF 1.798) + **D63.0** + **N18.31** = clinical picture preserved with auditable specificity.

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