AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Multiple Sclerosis

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: **Multiple sclerosis** (MS) is a chronic, immune-mediated inflammatory and neurodegenerative disease of the central nervous system in which autoreactive T and B cells breach the blood-brain barrier and **drive demyelination**, **axonal loss**, and **astrocytic gliosis**.[1,2] It is the leading non-traumatic cause of neurological disability in young and middle-aged adults.[1] Four standardized phenotypes are recognized: **clinically isolated syndrome** (**CIS**), **relapsing-remitting** MS (**RRMS**, the most common form), **primary progressive** MS (**PPMS**), and **secondary progressive** MS (**SPMS**), each modified by descriptors for activity (clinical relapses or MRI activity) and progression (disability worsening independent of relapses).[1,3]

ICD-10 Codes:

MS is reported with **phenotype- and activity-specific subcodes**. **G35** is the multiple sclerosis category, now subdivided into **G35.A** (RRMS), **G35.B0/B1/B2** (PPMS: unspecified/active/ non-active), **G35.C0/C1/C2** (SPMS: unspecified/active/ non-active), and **G35.D** (MS, unspecified). **Activity status** (active = recent clinical relapse, new MRI lesions, or documented progression; non-active = clinically and radiologically stable) **must be documented** to support the active-vs-non-active subcodes.[4] Commonly co-occurring manifestations are **coded separately**: **H46.1-** (retrobulbar/optic neuritis, specify laterality), **G37.3** (acute transverse myelitis in demyelinating disease), **N31.-** (neurogenic bladder), **R13.1-** (dysphagia), **R26.-** (gait abnormality), **G31.84** (mild cognitive impairment), **F32.-/F33.-** (depressive disorder), **R53.83** (fatigue), and **R25.2/M62.83** (spasm/muscle spasm).[4] Do **not** code **G12.21** (amyotrophic lateral sclerosis; ALS) for MS **unless ALS is independently diagnosed**.

Prevalence and Burden: MS affects an estimated nearly **1 million** adults in the United States, with a female-to-male ratio of approximately **3:1**.[1,5] Within the United States, prevalence increases significantly with latitude (r = 0.82) and ranges from ~161 per 100,000 in Hispanic populations to ~375 per 100,000 in White populations.[1,6] Although onset typically occurs between ages **20 and 40**, life expectancy is estimated at approximately 74–76 years (7–9 years shorter than the general population) and MS prevalence in Medicare beneficiaries ≥65 was 243 per 100,000 in 2021, increasing 15.5% over the prior decade.[1,7,8] The total per-person economic burden averages approximately **$88,000 per year** (2019 dollars), with direct medical costs of **~$65,600 per year**.[9]

HCC/RAF V28 Mapping

ICD-10 CODE(S)[10]	HCC CATEGORY (V28)[10]	RAF (CNA)[11]	DOCUMENTATION REQUIREMENT[4]
G35.A Relapsing-remitting multiple sclerosis	**HCC 198** Multiple Sclerosis	**0.647**	Document **relapsing-remitting multiple sclerosis** (**RRMS**); include relapse history, current disease activity, MRI findings when available, and disease-modifying therapy

ICD-10 CODE(S)[10]	HCC CATEGORY (V28)[10]	RAF (CNA)[11]	DOCUMENTATION REQUIREMENT[4]
G35.B1 Primary progressive multiple sclerosis, active/G35.C1 Secondary progressive multiple sclerosis, active	**HCC 198** Multiple Sclerosis	**0.647**	Specify active **PPMS or active SPMS**; document evidence of activity (clinical relapse, new/enlarging MRI lesion, or progression within the past year)
G35.B2 Primary progressive multiple sclerosis, non-active/ G35.C2 Secondary progressive multiple sclerosis, non-active	**HCC 198** Multiple Sclerosis	**0.647**	Specify **non-active PPMS or non-active SPMS**; document **absence of relapses** and new MRI activity while describing ongoing disability or progression status
G35.D Multiple sclerosis, unspecified	**HCC 198** Multiple Sclerosis	**0.647**	Use **ONLY** when MS subtype c**annot be determined**; whenever possible, document RRMS, PPMS, or SPMS to support **diagnostic specificity**
H46.1- Optic neuritis	No HCC	—	Document **laterality and relationship to demyelinating disease**; record as a clinically confirmed demyelinating event
G37.3 Acute transverse myelitis in demyelinating disease of central nervous system	No HCC	—	**Document**: neurologic deficits, spinal cord involvement, MRI findings, and association with demyelinating disease
N31.- Neurogenic bladder	No HCC	—	Document **neurogenic bladder attributable to MS**; include symptoms, catheterization requirements, and treatment plan when applicable.

ABBREVIATIONS: CNA = Community Non-Dual Eligible, Aged segment; CMS = Centers for Medicare & Medicaid Services; HCC = Hierarchical Condition Category; ICD-10 = International Classification of Diseases, 10th Revision; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; MA = Medicare Advantage; MEAT = Monitor, Evaluate, Assess, Treat; MRI = magnetic resonance imaging; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; RAF = Risk Adjustment Factor; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis; V28 = CMS Hierarchical Condition Category Model, Version 28RAF 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

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

Risk-Adjusted Care Resources per Patient/Year[10,11]

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

MULTIPLE SCLEROSIS

$6.7K

HCC 198 · RAF 0.647

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

AAVBC PERSPECTIVE

***From the AAVBC's perspective**, value-based care in MS begins at the point of first clinical suspicion: reducing diagnostic delay is the single highest-yield action a PCP can take. Delays remain common, are frequently physician-dependent, and are associated with greater disability at diagnosis.[12] Treatment initiation within 6 months of the first demyelinating event is associated with a lower risk of reaching disability milestones compared with later starts.[13]*

***The PCP's role follows a simple sequence**:*

***ORDER MRI FIRST, NOT LATER**. When a patient presents with optic neuritis, limb numbness evolving over days, new gait instability, or unexplained bladder dysfunction, order brain and spinal cord MRI with contrast rather than waiting for a second attack.[14]*

*Then **REFER PROMPTLY**; the 2024 McDonald Criteria now allow **earlier diagnosis** by recognizing the optic nerve as a **fifth dissemination-in-space site**, accepting **radiologically isolated syndrome as diagnosable**, and no longer requiring dissemination in time when l**esions span four or more locations**.[15] Every year of delayed diagnosis is a year of **untreated neurodegeneration**; axonal damage begins at the earliest stages, and early high-efficacy therapy may lower the long-term risk of conversion to **secondary progressive MS**.[1,13]*

2 RECOGNITION AND DIAGNOSIS

There is no USPSTF recommendation or population-based screening program for multiple sclerosis in asymptomatic adults; MS has no validated presymptomatic screening test.[5,16] All diagnostic evaluation is **symptom-triggered**, and all surveillance testing applies only to patients with an **established MS diagnosis**. Medicare Part B covers the following diagnostic and surveillance tests:

Diagnostic and Surveillance Tests Covered Under Medicare Part B (Diagnosed MS Population)

TEST	FREQUENCY	CPT/ HCPCS	CLINICAL INDICATION
MRI brain without and with contrast	**At diagnosis**;[17,18] new baseline **3–6 mo after DMT** start/switch; then **annually** on DMT	70553	**DIS/DIT** per 2024 McDonald Criteria; annual lesion surveillance[17,18]
MRI brain without contrast	Follow-up surveillance when **contrast not indicated**	70551	Routine surveillance once stable baseline established and **contrast not required**[17,18]
MRI cervical/ thoracic spine ± contrast	**At diagnosis**; when clinically indicated[17]	72156/ 72157	**Spinal cord lesion evaluation**; suspected DIS; partial myelitis[15,18]
Lumbar puncture/ CSF analysis	**Once at diagnosis** when MRI is non-diagnostic[15,19]	62270	**OCBs or kappa free light chains**; CSF-specific OCBs **substitute for DIT** under 2024 criteria[15,19,20]
Visual evoked potentials	When **optic nerve involvement** is in question[21]	95930	**Optic-nerve lesion documentation**; optic nerve = fifth DIS site under 2024 McDonald Criteria[15,21]
Depression screening (PHQ-2/ PHQ-9)	**Annually** and when clinically indicated	G0444	Depression affects **21–50%** of MS patients; AAN recommends routine screening[22]
Cognitive assessment/ care planning‡	**Annually**; SDMT preferred over MMSE[23]	99483	SDMT screens **processing-speed impairment**; MMSE is insensitive in MS[23]
Physical/ occupational therapy§	Per functional need[24]	97110–97542	Maintenance rehabilitation for gait, balance, and fall prevention[24]
Advance Care Planning (during AWV)†	**Annually** + when goals change	99497/ 99498	**Document directives, surrogate, and goals**; relevant in progressive MS with significant disability

ABBREVIATIONS: AAN = American Academy of Neurology; AWV = Annual Wellness Visit; CPT/HCPCS = Current Procedural Terminology/Healthcare Common Procedure Coding System; CSF = cerebrospinal fluid; DIS = dissemination in space; DIT = dissemination in time; DMT = disease-modifying therapy; MMSE = Mini-Mental State Examination; MRI = magnetic resonance imaging; MS = multiple sclerosis; OCB = oligoclonal band; PHQ = Patient Health Questionnaire; SDMT = Symbol Digit Modalities Test

Subtle Early Signs in Older Adults

SIGN/SYMPTOM	CLINICAL SIGNIFICANCE
Subacute monocular vision loss or painful eye movement (optic neuritis)	**Classic demyelinating presentation**; in older adults do not dismiss as cataract or ischemic optic neuropathy without considering MS → **order MRI and refer**[14,18]
New limb numbness, tingling, or a sensory 'band' developing over days	**Partial myelitis pattern**; sensory symptoms evolving over days (not seconds-to-minutes like stroke) warrant MRI rather than a wait-and-see approach[1]
Disabling fatigue out of proportion to activity	Affects roughly **80%** of people with MS; in older adults it is often **misattributed to aging** or depression rather than evaluated as an MS symptom[25]
New gait instability, ataxia, or unexplained falls	**May reflect cerebellar or spinal cord involvement**; in patients >65 this is frequently attributed to deconditioning, **masking progressive MS**[26]
Heat-triggered transient worsening (Uhthoff phenomenon)	Symptom worsening with fever, infection, or heat reflects conduction slowing, not new inflammation = a **pseudoexacerbation**; **do not reflexively give steroids**[27,28]
Progressive cognitive slowing (processing speed, memory)	Cognitive impairment affects **40–70%** of people with MS and is **poorly captured by the MMSE**; use the **SDMT** and code **G31.84** when present[23,29]
New or worsening bladder urgency, frequency, or retention	**Neurogenic bladder is common**, under-documented, and a driver of UTIs and ED visits; code **N31.-** and address proactively[30,31]
Insidious, steadily progressive weakness without discrete relapses	Suggests a progressive phenotype (**PPMS or SPMS**) or **PIRA**; reassess the phenotype rather than assuming stable RRMS[32]

ABBREVIATIONS: ED = emergency department; MMSE = Mini-Mental State Examination; MRI = magnetic resonance imaging; MS = multiple sclerosis; PIRA = progression independent of relapse activity; PPMS = primary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SDMT = Symbol Digit Modalities Test; SPMS = secondary progressive multiple sclerosis; UTI = urinary tract infection

CLINICAL PEARL: MULTIPLE SCLEROSIS AND EBV

Epstein-Barr Virus (EBV) seroconversion is present in **virtually all MS patients** and **increases MS risk 32-fold**, yet >95% of adults are EBV-seropositive and **only ~0.1–0.2%** develop MS.[33–35] **EBV is necessary but not sufficient**: disease requires additional genetic susceptibility (especially **HLA-DRB115:01**),[36] low vitamin D, smoking, or other cofactors. EBV seronegativity effectively **rules out MS** in the differential.

Geriatric Risk Factors

FACTOR	RISK SIGNAL	NOTES
Epstein-Barr virus infection	**RR 2.17** (95% CI 1.97–2.39); **32-fold risk after EBV seroconversion**[34,35]	**The dominant infectious driver**; near-universal EBV seropositivity means it is **necessary but not sufficient for MS**[37]
HLA-DRB1*15:01 haplotype	OR ~**3.0** (strongest single genetic effect)[38]	**More than 200 risk variants identified**; most involve immune-pathway genes[36]
Family history (first-degree relative)	**2–4% lifetime risk vs ~0.1% general**; twin concordance 30–50%[2]	**No validated genetic factor** reliably predicts clinical course[2]
Female sex	~**3:1** female-to-male ratio[6]	**Consistent across populations**; male patients with demyelinating symptoms still warrant full workup[2]
Cigarette smoking	**RR 1.48** (meta-analysis)[1]	**Also accelerates disability progression and SPMS conversion**; the most actionable modifiable risk factor[39]
Higher latitude/low vitamin D	Prevalence gradient (**5–300 per 100,000**)[1,38]	Vitamin D supplementation **has not been shown** in trials to improve MS outcomes[40]
Adolescent obesity	**HR 1.58** for BMI >95th percentile at age 13[1]	Interacts synergistically with HLA-DRB1*15:01, smoking, and EBV[41]
Older age at onset (≥50 y)	**Faster disability accumulation**; more progressive phenotype[42]	**Late-onset MS reaches EDSS milestones faster**; stricter MRI thresholds apply at ≥50 due to **vascular mimics**[43]
Vascular comorbidity at diagnosis	**HR 1.51** (95% CI 1.41–1.61) for ambulation disability[1,44]	**Reduces median time to a walking aid from 18.8 to 12.8 years**; the most validated modifier of outcome in older patients[44]

ABBREVIATIONS: BMI = body mass index; CI = confidence interval; EBV = Epstein-Barr virus; EDSS = Expanded Disability Status Scale; HLA = human leukocyte antigen; HR = hazard ratio; MRI = magnetic resonance imaging; MS = multiple sclerosis; OR = odds ratio; RR = relative risk; SPMS = secondary progressive multiple sclerosis

Diagnostic Thresholds

MS diagnosis and ongoing classification rely on **two primary frameworks in US clinical practice**: the **2024 McDonald Criteria** (published 2025), which establish the initial diagnosis, and the **Lublin Phenotype Classification** (2013, clarified 2020), which categorizes the clinical course and drives ICD-10 subcode selection, DMT eligibility, and surveillance planning.[3,15] Diagnosis hinges on demonstrating that demyelinating lesions are **disseminated in space** (**DIS**) across characteristic CNS locations and **disseminated in time** (**DIT**), with alternative biomarker pathways (CSF, CVS, PRLs) now available when conventional MRI evidence is insufficient.[15] Once

diagnosed, the clinical course is classified by **phenotype** (RRMS, PPMS, SPMS) with annual activity and progression modifiers, and disability is tracked **longitudinally using the EDSS**.[3,45]

Primary Diagnostic System: 2024 McDonald Criteria

The **2024 McDonald Criteria** provide a unified diagnostic framework for all MS presentations: relapsing, progressive, pediatric, and late-onset.[15] The diagnosis requires **DIS across five anatomical locations** (periventricular, juxtacortical/cortical, infratentorial, spinal cord, and now the optic nerve as a new fifth site) plus evidence of DIT or supportive biomarkers.[15,21]

Key changes from 2017 include: DIT/CSF is no longer mandatory if lesions are present in ≥4 of 5 locations; the central vein sign (**CVS**) and paramagnetic rim lesions (**PRLs**) serve as **optional high-specificity MRI biomarkers**; kappa free light chains can substitute for oligoclonal bands; and radiologically isolated syndrome (**RIS**) can now fulfill MS criteria **when supported by biomarker evidence**.[14,15] **Stricter thresholds apply for patients ≥50 years**, those with vascular comorbidities, and children **to reduce misdiagnosis risk**.[15,46]

2024 McDonald Criteria

PRESENTATION[15]	ANATOMICAL LOCATIONS INVOLVED[15]	REQUIREMENTS TO ESTABLISH DIAGNOSIS[15]
Attack or ≥1 year of progression	≥2	DIT or CSF+ or CVS+ or lesions in 4/5 anatomical locations
≥1 year of progression (PPMS pathway)	≥2 (including spinal cord lesions)	DIT or CSF+ or CVS+ or lesions in 4/5 anatomical locations
Attack or ≥1 year of progression	1	CSF+ and CVS+, or CSF+ and PRL+, or DIT and CVS+, or DIT and PRL+
Incidental imaging or symptoms not specific for MS	≥2	DIT or CSF+ or CVS+

ABBREVIATIONS: CSF+ = cerebrospinal fluid positive (oligoclonal bands or elevated kappa free light chains); CVS+ = central vein sign positive; DIT = dissemination in time; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; PRL+ = paramagnetic rim lesion positive

Primary Classification System: Lublin Phenotype Descriptors (2013/2020)

Once MS is diagnosed, the clinical course is classified using the **Lublin phenotype system**, which defines four core phenotypes (**CIS**, **RRMS**, **PPMS**, and **SPMS**) that are each modified by **activity** (clinical relapses or new/enlarging MRI lesions) and **progression** (gradual disability worsening independent of relapses).[3,47] These modifiers must be reassessed **at least annually** and are framed in time (e.g., "SPMS, active and progressing over the past 12 months").[3,47] The phenotype directly determines the **ICD-10-CM subcode**, **DMT eligibility**, and **surveillance intensity**.

PHENOTYPE	ACTIVITY MODIFIER	ICD-10-CM CODE	DMT ELIGIBILITY*
Relapsing-remitting MS (RRMS)	Active or non-active	**G35.A**	**All approved** relapsing-forms DMTs
Primary progressive MS (PPMS)	Active, with or without progression	**G35.B1** (active)	**Ocrelizumab** (only FDA-approved DMT for PPMS)
Primary progressive MS (PPMS)	Non-active, with or without progression	**G35.B2** (non-active)	**Ocrelizumab**
Secondary progressive MS (SPMS)	Active, with or without progression	**G35.C1** (active)	Siponimod, cladribine, ocrelizumab (relapsing-forms indication)
Secondary progressive MS (SPMS)	Non-active, with or without progression	**G35.C2** (non-active)	**Limited options**; no DMT with strong evidence for non-active SPMS
MS, unspecified	—	**G35.D**	Use only when subtype is **genuinely undetermined**; overuse = common MS **coding error**

ABBREVIATIONS: DMT = disease-modifying therapy; FDA = Food and Drug Administration; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Primary Disability Scale: Expanded Disability Status Scale (EDSS)

The EDSS is the most widely used measure of **MS-related disability**, ranging from **0** (normal neurologic exam) to **10** (death due to MS) in 0.5-point increments.[48,49] It is scored by a neurologist based on examination of **8 functional systems**. Key clinical milestones are **EDSS 3.0** (moderate disability, fully ambulatory), **4.0** (significant disability, walks ≥500 m unaided), and **6.0** (requires unilateral walking aid for ~100 m).[50,51] A sustained 1.0-point increase (or 0.5-point at EDSS ≥6.0) **confirmed over 3–6 months** defines confirmed **disability progression**.[51] Known limitations to the EDSS include poor inter-rater reliability, heavy weighting toward ambulation at scores ≥4.0, and poor capture of cognitive and upper-limb function.

Simplified EDSS Summary Table (Adapted from Kurtzke, 1983)[48]

EDSS SCORE	FUNCTIONAL MEANING	CLINICAL SIGNIFICANCE
0	Normal neurologic exam	**Baseline reference**
1.0–1.5	No disability, minimal signs in one functional system	Subclinical findings only

EDSS SCORE	FUNCTIONAL MEANING	CLINICAL SIGNIFICANCE
2.0–2.5	Minimal disability in 1–2 functional systems	Fully ambulatory; may have mild sensory or visual findings
3	Moderate disability, fully ambulatory	**First milestone**: disability present but no walking limitation
4	Significant disability, walks ≥500 m without aid or rest	**Second milestone**: key threshold for DMT escalation discussions
6	Requires unilateral walking aid for ~100 m	**Third milestone:** major functional transition; triggers assistive device and fall-prevention planning
7.0–7.5	Restricted to wheelchair; transfers independently or with aid	**Caregiver support typically required**
8.0–9.5	Bed-bound to helpless	**Advance care planning critical**
10	**Death due to MS**	**—**

ABBREVIATIONS: DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; MS = multiple sclerosis

Other Relevant Diagnostic and Monitoring Tools

SYSTEM/ TEST	BASIS	KEY FEATURES	PRIMARY USE
Symbol Digit Modalities Test (SDMT)[23,29]	Timed symbol-to-number matching task (~5 min)	Most sensitive single test for **MS cognitive impairment**; a **4-point decline** is clinically meaningful (associated with employment loss); **8-point decline** proposed as reliable threshold for cognitive worsening	**Annual cognitive screening**; recommended by AAN and BICAMS consensus as standard longitudinal outcome
MRI surveillance (T2 lesion threshold)[52]	Annual brain MRI comparing **new T2 lesions** to treated baseline	**≥2 new T2 lesions independently predict ~3-fold relapse risk and support DMT escalation**; 1 new T2 lesion did not significantly increase risk; rebaseline MRI 3–6 months after DMT initiation recommended	**Treatment response monitoring**; DMT escalation decision-making
Central vein sign (CVS)[15]	Susceptibility-sensitive MRI (**T2*-weighted**)	**Perivenular demyelination marker**; positive when **≥6 lesions show CVS or majority if 10 lesions**; 94% accuracy distinguishing MS from mimics at 3T	**Diagnostic specificity, especially in patients ≥50** or with vascular comorbidities

SYSTEM/ TEST	BASIS	KEY FEATURES	PRIMARY USE
Paramagnetic rim lesions (PRLs)[15]	Susceptibility-sensitive MRI	**Iron-laden microglia rim = chronic active ("smoldering") lesion**; ≥1 PRL is >95% specific for MS; present in 48% of CIS, 59% of RRMS	Diagnostic specificity and prognostic marker **for aggressive disease**
CSF analysis (OCBs/kappa free light chains)[15]	Lumbar puncture	CSF-specific OCBs present in 80–90% of MS; kappa free light chains now accepted as OCB substitute under 2024 criteria	**Supports DIT when MRI is non-diagnostic**; differentiates MS from NMOSD and MOGAD
Radiologically isolated syndrome (RIS)[15,53]	Incidental MRI findings meeting DIS criteria **without clinical symptoms**	**~50% develop clinical MS within 10 years**; risk factors: age 35, male sex, spinal cord lesions, OCBs	Now eligible for MS diagnosis under 2024 criteria **if DIS + DIT/CSF/CVS are satisfied**; early intervention may **delay first clinical attack**

ABBREVIATIONS: AAN = American Academy of Neurology; BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis; CIS = clinically isolated syndrome; CSF = cerebrospinal fluid; CVS = central vein sign; DIS = dissemination in space; DIT = dissemination in time; DMT = disease-modifying therapy; MOGAD = myelin oligodendrocyte glycoprotein antibody-associated disease; MRI = magnetic resonance imaging; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; OCB = oligoclonal band; PRL = paramagnetic rim lesion; RIS = radiologically isolated syndrome; RRMS = relapsing-remitting multiple sclerosis; SDMT = Symbol Digit Modalities Test

Clues to Dig Deeper

CLINICAL CLUE	WHY IT MATTERS	NEXT DIAGNOSTIC STEP
Demyelinating symptoms evolving over days in any adult	**Opportunity to shorten diagnostic delay** rather than 'wait and see'[54]	**Order brain and spinal cord MRI** (ideally 3T) and refer to neurology promptly[55]
Optic neuritis or partial myelitis	**Classic first demyelinating events**; early treatment improves long-term outcomes[18]	**MRI brain and spine with contrast**; neurology referral; consider CSF if MRI non-diagnostic[15]

CLINICAL CLUE	WHY IT MATTERS	NEXT DIAGNOSTIC STEP
Incidental MRI white-matter lesions (possible RIS)	**RIS can meet MS criteria** and may warrant early intervention before the first clinical attack[53,56]	**Compare with prior imaging**; refer to neurology; do not label as MS on imaging alone[17]
Worsening gait or function without a discrete relapse	May signal **SPMS transition or PIRA** rather than stable RRMS[32]	**Neurology reassessment** of phenotype and treatment plan; surveillance MRI[1,45]
New progressive deficit on natalizumab	New cognitive, visual, or motor changes raise concern for **PML** → medical emergency[57]	**Emergent brain MRI with DWI and CSF JCV PCR**; urgent neurology contact[57]
Disabling fatigue, mood change, or cognitive slowing	These non-physical symptoms are under-recognized yet central to function and adherence[1,29]	**PHQ-9 and SDMT screening**; code G31.84/ F32.- when present; address **before** DMT changes[22,23]
Sudden worsening with fever or heat	Distinguishing a true relapse from a pseudoexacerbation **prevents unnecessary steroids**[1]	Check for infection and manage temperature first; reassess once afebrile[28]

ABBREVIATIONS: CSF = cerebrospinal fluid; DMT = disease-modifying therapy; DWI = diffusion-weighted imaging; JCV = John Cunningham virus; MRI = magnetic resonance imaging; MS = multiple sclerosis; PCR = polymerase chain reaction; PHQ-9 = Patient Health Questionnaire-9; PIRA = progression independent of relapse activity; PML = progressive multifocal leukoencephalopathy; RIS = radiologically isolated syndrome; RRMS = relapsing-remitting multiple sclerosis; SDMT = Symbol Digit Modalities Test; SPMS = secondary progressive multiple sclerosis

Common Oversights

OVERSIGHT/SHORTCUT	WHY IT MATTERS — WHAT TO DO INSTEAD
Over-reading nonspecific MRI 'white spots' as MS	Age-related **small-vessel ischemia and migraine lesions** are common in older adults; interpret MRI in clinical context and apply stricter thresholds at age ≥50[58,59]
Treating sensory symptoms alone as a relapse	**Subjective numbness without objective exam findings** should not by itself satisfy a demyelinating attack; document the objective neurological exam[1,59]
Diagnosing MS after a single event without proving dissemination in time	**Confirm a second lesion** on follow-up MRI, CSF-specific OCBs, or a true second relapse before committing to the diagnosis[15,59]
Misinterpreting JCV testing	**Blood JCV PCR is typically negative** and does not exclude risk; use serum JCV antibody index for PML risk stratification on natalizumab[54,60]

OVERSIGHT/SHORTCUT	WHY IT MATTERS — WHAT TO DO INSTEAD
Treating MS as 'set it and forget it'	**Irreversible atrophy and smoldering progression continue between relapses**; the PCP must manage vascular risk and monitor function even when DMTs are specialist-managed[1,61]
Giving steroids for every symptom flare	**Rule out pseudoexacerbation** (infection, fever, Uhthoff phenomenon) before steroids; check for infection and manage temperature first[62]
Denying maintenance rehabilitation for 'lack of restoration potential'	Maintenance PT/OT/speech therapy to prevent functional decline is a **recognized Medicare benefit**[24]

ABBREVIATIONS: CSF = cerebrospinal fluid; DMT = disease-modifying therapy; JCV = John Cunningham virus; MRI = magnetic resonance imaging; MS = multiple sclerosis; OCB = oligoclonal band; OT = occupational therapy; PCP = primary care provider; PCR = polymerase chain reaction; PML = progressive multifocal leukoencephalopathy; PT = physical therapy

Key Differentials in Elderly

PRESENTATION	DIFFERENTIAL	KEY TESTS
First demyelinating event in a patient ≥50	**MS**; small-vessel ischemic white-matter disease; migraine-related lesions; vitamin B12 deficiency; NMOSD; MOGAD[58]	**MRI brain and spine with contrast**; B12/methylmalonic acid; AQP4-IgG and MOG-IgG; vascular risk assessment[15,63]
Acute bilateral or severe vision loss	Neuromyelitis optica spectrum disorder (NMOSD) rather than MS; MOGAD; ischemic optic neuropathy[58,63]	**AQP4-IgG serology**; MOG-IgG; urgent MRI orbits/brain; neurology referral[64]
Longitudinally extensive transverse myelitis	**NMOSD** (lesions spanning ≥3 vertebral segments); MOGAD; MS (usually short-segment); compressive or vascular myelopathy[63]	**Spinal MRI**; AQP4-IgG; MOG-IgG; CSF analysis[64]
Progressive cognitive or behavioral decline	**Smoldering MS/PIRA**; vascular cognitive impairment; neurodegenerative dementia; depression[29]	**SDMT**; brain MRI; depression screen; vascular risk review[1,29]
Steadily progressive weakness, no relapses	**PPMS/SPMS**; cervical spondylotic myelopathy; ALS (do not code G35-MS as G12.21); hereditary spastic paraplegia[58]	**MRI brain and spine**; clinical phenotyping; neurology referral[15]
Symptom worsening with fever or heat	**Pseudoexacerbation** (**Uhthoff phenomenon**) vs true relapse; intercurrent infection[28]	**Evaluate for infection**; recheck after temperature normalizes; reserve steroids for confirmed relapse[1,62]

PRESENTATION	DIFFERENTIAL	KEY TESTS

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; AQP4-IgG = aquaporin-4 immunoglobulin G; CSF = cerebrospinal fluid; MOG-IgG = myelin oligodendrocyte glycoprotein immunoglobulin G; MOGAD = myelin oligodendrocyte glycoprotein antibody-associated disease; MRI = magnetic resonance imaging; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; PIRA = progression independent of relapse activity; PPMS = primary progressive multiple sclerosis; SDMT = Symbol Digit Modalities Test; SPMS = secondary progressive multiple sclerosis

Comorbidity Screening

CONDITION	PREVALENCE/ASSOCIATION	SCREENING APPROACH
Vascular disease (I10, E11.-, E78.-)	Vascular comorbidity at diagnosis carries **HR 1.51** for ambulation disability and **1.5x higher CV mortality**[1,65]	**Aggressive control of hypertension, diabetes, and hyperlipidemia**; smoking cessation slows brain volume loss[62,66]
Depression/ anxiety (F32.-, F41.-)	Affects **21–50%** of people with MS =**2–3x** the general population[1,67]	**Annual PHQ-9** or BDI (BDI cutoff ≥13); address before DMT changes to support adherence[68]
Cognitive impairment (G31.84)	Affects **40–70%** of people with MS; processing speed, memory, executive function[1,29]	**Use SDMT, not MMSE**; document and code; offer cognitive rehabilitation[23,29]
Neurogenic bladder (N31.-)	Common; drives **recurrent UTIs and avoidable ED visits**[30]	**Proactive bladder management**; treat infection; consider urology referral for refractory symptoms[30]
Falls and osteoporosis (M81.0, Z91.81)	Gait impairment and long-term corticosteroid use **raise fracture risk**; falls are under-reported[69]	Annual fall screen; DEXA per osteoporosis guidelines; PT for balance and gait[69,70]
Infection risk on DMTs	Anti-CD20 and other immunosuppressive DMTs **raise infection risk, compounded by immunosenescence**[71,72]	**Monitor immunoglobulins on anti-CD20**; complete age-appropriate vaccines before B-cell depletion[73]
Fatigue (R53.83)	Affects roughly **80%** of people with MS[1]	**Exercise and CBT have the most consistent evidence**; stimulant pharmacotherapy was no better than placebo in TRIUMPHANT-MS[25]

ABBREVIATIONS: BDI = Beck Depression Inventory; CBT = cognitive behavioral therapy; CV = cardiovascular; DEXA = dual-energy X-ray absorptiometry; DMT = disease-modifying therapy; ED = emergency department; HR = hazard ratio; MMSE = Mini-Mental State Examination; MS = multiple sclerosis; PHQ-9 = Patient Health Questionnaire-9; PT = physical therapy; SDMT = Symbol Digit Modalities Test; UTI = urinary tract infection

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

These emergency conditions require **same-day ED transfer or emergent neurology consultation:**

- **New progressive neurological deficits** (cognitive change, visual disturbance, motor weakness) in a patient on natalizumab or other immunosuppressive DMT[57,74]
  - → **Emergent brain MRI with DWI and CSF JCV PCR to evaluate for PML**
  - × PML carries 30–50% mortality; early detection is the strongest predictor of survival
- **Acute severe myelitis with bilateral motor/sensory loss and bowel/bladder dysfunction**[57,74]
  - → **Emergent spinal cord MRI;** differentiate complete transverse myelitis from cord compression
  - × Cord compression requires neurosurgical evaluation; delay risks permanent paralysis
- **Acute encephalopathy or altered consciousness**[57,74]
  - → Emergent brain MRI, LP, and infectious workup; may reflect PML, severe relapse, or CNS infection
  - × Altered mental status is rare in typical MS relapses — assume PML or infection until proven otherwise
- **Acute bilateral vision loss**[75,76]
  - → Urgent ophthalmology and neurology evaluation; test AQP4 and MOG antibodies to differentiate NMOSD
  - × Bilateral simultaneous optic neuritis is atypical for MS and suggests NMOSD, which requires different treatment
- **Brainstem relapse with respiratory compromise**[1,38]
  - → ICU-level monitoring; high-dose IV methylprednisolone; consider PLEX if steroid-refractory
  - × Brainstem relapses affecting respiratory centers can be life-threatening

⚠ RED FLAG — URGENT (24-72 HOURS)

Expedited workup required = **do not** refer to routine follow-up:

- **New severe relapse** (significant motor weakness, optic neuritis with marked vision loss, or severe ataxia)[1,77]
  - → Contact neurology within 24 hours for steroid consideration; brain MRI to confirm inflammatory activity
  - × Delays in steroid treatment may worsen relapse recovery
- **First presentation of suspected MS:** acute optic neuritis, partial myelitis, or brainstem syndrome evolving over days[13,78]
  - → Brain and spinal cord MRI with contrast; **urgent neurology referral**
  - × Early diagnosis and DMT initiation reduce long-term disability accumulation
- **Rapid unexplained neurological decline not fitting a pseudoexacerbation** (no fever, no infection)[32,57]
  - → **Urgent neurology evaluation**; brain MRI; consider PML or SPMS transition
  - × True neurological worsening without an identifiable trigger warrants urgent reassessment
- **≥2 new T2 lesions on surveillance MRI**[52]
  - → Urgent neurology discussion for DMT escalation; confirms breakthrough disease activity
  - × ≥2 new T2 lesions independently predict ~3-fold relapse risk
- **JCV antibody seroconversion on natalizumab (index >1.5)**[60,79]
  - → **Urgent discussion of DMT switch**; risk of PML rises substantially above index 1.5, especially after 24 months
  - × Continuing natalizumab at high JCV index without reassessment exposes patient to preventable PML risk
- **Worsening gait or function not explained by relapse**[32,45]
  - → Reassess for SPMS transition; document EDSS trajectory; discuss DMT adjustment with neurology
  - × Unrecognized SPMS transition delays appropriate management and prognostic counseling

3 MEAT DOCUMENTATION ESSENTIALS

MS documentation translates a **fluctuating**, **lifelong neurological disease** into a record that supports continuity, quality measurement, and shared decision-making. **The most frequent pitfalls**: defaulting to the unspecified subcode (**G35.D**) instead of documenting phenotype and activity, omitting the activity modifier (active vs non-active) that distinguishes the progressive

subcodes, and failing to capture the non-physical symptoms (fatigue, depression, cognitive impairment, bladder dysfunction, gait abnormality) that **define a patient's real clinical complexity**. Each gap obscures the clinical picture and impedes coordination with neurology, rehabilitation, and mental health.[1,15] The MEAT framework below ties each element into **appropriate clinical action**:

*A 67-year-old woman with a 19-year history of relapsing-remitting MS presents for a chronic-care visit. Over the past year she reports **gradually worsening walking distance** and balance without a discrete relapse, disabling fatigue, and low mood. She is on **ocrelizumab** managed by neurology. PMH: hypertension (amlodipine), hyperlipidemia. **No new MRI lesions in two years**. Functional status: walks ~150 m with a cane; independent in most ADLs; **recent near-falls**.*

MONITOR: "Progressive gait decline over 12 months without relapse, suggesting progression independent of relapse activity or SPMS transition. **EDSS estimated ~6.0** (unilateral walking aid for ~100 m). PHQ-9 14 (moderate depression); **SDMT below expected for age**. Blood pressure 148/88; LDL above goal."

EVALUATE: "Surveillance brain MRI ordered (stable for 2 years on therapy) plus spinal cord MRI to **evaluate progressive gait change**. Immunoglobulin level checked given long-term anti-CD20 therapy. Vascular risk reassessed → hypertension and hyperlipidemia control reviewed because vascular comorbidity accelerates disability. PT referral for balance and falls; urinalysis given new urgency."

ASSESS: "Diagnoses to document: secondary progressive MS, non-active (no relapse or new MRI lesion in the past year): **G35.C2**. Major depressive disorder, moderate (**F33.-**). MS-related gait abnormality (**R26.-**) and fatigue (**R53.83**). Essential hypertension (**I10**) and hyperlipidemia (**E78.-**). Reassess phenotype annually."

TREAT: "Neurology coordinating DMT strategy → **de-escalation discussion** pending given age/infection risk vs noninferiority data. BP to goal, statin added. SSRI started for depression; CBT referral placed. PT/OT for gait/falls. **Vaccines reviewed**: anti-CD20 timing noted. SDM and ACP documented."

Clinical Documentation Elements

- **Document the MS phenotype explicitly**: relapsing-remitting (**G35.A**), primary progressive (**G35.B-**), or secondary progressive (**G35.C-**) → phenotype drives both treatment and the ICD-10 subcode[1,3,47]
- **Document activity status**: active (recent relapse, new MRI lesion, or progression) vs non-active (stable) = to support the progressive subcodes (**B1/C1 vs B2/C2**)[3,47]
- **Reassess and document the phenotype at least annually**; the RRMS-to-SPMS transition changes the subcode and the treatment plan[3,32,47]
- **Document disability and surveillance objectively**: EDSS or a patient-reported equivalent, T25FW or SDMT where available, and the most recent MRI date and findings[54]
- **Code each functional and non-physical manifestation addressed at the visit**: fatigue (**R53.83**), depression (**F32.-/F33.-**), cognitive impairment (**G31.84**), neurogenic bladder (**N31.-**), gait abnormality (**R26.-**), spasticity (**R25.2/M62.83**)[1,23]

- **Document**: DMT name, route, and monitoring (e.g., ocrelizumab IV q6 months; immunoglobulins and infection surveillance), and **distinguish a true relapse from a pseudoexacerbation**[28,54]
- **Document**: the vascular comorbidity burden (hypertension, diabetes, hyperlipidemia, smoking) = accelerate disability and are **squarely the PCP's responsibility**[1,65]
- **Document**: advance care planning and rehabilitation needs for patients with progressive disease and significant disability[80]

Reframing Common Documentation Shortcuts

INSTEAD OF...	DOCUMENT...[1,3,17,23,47,80]
'Multiple sclerosis'	'Relapsing-remitting multiple sclerosis (**G35.A**), last relapse 14 months ago, stable on ocrelizumab; **EDSS 2.5**'
'MS, progressive'	'Secondary progressive MS, non-active (**G35.C2**); no relapse or new MRI lesion in the past year; **EDSS 6.0**'
'MS, unspecified' (G35.D) by default	Specify phenotype and activity (**G35.A**/**G35.B1-2**/**G35.C1-2**); reserve G35.D **only when the subtype is genuinely undetermined**
'On MS medication'	'Ocrelizumab 600 mg IV q6 months (neurology-managed); immunoglobulins monitored; infection surveillance; vaccinations current'
'Patient feels worse'	**Distinguish relapse from pseudoexacerbation**: 'Symptom worsening with UTI and low-grade fever → pseudoexacerbation (Uhthoff); no steroids; treat infection'
'Chronic fatigue'	'MS-related fatigue (**R53.83**); exercise and CBT counseled; stimulants not initiated (no benefit over placebo in TRIUMPHANT-MS)'
'Depression'	'Major depressive disorder, moderate (**F33.-**), PHQ-9 14; sertraline initiated; addressing **before** any DMT change to support adherence'
'Memory complaints'	'MS-related cognitive impairment (**G31.84**); **SDMT below age expectation**; cognitive rehabilitation referral'
'Walks with a cane'	'Gait abnormality (**R26.-**), **EDSS 6.0**; maintenance PT for balance and falls (covered Medicare benefit)'
'Bladder problems'	'Neurogenic bladder (**N31.-**); recurrent UTIs addressed; proactive bladder management; urology referral if refractory'

ABBREVIATIONS: CBT = cognitive behavioral therapy; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IV = intravenous; MRI = magnetic resonance imaging; MS = multiple sclerosis; PHQ-9 = Patient Health Questionnaire-9; PT = physical therapy; SDMT = Symbol Digit Modalities Test; SPMS = secondary progressive multiple sclerosis; UTI = urinary tract infection

DOCUMENTATION IS COMPREHENSIVE CODING

Every MS encounter should document the **phenotype** (RRMS, PPMS, or SPMS) and **activity status** (active vs non-active),[3,38,47] the **current EDSS** or functional status and most recent **MRI date/findings**,[1,23] the **DMT** and its monitoring, and the full functional and comorbidity burden (fatigue, depression, cognitive impairment, bladder dysfunction, gait abnormality, and vascular risk factors).[1,44,81] **Reassess the phenotype annually** so the subcode reflects the **true disease course**.

4 TREATMENT AND REFERRAL QUICK GUIDE

MS treatment is driven by phenotype (relapsing vs progressive), disease activity, age, and comorbidity — not chronological age alone.[1,65] Disease-modifying therapy is initiated and escalated by neurology, but the **PCP's highest-value contributions are**: shortening diagnostic delay, sustaining adherence, managing the vascular risk that accelerates brain volume loss, proactively treating symptoms (spasticity, fatigue, bladder, mood) to reduce ED visits and hospitalizations, and co-monitoring DMT safety.[82] **In older adults the risk-benefit balance shifts**: high-efficacy DMTs show diminishing incremental benefit while **infection risk rises with immunosenescence**.[65] Social determinants of health **materially affect MS outcomes** and adherence and should be addressed in value-based models serving diverse Medicare populations.[83]

Therapy Escalation Criteria

TRIGGER	ACTION*[1,18,54,65,82]
Demyelinating symptoms over days (optic neuritis, partial myelitis, brainstem syndrome)	**Order brain and spinal cord MRI**; refer to neurology promptly → **do not** 'wait and see'
Confirmed relapsing MS, treatment-naive	**Neurology initiates a DMT**; AAN advises offering a DMT to patients with relapsing MS and recent clinical or MRI activity
Breakthrough disease on a moderate-efficacy DMT (≥1 relapse, ≥2 new MRI lesions, or progression over 1 year)	Discuss switching to a higher-efficacy DMT **or a different mechanism**
≥2 new T2 lesions on annual surveillance MRI	**Supports DMT escalation** even if clinically stable; neurology reassessment
Acute relapse (significant new deficit, not a pseudoexacerbation)	After excluding infection/fever, neurology may give **IV or oral methylprednisolone** 500–1,000 mg/day × 3–5 days; plasma exchange if **steroid-refractory**

TRIGGER	ACTION*[1,18,54,65,82]
Active SPMS	Neurology; **siponimod** is FDA-approved for **active SPMS** (relapsing forms)
Primary progressive MS	Neurology; **ocrelizumab** is the only DMT approved for **PPMS**
New progressive deficit on natalizumab	Emergent MRI with DWI and CSF JCV PCR to **evaluate for PML**; urgent neurology
Stable disease >2 years in a patient >60	**Discuss DMT de-escalation with neurology**; discontinuation has not shown non-inferiority for MRI activity
Disabling spasticity, bladder dysfunction, fatigue, or depression	**Initiate symptom-directed management**; refer to rehabilitation and mental health as needed
Progressive functional decline in older adult	Comprehensive functional assessment; maintenance rehabilitation; advance care planning

ABBREVIATIONS: AAN = American Academy of Neurology; CSF = cerebrospinal fluid; DMT = disease-modifying therapy; DWI = diffusion-weighted imaging; FDA = U.S. Food and Drug Administration; IV = intravenous; JCV = John Cunningham virus; MRI = magnetic resonance imaging; MS = multiple sclerosis; PCR = polymerase chain reaction; PML = progressive multifocal leukoencephalopathy; PPMS = primary progressive multiple sclerosis; SPMS = secondary progressive multiple sclerosis
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

AAN DMT Guideline–Aligned Treatment by Phenotype, Activity, and Patient Profile

SETTING/CLASS	PREFERRED OPTION(S)*	KEY NOTES*
Acute relapse management	IV or oral **methylprednisolone** 500–1,000 mg/day × 3–5 days; plasma exchange if steroid-refractory[1,38]	**Rule out pseudoexacerbation first**; oral methylprednisolone is noninferior to IV for relapse recovery[77]
Moderate-efficacy DMT (first-line for many)	Dimethyl fumarate, teriflunomide, interferon beta, glatiramer acetate[54,84]	Favorable safety; relative relapse reduction vs placebo 0.62–0.84; **well tolerated in older adults**[84]
High-efficacy DMT (escalation or early intensive)	Ocrelizumab, natalizumab, fingolimod, ofatumumab, ublituximab, alemtuzumab, cladribine[84,85]	**Strongest relapse reduction**; natalizumab had the largest real-world effect (HR 0.44 vs glatiramer)[86]

SETTING/CLASS	PREFERRED OPTION(S)*	KEY NOTES*
Anti-CD20 monoclonal antibodies	Ocrelizumab (IV q6 months), ofatumumab (SC monthly), ublituximab[1,86]	Most widely used high-efficacy class; ocrelizumab is the **only agent approved for PPMS**
Active secondary progressive MS	**Siponimod** (titrated; CYP2C9 genotyping)[32]	FDA-approved for active SPMS; **EXPAND trial** showed **~21% relative reduction** in 3-month confirmed disability progression[32]
Primary progressive MS	**Ocrelizumab**	**ORATORIO** showed a **~20–25%** relative reduction in 3-month confirmed disability progression vs placebo; the BTK inhibitor tolebrutinib reduced 6-month confirmed progression by **~31%** in **nonrelapsing SPMS in HERCULES**, signaling an emerging option for progressive disease[87,88]
Older adults (≥55–60 y)	Continue or de-escalate per shared decision-making[89]	High-efficacy benefit **narrows with age** while infection risk rises; discontinuation not proven non-inferior[89]
Spasticity	**Baclofen or tizanidine**; PT and structured exercise	**Second-line**: gabapentin, botulinum toxin (focal), intrathecal baclofen for refractory cases
Fatigue	Exercise and CBT (most consistent evidence)	Amantadine, modafinil, and methylphenidate were **no better than placebo in TRIUMPHANT-MS**[25]
Neurogenic bladder	**Antimuscarinics** (oxybutynin) or **mirabegron**; bladder training	Botulinum toxin for **refractory detrusor overactivity**; treat and prevent UTIs
Depression	SSRIs/SNRIs plus CBT	**Screen annually**; address before DMT changes to support adherence

ABBREVIATIONS: AAN = American Academy of Neurology; BTK = Bruton's tyrosine kinase; CBT = cognitive behavioral therapy; CYP2C9 = cytochrome P450 2C9; DMT = disease-modifying therapy; EXPAND = Exploring the Efficacy and Safety of Siponimod in Patients With Secondary Progressive Multiple Sclerosis; FDA = Food and Drug Administration; HERCULES = Phase 3 Trial of Tolebrutinib in Nonrelapsing Secondary Progressive Multiple Sclerosis; HR = hazard ratio; IV = intravenous; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; PT = physical therapy; q6 months = every 6 months; SC = subcutaneous; SNRI = serotonin-norepinephrine reuptake inhibitor; SPMS = secondary progressive multiple sclerosis; SSRI = selective serotonin reuptake inhibitor; TRIUMPHANT-MS = Trial of Amantadine, Modafinil, and Methylphenidate for MS-Related Fatigue; UTI = urinary tract infection
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL — PHENOTYPE & FUNCTION > CHRONOLOGIC AGE

Treat MS by phenotype and function, not chronological age.[54,65] In older adults the incremental benefit of high-efficacy DMTs over moderate-efficacy agents narrows, while infection risk rises with **immunosenescence compounded by immunosuppression**. Age alone should not preclude treatment: DMTs were as beneficial in late-onset RRMS as in adult-onset RRMS over 2 years.[90] **The highest-yield interventions in older patients are** proactive symptom management and vascular-risk control, which slow disability and reduce avoidable ED visits and hospitalizations.[90]

Non-Pharmacologic Care and Supportive Interventions

INTERVENTION	TARGET/RECOMMENDATION	NOTES
Exercise/structured physical activity	**Encourage as tolerated**; associated with improved fatigue, mood, and possibly brain volume[24]	**Low risk**; among the most consistently beneficial nonpharmacologic measures[24]
Maintenance PT/OT/speech therapy	**Prescribe proactively** to prevent functional decline[24]	**A covered Medicare benefit**; should not be denied for 'lack of restoration potential'[24]
Fatigue self-management	Energy conservation, heat avoidance, CBT	Exercise and CBT **outperform stimulant pharmacotherapy**, which was placebo-equivalent in **TRIUMPHANT-MS**[25]
Spasticity management	Stretching, PT, structured exercise, TENS alongside pharmacotherapy[26]	Multimodal care **reduces disability** and supports mobility[24,26]
Smoking cessation	Quitline; **pharmacotherapy as appropriate**[39]	**The most actionable modifiable risk factor**; smoking accelerates SPMS conversion[39]
Cognitive engagement and rehabilitation	**Intellectually challenging activity**; neuropsychological rehab and OT[29]	Associated with improved cognitive function; pair with **SDMT monitoring**[26,29]
Self-management education	Adjusting outlook, stress and symptom management, communication, planning	Structured, multicomponent self-management improves quality of life

INTERVENTION	TARGET/RECOMMENDATION	NOTES
Advance care planning	Annually and when goals change[91]	Especially relevant in **progressive MS** with significant disability[91]

ABBREVIATIONS: CBT = cognitive behavioral therapy; DMT = disease-modifying therapy; MS = multiple sclerosis; OT = occupational therapy; PT = physical therapy; SDMT = Symbol Digit Modalities Test; SPMS = secondary progressive multiple sclerosis; TENS = transcutaneous electrical nerve stimulation; TRIUMPHANT-MS = Trial of Amantadine, Modafinil, and Methylphenidate for MS-Related Fatigue

Medication Safety and Key Interactions

DRUG/CLASS	INTERACTION/TOXICITY*[1,60,65,92]	CLINICAL ACTION*[54,93–95]
Natalizumab	Progressive multifocal leukoencephalopathy (**PML**); risk rises with JCV antibody index, prior immunosuppression, and treatment duration	JCV antibody index **every 6 months**; emergent MRI + CSF JCV PCR for new progressive deficits; discuss switch if **index >1.5**
Ocrelizumab/ ofatumumab/ ublituximab (anti-CD20)	**Hypogammaglobulinemia**, infection risk, blunted vaccine response; infusion reactions	**HBV screening before start**; monitor immunoglobulins (especially in older adults); vaccinate before initiation
Fingolimod/ siponimod (S1P modulators)	**First-dose bradycardia/AV block**; macular edema; lymphopenia; may worsen hypertension	**First-dose cardiac monitoring**; baseline ophthalmologic exam; CBC; CYP2C9 genotyping for siponimod
Dimethyl fumarate	**Lymphopenia** (risk rises with age); GI effects; rare PML with prolonged lymphopenia	**CBC every 6 months**; monitor absolute lymphocyte count; hold if persistently low
Teriflunomide	**Hepatotoxicity**; may worsen hypertension; **teratogenicity**	**LFTs monthly** × 6 months then periodically; blood pressure; TB screening before start
Alemtuzumab/ cladribine	Autoimmune thyroid disease, ITP, nephropathy (**alemtuzumab**); lymphopenia, malignancy risk (**cladribine**)	Specialist-managed with REMS-level monitoring; limited data in older adults
High-dose corticosteroids (relapse)	Hyperglycemia, mood change, insomnia, osteoporosis with repeated courses	**Reserve for confirmed relapse** (not pseudoexacerbation); monitor glucose; bone health with recurrent use

DRUG/CLASS	INTERACTION/TOXICITY*[1,60,65,92]	CLINICAL ACTION*[54,93–95]
Polypharmacy in older adults	Symptomatic agents (anticholinergics, gabapentinoids) **add sedation and fall risk**	**Medication reconciliation each visit**; deprescribe where possible; weigh anticholinergic burden

ABBREVIATIONS: AV = atrioventricular; CBC = complete blood count; CSF = cerebrospinal fluid; CYP2C9 = cytochrome P450 2C9; FDA = Food and Drug Administration; GI = gastrointestinal; HBV = hepatitis B virus; ITP = immune thrombocytopenic purpura; JCV = John Cunningham virus; LFTs = liver function tests; MRI = magnetic resonance imaging; PCR = polymerase chain reaction; PML = progressive multifocal leukoencephalopathy; REMS = Risk Evaluation and Mitigation Strategy; S1P = sphingosine-1-phosphate; TB = tuberculosis
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

When to Refer

CRITERION[15,54,81]	SPECIALIST[1,22,23]	URGENCY[17,54,96]
Suspected PML on immunosuppressive DMT	Emergency department/ neurology	**Emergent**
Acute severe myelitis with bowel/bladder dysfunction	Emergency department/ neurology	**Emergent**
Acute bilateral vision loss (possible NMOSD)	Emergency department/ neurology/ophthalmology	**Emergent**
New severe relapse for steroid consideration	Neurology	**Urgent** (24–72 hours)
First presentation of suspected MS	Neurology (after MRI ordered)	**Urgent** (within days)
JCV seroconversion on natalizumab (index >1.5)	Neurology	**Urgent** (within days)
≥2 new T2 lesions on surveillance MRI	Neurology	**Expedited** (within days)
Worsening gait/function not explained by relapse	Neurology (phenotype reassessment)	**Expedited** (within days)
Refractory spasticity or neurogenic bladder	Rehabilitation medicine/ urology	**Routine**
Moderate-to-severe depression	Behavioral health	**Routine**
Progressive disability needing supportive care	Rehabilitation; palliative care when appropriate	**Routine**

CRITERION[15,54,81]	SPECIALIST[1,22,23]	URGENCY[17,54,96]

ABBREVIATIONS: DMT = disease-modifying therapy; JCV = John Cunningham virus; MRI = magnetic resonance imaging; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; PML = progressive multifocal leukoencephalopathy; T2 = T2-weighted magnetic resonance imaging

Follow-Up Timing

CATEGORY	FREQUENCY[1,17,54,96]	LABS/MONITORING[1,17,54,96]
Relapsing-remitting MS on DMT (G35.A)	Clinical review **q3–6 months**; brain MRI annually with a new baseline **3–6 months** after start/switch	Track relapses and new **T2/ enhancing lesions**; **≥2 new T2 lesions** supports escalation
Secondary progressive MS (G35.C-)	Clinical review **q3–6 months**; MRI per neurology	Reassess phenotype and activity; monitor **PIRA** and functional status (**EDSS, T25FW**)
Primary progressive MS (G35.B-)	Clinical review **q3–6 months**; MRI per neurology	**Function-focused monitoring**; ocrelizumab response and infection surveillance
Cognitive screening	**Annually** with SDMT	A **4-point SDMT decline** is clinically meaningful; MMSE is **insensitive in MS**
Depression screening	**Annually** (PHQ-9 or BDI, BDI cutoff ≥13)	Address **before DMT changes** to support adherence
Fall risk	**Annual** fall screen, especially with gait impairment or chronic steroids	PT for balance/gait; **DEXA** per osteoporosis guidelines
Vascular risk factors	**Every visit**	Blood pressure, glucose, lipids, smoking = **control slows brain volume loss and disability**
Anti-CD20 therapy safety	Immunoglobulins periodically; infection surveillance	More frequent attention in older adults given **immunosenescence**
Brain atrophy (where available)	**Per neurology**; incorporated into NEDA-4	Annual brain volume loss **>0.4%** suggests pathologic atrophy beyond normal aging

ABBREVIATIONS: DMT = disease-modifying therapy; MRI = magnetic resonance imaging; MS = multiple sclerosis; T2 = T2-weighted magnetic resonance imaging; PIRA = progression independent of relapse activity; EDSS = Expanded Disability Status Scale; T25FW = Timed 25-Foot Walk; SDMT = Symbol Digit Modalities Test; MMSE = Mini-Mental State Examination; PHQ-9 = Patient Health Questionnaire-9; BDI = Beck Depression Inventory; PT = physical therapy; DEXA = dual-energy X-ray absorptiometry; CD20 = cluster of differentiation 20; NEDA-4 = no evidence of disease activity-4

Comorbidity Management — Primary Care Role

COMORBIDITY	APPROACH	CAUTION*
Hypertension/ vascular risk (I10)	Treat BP, lipids, glucose **to goal**; smoking cessation at **every visit**	Vascular comorbidity a**ccelerates disability** and brain volume loss; not optional in MS care[1,66]
Depression/anxiety (F32.x, F41.x)	**Annual PHQ-9**; SSRI/SNRI plus CBT referral[22]	**Underdiagnosed**; impairs cognition and DMT adherence; address **before** attributing symptoms to MS progression[22]
Cognitive impairment (G31.84)	**SDMT annually**; cognitive rehabilitation; caregiver support[23,29]	**MMSE is insensitive for MS**; impairment affects **40–70%** and is rarely coded[23,29]
Neurogenic bladder (N31.x)	**Antimuscarinics or mirabegron**; bladder training; treat/prevent UTIs[26,31]	Drives **recurrent UTIs** and **avoidable ED visits** when neglected[26,31]
Osteoporosis/falls (M81.0, Z91.81)	**DEXA**; calcium/vitamin D; PT for balance; bisphosphonate if indicated[97]	Chronic corticosteroids and gait impairment **raise fracture risk**; screen annually[97]
Infection risk on immunosuppressive DMTs	**Vaccinate before B-cell depletion**; monitor immunoglobulins; treat infections promptly[81,98]	Immunosenescence compounds **DMT-related infection risk** in older adults[81,98]
Spasticity (R25.2/ M62.83)	Baclofen/tizanidine; PT; **botulinum toxin for focal spasticity**[26]	Untreated spasticity **worsens mobility, pain, and falls**[26]
Polypharmacy (Z79.x)	Medication reconciliation each visit; deprescribing review	Anticholinergic and sedating agents add fall and cognitive risk in older adults[1]

ABBREVIATIONS: BP = blood pressure; MS = multiple sclerosis; PHQ-9 = Patient Health Questionnaire-9; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitor; CBT = cognitive behavioral therapy; DMT = disease-modifying therapy; SDMT = Symbol Digit Modalities Test; MMSE = Mini-Mental State Examination; UTI = urinary tract infection; ED = emergency department; DEXA = dual-energy X-ray absorptiometry; PT = physical therapy; B-cell = B lymphocyte

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Cost-Smart Options

BRAND (EST. COST)[7,99]	GENERIC/ ALTERNATIVE (EST. COST)*[7,99,100]	EST. SAVINGS	COST-SMART TIP[7,101]
Copaxone (glatiramer acetate) 40 mg 3×/wk (~$22,000–$26,600/yr list)	**Generic** glatiramer acetate (Glatopa/Mylan) (**~$1,800–$6,000/yr**)	**~$16,000–$24,000/yr**	**Lowest-cost branded DMT**; moderate-efficacy injectable for low-activity RRMS; Part D OOP **capped at $2,000/yr**
Tecfidera (dimethyl fumarate) 240 mg BID (~$96,000/yr list)	**Generic** dimethyl fumarate (**~$130–$415/yr DTC**; **~$720–$1,050/yr Part D**)	**~$7,500–$8,000/yr OOP**	**Lowest-cost oral DMT** via DTC pharmacy (**~$415/yr**); monitor ALC q6 months
Gilenya (fingolimod) 0.5 mg daily (~$115,000/yr list)	**Generic** fingolimod (**~$1,040–$2,000/yr** post-IRA)	**~$6,800–$8,500/yr OOP**	**Generic high-efficacy oral**; first-dose 6-hour cardiac monitoring still required
Aubagio (teriflunomide) 14 mg daily (~$103,000/yr list)	**Generic** teriflunomide (**~$130–$210/yr DTC**)	**~$7,800–$9,300/yr OOP**	**Cheapest DMT at ~$133/yr DTC**; teratogenic = requires washout **before conception**
Ocrevus (ocrelizumab) 600 mg q6mo (~$67,000/yr list)	Off-label rituximab (**~$5,000–$10,000/yr** with biosimilars)	**~$35,000–$66,000 over 5 yr**	**WHO Essential Medicines List for MS**;[102] biosimilars reduce cost further; did not meet noninferiority to ocrelizumab in registry data
Tysabri (natalizumab) 300 mg q4wk (~$102,000/yr list; ~$75,000/yr net)	**No generic**; biosimilar FDA-approved 2023, US launch pending	Pending	**Highest-efficacy monotherapy**; extended-interval dosing (q6wk) may reduce cost and PML risk
Kesimpta (ofatumumab) 20 mg SC monthly (~$83,000–$88,000/yr list)	**No generic** (exclusivity through ~2032)	—	**Self-administered SC anti-CD20**; no infusion costs; MPPP reduces OOP to **~$167/mo**
Mayzent (siponimod) 2 mg daily (~$107,000/yr list)	**No generic** available	—	**Only S1P modulator with phase 3 SPMS data**; CYP2C9 genotyping required before initiation

BRAND (EST. COST)[7,99]	GENERIC/ ALTERNATIVE (EST. COST)*[7,99,100]	EST. SAVINGS	COST-SMART TIP[7,101]
All self-administered Part D DMTs	**IRA Part D $2,000 OOP cap + MPPP**	**Up to thousands/yr**	OOP reduced **68%–79%** for brand DMTs; MPPP spreads to **~$167/mo**; confirm LIS/Extra Help eligibility

ABBREVIATIONS: DMT = disease-modifying therapy; RRMS = relapsing-remitting multiple sclerosis; OOP = out-of-pocket; BID = twice daily; DTC = direct-to-consumer; ALC = absolute lymphocyte count; IRA = Inflation Reduction Act; q6mo = every 6 months; WHO = World Health Organization; MS = multiple sclerosis; FDA = Food and Drug Administration; US = United States; q4wk = every 4 weeks; PML = progressive multifocal leukoencephalopathy; SC = subcutaneous; CD20 = cluster of differentiation 20; MPPP = Medicare Prescription Payment Plan; S1P = sphingosine-1-phosphate; SPMS = secondary progressive multiple sclerosis; CYP2C9 = cytochrome P450 2C9; LIS = Low-Income Subsidy
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Patient Education and Adherence

MS patient education is distinguished by the **invisible nature of many symptoms** (fatigue, cognitive slowing, depression),[1] the concept of "**smoldering**" **disease activity** beneath clinical stability, which makes adherence feel counterintuitive when feeling well, the need to **differentiate true relapses from pseudoexacerbations** (which do not require steroids), and the complexity of DMT options spanning injectable, oral, and infusion platforms with distinct safety monitoring requirements.[1,27,54,103] **Education should emphasize**: why MRI surveillance and DMT adherence matter even during clinical stability, how vascular-risk control directly slows disability progression, and what cost-support resources exist to sustain access to therapy.

DOCUMENTATION — PATIENT EDUCATION

Document the following education topics, the patient and caregiver(s) present, materials provided, and patient understanding (**teach-back method**):

- **Diagnosis and phenotype in plain language**:[54] Document that the patient understands their MS subtype (RRMS, PPMS, SPMS), what "active" vs "non-active" means, and that MS is a lifelong condition requiring ongoing monitoring **even during periods of stability**
- **Smoldering progression and why monitoring matters when feeling well**:[29,103] Document counseling that brain volume loss and subclinical disease activity can occur **without noticeable symptoms**; this is why regular MRI surveillance and cognitive testing (**SDMT**) are essential even when the patient feels unchanged
- **Relapse vs pseudoexacerbation (Uhthoff phenomenon)**:[1,27] Document counseling on how to distinguish a **true relapse** (new or worsening neurologic symptoms lasting >24 hours without fever/infection) from a **pseudoexacerbation** triggered by heat, infection, or stress, which resolves with the trigger and **does not require steroids**
- **DMT plan, route, and monitoring**:[1,54,81] Document modalities discussed (injectable, oral, infusion); shared decision-making regarding efficacy, safety profile, and lifestyle fit; **specific monitoring requirements** (e.g., JCV index for natalizumab, immunoglobulins for anti-CD20 therapies, first-dose cardiac monitoring for S1P modulators); patient questions and preferences recorded
- **Vascular-risk control**:[1,39] Document counseling that hypertension, dyslipidemia, smoking, and diabetes each independently accelerate MS disability progression and brain volume loss; blood pressure, lipid, and glucose targets reviewed; **smoking cessation plan** documented
- **What to report between visits**:[1] New or worsening weakness, numbness, vision changes, or bladder dysfunction lasting >24 hours (possible relapse); fever or infection symptoms during immunosuppressive therapy; **signs of PML** (progressive confusion, visual changes, personality change) for patients on natalizumab or anti-CD20 therapies
- **Cost-support resources and adherence**:[7,104] Document counseling on the **IRA $2,000 Part D out-of-pocket cap**, manufacturer patient-assistance programs, specialty pharmacy support, and LIS/Extra Help enrollment; **cost is a leading driver of DMT nonadherence** in Medicare populations
- **Advance care planning**:[91] Surrogate designation, code status, goals of care; CPT 99497/99498 billable during AWV with no patient copay; particularly relevant as disability accumulates and at the SPMS transition
- **Caregiver assessment**: Document caregiver present, their understanding of DMT schedule, relapse recognition, and surveillance plan; screen for caregiver burden; **refer to social work if strain identified**

Quality Metrics Tie-In

No MS-specific HEDIS measures are currently active in MY2026, but MS intersects multiple quality measurement domains: depression screening (PHQ-9), fall risk, blood pressure control (vascular comorbidity acceleration of disability), bone health (immobility- and steroid-related osteoporosis), medication adherence (DMT access and Part D utilization), and advance care planning. **MS's combination of** lifelong DMT management, progressive disability with fall and fracture risk, underrecognized depression, vascular comorbidity–driven brain volume loss, and polypharmacy in advanced disease means that **cross-cutting national measures apply across the care trajectory** and can anchor quality reporting for any clinician managing an MS patient in a value-based program.

MEASURE	STANDARD	APPLICABILITY TO MS
HEDIS DMS-E: Utilization of the PHQ-9 to Monitor Depression Symptoms	**Denominator**: enrollees ≥12 with major depression/dysthymia AND PHQ-9 ≥10 **Numerator**: follow-up PHQ-9 within 4–8 months of index elevated score **Exclusions**: hospice	Depression prevalence in MS is **3x** the general population;[105] some DMTs and corticosteroid pulses may **exacerbate mood symptoms**[68]
HEDIS CBP: Controlling High Blood Pressure	**Denominator**: adults 18–85 with hypertension **Numerator**: BP 140/90 mmHg; **Exclusions**: hospice, ESRD, inpatient palliative care	Vascular comorbidities a**ccelerate MS disability progression** and brain volume loss;[1] hypertension and dyslipidemia **each independently worsen** EDSS trajectory[1,49]
HEDIS COA: Care for Older Adults — Medication Review	**Denominator**: MA enrollees ≥66, continuously enrolled **Numerator**: medication review documented annually **Exclusions**: hospice, ESRD	**DMT polypharmacy** (anti-CD20, S1P modulators) plus symptomatic medications (baclofen, gabapentin, anticholinergics) create **interaction and fall risk**;[106] medication review should reconcile immunosuppressive burden against infection and comorbidity risk[106,107]
HEDIS COA: Care for Older Adults — Functional Status Assessment	**Denominator**: enrollees ≥66; **Numerator**: functional status assessment documented annually; **Exclusions**: hospice, ESRD	**EDSS and SDMT** directly satisfy this sub-measure; document **at every visit** to guide **DMT continuation vs de-escalation** decisions in aging MS patients[29]
HEDIS ACP: Advance Care Planning	**Denominator**: enrollees ≥66; **Numerator**: advance care plan or surrogate decision-maker documented, OR ACP discussed but patient declined **Exclusions**: hospice	ACP should be addressed as disability accumulates, **particularly at SPMS transition**; billable as CPT 99497/99498 during AWV with no copay

MEASURE	STANDARD	APPLICABILITY TO MS
HEDIS Part D Medication Adherence	**Denominator**: Part D enrollees ≥18 with ≥2 fills of a medication in the target class (diabetes, hypertension, or cholesterol) during the measurement year **Numerator**: PDC ≥80% for the target medication class; **Exclusions**: hospice, ESRD	The **IRA $2,000 Part D out-of-pocket cap** supports DMT adherence and is a key VBC target[7,104]
MIPS #513: Patient-Reported Falls and Plan of Care	**Denominator**: patients ≥18 with documented fall in past year **Numerator**: plan of care for falls documented **Exclusions**: tic disorder, epilepsy, concussion/mTBI	MS patients have **50–60%** annual fall prevalence;[70] gait impairment, spasticity, and sensory loss are primary drivers

ABBREVIATIONS: PHQ-9 = Patient Health Questionnaire-9; MS = multiple sclerosis; DMT = disease-modifying therapy; HEDIS = Healthcare Effectiveness Data and Information Set; CBP = Controlling High Blood Pressure; BP = blood pressure; mmHg = millimeters of mercury; ESRD = end-stage renal disease; COA = Care for Older Adults; MA = Medicare Advantage; CD20 = cluster of differentiation 20; S1P = sphingosine-1-phosphate; EDSS = Expanded Disability Status Scale; SDMT = Symbol Digit Modalities Test; ACP = advance care planning; SPMS = secondary progressive multiple sclerosis; CPT = Current Procedural Terminology; AWV = Annual Wellness Visit; PDC = proportion of days covered; IRA = Inflation Reduction Act; VBC = value-based care; MIPS = Merit-based Incentive Payment System; mTBI = mild traumatic brain injury; SDoH = social determinants of health

QUALITY OUTCOME

When primary care shortens diagnostic delay by ordering MRI at the first demyelinating symptoms, documents phenotype and activity accurately, **sustains DMT adherence and vaccination**, controls vascular risk to slow brain volume loss, and proactively manages spasticity, fatigue, bladder, and mood — people with MS spend more time in stable rather than progressive states, with **fewer ED visits and hospitalizations**.

5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

- **Document MS phenotype at every encounter**:[4] **G35.A** relapsing-remitting; **G35.B-** primary progressive; **G35.C-** secondary progressive. **Specify activity status**: active (recent relapse, new MRI lesion, or progression) vs non-active (stable) = **completes the subcode** (e.g., G35.B1 active vs G35.B2 non-active). Defaulting to **G35.D** (unspecified) when the subtype is known = **most common MS coding error**

- **Reassess phenotype at least annually:** the RRMS-to-SPMS transition changes the subcode from **G35.A** to **G35.C-** and may **alter treatment eligibility**. Do not carry forward a stale phenotype **without clinical reassessment**
- **Functional and demyelinating manifestations coded separately and linked to MS**: fatigue **R53.83**; depression **F32.-/F33.-**; cognitive impairment **G31.84**; neurogenic bladder **N31.-**; gait abnormality **R26.-**; spasticity **R25.2/M62.83**. Code optic neuritis (**H46.1-** with laterality) and acute transverse myelitis (**G37.3**) distinctly, not as nonspecific complaints. **Do not assign G12.21** (ALS) for MS patients **unless** ALS is independently diagnosed
- **Comorbidities = frequently undercoded**: hypertension **I10**, hyperlipidemia **E78.-**, diabetes **E11.-**, osteoporosis **M81.0**, long-term DMT **Z79.-**. These are MS-relevant vascular and skeletal risk factors and should be coded when addressed
- **Definitive diagnostic language**: document MS only after dissemination in time and space is established; avoid committing to MS **from a single event or imaging alone**[1]

Annual Clinical Review and Confirmation

- **Annual reconfirmation and visit modality**: MS must be reassessed **once per calendar year** via in-person **or** synchronous audio-video encounter with MEAT documented = phenotype, activity status, current EDSS or functional status, most recent MRI findings, and DMT with monitoring data. Chart updates without an encounter do not satisfy MEAT. Under CMS-HCC V28, all MS subcodes (**G35.A** through **G35.D**) map to **HCC 198** (CNA RAF = **0.647**);[10,11] the documentation value of specifying active vs non-active lies in clinical accuracy and continuity, not additional risk capture
- **Status reconfirmation at every annual visit**: document current phenotype and activity status, current DMT with drug/dose/route/last infusion date, most recent MRI activity, EDSS, and SDMT.[3,15,17] "Stable on ocrelizumab" without objective data **does not satisfy MEAT**: include MRI date/result, IgG level, and functional scores
- **Reconfirm functional comorbidities annually**: fatigue, depression, cognitive impairment, neurogenic bladder, spasticity, and osteoporosis should be reviewed and recoded as currently active or resolved at each annual visit. Update vascular-risk documentation (BP, lipids, glucose, smoking) at each encounter
- **Avoid rollover**: **do not** copy last year's MS note forward **without updating**: phenotype/activity status, DMT and monitoring labs (JCV index, immunoglobulins, CBC), surveillance MRI results, EDSS/SDMT, vascular and functional comorbidity burden, and vaccination status

EHR Workflow Tips

- **[EHR TIP — Smartphrase]** Build a **.msvisit dot phrase** that auto-populates **G35.xx** subcode with phenotype/activity, current DMT (drug/dose/route/last infusion), EDSS, monitoring labs with dates (JCV index, immunoglobulins, CBC), last MRI date/activity,

vascular-risk fields, and SDMT/PHQ-9 scores. Companion **.msmeat block**: **Monitor** (relapses, MRI activity, EDSS trend, SDMT, vascular risk); **Evaluate** (neuro exam, MRI, labs, JCV trend); **Assess** (G35.xx phenotype/activity, trajectory); **Treat** (DMT details, vascular-risk plan, follow-up). Reduces unspecified G35 coding and supports MEAT in a single paste

- **[EHR TIP — Alert] Natalizumab JCV check**: BPA fires when JCV index >1.5 **or** not updated in 6 months. **Anti-CD20 IgG check**: BPA fires when ocrelizumab/ofatumumab is active without IgG in 12 months. **S1P first-dose**: BPA fires at fingolimod/siponimod initiation without documented cardiac monitoring or ophthalmology clearance
- **[EHR TIP — Best Practice] Problem list:** "Secondary progressive MS, non-active, EDSS 6.0, on ocrelizumab" — not "multiple sclerosis." Update phenotype/activity **at every visit**. Code MS comorbidities individually (spasticity, neurogenic bladder, depression, osteoporosis). **Flag Z86.16 persisting** while active DMT is on the med list → likely miscoded
- **[EHR TIP — Order Set]** "**MS Annual Workup**": CBC, CMP, immunoglobulins, JCV index (if natalizumab), 25-OH vitamin D, MRI brain/cord, SDMT, PHQ-9, fall screen, DEXA if indicated. "**MS Rebaseline MRI**": brain and cord MRI 3–6 months post-DMT switch = triggered when new DMT start is documented
- **[EHR TIP — Auto-prompt]** Annual MRI, SDMT, and PHQ-9 fire **if not completed in 11 months**. JCV index >1.5 on natalizumab fires DMT reassessment. IgG <500 on anti-CD20 fires dose-delay prompt. EDSS worsening ≥1.0 point sustained 6 months fires phenotype reassessment and neurorehab referral. One-click referral template auto-populates phenotype, EDSS, DMT, last MRI, and labs

Brief Case Examples

SUCCESS: COMPREHENSIVE DOCUMENTATION

SCENARIO

A 67-year-old woman with a 19-year history of **relapsing-remitting MS**; gradual gait decline over 12 months without a discrete relapse; disabling fatigue; low mood; on ocrelizumab; PMH hypertension, hyperlipidemia; walks ~150 m with a cane.

Documentation: "Secondary progressive MS, non-active (**G35**) — phenotype reassessed per Lublin criteria; no relapse or new MRI lesion in past year; EDSS ~6.0. PHQ-9 14 → MDD, moderate (F33.1); sertraline started MS-related gait abnormality (R26.89) and fatigue (R53.83). Ocrelizumab 600 mg IV q6 mo; immunoglobulins checked (hypogammaglobulinemia risk rises after ~3 years on anti-CD20). Vaccinations current per AAN guideline.Hypertension (I10) and hyperlipidemia (E78.5) — intensifying control; vascular comorbidities accelerate ambulatory disability. Maintenance PT authorized. ACP documented during AWV. Care coordinated with neurology."

Outcome: Phenotype reassessed from RRMS to SPMS with activity/progression modifiers evaluated annually. Vascular risk intensified; sertraline started for moderate MDD; maintenance PT for balance and falls authorized. Immunoglobulin surveillance initiated on anti-CD20 therapy. Vaccinations confirmed current. ACP documented during AWV. Care coordinated with neurology; no avoidable ED visit over the next year.

PITFALL: INSUFFICIENT DOCUMENTATION

Documentation as written: "72-year-old with MS, stable. Continue meds. Multiple sclerosis, unspecified (**G35**)."

Consequence: Phenotype and activity status **not documented**; **G35** used by default = the most common **MS coding gap**. Disabling fatigue, depression, and a recent fall went uncoded, understating complexity. [1,65] No vascular-risk reassessment **despite hypertension**, which is associated with **accelerated disability progression** in MS.

RAF Impact: MS maps to **HCC 198** (CNA RAF 0.647) whether or not the subtype is specified, so the RAF is unchanged; the unspecified note **misrepresents the clinical course**, omits functional comorbidities that define complexity, and **weakens continuity and quality reporting**.[4]

Fix: "Relapsing-remitting MS (**G35**) vs secondary progressive → reassess phenotype this year. MS-related fatigue (**R53.83**); depression screened (PHQ-9); recent fall → fall-risk assessment and PT. Hypertension control intensified (vascular comorbidities associated with increased ambulation disability). Immunoglobulins checked given anti-CD20 duration. Vaccinations reviewed per AAN guideline."

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