AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

ALS

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: Amyotrophic lateral sclerosis (ALS) — also called Lou Gehrig disease — is a progressive, uniformly fatal neurodegenerative disease that destroys **upper motor neurons (UMN)** in the brain and **lower motor neurons (LMN)** in the brainstem and spinal cord, producing relentless **muscle atrophy, paralysis, and ultimately respiratory failure**.[1] Median survival from symptom onset is **2-5 years**, and **respiratory failure is the cause of death in up to 95%** of people living with ALS.[2] Approximately **90-95% of cases are sporadic** (unknown cause); **5-10% are familial**, with pathogenic variants in C9orf72, SOD1, TARDBP, and FUS among the most characterized.[1] ALS is not purely a motor disease: up to **50% of patients develop cognitive or behavioral changes**, and roughly **15% develop frontotemporal dementia (ALS-FTD)** — a finding routinely missed in primary care with profound implications for advance care planning and decision-making capacity.[3]

ICD-10 Codes:

Primary diagnosis: **G12.21** — Amyotrophic lateral sclerosis — is the specific code for confirmed ALS and should be documented whenever the phenotype is known. Document "amyotrophic lateral sclerosis" or "ALS" explicitly; both familial and sporadic ALS map to **G12.21** (there is no separate code), so record genetic testing results (SOD1, C9orf72, FUS, TARDBP) in the chart to support specialist referral and **tofersen** eligibility. Avoid **G12.20** (motor neuron disease, unspecified) once the ALS phenotype is confirmed — it was the default before ICD-10 carried a specific ALS code and forfeits clinical specificity. Related motor neuron disease codes (**G12.22** progressive bulbar palsy; **G12.23** primary lateral sclerosis; **G12.25** progressive spinal muscular atrophy) describe distinct phenotypes and should not substitute for **G12.21** when ALS is confirmed. Because ALS progresses rapidly, comorbidity codes for respiratory, nutritional, mobility, and cognitive status must be updated at every encounter.[4]

Prevalence and Burden: The CDC National ALS Registry estimated approximately **33,000 people living with ALS** in the United States in 2022 (prevalence **~9.9 per 100,000**), projected to rise more than 10% to **over 36,000 by 2030** as the population ages; in the Medicare Advantage population specifically, 5-year period prevalence has been reported at **20.5 per 100,000**.[5,6] ALS incidence peaks between ages **55 and 75 years**, with a male-to-female ratio of approximately **1.2:1 to 1.5:1** for sporadic disease (1:1 for familial). The older population (>65 years) carries a disproportionate burden: in beneficiaries **≥65 years**, median time to diagnosis is **2.5 years for limb-onset** and **1.25 years for bulbar-onset**, and roughly **40% of Medicare ALS patients died within 1 year** of their first ALS diagnostic code or never saw a neurologist — with **25.5% dying within 6 months** — evidence of severe under-ascertainment in older adults.[1]

HCC/RAF V28 Mapping

ICD-10 CODE(S)	HCC CATEGORY (V28)	RAF (CNA)	DOCUMENTATION REQUIREMENT
G12.21 (ALS and Other Motor Neuron Disease/ Spinal Muscular Atrophy)	HCC 190— ALS and Other Motor Neuron Disease	1.175	Active **ALS**, current condition. State **"amyotrophic lateral sclerosis"** or **"ALS"** explicitly Document: El Escorial criteria or equivalent diagnostic criteria; UMN/LMN findings, onset type (bulbar vs. limb), rate of disease progression and affected body regions; update at **every** encounter.
G12.20 (motor neuron disease, unspecified)	HCC 190 — ALS and Other Motor Neuron Disease	1.175	AVOID: Motor neuron disease, **unspecified**. Document: Progressive motor dysfunction (weakness, atrophy, fasciculations); EMG/NCS results; UMN/ LMN exam signs; Rationale for undetermined subtype. Use **G12.21** once the ALS phenotype is documented
J96.12 (Chronic respiratory failure with hypercapnia)/ J96.11 (hypoxia)	HCC 213 — Cardio-Respiratory Failure and Shock	0.370	**Chronic respiratory failure** with **hypercapnia** (**J96.12**) or hypoxia (**J96.11**). Document **FVC % predicted**, MIP/SNIP, NIV use, underlying cause, ABG showing chronically elevated $PaCO^2$ with metabolic compensation (elevated bicarbonate indicating chronic state) or confirmed nocturnal hypoventilation
Z99.11 (Ventilator dependence)	HCC 211 — Respirator Dependence/ Tracheostomy Status	0.879	**Ventilator dependence** (NIV or invasive). Document type, hours/day of use, and date initiated — at **every** encounter once support begins
G31.09 (Other frontotemporal dementia) + F02.80 (Dementia in other diseases classified elsewhere, without behavioral disturbance)	HCC 127 — Dementia, Mild or Unspecified	0.341	**ALS-FTD** (frontotemporal dementia). Pair **G31.09** with **F02.80** for HCC credit; document **ECAS** or neuropsychological screening result

ICD-10 CODE(S)	HCC CATEGORY (V28)	RAF (CNA)	DOCUMENTATION REQUIREMENT
J69.0 (Aspiration pneumonia)	HCC 282 — Aspiration and Specified Bacterial Pneumonias	0.440	**Aspiration pneumonia** — high risk in bulbar-onset disease (in-hospital mortality **>10%**). Document aspiration events and swallow-evaluation results
Z51.5 (palliative care)/ R13.12 (oropharyngeal dysphagia)	No HCC	—	Encounter for **palliative care** (**Z51.5**) as a secondary code when palliative services are provided; **oropharyngeal dysphagia** (**R13.12**) supports medical necessity for PEG and speech therapy

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; CMS-HCC V28 = Centers for Medicare & Medicaid Services Hierarchical Condition Category Model V28; CNA = Community Non-Dual Eligible, Aged segment; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FTD = frontotemporal dementia; FVC = forced vital capacity; HCC = Hierarchical Condition Category; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; LMN = lower motor neuron; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; RAF = Risk Adjustment Factor; SNIP = sniff nasal inspiratory pressure; UMN = upper motor neuron. *Illustrative annual value at 2024 CMS-HCC base rate x CNA RAF coefficient — confirm payment year against current CMS tables.The impact of this condition varies across patient populations, particularly in individuals with disability, dual eligibility, or those receiving care in institutional settings

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

Risk-adjusted care resource allocation — MA base rate (~$10,402.34) × RAF coefficient for HCC 190 (ALS): 1.175 (CNA segment, CY2026)

ALS and Other Motor Neuron Disease/Spinal Muscular Atrophy

~$12.2K

HCC 190 · RAF 1.175 · per active patient/year

2 RECOGNITION AND DIAGNOSIS

Medicare Screenings and Surveillance (Adult and Geriatric)

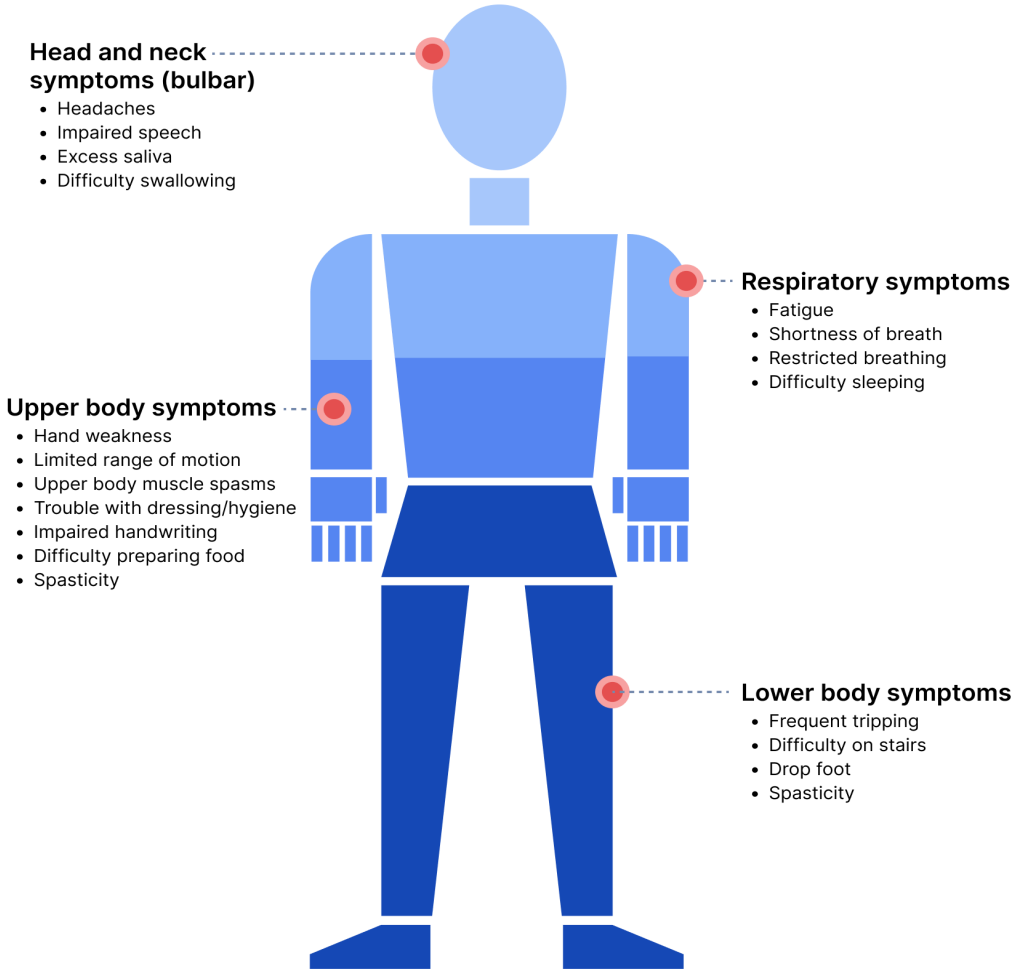
No population-level screening test exists for ALS. Unlike conditions with validated screening instruments (e.g., PHQ-9 for depression, LDCT for lung cancer), ALS has no biomarker, questionnaire, or imaging modality suitable for presymptomatic detection in the general population. The diagnosis remains clinical, based on recognition of concurrent upper and lower motor neuron signs with progressive spread across body regions. **The primary care imperative is therefore pattern recognition of early signs and symptoms** — particularly **asymmetric hand weakness, new fasciculations with progressive weakness, unexplained dysarthria or dysphagia**, and split-hand sign (preferential thenar > hypothenar wasting) — and prompt neurology referral when these features are identified.

Subtle Early Signs

SIGN/SYMPTOM[7,8]	CLINICAL SIGNIFICANCE
Painless, progressive, asymmetric limb weakness	The classic actionable trigger for ALS suspicion — **tripping, foot drop, hand clumsiness, or dropping objects that progresses and spreads**; warrants **same-encounter neurology referral**, not watchful waiting
Fasciculations with hyperreflexia or spasticity	**Combined LMN** (fasciculations, atrophy) **and UMN** (brisk reflexes, spasticity) signs in the same region are the **hallmark of ALS** — a pattern rarely produced by mimics
New dysarthria or dysphagia without structural cause	**Bulbar-onset** disease, more common in older adults; **slurred speech or swallowing difficulty without a structural lesion** should prompt neurologic evaluation, not empiric reflux or ENT-only workup
Unexplained weight loss with reduced oral intake	Early dysphagia and hypermetabolism drive malnutrition; **weight loss >5%** is a poor prognostic sign and a trigger for dietitian and PEG evaluation
Morning headache, unrefreshing sleep, orthopnea	Subtle signs of **nocturnal hypoventilation** from diaphragm weakness — often missed; check FVC/MIP rather than attributing to age or insomnia
Involuntary laughing or crying (pseudobulbar affect)	**Affects up to 50% of bulbar-phenotype patients** and is frequently misread as depression — emotional lability that does not match mood is a clue, not a psychiatric diagnosis
New disinhibition, apathy, or impaired judgment	Up to **50% develop cognitive/behavioral change** and ~15% develop ALS-FTD; screen with ECAS and assess decision-making capacity early
Recurrent aspiration or unexplained pneumonia	In a patient with **dysarthria or limb weakness, aspiration pneumonia** (in-hospital mortality **>10%**) may be the first recognized event — evaluate swallowing and motor function

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; ENT = ear, nose, and throat; FVC = forced vital capacity; LMN = lower motor neuron; MIP = maximum inspiratory pressure; PEG = percutaneous endoscopic gastrostomy; UMN = upper motor neuron

Anatomical Mapping of Symptoms



Geriatric Risk Factors

FACTOR	RISK SIGNAL	NOTES
Older age (peak 55-75y)	OR **1.44** (80-84 y) and OR **1.49** (85-90 y) vs. 66-69 y (US Medicare)	**Strongest demographic risk factor**; incidence continues rising through age 85-90 in Medicare data[1]
Male sex	Male:female ~**1.2-1.5:1** (sporadic); ratio narrows with age	**Familial ALS shows a 1:1 ratio**; alarm symptoms in women warrant the same workup[1]
Family history (familial ALS)	**5-10%** of cases; autosomal dominant	C9orf72 (**~2.2%**), SOD1 (**~2.1%**), TARDBP (**~1.7%**), FUS (**~1.7%**) are most common; document for genetic counseling and **tofersen** eligibility[8]

FACTOR	RISK SIGNAL	NOTES
Heavy metal (lead) exposure	OR **1.79-2.31**	Cumulative lifetime occupational exposure is relevant in older adults — document work history[9]
Pesticide exposure	OR **1.46-1.96**	Consistent across multiple meta-analyses[9]
Head trauma	OR **1.26-1.37**	Repeated trauma may carry higher risk[9]
Type 2 diabetes	OR **0.83** (protective)	**Paradoxically protective**; antidiabetic use OR ~0.52 — notable given high DM prevalence in Medicare[10]
Higher BMI (obesity)	OR **0.60** for incidence (protective)	Higher premorbid BMI is protective for incidence, but **low BMI at diagnosis is a poor prognostic sign**[10]
Specific military exposures (herbicides, pesticides, exhaust, radar, explosions)	ORs ranging from 1.50 to 7.75 depending on exposure type	Agent Orange exposure, burn pits, heavy metals, and high-intensity radar waves each independently associated with elevated ALS risk

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; BMI = body mass index; DM = diabetes mellitus; OR = odds ratio; VA = US Department of Veterans Affairs

Diagnostic Thresholds

Diagnosis of ALS is made **based on a combination** of **clinical findings** and results of **electrophysiological and neuroimaging tests**.

The diagnostic criteria for ALS requires **evidence of both upper and lower motor neuron involvement**, such as spasticity and overactive reflexes, as well as muscle weakness, fasciculations, and atrophy, respectively. These signs need to be present in different body regions, including the arms, trunk, legs, and bulbar muscles. Finally, ALS diagnosis **requires ruling out other conditions that may mimic its symptoms, such as myasthenia gravis, spinal cord lesions (e.g., tumors, herniated discs), and other neurodegenerative or autoimmune diseases.**

While there are no definitive tests for ALS, diagnostic tests may be performed to assist the diagnosis, such as laboratory testing to measure levels of creatinine kinase (CK). CK will typically be increased in ALS due to muscle wasting and atrophy. Nerve conduction studies (NCS) and needle electromyography (EMG) may be ordered to assess the function of muscles and nerve cells. Nerve conduction will typically be slowed on NCS in those with ALS, demonstrating nerve damage. On EMG, ALS typically presents with fibrillations and positive sharp waves, which reflect the characteristic spontaneous depolarization of denervated muscle fibers at rest.

TEST/SYSTEM	DIAGNOSTIC CRITERION	NOTES
Gold Coast Criteria (2020)[11]	**Binary (ALS vs. not ALS):** **(1)** progressive motor impairment by history/repeated assessment **(2)** UMN + LMN dysfunction in ≥1 region, or LMN in ≥2 regions **(3)** exclusion of mimics	Simplifies the older tiered categories and enables earlier diagnosis; lower specificity requires vigilance in older adults with comorbidities that mimic ALS
Revised El Escorial/ Awaji criteria[12]	Tiered (possible/probable/definite); specificity **~94%** at probable+ level; Awaji sensitivity **~90%** for bulbar onset	Most specific but a minority meet "definite" at diagnosis; poor inter-rater reliability prompted the shift toward Gold Coast
Needle EMG + NCS[1]	**EMG confirms LMN** involvement; **NCS excludes multifocal motor neuropathy** (conduction block), CIDP, compressive neuropathy	**Mainstay of confirmatory testing**; combine with brain/ cervical-spine MRI to exclude structural lesions
Serum/CSF neurofilament light (NfL)[13]	**Elevated in ALS**; correlates with progression; used as a trial surrogate (basis for **tofersen** accelerated approval)	**Not yet validated for routine diagnosis**; an emerging biomarker
Genetic testing (SOD[1]**, C9orf72)**[14]	Pathogenic SOD1 variant present in **~2%** of all ALS — defines tofersen eligibility	Document results in the chart; familial and sporadic ALS share code **G12.21**
ALSFRS-R functional rating[15]	12-item scale, range **0 (no function) to 48 (full function)**; rate of decline (deltaFS) categorizes progression speed	Gold-standard progression monitor and primary trial endpoint; informally tracked at PCP visits, formally at ALS clinic
King's College staging[15]	Stages 1-4B by regions involved and need for gastrostomy (4A) or NIV (4B)	More sensitive early in disease; bulbar-onset patients typically reach 4A before 4B
Brain + cervical-spine MRI[1,8]	**MRI is used primarily to exclude structural mimics of ALS** — not to confirm the diagnosis. Brain MRI without contrast excludes tumors, demyelinating disease (multiple sclerosis), and stroke in patients with bulbar symptoms; cervical-spine MRI excludes cervical spondylotic myelopathy, central disc herniation, and cord compression in patients with hand or upper limb weakness	Imaging the spinal cord by MRI is described as "essential" to rule out more common differential diagnoses

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; CIDP = chronic inflammatory demyelinating polyneuropathy; CSF = cerebrospinal fluid; deltaFS = rate of ALSFRS-R decline; EMG = electromyography; LMN = lower motor neuron; MRI = magnetic resonance imaging; NCS = nerve conduction studies; NfL = neurofilament light chain; NIV = non-invasive ventilation; UMN = upper motor neuron

Other Core Testing

The following table provides the most comprehensive listing of laboratory tests used in the ALS diagnostic workup to **exclude metabolic, autoimmune, infectious, and other mimic conditions.**

TEST	MIMIC EXCLUDED	EXPECTED FINDING IN ALS
CBC with differential, CMP (including calcium, phosphate, liver enzymes)	Systemic illness, malignancy, hypocalcemia, hypercalcemia, hypophosphatemia, hepatic myelopathy	Normal
Thyroid function tests (± PTH if calcium elevated)	Hyperthyroid myopathy, thyroid-related fasciculations, hyperparathyroidism	Normal
Creatine phosphokinase (CK)	Myopathies	Normal or mildly to moderately elevated (consistent with denervation)
ESR or hs-CRP	Infectious/inflammatory causes, vasculitis	Normal
ANA and rheumatoid factor	Autoimmune disease, vasculitis	Normal
Vitamin B12, syphilis serology, copper level	Myelopathy, subacute combined degeneration, copper deficiency myelopathy	Normal
Anti-GM1 antibody	Multifocal motor neuropathy (MMN)	Normal
Serum protein electrophoresis with immunofixation (SPEP/IFE)	Paraproteinemia, hematologic malignancy–related polyradiculoneuropathy	Normal
Acetylcholine receptor antibodies, MuSK antibodies, voltage-gated calcium channel antibodies	Myasthenia gravis, Lambert-Eaton myasthenic syndrome	Normal
HIV	HIV-related motor neuronopathy	Normal
HTLV-1/2	HTLV-associated ALS-like syndrome (tropical spastic paraparesis)	Normal
Lyme disease serology	Neuroborreliosis (Bannwarth syndrome)	Normal
West Nile virus	Poliomyelitis-like syndrome	Normal

TEST	MIMIC EXCLUDED	EXPECTED FINDING IN ALS
Heavy metal panel (lead, arsenic, mercury)	Lead/arsenic poisoning neuropathy	Normal
Celiac testing (anti-tTG, anti-endomysial)	Celiac-associated neuropathy	Normal
Paraneoplastic panel (anti-Hu, Yo, Ri, Ma2/Ta, CV2/CRMP5, amphiphysin)	Paraneoplastic motor neuron syndrome	Normal
Hexosaminidase A/B	Late-onset Tay-Sachs disease	Normal
Very-long-chain fatty acids (VLCFA)	Adrenomyeloneuropathy/ adrenoleukodystrophy	Normal
Kennedy disease genetic testing (AR CAG repeat)	Kennedy disease (X-linked spinal and bulbar muscular atrophy) — in males	Normal
ENA, ANCA, ACE, folate, vitamin B6, anti-MAG antibodies	Vasculitis, sarcoidosis, metabolic neuropathy	Normal
Lumbar puncture/CSF analysis	Infectious, inflammatory, or malignant causes	Normal
Neurofilament light chain (NfL) — blood or CSF (emerging)	ALS mimics (sensitivity 0.81–0.87); also prognostic (pooled HR 2.8–4.3)	**Elevated in ALS**; not yet standard clinical practice

ABBREVIATIONS: ACE = angiotensin-converting enzyme; ALS = amyotrophic lateral sclerosis; ANA = antinuclear antibody; ANCA = anti-neutrophil cytoplasmic antibody; AR = androgen receptor; CAG = cytosine-adenine-guanine (trinucleotide repeat); CBC = complete blood count; CK = creatine phosphokinase; CMP = comprehensive metabolic panel; CRMP5 = collapsin response mediator protein 5; CSF = cerebrospinal fluid; CV2 = crossveinless-2; ENA = extractable nuclear antigen; ESR = erythrocyte sedimentation rate; HIV = human immunodeficiency virus; HR = hazard ratio; hs-CRP = high-sensitivity C-reactive protein; HTLV = human T-lymphotropic virus; IFE = immunofixation electrophoresis; MAG = myelin-associated glycoprotein; MMN = multifocal motor neuropathy; MuSK = muscle-specific kinase; NfL = neurofilament light chain; PTH = parathyroid hormone; SPEP = serum protein electrophoresis; tTG = tissue transglutaminase; VLCFA = very-long-chain fatty acids

Diagnostic Pathway

DIAGNOSIS OF ALS → **MIMIC DISORDERS EXCLUDED**

CLINICAL (GOLD COAST CRITERIA)

- Previously normal function
- Progressive MOTOR weakness on repeat clinical examination/history

At least:

- UMN AND LMN involvement in 1 region
- LMN involvement in 2 regions
- Mimics excluded (see related flow diagram)

SUPPORTIVE INVESTIGATIONS

Lower motor neuron

1. **EMG**
   - Fibrillations and positive sharp waves
   - Complex fasciculation potentials
2. **Muscle imaging**
   - Fasciculations on ultrasound

Upper motor neuron

1. **NCS**
   - H reflex in muscles that do not have H reflex at rest e.g. tibialis anterior, extensor carpi radialis, abductor pollicis brevis
2. **TMS**
   - Reduced short interval intracortical inhibition
   - Reduced cortical silent period duration
   - Increased central motor conduction time
3. **Imaging**
   - MRI with FLAIR - increased corticospinal tract and corpus callosum intensities
   - Diffusion Tensor Imaging - cortical and subcortical atrophy
   - PET scan - quantifying brain metabolism and glial activation

Mimic disorders	Key findings
Immune-mediated neuropathies: Multifocal motor neuropathy Motor predominant CIDP	Clinically pure LMN; NCS: evidence of conduction block, demyelinating features; CSF: albumin-cytological dissociation in CIDP; Improvement with immunotherapy i.e. IVIG
Genetic neuropathies: Charcot-Marie-Tooth disease	Clinically pure LMN; NCS shows sensorimotor neuropathy; Genetic testing
Muscle disease: Inclusion body myositis	Clinically quadriceps and finger flexor weakness; EMG: myopathic units, early recruitment pattern; Raised serum CK; Muscle biopsy: rimmed vacuoles
Neuromuscular disorders: Myasthenia gravis	Clinically fatiguable weakness including ocular symptoms of diplopia; Decremental responses on RNS; Jitter analysis: abnormal and block; Improvement with immunotherapy i.e. IVIG, steroids
Degenerative LMN: Spinal muscular atrophy Spinobulbar muscular atrophy	Clinically LMN, perioral fasciculations in SBMA; NCS: sensory neuropathy in SBMA; Genetic testing for both
Spinal: Cervical myelopathy HIV/HTLV-1/syphilis	Clinically UMN-predominant; MRI spine abnormal; CSF shows infective changes in HIV/HTLV-1
Others: Cramp-fasciculation syndrome Peripheral nerve hyperexcitability e.g. neuromyotonia	Clinically pure LMN; NCS: myokymia, irregularly occurring doublet, or multiplet CMAPs; Serology: Antibodies Caspr2/LG1

Staging: Prognosis/Trajectory

ALS does not follow a predictable linear trajectory — disease progression varies substantially between individuals, making precise staging difficult. As the disease advances, muscle weakness and atrophy spread progressively, leading to dysarthria (difficulty speaking), dysphagia (difficulty swallowing), and dyspnea (respiratory compromise).[1,7,8,15]

Because of this variability, many clinicians frame ALS progression in three to four broad stages rather than rigid timelines:

- **Early stage** — **Focal**, often **asymmetric weakness** (typically hands or feet); patients remain largely independent; diagnosis is frequently still being established during this phase
- **Middle stage** — **Weakness spreads** to additional body regions; mobility becomes increasingly impaired; speech and swallowing difficulties emerge; assistive devices and therapy modifications become necessary
- **Late stage** — **Severe generalized weakness**; dependence on **non-invasive ventilation** (NIV); **PEG** tube placement often required for nutrition; communication may require augmentative devices
- **Final stage** — **Near-total paralysis**; **ventilator dependence** (invasive or non-invasive); focus shifts to comfort care, goals-of-care discussions, and hospice referral
- **Median survival from symptom onset is 2–5 years**, though approximately 10% of patients survive beyond 10 years. **Bulbar-onset ALS tends to progress more rapidly** than limb-onset disease, and younger age at onset is generally associated with longer survival[1,16]

STAGE	DESCRIPTION	AVERAGE DURATION
Early Stage	Mild muscle weakness and atrophy, difficulty speaking, swallowing, or walking, maintained independence in daily activities	0–2 years from onset
Middle Stage	Increased muscle weakness and atrophy, increased difficulty in mobility and daily activities, possible need for assistive devices for mobility or communication	2–4 years from onset
Late Stage	Severe muscle weakness and atrophy, dependency in most daily activities, possible respiratory insufficiency	4–6 years from onset
End Stage	Near-total paralysis, significant respiratory compromise, high dependency for care	5+ years from onset

Two complementary staging systems have been developed for ALS — the King's College staging system and the Milano-Torino Staging (MiToS) system — each capturing different dimensions of disease progression. Both can be derived from the ALSFRS-R scale, and neither is yet in widespread clinical use, though both are increasingly applied in clinical trials.

King's College Staging System

The King's system is based on the anatomical spread of motor involvement across body regions (bulbar, upper limbs, lower limbs) and the need for nutritional/respiratory support.[17]

STAGE	DEFINITION	STANDARDIZED DISEASE COURSE TIMING
1	Symptom onset — 1 body region involved	0% (onset)

STAGE	DEFINITION	STANDARDIZED DISEASE COURSE TIMING
2A	Diagnosis established	~35% through disease course
2B	2 body regions involved	~38% through disease course
3	3 body regions involved	~61% through disease course
4A	Needs gastrostomy (nutritional failure)	~77% through disease course
4B	Needs non-invasive ventilation (respiratory failure)	~80% through disease course
5	Death	100%

Milano-Torino Staging (MiToS) System

MiToS is a functional milestone-based system that tracks the cumulative loss of independence across four domains: walking/self-care, swallowing, communication, and breathing.[18]

STAGE	DEFINITION
0	Functional involvement present but no loss of independence in any domain
1	Loss of independence in 1 domain
2	Loss of independence in 2 domains
3	Loss of independence in 3 domains
4	Loss of independence in all 4 domains
5	Death

The systems are complementary rather than competing:

- **King's is more sensitive early in the disease course** — it captures regional spread before functional independence is lost, making it better for staging patients at diagnosis and in early disease
- **MiToS is more sensitive late** — it captures progressive functional dependence with greater resolution in advanced disease, where King's stages tend to compress (most late patients cluster in stage 4)
- Both show a progressive increase in mortality risk with each stage, and patients generally progress sequentially without skipping stages
- **Neither system is currently in routine clinical practice, but both are considered valid tools for clinical trial design, prognostication, and resource planning**

Clues to Dig Deeper

CLINICAL CLUE[3,8]	WHY IT MATTERS	NEXT DIAGNOSTIC STEP
Asymmetric, painless weakness with fasciculations	**Combined UMN + LMN signs** are the ALS hallmark; diagnosis is delayed **~1 year** on average, costing the therapy and ACP window	**Same-encounter** neurology/ALS-clinic referral; needle EMG/NCS; brain + cervical-spine MRI
New dysarthria or dysphagia without structural cause in patient ≥65	Bulbar-onset is more common and faster-progressing in older adults; mimics include stroke and Parkinson disease	**Neurology referral**; **speech/swallow evaluation**; do not stop at ENT or empiric reflux therapy
Morning headache or orthopnea with normal pulse oximetry	Suggests early **nocturnal hypoventilation** from diaphragm weakness — oximetry by day can be normal	**FVC**, MIP/SNIP, and **nocturnal oximetry**/ transcutaneous CO2; pulmonology referral if abnormal
Disinhibition, apathy, or impaired judgment	Up to **50%** have cognitive/behavioral change and **~15% develop ALS-FTD** — affects capacity and caregiver burden	**ECAS** or neuropsychological screen; assess decision-making capacity and engage surrogate early
Family history of ALS or early-onset dementia	**Familial ALS (~5-10%)** and C9orf72 expansions carry treatment and counseling implications	**Genetic counseling**; SOD1/C9orf72 testing; document results for tofersen eligibility
Recurrent aspiration or unexplained weight loss	Early bulbar dysfunction drives aspiration (in-hospital mortality **>10%**) and malnutrition	**Swallow evaluation**; **dietitian** referral; consider PEG while **FVC >50%**

ABBREVIATIONS: ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; CO2 = carbon dioxide; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; EMG = electromyography; ENT = ear, nose, and throat; FVC = forced vital capacity; LMN = lower motor neuron; MIP = maximum inspiratory pressure; MRI = magnetic resonance imaging; NCS = nerve conduction studies; PEG = percutaneous endoscopic gastrostomy; SNIP = sniff nasal inspiratory pressure; UMN = upper motor neuron

Common Oversights

OVERSIGHT/ SHORTCUT[8,19,20]	WHY IT MATTERS — WHAT TO DO INSTEAD
Treating diagnosis as "wait-and-see" until spread is definitive	Diagnostic delay averages **~1 year** and forfeits the window for disease-modifying therapy and capacity-intact ACP. Refer to a multidisciplinary ALS clinic or neurologist at **first suspicion**

OVERSIGHT/ SHORTCUT[8,19,20]	WHY IT MATTERS — WHAT TO DO INSTEAD
Attributing dysarthria/ dysphagia to age, reflux, or stroke alone	Bulbar-onset ALS is more common in older adults; misdiagnosis occurs in **30-40%** of cases. Pursue neurologic evaluation when no structural cause is found
Assuming cognition is intact	Up to **50%** of people with ALS have cognitive/behavioral change and **~15% develop ALS-FTD**. Screen with ECAS at diagnosis and every 6 months, and assess capacity before it is lost
Waiting for FVC <50% before discussing NIV	The traditional Medicare **FVC <50%** threshold is widely recognized as too restrictive; evidence supports NIV at **FVC <80% with symptoms**. MA plans have flexibility to authorize earlier
Reading pseudobulbar affect as depression	Involuntary laughing/crying that does not match mood is pseudobulbar affect (up to 50% of bulbar phenotype) — treatable with dextromethorphan/quinidine, distinct from a mood disorder
Letting comorbidity codes lag behind disease	ALS progresses fast — a note from 3 months ago may understate current burden. Update respiratory (**J96.12**), ventilator (**Z99.11**), malnutrition (**E43**), and cognitive (**G31.09 + F02.80**) status at every visit
Delegating advance care planning to specialists	ACP is a primary-care deliverable, billable (99497/99498), and significantly under-used in ALS. Initiate and document at every encounter — do not wait for the ALS clinic

ABBREVIATIONS: ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; MA = Medicare Advantage; NIV = non-invasive ventilation

Key Differentials in Elderly

PRESENTATION[1,3,8,16,20]	DIFFERENTIAL	KEY TESTS
Progressive asymmetric limb weakness, patient ≥65	ALS **vs** cervical spondylotic myelopathy; multifocal motor neuropathy (MMN); inclusion body myositis; peripheral neuropathy	Needle **EMG/NCS**; **cervical-spine MRI**; **anti-GM1 antibodies** if MMN suspected
New dysarthria/ dysphagia	Bulbar-onset ALS **vs** brainstem stroke; myasthenia gravis; Parkinson disease; structural/oropharyngeal lesion	**Brain MRI**; **acetylcholine-receptor antibodies**; **speech/swallow evaluation**; neurology referral

PRESENTATION[1,3,8,16,20]	DIFFERENTIAL	KEY TESTS
UMN-predominant spasticity/hyperreflexia	Primary lateral sclerosis **vs** hereditary spastic paraplegia; cervical myelopathy; multiple sclerosis	**Brain/cervical MRI**; consider genetic testing; longitudinal **EMG** to detect emerging LMN signs
LMN-predominant atrophy/weakness	Progressive muscular atrophy **vs** multifocal motor neuropathy; spinal muscular atrophy; radiculopathy	**EMG/NCS** with conduction-block studies; consider SMN gene testing; spine imaging
Fatigable weakness, ptosis, diplopia	Myasthenia gravis (key treatable mimic) **vs** ALS with bulbar involvement	**Acetylcholine-receptor and MuSK antibodies**; repetitive nerve stimulation; edrophonium/ice-pack testing
Cognitive/behavioral change with motor signs	ALS-FTD **vs** Alzheimer disease; other dementias; depression	**ECAS** or neuropsychological testing; brain **MRI**; C9orf72 testing if familial

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; EMG = electromyography; GM1 = ganglioside monosialic acid 1; LMN = lower motor neuron; MMN = multifocal motor neuropathy; MRI = magnetic resonance imaging; MuSK = muscle-specific kinase; NCS = nerve conduction studies; SMN = survival motor neuron; UMN = upper motor neuron

Comorbidity Screening

CONDITION	PREVALENCE/ASSOCIATION	SCREENING APPROACH
Respiratory insufficiency (J96.x)[22]	**Respiratory failure is the cause of death in up to 95% of ALS patients**; nocturnal hypoventilation often precedes daytime symptoms	**FVC**, MIP/SNIP every 3–6 months; **nocturnal oximetry/transcutaneous CO_2**; NIV initiation at FVC ≤80% or symptomatic hypoventilation; supine FVC may detect diaphragm weakness earlier than erect FVC
Dysphagia and malnutrition (R13.x, E46)[23]	Weight loss is multifactorial (**dysphagia, hypermetabolism, muscle wasting**); >50% are hypermetabolic; weight loss >5% is a poor prognostic sign	Serial weight at every visit; **SLP swallow evaluation at diagnosis** and with any new symptom; dietitian referral; consider PEG while FVC >50%; high-calorie supplementation (25–30 kcal/kg/day)
Cognitive/behavioral impairment and FTD (F02.80, G31.09)[3,8]	**35–50% develop cognitive or behavioral changes**; ~15% meet criteria for frontotemporal dementia (ALS-FTD); associated with C9orf72 mutations and bulbar onset	**ECAS or neuropsychological screen** at diagnosis and periodically; assess decision-making capacity early; engage surrogate and advance care planning before capacity declines

CONDITION	PREVALENCE/ASSOCIATION	SCREENING APPROACH
Depression (F32.x, F33.x)[24]	Pooled prevalence ~34% (range 23–50%); adjusted HR 9.1 vs. non-ALS controls; **associated with reduced quality of life and poorer survival**	**PHQ-9** at every visit; **SSRI first-line** (avoid TCAs due to anticholinergic burden); coordinate with multidisciplinary team; distinguish from pseudobulbar affect
Pseudobulbar affect (F48.2)[25]	**20–50% of ALS patients**; prevalence ~38.5% in meta-analysis; more common with bulbar UMN involvement	**CNS-Lability Scale**; **distinguish from depression** (involuntary emotional episodes incongruent with mood); dextromethorphan/quinidine (Nuedexta) FDA-approved for PBA
Pain (G89.x, M79.x)[26]	Pooled prevalence ~60%; **most common in upper limbs/ shoulders**; moderate-severe in majority; increases in later disease stages	**Pain assessment at every visit** (VAS or Brief Pain Inventory); identify type (cramp, nociceptive, neuropathic, spasticity-related); NSAIDs, gabapentin, or opioids as appropriate; PT/positioning
Sleep disorders (G47.x)[27]	**50–63% have poor sleep quality** (PSQI >5); pooled prevalence of poor sleepers 56.7%; driven by respiratory insufficiency, pain, cramps, anxiety, and immobility	PSQI screening; nocturnal oximetry; **NIV optimization improves sleep quality**; address contributing factors (pain, anxiety, cramps, positioning); avoid sedative-hypnotics that suppress respiratory drive
Sialorrhea (K11.7)[1,25]	**Up to 50% of patients; distressing, increases aspiration risk**; driven by impaired swallowing rather than excess production	**Anticholinergics first-line** (glycopyrrolate, scopolamine patch, sublingual atropine); botulinum toxin to salivary glands if refractory; salivary gland radiation as third-line; portable suction device
Venous thromboembolism (I82.x, I26.x)[28]	**1-year VTE incidence 11.2%** (prospective data); aHR 2.7 vs. controls; leg-onset ALS with significant weakness: 35.5% 1-year incidence	Clinical vigilance for DVT/PE symptoms; lower threshold for duplex ultrasound in patients with leg weakness and swelling; no current guideline for routine prophylaxis, but awareness is critical
Constipation (K59.0)[29]	Common due to immobility, reduced fluid/fiber intake, and medication effects (anticholinergics, opioids)	**Increase fluid and fiber intake**; osmotic or stimulant laxative; adjust enteral nutrition formula; increase physical activity as tolerated
Frailty/sarcopenia (M62.84)[30]	**Progressive muscle wasting is intrinsic to ALS**; lower BMI at diagnosis is a poor prognostic sign; sarcopenia accelerates functional decline	Serial weight, BMI, and grip strength; ALSFRS-R at every visit; high-protein diet (1.2–1.5 g/kg/day); early PT/OT referral; frailty assessment guides treatment intensity and goals of care

CONDITION	PREVALENCE/ASSOCIATION	SCREENING APPROACH
Cardiovascular disease (I25.x, I50.x)[31]	**Coronary heart disease associated with faster ALS progression**; hypertension may negatively affect disease course	**Baseline CVD risk assessment**; manage modifiable risk factors; coronary heart disease coexistence may accelerate respiratory involvement

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALS-FTD = amyotrophic lateral sclerosis-frontotemporal dementia; CNS = central nervous system; CO_2 = carbon dioxide; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FTD = frontotemporal dementia; FVC = forced vital capacity; HR = hazard ratio; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; NSAID = nonsteroidal anti-inflammatory drug; PBA = pseudobulbar affect; PEG = percutaneous endoscopic gastrostomy; PHQ-9 = Patient Health Questionnaire 9-item; PT = physical therapy; SLP = speech-language pathology; SNIP = sniff nasal inspiratory pressure; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; UMN = upper motor neuron; VAS = visual analog scale
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CNS-Lability Scale

The CNS-Lability Scale is a 7-item self-report questionnaire scored on a 5-point Likert scale (1 = "Applies Never" to 5 = "Applies Most of the Time"), with a total score range of 7–35. The 7 items assess the frequency of involuntary emotional episodes across two domains — pathological laughing and pathological crying.

Labile Laughter subscale (4 items):

- Episodes of laughing for no apparent reason
- Laughing that is difficult to control once it starts
- Laughing that is exaggerated or inappropriate to the situation
- Laughing that occurs suddenly without warning

Labile Crying/Tearfulness subscale (3 items):

- Episodes of tearfulness or crying for no apparent reason
- Crying that is difficult to control once it starts
- Crying that is exaggerated or inappropriate to the situation

SCORE RANGE	INTERPRETATION	CLINICAL ACTION
7–12	Below threshold; PBA unlikely	No specific PBA treatment indicated; reassess if new emotional lability develops
≥13	Screening-positive for PBA in ALS (sensitivity 0.84, specificity 0.81)	Confirm episodes are involuntary, sudden, and mood-incongruent; consider dextromethorphan/quinidine
≥17	Alternative cutoff validated in MS (sensitivity 0.94, specificity 0.83)	Used in MS populations; correctly diagnosed PBA 89% of the time without comorbid depression

SCORE RANGE	INTERPRETATION	CLINICAL ACTION
≥21	Stringent threshold used in some studies	Greater specificity for severe PBA; used in research settings
Higher scores	Greater emotional lability	Correlates with bulbar dysfunction, UMN burden, cognitive impairment, and lower quality of life

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; MS = multiple sclerosis; PBA = pseudobulbar affect; UMN = upper motor neuron

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE[32]

- **Acute respiratory failure** — new dyspnea at rest, accessory-muscle use, **oxygen saturation <90%**, altered mental status, or acute hypercapnia (PCO2 >65 mmHg) Respiratory failure is the cause of death in **up to 95%** of people with ALS and may be triggered by aspiration, pneumonia, or mucus plugging
- **Aspiration pneumonia with respiratory distress** — fever, productive cough, hypoxia in a patient with known dysphagia (in-hospital mortality **>10%**)
- **Acute airway obstruction** — inability to clear secretions, stridor, or a choking episode unresponsive to cough assist
- **Activate emergency department transfer and emergent airway management**

⚠ RED FLAG — URGENT (24-72RS)[3,8,20,22]

- **Rapid FVC decline** (>10% drop between visits or FVC approaching **50%**) — accelerating respiratory-muscle weakness; **expedite pulmonology referral for NIV initiation** (median survival after diaphragmatic weakness is **~6 months**)
- **Acute dysphagia with inability to maintain oral intake** — risk of dehydration and aspiration; urgent speech-therapy and gastroenterology referral for PEG (place before **FVC <50%** to reduce procedural risk)
- **New cognitive/behavioral change suggesting ALS-FTD** — disinhibition, apathy, or loss of decision-making capacity; urgent neuropsychological evaluation to address advance-directive capacity
- **Progressive weight loss >5% over 1 month** — expedited dietitian evaluation and PEG consideration
- **Caregiver crisis or unsafe home environment** — expedited social work and palliative care to prevent premature institutionalization

3 MEAT DOCUMENTATION ESSENTIALS

ALS documentation translates a rapidly evolving clinical picture into a record that supports continuity, care coordination, and accurate representation of clinical complexity. Because ALS progresses fast, a note from three months ago may significantly understate the current disease burden. The most common gaps are coding **G12.20** when the **ALS** phenotype is confirmed, failing to update respiratory, nutritional, mobility, and cognitive status at each encounter, missing **ALS-FTD** because cognition was assumed intact, and delegating advance care planning to specialists. Each gap obscures the person's real clinical picture and impedes shared decision-making with the multidisciplinary team.

Case: 72M, Medicare Advantage, Army veteran (6 yrs). PMH: HTN, T2DM, 30 pack-year smoking (quit 10 yrs ago). Presents with 8 months progressive R hand weakness/clumsiness → R forearm, bilateral calf fasciculations, 12-lb weight loss over 4 months. Wife reports impulsivity and inappropriate laughter. Exam: R hand intrinsic atrophy with fasciculations, hyperreflexia in all extremities (including atrophic muscles), bilateral positive Hoffmann sign, tongue fasciculations

MONITOR: "Weight 168 lbs (↓12 lbs/4 mo; >5% loss — poor prognostic sign), BMI 24.1. ALSFRS-R 38/48 (deltaFS 1.25 pts/mo — intermediate progressor). FVC 72% erect, 58% supine — significant diaphragm weakness with symptomatic nocturnal hypoventilation; MIP −42 cmH_2O, SNIP 38 cmH_2O (both below threshold). **PHQ-9:** 8 (mild depression). **CNS-Lability Scale:** 14 (pseudobulbar affect). **ECAS:** executive dysfunction <5th percentile, verbal fluency impaired. Pain VAS 4/10, bilateral shoulder cramping. Caloric intake ~1,400 kcal/day (target 1,900–2,300 kcal/day). **Caregiver:** wife — increasing burden and sleep disruption."

EVALUATE: **'**EMG/NCS confirms active/chronic denervation in 3 regions (cervical, thoracic, lumbosacral) with fasciculations in all regions and normal sensory conduction. Brain MRI shows no structural lesion; C-spine MRI shows mild spondylosis without cord compression. Anti-GM1 negative, CK 380 U/L (mildly elevated). Gold Coast Criteria met. ECAS demonstrates executive dysfunction (letter fluency 12, <5th percentile) with intact language/memory; spouse confirms disinhibition and apathy, consistent with ALSci/ALSbi (not full ALS-FTD). Genetics: SOD1 negative, C9orf72 pending. Swallow evaluation shows mild oropharyngeal dysphagia with thin-liquid penetration on VFSS, no aspiration — nectar-thick liquids recommended.'

ASSESS: 'Amyotrophic lateral sclerosis (**G12.21**), King's stage 3, intermediate progressor (deltaFS 1.25/mo). Respiratory insufficiency with diaphragm weakness (**J96.10**) — symptomatic nocturnal hypoventilation. Oropharyngeal dysphagia (**R13.12**) with weight loss >5% (**R63.4**) and malnutrition risk (**E46**). ALS-associated cognitive impairment with executive dysfunction (**R41.840**) and behavioral changes — capacity intact but declining trajectory. Pseudobulbar affect (**F48.2**), CNS-Lability Scale 14, distinct from depression. Mild depression (**F32.0**), PHQ-9 = 8. Bilateral shoulder cramping (**M79.621**, **M79.622**). Former tobacco use in remission (**Z87.891**), HTN (I10), T2DM (**E11.9**). Military service documented — VA service-connected ALS eligibility to be explored.'

TREAT: 'Multidisciplinary ALS clinic referral placed. Riluzole 50 mg BID started; LFTs at baseline, monthly × 3, then periodically; counseled on modest survival benefit and hepatotoxicity risk. Edaravone IV deferred pending ALS clinic eval and insurance auth. Tofersen not indicated (SOD1 neg); C9orf72 result pending. NIV initiated at home(FVC 58% supine with symptoms); bilevel PAP titrated; nocturnal oximetry/$TcCO_2$ ordered; MI-E prescribed; pulmonology q3mo with serial FVC/MIP/SNIP. Dietitian referral for high-calorie, high-protein diet (25–30 kcal/kg/day) with oral supplements. PEG discussion initiated — recommend placement while FVC >50%; GI referral placed. Nectar-thick liquids per SLP; serial swallow evals planned. Dextromethorphan/quinidine 20/10 mg BID for PBA (QTc normal). Sertraline 25 mg daily for depression; Na^+ at 2 wks. Gabapentin 100 mg TID (eGFR 62) for cramping. Baclofen 5 mg TID for spasticity; titrate slowly. ACP (CPT 99497) completed —

HCP designated (wife); DNI elected; POLST completed. Social work referral for caregiver support; connected to ALS Association. VA benefits eligibility being explored. PT/OT for adaptive equipment and home safety; AAC device eval planned. Follow-up: PCP q1–3 mo; ALS clinic q3 mo; pulmonology q3 mo; serial ALSFRS-R, FVC, weight, PHQ-9, ECAS each visit.'

Clinical Documentation Elements

- Document **"amyotrophic lateral sclerosis"** or **"ALS"** explicitly and assign **G12.21** — not "motor neuron disease" (**G12.20**) — once the phenotype is confirmed. Record UMN/LMN findings, onset type (bulbar vs. limb), and progression rate
- **Update respiratory status at every encounter: FVC % predicted**, MIP/SNIP, NIV use, and nocturnal-hypoventilation symptoms — chronic respiratory failure maps to HCC 213 (**J96.11/J96.12**)
- **Update nutritional status:** weight trend (% loss), BMI, swallow-evaluation results, and PEG status — **weight loss >5%** triggers urgent dietitian and PEG evaluation
- Document ventilator dependence (**Z99.11** → HCC 211) once NIV or invasive ventilation begins, including type and hours/day of use
- **Screen cognition/behavior: ECAS** at diagnosis and every 6 months; document ALS-FTD when present (**G31.09 + F02.80** → HCC 127) and assess decision-making capacity
- **Record genetic testing results:** SOD1, C9orf72, FUS, TARDBP — familial and sporadic ALS share **G12.21**, and SOD1 status determines **tofersen** eligibility
- Document the **ALSFRS-R** score and rate of decline (deltaFS) when available, plus King's or MiToS stage, to convey current functional burden
- **Document advance care planning at every encounter** (NIV, PEG, tracheostomy, hospice, DNR/Z66) — a primary-care deliverable, billable via CPT 99497/99498

Reframing Common Documentation Shortcuts

INSTEAD OF...	DOCUMENT...
'Motor neuron disease'	'**Amyotrophic lateral sclerosis (ALS)**, bulbar-onset, mixed UMN/LMN signs across bulbar and cervical regions (**G12.21**); diagnosed by Gold Coast criteria' — use **G12.20** only when the phenotype is truly unspecified
'Weakness, monitoring'	'ALS (**G12.21**) — right-hand intrinsic atrophy and tongue fasciculations; ALSFRS-R 38; deltaFS ~0.8/month'
'Breathing OK on room air'	'FVC 78% predicted with orthopnea and morning headache; nocturnal hypoventilation suspected — pulmonology referral for NIV discussion'
'On a ventilator'	'Ventilator dependence (**Z99.11** → HCC 211): nocturnal NIV ~8 h/night, initiated 2026-04; tolerating full-face mask'

INSTEAD OF...	DOCUMENT...
'Some memory issues'	'ALS-FTD — ECAS executive dysfunction; **G31.09 + F02.80** (HCC 127); decision-making capacity assessed, surrogate designated'
'Losing weight'	'Abnormal weight loss (**R63.4**), 4 kg over 3 months (>5% from baseline); oropharyngeal dysphagia (**R13.12**); dietitian referral and PEG counseling while FVC >50%'
'Discussed goals of care'	'Advance care planning (CPT 99497): NIV and PEG preferences reviewed; DNR (**Z66**) in effect; revisited with surrogate present given cognitive change'
'Started medication'	'**Riluzole** 50 mg PO BID started; baseline LFTs obtained; DMP discussed and offered per AAN Quality Measurement Set'

ABBREVIATIONS: AAN = American Academy of Neurology; ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; ALS-FTD = ALS-frontotemporal dementia; deltaFS = rate of ALSFRS-R decline; DMP = disease-modifying pharmacotherapy; DNR = do not resuscitate; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; HCC = Hierarchical Condition Category; LFT = liver function test; LMN = lower motor neuron; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; UMN = upper motor neuron

DOCUMENTATION REMINDER IS COMPREHENSIVE CODING

Every active ALS encounter should document the confirmed diagnosis (**G12.21**, onset type, UMN/LMN findings), current **FVC** and respiratory status,[14] nutritional status and weight trend, ventilator and gastrostomy status when present, cognitive/behavioral screen (**ECAS**) and capacity, **ALSFRS-R** or staging, disease-modifying therapy discussion, the full comorbidity burden, and an updated **advance care planning** note. Because ALS progresses rapidly, do not copy forward prior notes — re-document current burden at each visit.

4 TREATMENT AND REFERRAL QUICK GUIDE

Therapy Escalation Criteria

Aggressive clinical management, targeted medications, and specialized supportive care can meaningfully slow down functional decline, preserve independence, and prolong survival.

TRIGGER[1,3,8,21,33]	ACTION
Painless, progressive, asymmetric motor weakness ± fasciculations	**Same-encounter** referral to a multidisciplinary ALS clinic or neurologist; do not adopt a wait-and-see approach

TRIGGER[1,3,8,21,33]	ACTION
Confirmed ALS at diagnosis	Discuss and document **disease-modifying pharmacotherapy** (riluzole; edaravone; tofersen if SOD1) per AAN QMS; enroll in multidisciplinary clinic
FVC <80% predicted with respiratory symptoms	Pulmonology referral for **NIV** discussion now — do not wait for the FVC <50% Medicare DME threshold
FVC ≤50%, MIP ≤ -60 cmH2O, or SNIP ≤ -40 cmH2O	Urgent NIV initiation; MA plans may authorize earlier than traditional Medicare
Dysphagia or weight loss >5%	Speech/swallow and dietitian evaluation; consider **PEG** while **FVC >50%** to reduce procedural risk
SOD1 mutation confirmed (~2% of ALS)	Refer to ALS specialist for **tofersen** (intrathecal) consideration; document SOD1 status
Cognitive/behavioral change or positive ECAS	**Neuropsychological evaluation**; assess decision-making capacity; engage surrogate before capacity is lost
Pseudobulbar affect interfering with function	Dextromethorphan/quinidine (FDA-approved); distinguish from depression
Any ALS encounter	Initiate or revisit **advance care planning** (NIV, PEG, tracheostomy, hospice, DNR); document via CPT 99497/99498
Caregiver strain or unsafe home environment	Social work referral; ALS Association chapter linkage; respite/home-health planning to prevent premature institutionalization

ABBREVIATIONS: AAN = American Academy of Neurology; ALS = amyotrophic lateral sclerosis; DME = durable medical equipment; DNR = do not resuscitate; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; MA = Medicare Advantage; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; QMS = Quality Measurement Set; SNIP = sniff nasal inspiratory pressure; SOD1 = superoxide dismutase 1

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

AAN-Aligned Treatment and Multidisciplinary Care by Setting

SETTING/ INDICATION	PREFERRED APPROACH	KEY NOTES
All people with ALS, at diagnosis[25,34]	**Riluzole** 50 mg PO BID (tablet, suspension, or oral film)	**Prolongs tracheostomy-free survival** by **60-90 days** vs. placebo. No age dose adjustment; monitor ALT at baseline, monthly x3 months, then periodically — important given polypharmacy Riluzole is a benzothiazole derivative that exerts neuroprotection through multiple complementary mechanisms **targeting glutamate excitotoxicity and neuronal hyperexcitability**
Early-stage ALS (duration ≤2 y, FVC ≥80%)[35,36]	**Edaravone** (Radicava ORS) 105 mg PO daily in cycles	~2.5-point **lower ALSFRS-R decline over 24 week**s in early disease. **IV formulation discontinued in the US (April 2025)**; oral suspension remains. Shown to reducing physical function decline by up to 33% in certain patient groups. Limited data >75 y; gait disturbance and fall risk Edaravone acts as a free-radical scavenger that reduces oxidative stress-mediated motor neuron injury
SOD1-mutation ALS (~2% of cases)[14]	**Tofersen** (Qalsody) 100 mg intrathecal — 3 loading doses q14d, then q28d	Early-start tofersen: ALSFRS-R decline **-6.0 vs. -9.5 points at 52 weeks** with NfL reduction. Intrathecal access may be limited by spinal degenerative disease in older adults **Tofersen is currently the most effective and only genetically targeted disease-modifying therapy for SOD1-mutation ALS. The long-term data has demonstrated that early-start tofersen slowed decline of respiratory capacity and muscle strength**[14,37]
Multidisciplinary clinic care[25,33]	Neurology + ≥4 disciplines (pulmonology, dietitian, speech, PT/OT, social work, palliative care)	**Standard of care**, not optional — improves survival and quality of life. The PCP coordinates when geographic or access barriers limit direct enrollment
Respiratory support[3]	**NIV** when FVC <80% with symptoms, FVC ≤50%, MIP ≤ -60, or SNIP ≤-40 cmH2O	Single most impactful intervention after diagnosis that can be arranged at home setting— prolongs survival up to **7 months** (up to ~11 with good adherence). Add cough assist (E0482) when cough peak flow is inadequate

SETTING/ INDICATION	PREFERRED APPROACH	KEY NOTES
Nutrition[38]	**PEG** while **FVC >50%** and before severe malnutrition	Aspiration and malnutrition increase death risk **7.7-fold**. BMI <20 at gastrostomy predicts poor outcomes; high-calorie diet may slow weight loss
Palliative care[39]	Introduce **early — at or shortly after diagnosis** in VBC geriatric populations	Pain and muscle spasms are the most common symptoms managed; concurrent with disease-directed care, not end-of-life only
Older adult with frailty[40]	Decisions on **functional status, not chronologic age**; reduced-intensity, goal-concordant plans	Bulbar-onset (more common in elderly) progresses faster — Medicare median survival may be as low as ~2 years from diagnosis

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; ALT = alanine aminotransferase; BMI = body mass index; FVC = forced vital capacity; IV = intravenous; MIP = maximum inspiratory pressure; NfL = neurofilament light chain; NIV = non-invasive ventilation; OT = occupational therapy; PEG = percutaneous endoscopic gastrostomy; PT = physical therapy; SNIP = sniff nasal inspiratory pressure; SOD1 = superoxide dismutase 1; VBC = value-based care
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL — DO NOT WAIT FOR FVC <50% TO DISCUSS NIV AND HOME VENTILATION

Do not wait for **FVC <50%** to discuss respiratory support. The traditional Medicare DME threshold is widely recognized as too restrictive; the CHEST 2023 guideline support **NIV at FVC <80% with symptoms**, FVC ≤50% regardless of symptoms, MIP ≤-60 cmH2O, or SNIP ≤-40 cmH2O. **NIV is the single most impactful intervention after diagnosis** — prolonging survival up to **7 months** (up to ~11 with good adherence) and improving quality of life. Median survival after diaphragmatic weakness develops is only **~6 months**, so monitor FVC every 3 months and refer to pulmonology early — Medicare Advantage plans can authorize NIV ahead of the traditional threshold.[32]

Home Ventilation: Patient-Centered, Better Outcomes, Cost-Smart

Home bilevel ventilation (BiPAP) is one of the most impactful interventions after an ALS diagnosis, with a survival effect potentially greater than any available medication. Beyond survival benefits discussed above, home ventilation improves sleep quality, reduces daytime fatigue, alleviates morning headaches, and slows the rate of overall functional decline, even in patients with bulbar involvement.[3]

Home ventilation also keeps patients where they want to be. A multicenter randomized trial demonstrated that home-initiated BiPAP achieves the same improvement in gas exchange and quality of life as hospital-based initiation, while patients report substantial advantages including reduced travel burden, greater comfort, and a more trustworthy care environment. **A network meta-analysis of 8 studies confirmed that home and outpatient initiation are not inferior to in-hospital initiation on any measured outcome**.[41]

Home ventilation is also cost-smart. Home initiation can save well over $10,000–$20,000/month. ***See chart below***. Pairing BiPAP with a cough-assist device further prevents aspiration-related emergency visits and admissions. Telemonitoring through ventilator software platforms enables real-time adjustments at home, reducing the need for in-person hospital visits and supporting sustained adherence.[42]

A secondary benefit of home mechanical ventilation is a significantly lower risk of nosocomial (hospital-acquired) infections, which is critically important in medically complex, vulnerable populations.[43]

Cost Savings for Home Ventilation

SETTING[44,45]	ESTIMATED MONTHLY COST (USD)	SOURCE
LTACH (ventilator-dependent)	~$45,000–$90,000	$1,500–$3,000/day × 30 days (Medicare program cost)
Acute care hospital (prolonged MV)	~$55,000–$78,000/stay	Median hospital costs $55,014 (PAMV); $78,474 (nontransferred)

SETTING[44,45]	ESTIMATED MONTHLY COST (USD)	SOURCE
Home NIV (ALS, all health system costs)	~$3,000–$5,300	Annual ~$63,693 (majority DME); median $3,925 CAD/month for NIV users
Home invasive MV (tracheostomy)	~$6,800–$8,700	Median $8,733 CAD/month for invasively ventilated home users
Estimated monthly savings (LTACH → home)	~$36,000–$85,000	Derived from above comparisons

Abbreviations: ALS = amyotrophic lateral sclerosis; CAD = Canadian dollars; DME = durable medical equipment; LTACH = long-term acute care hospital; MV = mechanical ventilation; NIV = non-invasive ventilation; PAMV = prolonged acute mechanical ventilation; USD = United States dollars

Non-Pharmacologic Care and Supportive Interventions

Beyond disease-modifying agents described in the next section, symptom management remains central to ALS care: muscle relaxants and antispasticity agents for spasticity and cramps, dextromethorphan/quinidine for pseudobulbar affect, non-invasive ventilation to improve survival and quality of life, and tracheostomy with artificial feeding as disease progresses.[1,8,25,32,33,36]

INTERVENTION	TARGET/ RECOMMENDATION	NOTES
Non-invasive ventilation (NIV)	Initiate per CHEST/ONMAP criteria; encourage nightly + nap use	**Consistent use yields the greatest survival benefit**; severe bulbar impairment may limit tolerance — address sialorrhea and mask fit first
Cough assist (mechanical insufflation-exsufflation)	When cough peak flow is inadequate; covered under Medicare Part B (E0482)	Reduces mucus plugging and aspiration risk; especially valuable in bulbar disease
Percutaneous endoscopic gastrostomy (PEG)	Offer while **FVC >50%** and before severe malnutrition	**Both NIV and PEG improve survival;** PEG at FVC <50% carries higher procedural risk
Nutrition support	High-calorie, high-fat diet once dysphagia or active weight loss begins; dietitian-set caloric targets	Weight loss >5% triggers urgent evaluation; BMI <20 at gastrostomy predicts poor outcomes
Speech therapy + communication	Early referral; **voice banking while speech is intelligible**; augmentative/alternative communication devices	**Dysarthria affects ~70%**; early voice banking preserves the person's own voice for later use[1]

INTERVENTION	TARGET/ RECOMMENDATION	NOTES
Mobility and DME	Wheelchair (manual/power), hospital bed, lifts; fast-track authorization in MA	Proactive DME prevents falls and avoidable ED visits; document mobility status (**Z99.3**)
Physical and occupational therapy	Maintain function and reduce fall risk early; adaptive-equipment training	Preserves independence and safety as the disease progresses
Palliative care + hospice	Introduce palliative care **early**; hospice when goals align	Pain and muscle spasms are most commonly managed; **subcutaneous morphine relieves dyspnea at rest in advanced disease**
Caregiver and social support	Social work at diagnosis; ALS Association chapter; respite and home-health planning	Caregiver burnout is a leading **driver of premature institutionalization**
Advance care planning	Iterative — initiate at diagnosis, revisit at every encounter	Billable (CPT 99497/99498); document NIV, PEG, tracheostomy, hospice, and DNR (Z66) preferences

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; DME = durable medical equipment; DNR = do not resuscitate; ED = emergency department; FVC = forced vital capacity; MA = Medicare Advantage; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Medication Options, Safety, and Key Interactions

Although there is currently no known cure, **ALS can be managed using disease-modifying agents**. As of January 2025, there are several FDA-approved medications in the United States, including riluzole, edaravone, combination therapy with sodium phenylbutyrate and taurursodiol, and more recently, tofersen.

Riluzole (Rilutek®) blocks the transmission of glutamate in the central nervous system, thereby decreasing the rate of neuronal degeneration and symptom progression.[34] Riluzole is indicated for mild to moderate disease of less than 5-years' duration. On the other hand, edaravone (Radicava®) is a drug for the treatment of ALS that acts as a free-radical scavenger and reduces oxidative stress on neurons. Similarly, combination therapy with sodium phenylbutyrate and taurursodiol (Relyvrio®) is thought to protect motor neurons by reducing metabolic stress and cellular dysfunction. Finally, tofersen (Qalsody®) is designed to reduce the production of SOD1 protein in patients with known SOD1 gene mutations, which account for a subset of familial ALS cases.

DRUG/CLASS[1,34,47-50]	INTERACTION/TOXICITY	CLINICAL ACTION
Riluzole + CYP1A2 inhibitors (ciprofloxacin, fluvoxamine)	Inhibition raises riluzole exposure and **hepatotoxicity risk**; ciprofloxacin is commonly used for UTIs in older adults	**Avoid when possible**; if unavoidable, increase LFT monitoring; discontinue riluzole if ALT >5x ULN

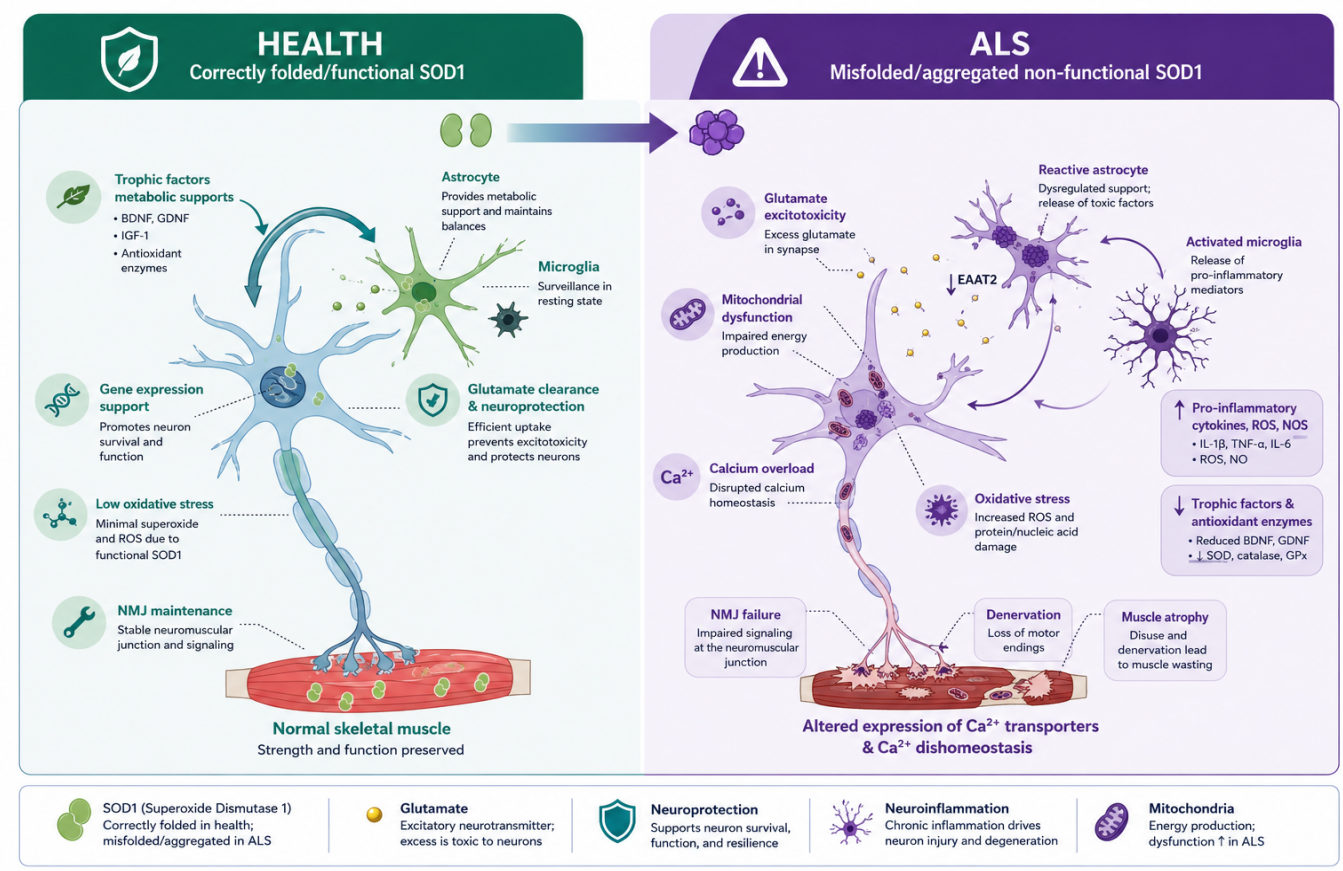
DRUG/CLASS[1,34,47-50]	INTERACTION/TOXICITY	CLINICAL ACTION
Riluzole + hepatotoxic agents (statins, amiodarone, methotrexate)	Additive liver injury risk, elevated in polypharmacy	Monitor ALT/AST; consider alternative lipid-lowering if LFT elevation occurs on riluzole
Riluzole + CYP1A2 inducers (tobacco, omeprazole)	**Can lower riluzole levels by up to ~50%, reducing effect**	Document smoking status; counsel cessation; note PPI co-use
Dextromethorphan/ quinidine + CYP2D6 substrates (metoprolol, fluoxetine, paroxetine)	Quinidine inhibits CYP2D6, raising substrate levels — **metoprolol bradycardia/hypotension** risk in elderly cardiac patients	Review full medication list before prescribing; reduce or avoid CYP2D6 substrates; check ECG (QT)
Baclofen/tizanidine + CNS depressants (opioids, benzodiazepines, gabapentinoids)	Additive CNS and **respiratory depression** — critical given baseline respiratory-muscle compromise	Titrate slowly, lowest effective dose; **in FVC <50% or on NIV use with extreme caution** and document respiratory monitoring
Anticholinergics for sialorrhea (amitriptyline, glycopyrrolate)	Amitriptyline: anticholinergic burden, sedation, falls, QTc (Beers list)	Prefer glycopyrrolate if cognitive impairment or fall risk; monitor for urinary retention/constipation
Morphine (dyspnea) + benzodiazepines (anxiety)	Additive respiratory depression in late-stage disease	Coordinate with palliative care; document comfort-focused goals when combined
Benzodiazepines for insomnia	Respiratory depression risk; Beers list in older adults	**Avoid;** prefer sleep hygiene, low-dose trazodone/mirtazapine; adjust NIV settings for sleep-disordered breathing
Citalopram for depression	QT prolongation; max 20 mg/day in elderly	**Screen mood at every visit**; prefer escitalopram/sertraline; review QT-prolonging co-medications
Tofersen (intrathecal ASO) + immunomodulatory agents	**Tofersen can cause myelitis, aseptic meningitis, and papilledema** (~7% neurologic serious adverse events); concurrent immunosuppressants may mask or complicate recognition of these CNS inflammatory reactions	**Hold or closely coordinate immunomodulatory therapy around dosing**; monitor for back pain, leg weakness, urinary retention, headache, and papilledema after each intrathecal injection; obtain urgent MRI spine if myelitis suspected

DRUG/CLASS[1,34,47-50]	INTERACTION/TOXICITY	CLINICAL ACTION

ABBREVIATIONS: ALT = alanine aminotransferase; ASO = antisense oligonucleotide; AST = aspartate aminotransferase; CNS = central nervous system; CYP1A2 = cytochrome P450 1A2; CYP2D6 = cytochrome P450 2D6; ECG = electrocardiogram; FVC = forced vital capacity; LFT = liver function test; MRI = magnetic resonance imaging; NIV = non-invasive ventilation; PPI = proton pump inhibitor; QT/QTc = corrected QT interval; ULN = upper limit of normal; UTI = urinary tract infection

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

Proposed Mechanism of SOD1 in ALS



Description: SOD1-related ALS pathogenesis involves disrupted SOD1 protein metabolism — whether through toxic aggregation of misfolded SOD1 species, loss of normal enzyme function, or both — that impairs multiple cellular processes across motor neurons, glial cells, and skeletal muscle cells, with pathological cross-talk between these cell types collectively driving the disease phenotype.

When to Refer

CRITERION[2,8,41]	SPECIALIST	URGENCY
Acute respiratory failure (dyspnea at rest, SpO2 <90%, hypercapnia)	Emergency department/ pulmonology	**Emergent**
Aspiration pneumonia with respiratory distress	Emergency department	**Emergent**
Acute airway obstruction/ unrelieved choking	Emergency department	**Emergent**
Painless progressive asymmetric weakness ± fasciculations	Multidisciplinary ALS clinic/ neurology	**Urgent (same/next day)**
Rapid FVC decline (>10% between visits or approaching 50%)	Pulmonology for NIV	**Urgent (same/next day)**
Acute dysphagia, unable to maintain oral intake	Speech therapy + gastroenterology for PEG	**Urgent (within days)**
New cognitive/behavioral change suggesting ALS-FTD	Neuropsychology	**Urgent (within days)**
SOD1 mutation confirmed	ALS specialist for tofersen consideration	**Routine (within 2-4 weeks)**
Progressive weight loss >5% in 1 month	Dietitian; consider PEG	**Expedited (within days)**
Caregiver crisis or unsafe home environment	Social work + palliative care	**Expedited (within days)**
Goals-of-care or hospice eligibility	Palliative care/hospice (Medicare Hospice Benefit)	**When goals align**

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; FVC = forced vital capacity; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; SOD1 = superoxide dismutase 1; SpO2 = peripheral oxygen saturation
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Follow-Up Timing

PARAMETER[22,25,51,52]	FREQUENCY	ACTION THRESHOLD/MONITORING
ALSFRS-R	**Every 3 months** at ALS clinic; informally at PCP visits	Decline **>1 point/month** signals rapid progression — trigger escalation and ACP update
Forced vital capacity (FVC)	**Every 3 months** (more often if declining)	**FVC <80% + symptoms**: NIV discussion; ≤50%: urgent NIV; near 25%: median survival ~6 months
MIP/SNIP	**Every 3 months** with FVC	MIP ≤-60 cmH2O or SNIP ≤-40 cmH2O: NIV criteria met
Nocturnal oximetry/ transcutaneous CO2	**When FVC <80%** with symptoms or suspected nocturnal hypoventilation	**Sustained desaturation or rising CO2: initiate NIV**
Riluzole LFTs (ALT/ AST)	**Baseline; monthly x3 months;** periodically thereafter	ALT >3x ULN: dose-reduction discussion; >5x ULN: discontinue
Weight/BMI/nutrition	**Every visit**; monthly if active weight loss	Loss **>5%** from baseline: urgent dietitian referral and PEG discussion; BMI <20: prioritize PEG
Dysphagia/swallow function	**Every ALS clinic visit**; at PCP visit if bulbar symptoms worsen	New difficulty: formal **swallow evaluation**; aspiration suspected: modified barium swallow/FEES
Cognitive/behavioral screen (ECAS)	At diagnosis; **every 6 months** or with behavioral change	Disinhibition, apathy, executive dysfunction: neuropsychological evaluation; assess capacity
Advance care planning	At **every** encounter; document current status	Revisit NIV/PEG/tracheostomy/hospice/DNR preferences; CPT 99497 billable (first 30 min)
Caregiver burden/ social support	**Every 3 months**; escalate with progression	Burnout or isolation: social work referral; palliative care consultation

ABBREVIATIONS: ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; CO2 = carbon dioxide; DNR = do not resuscitate; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FEES = fiberoptic endoscopic evaluation of swallowing; FVC = forced vital capacity; LFT = liver function test; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; SNIP = sniff nasal inspiratory pressure; ULN = upper limit of normal

Comorbidity Management

COMORBIDITY[1,8,22,25,32]	PCP APPROACH	CAUTION
Chronic respiratory failure (J96.1x)	Serial FVC/MIP; NIV per CHEST/ONMAP; cough assist when peak flow inadequate	Median survival after diaphragmatic weakness ~6 months — **act early, not at the FVC <50% threshold**
Dysphagia/malnutrition (R13.12, R63.4)	Swallow and dietitian evaluation; high-calorie diet; PEG while FVC >50%	**Aspiration + malnutrition raise death risk 7.7-fold;** BMI <20 at gastrostomy predicts poor outcomes
ALS-FTD/cognitive impairment (G31.09 + F02.80)	ECAS at diagnosis and q6 months; capacity assessment; surrogate engagement	Affects adherence, ACP capacity, and caregiver burden — **do not assume intact cognition**
Pseudobulbar affect (F48.2)	Dextromethorphan/quinidine (FDA-approved)	Frequently misread as depression; quinidine prolongs QT and inhibits CYP2D6
Depression/anxiety (F32.x, F41.x)	Screen every visit; SSRI first-line (escitalopram, sertraline)	Citalopram max 20 mg/day in elderly (QT); **avoid benzodiazepines** (respiratory depression)
Spasticity/cramps	Baclofen or tizanidine, titrated slowly	Sedation, falls, and additive respiratory depression in patients with compromised FVC
Sialorrhea	Glycopyrrolate or atropine drops; botulinum toxin if refractory	**Anticholinergic burden in elderly**; prefer glycopyrrolate over amitriptyline if cognitive/fall risk
Venous thromboembolism (I26.x, I82.x)	Mobility support; clinical vigilance for DVT/PE	Immobility and wheelchair dependence elevate risk
Caregiver burden (Z74.x)	Social work, respite, ALS Association linkage, home health	A leading driver of premature institutionalization

ABBREVIATIONS: ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; BMI = body mass index; CYP = cytochrome P450; DVT = deep vein thrombosis; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; NIV = non-invasive ventilation; PE = pulmonary embolism; PEG = percutaneous endoscopic gastrostomy; QT = QT interval; SSRI = selective serotonin reuptake inhibitor

Cost-Smart Options

ITEM	COST	ALTERNATIVE /OPTION	EST. SAVINGS	COST-SMART TIP
Riluzole (Rilutek, Tiglutik, Exservan)[34]	**Tiglutik**: $1,500–$2,500/month **Exservan**: $1,000–$2,000/month	Generic riluzole tablet ($100–$300/month)	$1,000–$2,000+/ month	Generic tablet is low-cost; reserve suspension/film for documented dysphagia
Edaravone (Radicava ORS)[36]	$713–$1600 per 30-day fill	No generic; single-source brand	Patient assistance variable	Manufacturer assistance for eligible patients; confirm early-stage criteria before initiating
Tofersen (Qalsody)[53]	$2,805 per dose (procedural/ operational costs) $36,000–$42,000/ year	No generic; SOD1-only	—	Reserve for confirmed SOD1 mutation; manufacturer support programs; document genetic eligibility
NIV/BiPAP equipment[52]	**Medicare:** ~$200/ month for a home ventilator $1,500 and $3,500 out-of-pocket for standard devices, while highly advanced ventilator-integrated models can exceed $5,000	Medicare Part B DME (E0470-E0472)	Home initiation of NIV saves over $3,700 per patient over 6 months compared to hospital-based setup, with no difference in clinical outcomes (gas exchange, quality of life)	MA plans can fast-track authorization at FVC <80% with symptoms — earlier than traditional threshold
Cough assist device[33]	~$6,500 (without coverage)	Medicare Part B (E0482)	Prevents ED visits	Authorize when cough peak flow is inadequate; reduces aspiration-related admissions

ITEM	COST	ALTERNATIVE /OPTION	EST. SAVINGS	COST-SMART TIP
Antidepressants/ anticholinergics	Generic sertraline (50–200 mg/day): **$15–$25/month vs. ~$310–$625/ month (Zoloft)** and generic **escitalopram (10–20 mg/day): $10/month vs. ~$350/month for brand (Lexapro)**	Generic glycopyrrolate, sertraline, escitalopram	~$285–$600/ month	Generics effective; choose by anticholinergic burden and QT profile in elderly
Avoidable ED visits/admissions	**See Cost Savings for Home Ventilation Section**	**Home-based** respiratory, nutrition, and palliative support	Substantial	Proactive DME, dysphagia management, and caregiver support prevent crisis utilization

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; DME = durable medical equipment; ED = emergency department; FVC = forced vital capacity; MA = Medicare Advantage; NIV = non-invasive ventilation; SOD1 = superoxide dismutase 1
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Patient and Caregiver Education

What makes ALS patient education unique is the convergence of diagnostic delay, rapid functional decline, and the need for anticipatory decision-making in a disease where most patients and families have no prior knowledge of the condition.

Unlike chronic diseases where education can unfold over years, ALS demands that patients and caregivers absorb complex information about respiratory support, nutritional intervention, communication devices, and end-of-life planning within a compressed and emotionally challenging timeline — while the patient's ability to communicate and participate in decisions is actively deteriorating.

Nearly 56% of patients rate the quality of diagnostic communication as average or worse, and caregivers consistently report being underprepared for managing the final stages of the disease.[54] Education must be disease-stage-specific and continuously updated: information needs shift from diagnosis comprehension and treatment options in early disease, to equipment training, swallowing management, and ventilation decisions in middle stages, to end-of-life care and bereavement support in late disease.

Caregivers in particular need practical **training in transfers, positioning, NIV management, PEG care, and suctioning.** Older adults face compounding barriers: limited health literacy (more than one-third of U.S. adults), sensory impairment, cognitive changes (up to 50% of AlS patients),[8] and caregiver dependence.

DOCUMENTATION REMINDER — PATIENT EDUCATION

Document the education topics covered (diagnosis and prognosis, disease-modifying therapy, NIV adherence, urgent-care triggers, weekly self-monitoring, voice banking, advance care planning), the person's understanding (teach-back when appropriate), and caregiver involvement. Education documentation supports continuity, shared decision-making, and signals to the multidisciplinary team that the plan is person-aligned.

Quality Metrics Tie-In

MEASURE (MY2026)[4]	STANDARD	APPLICABILITY TO ALS CARE
AAN QMS: Disease-Modifying Pharmacotherapy (DMP) Discussion	**Denominator:** patients with ALS diagnosis **Numerator:** documented discussion of FDA-approved disease-modifying therapies (riluzole, edaravone, tofersen if SOD1+) at least once annually	**Riluzole remains underprescribed even in specialized clinics** (38–86% use).[33] This measure ensures all patients are offered and counseled on available therapies, including newer agents. Updated to incorporate all FDA-approved therapies as the field evolves. Satisfies CMS QPP reporting
AAN QMS: Respiratory Screening and Appropriate Intervention	**Denominator:** patients with ALS **Numerator:** screened for respiratory impairment (FVC, MIP, SNIP, symptoms) and referred for NIV/cough assist when criteria met, at least once annually	**The single most impactful quality measure** — NIV use remains low despite survival benefit. Updated to support earlier NIV initiation at FVC >80% with symptoms or >65% if asymptomatic, per ATS recommendations. Cough assist referral when peak cough flow <270 L/min. Captures the most critical existing gap in ALS care[33]
AAN QMS: Nutrition and Dysphagia Screening	**Denominator:** patients with ALS **Numerator:** screened for dysphagia, weight loss, and malnutrition with validated tools and referred for dietitian/SLP evaluation at least once annually	**Weight loss >5% is a poor prognostic sign; aspiration and malnutrition raise death risk 7.7-fold**. Screen weight, BMI, and swallowing at every visit. PEG discussion while FVC >50% to reduce procedural risk. Combines former dysphagia and nutritional support measures[55]
AAN QMS: Multidisciplinary Care Plan	**Denominator:** patients with ALS **Numerator:** documented multidisciplinary care plan addressing ≥4 disciplines (neurology, pulmonology, SLP, dietitian, PT/OT, social work, palliative care) at least once annually	**Multidisciplinary clinic care improves survival and quality of life** — standard of care, not optional. Subsumes retired measures for cognitive/behavioral screening, symptomatic therapy, communication support, and falls. Telehealth encounters qualify[33]

MEASURE (MY2026)[4]	STANDARD	APPLICABILITY TO ALS CARE
AAN QMS: ALS Support Services	**Denominator:** patients with ALS **Numerator**: provided written or electronic material highlighting ALS patient or care partner resources and support services at least once annually	New measure addressing the gap in connecting patients and caregivers to ALS Association chapters, respite care, home-health resources, and community support. Caregiver burnout is a leading driver of premature institutionalization
AAN QMS: Patient Care Preferences (CMS QPP #386)	**Denominator:** patients with ALS **Numerator:** advance care planning documented at least once annually or at key disease milestones (diagnosis, dysphagia onset, respiratory impairment); CPT 99497/99498	Adopted by CMS QPP; performance ranges only 49–74% (2018–2020), confirming a persistent gap. Initiate while decisional capacity is intact — **ALS-FTD affect**s **up to 50%**.[8] Document NIV, PEG, tracheostomy, hospice, and DNR preferences. POLST completion. Renamed from "end-of-life planning" to reflect importance at all disease stages
HEDIS COA: Care for Older Adults — Medication Review	**Denominator:** MA/SNP enrollees ≥66, continuously enrolled **Numerator:** medication review documented annually. **Exclusions:** hospice, ESRD	**Polypharmacy is universal in elderly ALS** (riluzole, dextromethorphan/quinidine, baclofen, gabapentin, antidepressants, antihypertensives, statins). Medication review should reconcile: CYP1A2 interactions with riluzole (ciprofloxacin, omeprazole), CYP2D6 interactions with quinidine, anticholinergic burden (Beers Criteria), CNS depressant stacking (baclofen + gabapentin + opioids), and respiratory-depressant risk given compromised FVC[56]
HEDIS COA: Care for Older Adults — Functional Status Assessment	**Denominator:** MA/SNP enrollees ≥66 **Numerator:** functional status assessment documented annually **Exclusions:** hospice, ESRD	ALSFRS-R directly satisfies this sub-measure. Document at every visit to track functional trajectory (deltaFS >1 point/month = rapid progressor), guide rehabilitation intensity, and trigger escalation of respiratory support, nutritional intervention, and advance care planning[56]
HEDIS COA: Care for Older Adults — Pain Assessment	Denominator: MA/SNP enrollees ≥66. Numerator: pain assessment documented annually. Exclusions: hospice, ESRD	**Pain affects ~40% of ALS patients** — shoulder cramping, spasticity-related pain, and musculoskeletal pain from compensatory movement patterns. Document pain type, location, severity, and functional impact at every visit. Gabapentin and baclofen require careful titration given respiratory compromise[56]

MEASURE (MY2026)[4]	STANDARD	APPLICABILITY TO ALS CARE
HEDIS COA: Care for Older Adults — Advance Care Planning	Denominator: enrollees ≥66. Numerator: advance care planning documented annually; CPT 99497/99498	Overlaps with AAN QMS Patient Care Preferences. Billable during AWV with no copay. ALS-specific decision points are predictable (NIV, PEG, tracheostomy, hospice) — disease-specific advance directives have been developed for ALS. The AAN neuropalliative care position statement encourages early engagement given poor prognosis and progressive loss of communication ability[56]
HEDIS TSC-E: Tobacco Use Screening and Cessation Intervention	**Denominator 1:** enrollees ≥12. **Denominator 2:** positive tobacco users. Numerator 1: screened with documented tobacco status **Numerator 2:** received cessation counseling or pharmacotherapy **Exclusions:** death, hospice	**Tobacco use induces CYP1A2, which can lower riluzole levels by up to ~50%**, reducing therapeutic effect. Document tobacco status at every visit. Active smoking is a modifiable factor that directly undermines the only broadly indicated disease-modifying therapy. Former smokers (like the index patient) should be documented as **F17.211**[57]
HEDIS DMS-E: Utilization of the PHQ-9 to Monitor Depression Symptoms	**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 ALS is ~34%**. PHQ-9 is validated across neurologic populations. Distinguish depression from pseudobulbar affect (CNS-Lability Scale). Follow-up PHQ-9 within 4–8 months if ≥10. Avoid TCAs (anticholinergic burden) and benzodiazepines (respiratory depression); prefer sertraline or escitalopram[24]
HEDIS DAE: Use of High-Risk Medications in Older Adults	**Denominator:** enrollees ≥67 **Numerator:** received ≥1 high-risk medication per Beers Criteria. Lower rate = better performance	**High-yield in ALS: benzodiazepines compound respiratory depression in patients with compromised FVC**; anticholinergics (amitriptyline for sialorrhea) worsen cognitive impairment in ALS-FTD; first-generation antipsychotics increase EPS risk. Prefer glycopyrrolate over amitriptyline if cognitive/fall risk. Document Beers review at each visit[25,58]
CMS Star: Controlling Blood Pressure (CBP)	**Denominator:** enrollees 18–85 with HTN diagnosis **Numerator:** most recent BP <140/90 mmHg	**Hypertension is a common comorbidity in elderly ALS**[31]

MEASURE (MY2026)[4]	STANDARD	APPLICABILITY TO ALS CARE

ABBREVIATIONS: AAN = American Academy of Neurology; ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALS-FTD = amyotrophic lateral sclerosis–frontotemporal dementia; ALSFRS-R = ALS Functional Rating Scale–Revised; ATS = American Thoracic Society; AWV = Annual Wellness Visit; BMI = body mass index; BP = blood pressure; CBP = Controlling Blood Pressure; CMS = Centers for Medicare & Medicaid Services; CNS = Center for Neurologic Study; COA = Care for Older Adults; CPT = Current Procedural Terminology; CYP1A2 = cytochrome P450 1A2; CYP2D6 = cytochrome P450 2D6; DAE = Use of High-Risk Medications in Older Adults; deltaFS = delta functional score; DMP = disease-modifying pharmacotherapy; DMS-E = Utilization of the PHQ-9 to Monitor Depression Symptoms; DNR = do not resuscitate; EPS = extrapyramidal symptoms; ESRD = end-stage renal disease; FDA = Food and Drug Administration; FTD = frontotemporal dementia; FVC = forced vital capacity; HEDIS = Healthcare Effectiveness Data and Information Set; HF = heart failure; HTN = hypertension; LFT = liver function test; MA = Medicare Advantage; MIP = maximal inspiratory pressure; MY = measurement year; NIV = non-invasive ventilation; OT = occupational therapy; PEG = percutaneous endoscopic gastrostomy; PHQ-9 = Patient Health Questionnaire-9; POLST = Physician Orders for Life-Sustaining Treatment; PT = physical therapy; QMS = Quality Measurement Set; QPP = Quality Payment Program; SLP = speech-language pathology; SNIP = sniff nasal inspiratory pressure; SNP = Special Needs Plan; SOD1 = superoxide dismutase 1; TCA = tricyclic antidepressant; TSC-E = Tobacco Use Screening and Cessation Intervention

QUALITY OUTCOME

When primary care refers at first suspicion of ALS rather than waiting, monitors FVC every 3 months and advocates for **NIV** before the FVC <50% threshold, supports timely **PEG** while FVC >50%, screens cognition with **ECAS** and assesses capacity early, captures the evolving comorbidity burden at every encounter, and leads iterative **advance care planning** — people living with ALS receive coordinated, goal-concordant care that preserves dignity, prevents avoidable hospitalizations, and supports caregivers through a terminal illness.

5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

ELEMENT	DOCUMENTATION REQUIREMENT
Primary ALS diagnosis (G12.21)	State **"amyotrophic lateral sclerosis"** or **"ALS"** explicitly — not "motor neuron disease" alone. Coders require the specific phenotype to assign **G12.21**
Avoid G12.20 once phenotype is known	Motor neuron disease, unspecified (**G12.20**) maps to the same HCC but forfeits specificity; use **G12.21** when ALS is confirmed
Familial vs. sporadic — same code	Both map to **G12.21**; document genetic results (SOD1, C9orf72, FUS, TARDBP) for counseling and tofersen eligibility
Respiratory status	Chronic respiratory failure (**J96.11/J96.12** → HCC 213); document FVC, MIP/SNIP, NIV use; ventilator dependence (**Z99.11** → HCC 211)

ELEMENT	DOCUMENTATION REQUIREMENT
Nutritional status	Oropharyngeal dysphagia (**R13.12**); abnormal weight loss (**R63.4**); severe malnutrition (**E43** — no HCC under V28 but clinically necessary)
Cognitive status (ALS-FTD)	Pair **G31.09 + F02.80** (→ HCC 127) with documented ECAS/ neuropsychological screening
Aspiration pneumonia	**J69.0** (→ HCC 282) with documented aspiration events and swallow evaluation
Functional/device-dependence codes	Wheelchair dependence (**Z99.3**), gastrostomy status (**Z93.1**), tracheostomy status (**Z93.0**), palliative-care encounter (**Z51.5**) — document to convey complexity and support medical necessity
Update every encounter	ALS progresses rapidly; refresh respiratory, nutritional, mobility, and cognitive codes each visit — a 3-month-old note understates current burden
Advance care planning/ DNR	Document DNR (Z66) when in effect; ACP discussions billable via CPT 99497/99498

ABBREVIATIONS: ALS = amyotrophic lateral sclerosis; ALS-FTD = ALS-frontotemporal dementia; CNA = Community Non-Dual Eligible, Aged segment; DNR = do not resuscitate; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; HCC = Hierarchical Condition Category; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; SNIP = sniff nasal inspiratory pressure; SOD1 = superoxide dismutase 1; V28 = CMS-HCC Model Version 28

Annual Clinical Review and Confirmation

- **Annual review:** Active **ALS** must be reassessed at least annually with MEAT documented; because the diagnosis is lifelong and progressive, **G12.21** remains current and requires ongoing documentation of evolving disease burden each year
- **Visit modality:** Face-to-face or synchronous audio-video telehealth qualifies when it supports meaningful clinical evaluation; the AAN Quality Measurement Set explicitly includes telehealth encounters. Chart updates without an encounter do not satisfy MEAT
- **Clinical context:** Under CMS-HCC V28, ALS maps to **HCC 190** (CNA RAF **1.175**). Comorbidities that frequently co-occur carry additional, separately documented HCC weight: chronic respiratory failure (**J96.11/J96.12** → HCC 213, CNA RAF 0.370), ventilator dependence (**Z99.11** → HCC 211, CNA RAF 0.879), ALS-FTD (**G31.09 + F02.80** → HCC 127, CNA RAF 0.341), and aspiration pneumonia (**J69.0** → HCC 282, CNA RAF 0.440). HCC 190 alone significantly understates total disease burden — comorbidity documentation is essential for accurate representation of clinical complexity. **Avoid rollover:** Do not copy forward a prior note without updating onset type and current UMN/LMN findings, **FVC** and respiratory status, weight/BMI and nutritional status, NIV/PEG/ventilator status, ECAS/ cognitive status, ALSFRS-R or stage, disease-modifying therapy discussion, and current advance-care-planning preferences.

Good Documentation — EHR Tips

EHR TIP	WHAT TO INCLUDE
Problem-list precision	'**Amyotrophic lateral sclerosis**, bulbar-onset, mixed UMN/LMN (**G12.21**); King's Stage 3; on riluzole; nocturnal NIV' — not 'motor neuron disease'
Smart phrases/dot phrases	Build macros for Respiratory Monitoring (FVC, MIP/SNIP, NIV hours), Nutrition/Swallow (weight trend, BMI, PEG status), Cognitive Screen (ECAS result, capacity), and ACP (preferences, CPT 99497)
Status field at top of note	'Early limb-onset, ALSFRS-R 40' vs. 'Advanced bulbar, NIV-dependent, PEG in place, hospice-eligible' — orient every reader to current burden
Surveillance flags	Recurring reminders for q3-month FVC/MIP, q6-month ECAS, weight checks, riluzole LFT schedule, and ACP review at every visit
Genetic-result linking	Link SOD1/C9orf72 results to the active G12.21 problem to support tofersen eligibility and familial counseling
Comorbidity capture prompts	Discrete prompts for **J96.11/J96.12** (HCC 213), **Z99.11** (HCC 211), **G31.09 + F02.80** (HCC 127), **J69.0** (HCC 282) when clinically present
ACP/DNR templates	Templates documenting NIV, PEG, tracheostomy, hospice, and DNR (Z66) preferences as patient-understood and surrogate-confirmed
Education/teach-back templates	Templates so diagnosis, therapy, NIV adherence, urgent-care triggers, and advance care planning are documented as patient/caregiver-understood

ABBREVIATIONS: ACP = advance care planning; ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; DNR = do not resuscitate; ECAS = Edinburgh Cognitive and Behavioural ALS Screen; FVC = forced vital capacity; HCC = Hierarchical Condition Category; LFT = liver function test; LMN = lower motor neuron; MIP = maximum inspiratory pressure; NIV = non-invasive ventilation; PEG = percutaneous endoscopic gastrostomy; SNIP = sniff nasal inspiratory pressure; SOD1 = superoxide dismutase 1; UMN = upper motor neuron

Brief Case Examples

SUCCESS — Same-Encounter Referral, Comprehensive Documentation

Patient: 72-year-old man; 8 months of progressive dysarthria, dysphagia, and right-hand weakness; tongue fasciculations and brisk jaw jerk on examination; caregiver reports new apathy; PMH hypertension, type 2 diabetes.

Documentation: 'Progressive bulbar and limb signs without structural cause — same-encounter referral to multidisciplinary ALS clinic. Brain/cervical-spine MRI and needle EMG/NCS arranged to confirm LMN involvement and exclude mimics. Neurology confirmed amyotrophic lateral sclerosis by Gold Coast criteria. Diagnoses: ALS (**G12.21**); oropharyngeal dysphagia (**R13.12**); abnormal weight loss (**R63.4**). ECAS: executive dysfunction — evaluate ALS-FTD (**G31.09 + F02.80**). SOD1/C9orf72 sent.[12] FVC 78% with orthopnea — pulmonology referral for NIV.'

Outcome: Riluzole 50 mg BID started with baseline LFTs; DMP documented per AAN QMS. Multidisciplinary clinic enrollment confirmed. NIV discussed at FVC 78% rather than waiting for <50%; PEG counseling while FVC >50%. Iterative advance care planning documented with the patient's wife present (CPT 99497). Comorbidity codes (**J96**, **Z99.11** as applicable, **G31.09 + F02.80**) updated each visit.

PITFALL — Unspecified Coding and Assumed Intact Cognition

Documentation as written: '70-year-old with motor neuron disease (**G12.20**). Some trouble swallowing and a bit weaker. Breathing fine. Cognition intact. Follow up in 3 months.'

Consequence: G12.20 used despite a confirmed ALS phenotype — forfeits specificity for tracking and research. Respiratory status undocumented (no FVC), nutrition uncharacterized, and cognition assumed intact without an ECAS screen. A 3-month follow-up interval is too long for a rapidly progressive disease and delays NIV, PEG, and advance care planning.

RAF Impact: ALS coded as **G12.20** still maps to HCC 190 (CNA RAF 1.175), but co-occurring complexity is lost: chronic respiratory failure (**J96.11/J96.12** → HCC 213, RAF 0.370), ventilator dependence (**Z99.11** → HCC 211, RAF 0.879), and ALS-FTD (**G31.09 + F02.80** → HCC 127, RAF 0.341) go undocumented, understating clinical complexity for care planning.

Fix: Document explicitly: 'Amyotrophic lateral sclerosis (**G12.21**), bulbar-onset, mixed UMN/LMN. FVC 72% with orthopnea — pulmonology referral for NIV. Oropharyngeal dysphagia (**R13.12**); weight down 6% — dietitian and PEG evaluation while FVC >50%.[16] ECAS: executive dysfunction —ALS-FTD (**G31.09 + F02.80**). Advance care planning initiated (CPT 99497); shorten follow-up to align with rapid progression.'

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