AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Thalassemia

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: Thalassemia is a group of autosomal recessive hemoglobinopathies caused by defective synthesis of the alpha- or beta-globin chains of hemoglobin, producing chain imbalance, ineffective erythropoiesis, and chronic hemolytic anemia.[1] Severity spans a wide spectrum, so a single chart label of "thalassemia" can mean anything from an asymptomatic carrier to a patient in heart failure from decades of iron overload. Two axes define the condition: **alpha** (deletions of one to four **HBA1/HBA2** genes) versus **beta** (point mutations of the **HBB** gene), and carrier/trait versus clinically significant disease.[1] For management, the operative framework is **transfusion-dependent thalassemia (TDT)** versus **non-transfusion-dependent thalassemia (NTDT)** — the classification that drives transfusion protocol, chelation thresholds, monitoring frequency, and therapy eligibility. Thalassemia is best understood as a multisystem disease of iron overload, not simply as anemia: cardiac siderosis, endocrinopathy, hepatic fibrosis, and osteoporosis are the long-term drivers of morbidity, mortality, and cost.[2]

ICD-10 Codes:

Thalassemia is reported under the **D56** family, with subtype specificity directly determining risk-adjustment documentation. **D56.0** (alpha thalassemia) covers HbH disease (3-gene deletion); **D56.1** (beta thalassemia) covers both major/TDT and intermedia/NTDT; **D56.2** (delta-beta thalassemia); **D56.5** (hemoglobin E-beta thalassemia, common in Southeast Asian populations); **D56.8** (other thalassemias); and **D56.9** (thalassemia, unspecified). Trait and carrier states use **D56.3** (thalassemia minor) and **D56.4** (hereditary persistence of fetal hemoglobin) — neither maps to an HCC. Sickle-cell thalassemia is coded separately: **D57.42** (beta-zero without crisis) and **D57.44** (beta-plus without crisis). Iron overload is coded distinctly from the thalassemia itself — **E83.111** for hemochromatosis due to repeated transfusions (TDT) and **E83.118** for absorption-related overload (NTDT) — and other documentable complications include **I43** (cardiomyopathy), **K74.60** (cirrhosis), **C22.0** (hepatocellular carcinoma), **M81.0** (osteoporosis), **E03.9** (hypothyroidism), **E13.–** (secondary diabetes), and **F32.–/F41.–** (depression/anxiety). Document alpha-vs-beta, TDT-vs-NTDT status, and genetic-testing results to support the most specific code the record allows.[3]

Prevalence and Burden: Thalassemias are the most common monogenic disorders worldwide — roughly **1.5%** of the global population carries a beta-thalassemia allele and about **5%** an alpha-thalassemia allele, with more than **90%** of clinically affected patients living in a belt extending from the Mediterranean through the Middle East, Indian subcontinent, and Southeast Asia.[4] US data are sparse and rely on registry extrapolation: an estimated **11,262** patients have clinically significant thalassemia, a combined alpha- and beta-thalassemia prevalence of about **3.5 per 100,000**, and roughly **27%** of US thalassemia patients are foreign-born.[5,6] No published data describe thalassemia prevalence in Medicare or Medicare Advantage populations; patients surviving to age 65+ are a growing but poorly characterized cohort, the product of improved chelation and transfusion practice.[4,7]

HCC/RAF V28 Mapping

ICD-10[3]	CONDITION/HCC V28	RAF (CNA)	DOCUMENTATION REQUIRED
D56.1 (Beta thalassemia), D56.2 (Delta-beta thalassemia), D56.5 (Hemoglobin E-beta thalassemia)	**HCC 108** (Sickle Cell Disorders and Beta Thalassemia Major)	0.146	Specify subtype; document **TDT vs. NTDT** status and transfusion dependence; record genetic-testing results when available
D57.42 (Sickle-cell thalassemia, beta-zero without crisis)	**HCC 107** (Sickle Cell Anemia and Thalassemia Beta Zero)	0.457	Document beta-zero genotype explicitly and crisis status; distinguish from beta-plus **(D57.44)**
D57.44 (Sickle-cell thalassemia, beta-plus without crisis)	**HCC 108** (Sickle Cell Disorders and Beta Thalassemia Major)	0.146	Distinguish from beta-zero; beta-plus maps to HCC 108, not HCC 107
D56.0 (Alpha thalassemia), D56.8 (other thalassemias)	**No HCC** in the FY2026 mapping	—	Code the most specific subtype; document HCC-eligible iron-overload and organ complications separately (see below)
D56.3 (Thalassemia minor), D56.4 (HPFH)	(trait)/ → **No HCC**	—	Trait/carrier only; never apply **D56.3** to HbH disease or symptomatic alpha-thalassemia
E83.111 (Hemochromatosis due to repeated red blood cell transfusions) / E83.118(Hemochromatos due to repeated red blood cell transfusions)	Iron overload — transfusional (TDT)/ absorption-related (NTDT)	—	Code iron overload separately at every encounter; almost universally undercoded and a frequent documentation gap

ICD-10[3]	CONDITION/HCC V28	RAF (CNA)	DOCUMENTATION REQUIRED

ABBREVIATIONS: CNA = Community Non-Dual Eligible, Aged; RAF = Risk Adjustment Factor; HCC = Hierarchical Condition Category; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; HbE = hemoglobin E; HPFH = hereditary persistence of fetal hemoglobin
***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[8]

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

Thalassemia Beta Zero	Beta Thalassemia Major
$4,754	**$1,516**
HCC 107 · RAF 0.457	HCC 108 · RAF 0.146

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

2 RECOGNITION AND DIAGNOSIS

Medicare Screenings and Surveillance (Adult and Geriatric)

SERVICE/TEST	CPT/COVERAGE	FREQUENCY	CLINICAL PURPOSE
CBC with RBC indices[9]	85025; covered for anemia evaluation/ monitoring	Every **3–4 weeks**(TDT); every **3–4 months**(NTDT)	Track pre-transfusion Hb; microcytosis (MCV **<80 fL**) with normal/high RBC count suggests thalassemia over IDA
Hemoglobin electrophoresis[10]	83020; covered for hemoglobinopathy diagnosis	As needed for diagnosis	HbA_2 **>3.5%** confirms beta-thalassemia trait; **normal in alpha-thalassemia** — does not exclude it
Genetic (DNA) testing[4]	S3845 (alpha)/S3846 (beta); prior auth may apply	Once for diagnosis	**Gold standard, required for alpha-thalassemia** where electrophoresis is unreliable

SERVICE/TEST	CPT/COVERAGE	FREQUENCY	CLINICAL PURPOSE
Serum ferritin[11]	82728[1]; covered for iron-overload monitoring[1]	Every **3 months**	Best initial test to **distinguish thalassemia from IDA**; guides chelation initiation
Liver MRI (R2/R2*) iron quantification[11]	74181/74183; document medical necessity	Annually (adult TDT)	Liver iron concentration **>5 mg/g** → chelation; **>15 mg/g** → aggressive chelation
Cardiac MRI T2*[12]	75557/75561; document cardiac iron assessment[8]	Annually (from age 10)	T2* **<20 ms** → intensify chelation; **<10 ms**→ urgent combination therapy (highest heart-failure risk)
DEXA bone densitometry[9]	77080; Medicare covers q2 years	Every **1–2 years**	T-score **≤−2.5** → bisphosphonates + vitamin D + calcium; fracture risk compounded in older adults

ABBREVIATIONS: CPT = Current Procedural Terminology; CBC = complete blood count; RBC = red blood cell; MCV = mean corpuscular volume; Hb = hemoglobin; HbA_2 = hemoglobin A2; IDA = iron-deficiency anemia; MRI = magnetic resonance imaging; DEXA = dual-energy x-ray absorptiometry; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia

Subtle Early Signs in Adults

SUBTLE SIGN IN OLDER ADULTS	WHAT IT MAY SIGNAL	ACTION
Microcytic anemia not responding to iron[7]	Previously undiagnosed thalassemia trait or HbH disease misattributed to IDA	**Obtain ferritin + electrophoresis before further iron**; add genetic testing if alpha suspected
New exertional dyspnea or reduced exercise tolerance[12]	Iron-overload cardiomyopathy emerging on a background of age-related heart disease	**Echocardiogram + cardiac MRI T2*** to separate iron-mediated from age-related dysfunction
Unexplained fragility fracture or back pain[13]	Thalassemic osteopathy (lumbar osteoporosis **50.7–74.1%**) compounded by age-related bone loss	DEXA; assess for vertebral fracture; treat per **osteoporosis pathway**

SUBTLE SIGN IN OLDER ADULTS	WHAT IT MAY SIGNAL	ACTION
New glucose intolerance, hypothyroid or hypogonadal symptoms[4]	Endocrine iron deposition overlapping age-related endocrine decline	Annual TSH, fasting glucose/ HbA1c, gonadal hormones, calcium/PTH; endocrinology referral if abnormal
Rising ferritin in a patient labeled "trait"[11]	Mislabeled HbH disease or NTDT with absorptive iron loading, **not benign trait**	Re-stage with genetic testing and liver MRI; reconsider chelation

ABBREVIATIONS: IDA = iron-deficiency anemia; MRI = magnetic resonance imaging; T2* = transverse relaxation time; DEXA = dual-energy x-ray absorptiometry; TSH = thyroid-stimulating hormone; HbA1c = glycated hemoglobin; PTH = parathyroid hormone; HbH = hemoglobin H; NTDT = non-transfusion-dependent thalassemia

Geriatric Risk Factors

RISK FACTOR	RISK SIGNAL	WHY IT MATTERS IN OLDER ADULTS
Advancing age[11]	One of the **most important** risk factors for complications	**Vascular, hepatic, endocrine, and malignant complications accumulate** over decades of disease
Iron overload (ferritin >800 ng/ mL; liver iron >5 mg/g)	Hepatic fibrosis, HCC, endocrine and bone disease; in TDT, ferritin **>1000 µg/L** raises morbidity and mortality[11]	**Cumulative iron burden after 40–60 years** of disease is far higher than in the textbook young patient
Cardiac iron (T2* <10 ms)	Strongest predictor of heart failure; myocardial siderosis in **~25%** and cardiac complications in **~42%** of TDT[14]	**Iron cardiomyopathy overlaps with age-related HTN, CAD, and atrial fibrillation**, complicating diagnosis
Prior splenectomy[11]	**4–5-fold** higher venous thrombosis risk in NTDT; thrombotic events **4.38×** more frequent in NTDT than TDT	**Compounds age-related VTE risk** and confers lifelong OPSI risk from encapsulated organisms
Osteoporosis	Lumbar osteoporosis **50.7–74.1%;**[13] osteopenia/osteoporosis the most common complication (**69.8%**) in one adult cohort[15]	Adds to **age-related bone loss and hypogonadism**, producing very high fracture risk
Hepatitis C co-infection (historical transfusions)[5]	Accelerates hepatic fibrosis and HCC risk in older transfused patients	Warrants AFP + ultrasound surveillance in those **≥40 with cirrhosis or HCV**

RISK FACTOR	RISK SIGNAL	WHY IT MATTERS IN OLDER ADULTS

ABBREVIATIONS: HCC (clinical) = hepatocellular carcinoma; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; T2* = transverse relaxation time; HTN = hypertension; CAD = coronary artery disease; VTE = venous thromboembolism; OPSI = overwhelming post-splenectomy infection; AFP = alpha-fetoprotein; HCV = hepatitis C virus

Diagnostic Thresholds (TIF/AHA Staging)

TEST/INDEX	THRESHOLD	INTERPRETATION
CBC — mean corpuscular volume	MCV **<80 fL**, hypochromic, with normal or elevated RBC count and normal RDW[7]	**Microcytic, hypochromic anemia** disproportionate to mild Hb reduction suggests thalassemia over IDA
Serum ferritin[7]	Normal or elevated in microcytic anemia	Points away from IDA and toward thalassemia; **the best initial discriminating test**
Hemoglobin electrophoresis (HbA_2)	HbA_2 **>3.5%**[10]	Characteristic of beta-thalassemia trait; **normal in alpha-thalassemia** — a critical diagnostic gap
Mentzer Index (MCV/RBC count)	**<13** suggests thalassemia **≥13** suggests IDA[7]	Useful screen (sensitivity **74–100%**, specificity **63–88%** for beta-trait); not definitive[16]
Cardiac iron (T2* MRI, AHA 2013)	>20 ms normal 10–20 ms moderate **<10 ms severe**[12]	**Directly guides chelation intensit**y; the most widely used cardiac staging tool
Liver iron concentration (R2/R2* MRI)	<5 mg/g acceptable 5–15 mg/g moderate **>15 mg/g** severe[11]	**Guides chelation**; severe loading predicts progressive fibrosis and cardiac mortality
Complication Risk Score (CoRS, Vitrano 2021)	Validated on **7,910** patients; AUC **80–84.5%**across TDT and NTDT models[17]	**Stratifies low/intermediate/high/very-high complication risk**; not yet widely adopted in US practice
TDT vs. NTDT classification (TIF)[4]	Based on need for **regular lifelong transfusion**	Primary management framework; categories are fluid and may shift over time or with new therapy

TEST/INDEX	THRESHOLD	INTERPRETATION

ABBREVIATIONS: CBC = complete blood count; MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width; Hb = hemoglobin; HbA_2 = hemoglobin A2; IDA = iron-deficiency anemia; MRI = magnetic resonance imaging; T2* = transverse relaxation time; AHA = American Heart Association; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; TIF = Thalassemia International Federation

Clues to Dig Deeper

SURFACE FINDING	CLUE TO DIG DEEPER	NEXT STEP
"Iron-deficiency anemia" that never corrects[7]	Normal/high ferritin with persistent microcytosis is not IDA	**Stop empiric iron**; obtain electrophoresis and, if alpha suspected, genetic testing
Normal hemoglobin electrophoresis but persistent microcytosis[10]	Electrophoresis is normal in alpha-thalassemia trait/carrier states	**Order genetic (DNA) testing** (S3845) — the only reliable confirmation for alpha
A chart label of "thalassemia minor" in a symptomatic patient[18]	HbH disease is symptomatic but is often mislabeled as trait	**Re-confirm genotype**; HbH (3-gene deletion) is alpha-thalassemia disease, not trait
Ferritin rising despite "on chelation"[11]	Suggests non-adherence or chelation failure rather than disease progression	Review adherence and dosing; rapid rise **(>2500 ng/mL or doubling in 3 months)** needs urgent hematology review
NTDT patient who has never been transfused with iron overload[11]	Iron loading in NTDT comes from increased GI absorption, not transfusion	**Monitor ferritin and liver MRI**; code overload as E83.118; consider chelation

ABBREVIATIONS: IDA = iron-deficiency anemia; HbH = hemoglobin H; NTDT = non-transfusion-dependent thalassemia; GI = gastrointestinal; MRI = magnetic resonance imaging

Common Oversights

CLINICAL OVERSIGHT	CONSEQUENCE	BETTER PRACTICE
Treating persistent microcytic anemia with empiric iron[7]	**Accelerates iron overload** (especially in NTDT)and the cardiac, hepatic, and endocrine complications that follow	**Confirm ferritin + electrophoresis** (and genetic testing for alpha) **before any iron**

CLINICAL OVERSIGHT	CONSEQUENCE	BETTER PRACTICE
Accepting a normal electrophoresis as ruling out thalassemia[10]	Misses alpha-thalassemia, including HbH disease, the most commonly missed form	**Pursue genetic DNA testing when microcytosis persists** with a normal electrophoresis
Deferring annual cardiac and hepatic iron imaging[9,12]	Cardiac siderosis **(T2* <10 ms)** is the leading mortality driver and is silent until late	Schedule **annual cardiac MRI T2*** and **liver R2/R2*** in all adult TDT patients
Overlooking thrombosis risk in splenectomized NTDT patients[11]	**4–5-fold** venous thrombosis risk; pulmonary hypertension and silent cerebral infarcts go undetected	**Stratify thrombotic risk at surgery**, admission, and pregnancy; consider prophylaxis
Treating thalassemia as "anemia" alone in older adults[4]	Endocrinopathy, osteoporosis, and hepatic disease accumulate undetected for years	Run a **structured annual multisystem surveillance review** across cardiac, hepatic, endocrine, and bone domains
Applying pediatric/young-adult protocols unchanged to patients >65[9]	Misses geriatric needs — fall risk, lower osteoporosis thresholds, cardiac comorbidity overlap	**Individualize monitoring intensity** and integrate fall-risk and depression screening

ABBREVIATIONS: NTDT = non-transfusion-dependent thalassemia; TDT = transfusion-dependent thalassemia; HbH = hemoglobin H; MRI = magnetic resonance imaging; T2* = transverse relaxation time

Key Differentials in Elderly

DIFFERENTIAL	DISTINGUISHING FEATURES	CONFIRMATORY STEP
Iron-deficiency anemia[7]	Low ferritin, high RDW, Mentzer Index **≥13**; corrects with iron	**Serum ferritin** (low in IDA, normal/high in thalassemia); iron studies
Anemia of chronic disease/ inflammation[19]	Normal-to-high ferritin from inflammation, but with low/normal RBC count, not the high count of trait	**Inflammatory markers**, ferritin trend in clinical context; electrophoresis if microcytosis persists
Myelodysplastic syndrome[20]	Macrocytic or normocytic with dysplasia/cytopenias, typically older onset; not lifelong microcytosis	**Peripheral smear** and, if indicated, **marrow evaluation**

DIFFERENTIAL	DISTINGUISHING FEATURES	CONFIRMATORY STEP
Sideroblastic anemia[21]	Ring sideroblasts; dimorphic RBC population; may be acquired in older adults	**Marrow iron stain**; rule out **before** attributing microcytosis to trait
Sickle-cell thalassemia[22]	Vaso-occlusive features; distinct genotype (beta-zero vs. beta-plus)	**Electrophoresis + genetic testing**

ABBREVIATIONS: RDW = red cell distribution width; RBC = red blood cell; IDA = iron-deficiency anemia

Comorbidity Screening

COMORBIDITY DOMAIN	SCREENING APPROACH
Cardiac (iron cardiomyopathy, arrhythmia)[12]	Annual echocardiogram + ECG; cardiac MRI T2*; **watch for new atrial fibrillation**
Endocrine (diabetes, thyroid, gonadal, parathyroid)[4]	Annual TSH, fasting glucose/HbA1c, gonadal hormones, calcium/PTH
Hepatic (fibrosis, cirrhosis, HCC)[9]	Liver MRI, LFTs; AFP + ultrasound **q6–12 mo if ≥40** with cirrhosis or HCV
Bone (osteoporosis, fracture)[23]	**DEXA** every **1–2 years**; assess fall risk and vitamin D
Thromboembolic[11]	Risk-stratify at admission, surgery, pregnancy; higher risk post-splenectomy
Mental health[24]	Annual **PHQ-9/GAD-7**; psychosocial burden is high but under-addressed

ABBREVIATIONS: ECG = electrocardiogram; MRI = magnetic resonance imaging; T2* = transverse relaxation time; TSH = thyroid-stimulating hormone; HbA1c = glycated hemoglobin; PTH = parathyroid hormone; LFTs = liver function tests; AFP = alpha-fetoprotein; HCV = hepatitis C virus; HCC = hepatocellular carcinoma; DEXA = dual-energy x-ray absorptiometry; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder-7; HEDIS = Healthcare Effectiveness Data and Information Set; DSF = Depression Screening and Follow-Up

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

- **Acute decompensated heart failure** — dyspnea, orthopnea, edema in a patient with known cardiac iron overload
  → Urgent continuous **IV deferoxamine plus oral deferiprone**
- **Severe symptomatic anemia** (Hb <5 g/dL) with hemodynamic instability, syncope, or chest pain
  → Emergent transfusion
- **Acute hemolytic crisis** — sudden Hb drop, jaundice, dark urine; particularly in **HbH disease** during febrile illness
  → Emergency evaluation
- **Sepsis in a splenectomized patient (OPSI)** from encapsulated organisms — any fever **>38.5°C** is an emergency
  → Immediate evaluation and empiric antibiotics
- **Agranulocytosis on deferiprone** (ANC <500/µL)
  → Discontinue immediately; begin infection workup and **G-CSF**

⚠ RED FLAG — URGENT (24-72 HOURS)

- **Cardiac T2* <10 ms** — highest risk for heart failure and arrhythmia
  → Intensified chelation; same-day hematology or cardiology contact
- **New arrhythmia** (atrial fibrillation, ventricular ectopy) suggesting siderosis progression
  → Urgent cardiology and hematology contact
- **Acute thromboembolic event** — DVT, PE, or stroke; especially in post-splenectomy patients or those on luspatercept
  → Same-day evaluation and anticoagulation assessment
- **Rapidly rising ferritin** (>2,500 ng/mL or doubling within 3 months) suggesting chelation failure or non-adherence
  → Urgent hematology contact; reassess chelation regimen
- **Acute renal injury on deferasirox** — creatinine ≥33% above baseline
  → Interrupt therapy immediately and reassess with hematology

AAVBC PERSPECTIVE

*AAVBC encourages primary care providers to **consider thalassemia** in the differential diagnosis of any patient presenting with persistent microcytic anemia **before initiating empiric iron supplementation**. Thalassemia produces a hypochromic, microcytic CBC picture that is **indistinguishable from iron-deficiency anemia on routine laboratory***

> ***review**, and iron supplementation in a thalassemia patient accelerates iron overload, which is a potentially **organ-damaging complication**.*
> ***The appropriate first step is thalassemia screening**, including CBC with RBC indices and hemoglobin electrophoresis. When alpha-thalassemia is suspected, DNA analysis is required, as electrophoresis cannot detect alpha-thalassemia trait and may appear entirely normal. Clinical suspicion should be elevated when **MCV is low but RBC count is normal or elevated, when a positive family history is present, or when the patient has Mediterranean, South or Southeast Asian, Middle Eastern, or African ancestry**. Iron overload can also develop in non-transfusion-dependent thalassemia through increased gastrointestinal absorption, independent of any transfusion history, and should be monitored accordingly. **This helps ensure the right diagnosis is established for the right patient at the right time.***

3 MEAT DOCUMENTATION ESSENTIALS

Each encounter should document the subtype, transfusion status (TDT vs. NTDT), and active complications under management. Thalassemia is a lifelong condition with multisystem complications that accrue over time; a note that records only "history of thalassemia" without addressing active clinical complexity does not meet documentation standards.

Case vignette: A female patient, 71, with transfusion-dependent beta-thalassemia is seen for an annual review. Her note records pre-transfusion Hb 9.2 g/dL, serum ferritin 1,840 ng/mL on deferasirox, a cardiac MRI T2 of 14 ms, and a DEXA T-score of −2.7. The clinician documents "D56.1 beta-thalassemia (TDT), transfusional iron overload **(E83.111)**, iron cardiomyopathy monitored by T2* **(I43)**, and osteoporosis **(M81.0)**," with the chelation plan adjusted and endocrine labs ordered.*

MONITOR:"Transfusion-dependent beta-thalassemia, annual review. Pre-transfusion Hb **9.2 g/dL** — stable at transfusion target. Serum ferritin **1,840 ng/mL** on deferasirox — trending down from **2,210 ng/mL** at last visit; chelation response being tracked. Cardiac MRI T2* **14 ms** (date) — above the **<10 ms** high-risk threshold; mild-to-moderate cardiac iron burden. LIC not remeasured this cycle. LFTs within normal limits; renal function stable on current deferasirox dose — creatinine at baseline. DEXA T-score **−2.7** (date) — meets osteoporosis threshold. Endocrine panel ordered this visit. Functional status: independent ADLs; G-8 score pending."

EVALUATE: "Ferritin trajectory suggests adequate chelation response; non-adherence or chelation failure less likely given downward trend. Cardiac T2* **14 ms** — not in the highest-risk zone (**<10 ms**) but warrants continued annual cardiac MRI surveillance; no new dyspnea, palpitations, or exertional limitation reported. DEXA T-score **−2.7** consistent with thalassemia-related bone disease driven by ineffective erythropoiesis and cumulative iron deposition; bisphosphonate eligibility reviewed. Endocrine labs pending — prior hypogonadism and subclinical hypothyroidism on problem list; results will determine dose adjustment."

ASSESS: "Beta-thalassemia, transfusion-dependent (**D56.1**); transfusional iron overload (**E83.111**) — ferritin **1,840 ng/mL**, actively chelated with deferasirox; iron cardiomyopathy under T2* surveillance (**I43**) — T2* **14 ms**, no decompensation; osteoporosis (**M81.0**) — T-score **−2.7**, bisphosphonate initiated; hypothyroidism (**E03.9**) — replacement dose under review pending labs; hypogonadism (**E29.1**) — endocrine co-management ongoing. Comorbidities: essential hypertension (**I10**); CKD stage 2 (**N18.2**) — renal function monitored given deferasirox use."

TREAT: "Transfusion schedule maintained at **q3–4 weeks** with pre-transfusion Hb target **≥9.0 g/dL**. Deferasirox dose adjusted based on ferritin trend and renal function — dose confirmed in chart; renal function recheck in 4 weeks. Bisphosphonate initiated for osteoporosis (T-score **−2.7**); calcium **1,200 mg/day** and vitamin D **800 IU/day** continued. Endocrine labs resulted — levothyroxine and testosterone replacement doses to be reviewed at follow-up. Surveillance plan: serum ferritin and CBC q3 months; LFTs and creatinine q3 months on deferasirox; cardiac MRI T2* annually; DEXA every 2 years; endocrine panel annually. Referrals: hematology co-management ongoing; endocrinology follow-up scheduled; bone health confirmed with ordering provider. ACP documented (CPT **99497**): surrogate named, goals of care discussed given progressive multisystem disease trajectory."

Clinical Documentation Elements

- **Thalassemia type and genotype:** Alpha vs. beta, and where known the genotype (e.g., beta-zero vs. beta-plus, 3-gene-deletion HbH disease)
- **Transfusion status:** Explicitly **TDT or NTDT**, with transfusion interval and pre-transfusion Hb target for TDT patients
- **Iron-overload status and its mechanism:** Transfusional **(E83.111)** versus absorptive in NTDT **(E83.118)**, with the most recent ferritin and organ iron measures
- **Active complications by organ system:** Cardiac **(I43)**, hepatic **(K74.60/C22.0)**, bone **(M81.0)**, endocrine **(E03.9, E13.–)**, and psychiatric (**F32.–/F41.–)** — each coded separately when present
- **Surveillance performed and due:** Cardiac MRI T2*, liver MRI, DEXA, endocrine panel, and infection serology, with dates
- **Current therapy and monitoring requirements:** Chelation agent and the safety monitoring it mandates (e.g., weekly CBC on deferiprone)

Reframing Common Documentation Shortcuts

COMMON DOCUMENTATION SHORTCUT	WHY IT FALLS SHORT	REFRAME THAT REFLECTS COMPLEXITY
"History of thalassemia"	Reads as inactive past history; loses subtype, transfusion status, and active complications	"Transfusion-dependent beta-thalassemia **(D56.1)**, active, with transfusional iron overload **(E83.111)**"
"Thalassemia" with no subtype	Defaults toward unspecified coding and obscures the alpha/beta and TDT/NTDT distinctions that drive care	Name **alpha vs. beta and TDT vs. NTDT** every encounter; cite genetic results when available

COMMON DOCUMENTATION SHORTCUT	WHY IT FALLS SHORT	REFRAME THAT REFLECTS COMPLEXITY
"Anemia, on transfusions"	Frames a multisystem disease as anemia alone and omits iron overload and organ complications	Document the disease plus **each iron-overload** complication being monitored
"Iron overload" without mechanism	Misses the transfusional-vs-absorptive distinction; risks miscoding NTDT overload	Specify **E83.111** (transfusional, TDT) or **E83.118** (absorptive, NTDT)
HbH disease coded as "trait" (D56.3)	**D56.3** maps to no HCC; mislabels a symptomatic condition and loses all complexity documentation	Code HbH disease as **D56.0** alpha thalassemia and document its symptomatic course

ABBREVIATIONS: TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; HbH = hemoglobin H; HCC = Hierarchical Condition Category; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification

DOCUMENTATION IS COMPREHENSIVE CODING

Accurate documentation for thalassemia means **naming the subtype, transfusion status, and each active complication** at every encounter. This ensures that the true complexity of this disease that affects the heart, liver, bones, and endocrine system simultaneously is reflected. Code iron overload and organ-specific complications alongside the primary **D56** code at **every visit**.

4 TREATMENT AND REFERRAL QUICK GUIDE

Treatment is organized by the **TDT versus NTDT framework per Thalassemia International Federation guidelines** (TIF 2021/2017).[11,21] **Transfusion-dependent thalassemia (TDT)** requires lifelong transfusions, typically every 2-5 weeks, combined with iron chelation to prevent transfusional iron overload. **Non-transfusion-dependent thalassemia (NTDT)**requires transfusion only as needed, with chelation initiated once iron overload develops, since these patients absorb iron more efficiently from the gut even in the absence of transfusion. Accurate, complete documentation of active complications at every encounter is essential to guiding this pathway.

Curative options (hematopoietic stem cell transplantation and gene therapy) are generally **not appropriate** in patients aged 65 and older due to conditioning toxicity and graft-versus-host disease risk.

Therapy Escalation Criteria

ESCALATION STEP	TRIGGER/THRESHOLD*	ACTION
Initiate chelation	Ferritin **≥1000 ng/mL** (TDT) or **≥800 ng/mL** (NTDT); or liver iron **>5 mg/g**[11]	**Start first-line oral deferasirox**; classify TDT vs. NTDT and set monitoring
Intensify chelation	Cardiac T2* **10–20 ms** or liver iron **>15 mg/g**[12]	**Increase chelation**; add second agent if cardiac iron is **rising**
Urgent combination chelation	Cardiac T2* **<10 ms**[25]	Combination deferoxamine + deferiprone; **urgent hematology/cardiology** consult
Adjust transfusion	Pre-transfusion Hb persistently below target (9–10.5 g/dLTDT); NTDT Hb **<7 g/dL**with symptoms[11]	**Revise transfusion interval**; refer hematology
Add luspatercept	Adult TDT with high transfusion burden despite optimal support[21]	**Hematology-led**; monitor BP and thromboembolic events
Refer for curative therapy	Younger, well-chelated TDT with suitable donor; not generally appropriate at **≥65**[4]	**Hematology referral** for HSCT or gene-therapy candidacy discussion

ABBREVIATIONS: TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; T2* = transverse relaxation time; Hb = hemoglobin; BP = blood pressure; HSCT = hematopoietic stem cell transplantation
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

TIF-Aligned Treatment by Transfusion Status and Patient Profile

PATIENT PROFILE	RECOMMENDED APPROACH*	NOTES FOR OLDER ADULTS
TDT (regular transfusions required)	Transfuse every **2–5 weeks** to pre-transfusion Hb **9–10.5 g/dL**(11–12 g/dL if cardiac disease); chelate to organ-iron targets[11]	**Individualize** Hb target to cardiac tolerance and fluid status; **no thalassemia-specific geriatric transfusion guideline exists**

PATIENT PROFILE	RECOMMENDED APPROACH*	NOTES FOR OLDER ADULTS
NTDT (intermittent or no transfusion)	Transfuse for symptomatic anemia (Hb **<7 g/dL**), pregnancy, surgery, or worsening complications; folic acid supplementation[7]	Iron loading still occurs from absorption — monitor ferritin and liver MRI **even without transfusion**
Iron chelation, first-line	**Deferasirox** (Jadenu) oral, 14 mg/kg/dayTDT/7 mg/kg/ dayNTDT[26]	Contraindicated if **eGFR <40**; reduce **50%** at eGFR 40–60; review polypharmacy (CYP2C8/CYP1A2)
Iron chelation, cardiac/second-line	**Deferiprone** (Ferriprox) **75–100 mg/kg/day**; **deferoxamine** (Desferal) **20–60 mg/kg** infusion for acute cardiac iron[27]	Weekly CBC on deferiprone (agranulocytosis); deferoxamine adherence is hard in older adults
Transfusion-burden reduction	**Luspatercept** (Reblozyl) **1.0 mg/kgSC** q3 weeks, titrate to **1.25 mg/kg**[21]	BELIEVE: **21.4%** vs 4.5% achieved **≥33**%transfusion reduction (P<0.001); watch thrombosis and hypertension; Durability is sustained through **192** weeks with no new safety signals[21]

ABBREVIATIONS: TIF = Thalassemia International Federation; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; Hb = hemoglobin; HbF = fetal hemoglobin; MRI = magnetic resonance imaging; eGFR = estimated glomerular filtration rate; SC = subcutaneous; CBC = complete blood count; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL — HYDROXYCHLOROQUINE IS A PRIMARY-CARE MEDICATION

Do not prescribe empiric iron for persistent microcytic anemia without first excluding thalassemia. In thalassemia, **particularly NTDT** where gastrointestinal iron absorption is already elevated, iron supplementation accelerates iron overload and **increases the risk of cardiac, hepatic, and endocrine complications**. Confirm serum ferritin and hemoglobin electrophoresis before prescribing iron. For suspected alpha-thalassemia, genetic testing is required.

Non-Pharmacologic Care and Supportive Interventions

SUPPORTIVE INTERVENTION	RATIONALE	PRIMARY-CARE ACTION
Avoid iron-fortified foods and iron-containing multivitamins[11]	Increased GI iron absorption in thalassemia (especially NTDT) **worsens overload**	Counsel on **iron avoidance** unless documented coexisting iron deficiency
Vitamin D and calcium; bisphosphonate when indicated[23]	Lumbar osteoporosis prevalence **50.7–74.1%**; high fracture risk	Supplement and coordinate with **DEXA results and endocrinology**
Folic acid supplementation (NTDT)[9]	Supports erythropoiesis in non-transfused patients	Prescribe folic acid for NTDT patients
Vaccination + antibiotic prophylaxis (splenectomized)[29]	**Lifelong OPSI risk** from encapsulated organisms	**Ensure pneumococcal, meningococcal, and Hib vaccination**; educate on fever as emergency
Fall-risk and bone-health program (older adults)[30]	Compounded osteoporosis + age-related bone loss	**STEADI fall assessment**; physical therapy; environmental review

ABBREVIATIONS: GI = gastrointestinal; NTDT = non-transfusion-dependent thalassemia; DEXA = dual-energy x-ray absorptiometry; OPSI = overwhelming post-splenectomy infection; Hib = Haemophilus influenzae type b; STEADI = Stopping Elderly Accidents, Deaths and Injuries

Medication Safety and Key Interactions

AGENT/COMBINATION*	STATUS	SAFETY CONCERN AND ACTION
Deferasirox (Jadenu)[26,31]	FDA-approved	Renal toxicity — **contraindicated at eGFR <40**, reduce **50% at 40–60** ; monitor creatinine monthly, LFTs
Deferasirox + NSAIDs/ aspirin[32]	**Caution****	Additive GI mucosal toxicity and bleeding risk — **avoid**; if needed, lowest dose, shortest duration, consider PPI
Deferasirox + nephrotoxic agents (aminoglycosides, IV contrast)[33]	**Caution****	Additive renal injury — hold/dose-reduce before exposure; check creatinine **within 7 days**
Deferasirox + antacids/ CYP3A4 inducers[31]	**Caution****	Antacids and inducers (rifampin, phenytoin) reduce chelation — separate from antacids; monitor ferritin

AGENT/COMBINATION*	STATUS	SAFETY CONCERN AND ACTION
Deferiprone (Ferriprox)[34]	FDA-approved	**Agranulocytosis** — weekly CBC throughout therapy; ANC **<500/µL** → discontinue, begin G-CSF
Deferoxamine (Desferal)[35]	FDA-approved	Retinal/auditory toxicity — annual eye and hearing exams; injection-site reactions; zinc deficiency
Luspatercept (Reblozyl)[36]	FDA-approved (adult TDT)	Thromboembolic events **3.6%** vs 0.9%and hypertension **8.1%** vs 2.8%— monitor BP and thrombosis, especially post-splenectomy
Empiric oral iron in undiagnosed microcytic anemia[11]	**Contraindicated**	**Accelerates iron overload in thalassemia** — never prescribe without excluding thalassemia first

ABBREVIATIONS: FDA = US Food and Drug Administration; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; PPI = proton pump inhibitor; LFTs = liver function tests; CBC = complete blood count; ANC = absolute neutrophil count; G-CSF = granulocyte colony-stimulating factor; BP = blood pressure; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions **Caution combinations are flagged because they are high-risk**

When to Refer

TRIGGER	REFER TO	TIMING
Confirmed or suspected thalassemia disease (not trait)[4]	Hematology (first-line); genetic counseling for family	**At diagnosis**; genetic counseling as indicated
Cardiac T2* <20 ms, new arrhythmia, or declining LVEF[4]	Cardiology + hematology	**Urgent** if T2* <10 ms or new arrhythmia
LIC >15 mg/g, ALT >2× ULN, or HCC suspicion[4]	Hepatology	**Expedited** (within days)
New endocrinopathy (diabetes, thyroid, gonadal)[4]	Endocrinology	Within 1–2 weeks
Fragility fracture or T-score ≤−2.5[4]	Endocrinology or rheumatology	**Expedited**; immediate after fracture
Curative-therapy candidacy questions[4]	Hematology (HSCT/gene therapy)	**Routine**; counsel on age/risk limits at ≥65

ABBREVIATIONS: T2* = transverse relaxation time; LVEF = left ventricular ejection fraction; LIC = liver iron concentration; ALT = alanine aminotransferase; ULN = upper limit of normal; HCC = hepatocellular carcinoma; HSCT = hematopoietic stem cell transplantation

Follow-Up Timing

PARAMETER	INTERVAL	ACTION THRESHOLD
CBC with RBC indices[9]	q3–4 weeks(TDT); q3–4 months(NTDT)	Pre-transfusion Hb below target → adjust transfusion schedule
Serum ferritin[12]	Every 3 months	≥1000 (TDT)/≥800 (NTDT) → chelate **>2500 or doubling in 3 months**[7] → urgent review
Cardiac MRI T2*[12]	Annually	10–20 ms→ intensify **<10 ms → urgent** combination chelation
Liver MRI R2/R2*[4]	Annually	>5 mg/g → chelate **>15 mg/g → aggressive chelation** + hepatology
Creatinine/eGFR (deferasirox)[33]	Weekly for 1st month, then monthly	≥33% rise from baseline → **reduce dose by 7mg/kg**
CBC (deferiprone)[34]	Weekly throughout therapy	ANC <1500/µL → interrupt **<500/µL → discontinue** + G-CSF
DEXA; endocrine panel; Hep B/ C/HIV serology[7]	DEXA q1–2 yr; endocrine annually; serology annually if transfused	**T-score ≤−2.5 → treat**; abnormal endocrine → refer; positive serology → treat

ABBREVIATIONS: CBC = complete blood count; RBC = red blood cell; Hb = hemoglobin; MRI = magnetic resonance imaging; T2* = transverse relaxation time; eGFR = estimated glomerular filtration rate; ANC = absolute neutrophil count; G-CSF = granulocyte colony-stimulating factor; DEXA = dual-energy x-ray absorptiometry; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia

Comorbidity Management — Primary Care Role

COMORBIDITY	PRIMARY-CARE ROLE	COORDINATION
Iron cardiomyopathy/ arrhythmia[12]	Monitor symptoms, BP, ECG; reconcile cardiac meds	Cardiology + hematology for chelation intensification
Secondary diabetes/ endocrinopathy[4]	Annual metabolic and endocrine screening; manage glucose	Endocrinology; code **E13.–** when iron-related
Hepatic disease/HCC risk[11]	LFTs, AFP, ultrasound surveillance in high-risk	Hepatology for cirrhosis or rising AFP

COMORBIDITY	PRIMARY-CARE ROLE	COORDINATION
Osteoporosis[37]	DEXA, vitamin D/calcium, fall-risk program	Endocrinology/rheumatology for fracture or severe loss
Depression/anxiety[38]	Annual PHQ-9/GAD-7; initiate treatment or referral	Behavioral health; document HEDIS DSF follow-up

ABBREVIATIONS: BP = blood pressure; ECG = electrocardiogram; LFTs = liver function tests; AFP = alpha-fetoprotein; HCC = hepatocellular carcinoma; DEXA = dual-energy x-ray absorptiometry; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder-7; HEDIS = Healthcare Effectiveness Data and Information Set; DSF = Depression Screening and Follow-Up

Cost-Smart Options

BRAND (EST. COST)	COST-SMART OPTION	EST. SAVINGS	COST-SMART TIP
Jadenu (deferasirox extended-release) 360 mg daily: ~$7,113/month[39] **Exjade (deferasirox dispersible) 500 mg daily: ~$6,219/month**[40]	**Generic deferasirox**: from ~$306/month to ~$553/month [41]	~$6,560/month vs. Jadenu brand; ~$5,666/month vs. Exjade	Use **generic** when available at specialty pharmacy
Desferal (deferoxamine mesylate) SC 500 mg vials: ~$36/vial brand; estimated ~$2,150/month for typical SC regimen (20 mg/kg/night x 5 nights/week)[42]	**Generic deferoxamine mesylate**: ~$17.53/vial,~$1,050/month	~$1,100/month brand vs. generic	Use **generic**; reserve SC/IV for cardiac iron rescue — not routine maintenance; oral deferasirox preferred for maintenance adherence[43]
Ferriprox (deferiprone) 500 mg tablets: ~$1,337/100 tablets; ~$2,400/month at 3 g/day (6 tablets daily)[44]	**Generic deferiprone tablets: FDA-approved but not commercially available**	—	Chiesi patient assistance program available for eligible patients

BRAND (EST. COST)	COST-SMART OPTION	EST. SAVINGS	COST-SMART TIP
Reblozyl (luspatercept) 75 mg/injection: ~$12,302/ injection; ~$17,200–$19,700/month[45]	No biosimilar available	Up to ~$19,700/month patient cost eliminated via manufacturer program for eligible patients	**Prior authorization required**; confirm TDT/NTDT indication and transfusion-burden threshold before referral; billed under Medicare Part B when administered in clinic
Inpatient management of iron-induced heart failure: ~$20,000–$50,000+/ admission (ICU, vasopressors, IV chelation)[46]	**Annual cardiac MRI T2* surveillance**: ~$600–$1,500/year; ~$50–$125/month amortized[46]	Preventing one heart failure admission saves ~$20,000–$50,000+;	**T2* <10 ms requires intensified chelation** before decompensation; annual **T2* is the single highest-yield preventive investment** in thalassemia care

ABBREVIATIONS: BMS = Bristol Myers Squibb; CBC = complete blood count; GoodRx = GoodRx Holdings Inc.; ICU = intensive care unit; MA = Medicare Advantage; NTDT = non-transfusion-dependent thalassemia; SC = subcutaneous; TDT = transfusion-dependent thalassemia; VBC = value-based care

Patient Education and Adherence

Cover the following topics at education visits and document topics addressed, patient understanding, and caregiver involvement:

- **Chelation adherence** — adherence is the single most important factor in preventing heart, liver, and hormone complications. Oral deferasirox is taken on an empty stomach, 30 minutes before food, at the same time each day. Doses should never be skipped
- **Symptoms requiring prompt reporting** — new or worsening shortness of breath, leg swelling, irregular heartbeat, extreme fatigue, or jaundice should be reported without delay
- **Fever in splenectomized patients** — any fever above **38.5°C** is a medical emergency. Patients and caregivers must understand this threshold and act on it immediately
- **Dietary guidance** — avoid iron-fortified foods and iron-containing supplements unless a coexisting iron deficiency has been confirmed

DOCUMENTATION — PATIENT EDUCATION

Record education topics covered, the patient's demonstrated understanding, and caregiver involvement. Document chelation adherence counseling, fever-as-emergency teaching for splenectomized patients, and dietary iron guidance. **A documented shared plan reflects the coordination work that protects this patient from avoidable complications.**

Quality Metrics Tie-In

MEASURE	PROGRAM	APPLICABILITY TO THALASSEMIA
Controlling High Blood Pressure (HEDIS CBP; MIPS #236)[47]	**Denominator:** patients 18-85 with hypertension (≥2 outpatient visits with HTN diagnosis in MP or year prior) **Numerator:** most recent BP <140/90 mmHg during MP **Exclusions** ESRD, hospice, palliative care, pregnancy	**Hypertension** occurs in **~8%** of patients on luspatercept and is compounded by iron cardiomyopathy; heighten BP monitoring after luspatercept initiation and when T2* MRI identifies cardiac iron loading[21]
Comprehensive Diabetes/ Glycemic Care (HEDIS GSD; MIPS #1)[48]	**Denominator:** patients 18-75 with diabetes (≥2 diagnoses on different service dates in MP or prior year, or diagnosis + dispensed diabetes medication) **Numerator:** most recent HbA1c or GMI during MP (flag >9.0%; inverse measure) **Exclusions:** hospice, palliative care, frailty + advanced illness (≥66)	**Secondary diabetes from pancreatic iron deposition**; code as **E13.–** (other specified) rather than **E11** when iron-related. Note: chronic red cell turnover in thalassemia causes artifactually low HbA1c — fructosamine may be more accurate in transfusion-dependent patients
Osteoporosis Management after Fracture (HEDIS OMW; MIPS #418)[13]	**Denominator:** women 50-85 with a fracture during MP or year prior **Numerator:** BMD test or pharmacotherapy for osteoporosis prescribed within 180 days of fracture **Exclusions:** fractures of finger, toe, face, skull; hospice; frailty + advanced illness (≥66)	**Lumbar osteoporosis** affects thalassemia patients; fracture risk is compounded in older adults. HEDIS OMW and MIPS #418 apply to women only and are triggered only after a fracture — proactive DXA surveillance in thalassemia patients (both sexes, often before age 65) is an internal practice metric with no external measure equivalent

MEASURE	PROGRAM	APPLICABILITY TO THALASSEMIA
Statin Therapy for Cardiovascular Disease (HEDIS SPC; MIPS #438)[14]	**Denominator:** patients with ASCVD diagnosis; OR age ≥20 with LDL-C ≥190 mg/dL or familial hypercholesterolemia; OR age 40-75 with diabetes; OR age 40-75 with 10-year ASCVD risk ≥20% **Numerator:** statin therapy prescribed or active during performance period **Exclusions:** active liver disease, ESRD, hospice, palliative care	**Applies to iron-related cardiomyopathy and age-related ASCVD**; standard risk calculators may underestimate cardiovascular risk in thalassemia given chronic anemia, non-atherogenic cardiac iron loading, and early endocrine comorbidities
Depression Screening and Follow-Up (HEDIS DSF; MIPS #134)[49]	**Denomintor:** all patients ≥12 years seen during the performance period **Numerator:** screened with a standardized tool AND follow-up plan documented if positive **Exclusions:** documented reason for not screening; hospice	High but **under-addressed psychiatric burden** in aging thalassemia patients; PHQ-9 at each relevant encounter; chronic transfusion burden, chelation fatigue, and disease-related functional limitations are independent depression risk factors
Medication Adherence, chronic meds (CMS Star)[50]	**Denominator:** Medicare Part D enrollees dispensed a chronic medication class with ≥2 fills during MP **Numerator:** PDC ≥0.80 for the medication class during MP **Exclusions:** hospice, long-term care, end-stage conditions	No MIPS equivalent; CMS calculates automatically from pharmacy claims — clinicians cannot submit individually. Oral chelation adherence (deferasirox, deferiprone) is the most impactful modifiable factor in thalassemia-related organ damage; poor adherence should trigger shared decision-making review

ABBREVIATIONS: HEDIS = Healthcare Effectiveness Data and Information Set; PDC = proportion of days covered; OMW = Osteoporosis Management in Women who had a fracture; SPC = Statin Therapy for patients with Cardiovascular disease; DSF = Depression Screening and Follow-Up; CMS = Centers for Medicare & Medicaid Services. No HEDIS or CMS Star measure is dedicated specifically to thalassemia; the measures above apply through its comorbidities[29]

QUALITY OUTCOME

When the care team documents **subtype, transfusion status, and each active complication** (such as iron cardiomyopathy, hepatic fibrosis, endocrinopathy, osteoporosis) and **maintains surveillance on schedule**, patients experience **fewer avoidable hospitalizations, earlier detection of organ-threatening complications, and more appropriate treatment intensity** calibrated to their functional status.

AAVBC PERSPECTIVE

*AAVBC supports an active, longitudinal primary care role in thalassemia management, recognizing that **standard guidelines are largely oriented toward pediatric and young adult populations and do not adequately address the clinical complexity of aging patients with a lifelong genetic condition**.*
*In the geriatric population, the management framework shifts from transfusion protocols and growth milestones to **cumulative iron overload, organ aging, and multimorbidity**. Diabetes, hypothyroidism, osteoporosis, pulmonary hypertension, and cardiac arrhythmias each requiring active co-management rather than specialist deferral.*
*AAVBC encourages primary care providers to **take ownership of** chelation therapy adherence **monitoring**, renal and hepatic **function tracking**, and **coordination** of annual audiological and ophthalmological **evaluations** as part of a **structured longitudinal care plan**.*
***Psychosocial burden** (including depression, anxiety, and caregiver fatigue) is a meaningful and **underaddressed dimension of aging** with a chronic genetic condition, therefore, mental health screening also belongs in the primary care encounter. As patients age and travel to specialized hematology centers becomes less feasible, the primary care provider becomes the central coordinator of a condition that requires continuous, integrated oversight. This helps ensure the right patients receive the right longitudinal care within the right clinical framework.*

5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

ICD-10	DOCUMENTATION	SPECIFICITY REQUIREMENT
D56.0	**Alpha thalassemia** (includes HbH disease) — **No HCC** in FY2026 mapping	Document gene-deletion count (1–4) and genetic results; **HbH disease is D56.0, never D56.3**

ICD-10	DOCUMENTATION	SPECIFICITY REQUIREMENT
D56.1	**Beta thalassemia** (major/TDT and intermedia/NTDT) → **HCC 108**	Specify major vs. intermedia and **TDT vs. NTDT** status
D56.2/D56.5	**Delta-beta**/hemoglobin E-beta thalassemia → **HCC 108**	Confirm via electrophoresis and genetics; **D56.5** — document severity and transfusion status
D56.3/D56.4	**Thalassemia minor** (trait)/HPFH — **No HCC** in FY2026 mapping	Trait/carrier only; never apply to symptomatic disease
D56.8/D56.9	Other/unspecified thalassemia — **No HCC** in FY2026 mapping	Avoid **D56.9** when a subtype is determinable; specify alpha vs. beta whenever the record supports it
D57.42/D57.44	**Sickle-cell thalassemia,** beta-zero → **HCC 107**; beta-plus → **HCC 108**	Document genotype explicitly; beta-zero carries the higher complexity weight
E83.111/E83.118	**Iron overload** — transfusional (TDT)/ absorption-related (NTDT)	Code separately at every encounter; specify mechanism; routinely undercoded

ABBREVIATIONS: ICD-10 = International Classification of Diseases, 10th Revision; HCC = Hierarchical Condition Category; RAF = Risk Adjustment Factor; CNA = Community Non-Dual Eligible, Aged; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; HbH = hemoglobin H; HPFH = hereditary persistence of fetal hemoglobin; FY = fiscal year

Annual Clinical Review and Confirmation

- **Annual Clinical Review and Confirmation:** Thalassemia is a chronic condition that must be re-confirmed and re-documented each year. At the annual review, restate the subtype (alpha vs. beta), the genotype where known, and the current transfusion status (TDT vs. NTDT) — this status can change over time and with therapies such as luspatercept, so it should never be carried forward unexamined
- **Confirm and document each active complication by organ system:** iron overload and its mechanism (**E83.111** transfusional vs. **E83.118** absorptive), cardiomyopathy **(I43)**, cirrhosis **(K74.60)** or hepatocellular carcinoma **(C22.0)**, osteoporosis **(M81.0)**, endocrinopathies **(E03.9, E13.–)**, and depression or anxiety **(F32.–/F41.–)**. Each is a separately documentable condition that reflects real clinical work
- **Record the surveillance performed and due during the visit:** cardiac MRI T2*, liver MRI, DEXA, endocrine panel, and infection serology — with dates and results. A structured annual review that covers all complication domains in one encounter closes the documented real-world gap between guideline-recommended surveillance and actual practice
- **Confirm the chelation and transfusion plan and the monitoring each agent requires** (for example, weekly CBC on deferiprone and monthly creatinine on deferasirox),

and reconcile the full medication list given the polypharmacy typical of older thalassemia patients

Good Documentation — EHR Tips

EHR TIP	HOW TO APPLY	WHY IT HELPS
Problem-list specificity	Replace “thalassemia” with the specific subtype and TDT/NTDT status on the problem list	Prevents default to unspecified coding and carries the distinction into every note
Iron-overload SmartPhrase	Build a phrase prompting **E83.111** vs. **E83.118** with current ferritin and organ-iron values	Documents the most commonly missed comorbidity at each encounter
Annual surveillance template	Single template listing cardiac MRI, liver MRI, DEXA, endocrine panel, serology with due dates	Reduces fragmented care and missed screenings
Coding-trap alert	Flag any **D56.3** entry to confirm it is true trait, not HbH disease	Stops the highest-impact undercoding error before the claim is filed
Chelation-monitoring reminder	Link deferiprone orders to a weekly-CBC reminder and deferasirox to monthly renal labs	Prevents agranulocytosis and renal-injury safety lapses

ABBREVIATIONS: EHR = electronic health record; TDT = transfusion-dependent thalassemia; NTDT = non-transfusion-dependent thalassemia; MRI = magnetic resonance imaging; DEXA = dual-energy x-ray absorptiometry; CBC = complete blood count; HbH = hemoglobin H

Brief Case Examples

SUCCESS — Subtype, NTDT Status, and Iron Mechanism All Documented

Patient: Male patient, 68, with hemoglobin E-beta thalassemia, non-transfusion-dependent (NTDT), seen for annual review.

Documentation: Note records “**D56.5** hemoglobin E-beta thalassemia (NTDT); absorptive iron overload **(E83.118)**, ferritin 920 ng/mL; osteoporosis **(M81.0)**, T-score −2.6.” Liver MRI, DEXA, and endocrine panel dates recorded; folic acid and chelation plan documented.

Outcome: The record reflects the full multisystem burden — subtype, NTDT status, absorptive (not transfusional) iron overload, and active bone disease — supporting accurate complexity documentation and a clear surveillance plan.

PITFALL — HbH Disease Miscoded as Trait, Empiric Iron Continued

Documentation as written: "Thalassemia minor **(D56.3)**, stable. Continue iron supplement for anemia."

Consequence: The patient in fact has HbH disease (3-gene-deletion alpha-thalassemia), a symptomatic condition. Coding it as **D56.3** maps to no HCC, and empiric iron worsens the patient's iron overload.

RAF Impact: HbH disease should be coded **D56.0** alpha thalassemia; the "trait" miscode loses all condition documentation and, more importantly, the empiric iron is clinically harmful.

Fix: Re-confirm genotype, code **D56.0**, stop empiric iron, obtain ferritin and liver MRI, and document the active iron overload **(E83.118).**

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