KDIGO 2026 - Anemia in CKD: Clinical Practice Guide

Based on: Babitt JL et al. KDIGO 2026 Clinical Practice Guideline for Anemia in CKD. Kidney Int. 2026;109(1S):S1–S99 | Fully Published

1. Definitions & Diagnostic Workup

Anemia thresholds remain unchanged from WHO/KDIGO 2012: Hb <13 g/dL in adult men, <12 g/dL in adult women, with age-specific thresholds in children.

New 2026 Terminology — Critical Update:

Old Term (2012)	New Term (2026)	Mechanistic Rationale
Absolute iron deficiency	**Systemic iron deficiency**	TSAT <20% + ferritin <100 ng/mL (non-dialysis) or <200 ng/mL (G5HD)
Functional iron deficiency	**Iron-restricted erythropoiesis**	Low TSAT despite normal/high ferritin — reflects hepcidin-mediated sequestration

Expanded Initial Workup (2026):

The 2012 guide focused narrowly on iron and EPO. The 2026 guideline mandates a **multi-cause evaluation** before attributing anemia to CKD alone:

Test Category	Parameters
Hematologic	CBC + differential, reticulocyte count, peripheral smear
Iron stores	Ferritin, TSAT
Inflammation	CRP (to contextualize ferritin)
Nutritional	Vitamin B12, folate
Endocrine	TSH
Hematologic malignancy screening	SPEP, serum free light chains (SFLC), BJP (as warranted)
Other	Fecal occult blood, haptoglobin, LDH, PTH as clinically indicated

Structured Monitoring Schedule (NEW):

CKD Stage	Minimum Monitoring Frequency
G3	≥ Annually
G4	Twice per year
G5 / G5D (HD or PD)	Every 3 months

2. Iron Management

a. Initiation Thresholds

Population	Ferritin	TSAT	Action
CKD G5 Hemodialysis	≤ 500 ng/mL	≤ 30%	Start IV iron — **proactive** strategy (~400 mg/month) [Rec 2.1, 2.2 —

Population	Ferritin	TSAT	Action
			2D]
Non-dialysis CKD / PD	< 100 ng/mL	< 40%	Start iron (oral or IV per preference & severity) [Rec 2.3, 2.4 — 2D]
Non-dialysis CKD / PD (alt)	100–300 ng/mL	< 25%	Start iron; switch oral → IV if insufficient response after 1–3 months
Profound iron deficiency (no anemia)	< 30 ng/mL	< 20%	**Consider** iron even without anemia — non-hematologic benefits recognized [PP]
⛔ **WITHHOLD iron — all patients**	**> 700 ng/mL**	**≥ 40%**	Suspend routine iron. Also withhold during active systemic infection [PP 2.2]

Key Conceptual Shift: The 2012 guideline used a *reactive* iron strategy (treat when deficient). KDIGO 2026 adopts a *proactive* iron maintenance strategy in HD patients, driven by the **PIVOTAL trial** (N=2,141), which showed that high-dose proactive IV iron reduced the composite CV endpoint (HR 0.85), lowered ESA requirements by ~25%, and did not increase infection risk. This single trial is the backbone of multiple iron-related changes in 2026.

Raising the Withholding Ceiling: The ferritin ceiling for withholding iron was raised from >500 ng/mL (2012) to **>700 ng/mL** (2026), based on PIVOTAL safety data showing no harm up to this threshold.

b. IV Iron Administration

Parameter	KDIGO 2026 Guidance
Test dose	❌ NOT required with ***modern formulations***
Premedication	Corticosteroids / antihistamines — NOT routinely recommended
Anaphylaxis incidence	< 1 : 200,000 administrations (modern formulations)

Parameter	KDIGO 2026 Guidance
Mandatory safety requirement	Administer ONLY where acute hypersensitivity & hypotension can be managed; observe ≥ 30 min post-infusion
Exception	Prior serious reaction to a specific formulation → switch to an alternative preparation
Hypophosphatemia warning (NEW)	Monitor phosphate with ferric carboxymaltose, saccharated iron oxide, and iron polymaltose — risk of iFGF23-mediated hypophosphatemia

The removal of the routine test dose applies specifically to **modern high-molecular-weight-free formulations**: ferric carboxymaltose, iron isomaltoside/ferric derisomaltose, ferumoxytol. This is a major clinical workflow change.

Iron Monitoring on Therapy: Check Hb, ferritin, TSAT every 1–3 months in G5HD; every 3 months in non-dialysis CKD/PD. Increase frequency if: starting/increasing ESA or HIF-PHI, recent blood loss, hospitalization, or ferritin overshoot.

3. ESA Therapy

a. Pre-Treatment Workup — Expanded

Before initiating ESA, KDIGO 2026 requires addressing **all correctable causes of anemia** — not just iron deficiency. This includes: iron, vitamin B12, folate, thyroid dysfunction, suboptimal dialysis adequacy, active inflammation, and occult blood loss. [PP 3.1.2]

b. Initiation Thresholds

Population	Initiation Hb	Notes
G5D (HD/PD)	≤ 9.0–10.0 g/dL	Lower threshold (9.0) for higher-risk patients: prior stroke, vascular access thrombosis history [Rec 3.2.1 — 2D]
Non-dialysis CKD	8.5–10.0 g/dL (individualized)	Factor in: symptoms, CV risk, patient preference, transfusion harm avoidance [Rec 3.2.2 — 2D]

c. Hb Target & Dose Adjustment

Parameter	KDIGO 2026
Hb target upper limit	**< 11.5 g/dL** [Rec 3.3.1 — 1D] — Do NOT target normal-range Hb
Dose adjustment frequency	No more frequently than every **4 weeks**
Rapid rise response	Hb rise > 1 g/dL in 2 weeks → reduce ESA dose by **25–50% immediately**
Response to Hb >11.5	**Dose reduction** (not discontinuation)

The Hb target of <11.5 g/dL carries a **Grade 1D** — the strongest recommendation grade despite very low evidence certainty. This reflects the consistent CV and stroke harm signals from the CHOIR and TREAT trials when targeting normal hemoglobin, making this a firm safety ceiling regardless of evidence quality.

d. When to Suspend ESA

ESA (and HIF-PHI) should be **suspended** in: acute stroke, myocardial infarction, thromboembolic events (DVT, PE), vascular access thrombosis, or newly diagnosed malignancy. Restart decision via shared decision-making.

ESA Hyporesponsiveness — Formal 2026 Definition: Failure to reach target Hb despite ESA doses 2–3× higher than typical. This is now recognized as a **cardiovascular risk marker** in its own right. The structured management algorithm is: investigate → correct underlying cause → consider 3–4 month HIF-PHI trial or RBC transfusion.

4. HIF-PHI (Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors)

This is an **entirely new section** in KDIGO 2026, reflecting the class's post-2012 regulatory approval.

Parameter	Guidance
Position	**Second-line** after ESA [Rec 3.1.1 — 2D]
Indications	ESA-intolerant, ESA-hyporesponsive, or barriers to parenteral therapy
Combination rule	❌ NEVER combine ESA + HIF-PHI simultaneously
Monitoring	Thrombosis, VEGF-related angiogenesis, thyroid function (especially roxadustat)

HIF-PHI Absolute Contraindications:

Children, kidney transplant recipients, history of CV events or thromboembolism, active cancer, hepatic impairment, seizures, proliferative retinopathy, pulmonary arterial hypertension (PAH), polycystic kidney disease (PKD), pregnancy.

Why second-line? Not because HIF-PHIs fail to raise Hb (RCTs show non-inferiority vs. ESAs), but because: (1) ESAs carry 40+ years of safety surveillance data; (2) some HIF-PHIs show potentially higher thrombotic/MACE risk in non-dialysis CKD; and (3) long-term comparative safety data are still accumulating.

5. RBC Transfusion

Setting	Hb Threshold	Notes
Asymptomatic, hemodynamically stable inpatient	< 7 g/dL	Unchanged from 2012
Pre-cardiac surgery	< 7.5 g/dL	**New threshold**
Pre-orthopedic surgery / significant CVD	< 8 g/dL	**New threshold**
All other contexts	Symptom-driven	Hb is a guide, not an absolute trigger

Conceptual shift in 2026: Transfusion decisions are now explicitly **symptom-driven** rather than purely numeric. Hb thresholds serve as background guides, not automatic triggers. For patients awaiting kidney transplantation, **alloimmunization protection** is explicitly elevated as a central reason to maintain a restrictive transfusion strategy.

System-level stewardship additions (2026): Standardized iron deficiency correction protocols, patient education tools, decision aids, and limiting phlebotomy-associated blood loss during hospitalization.

6. Head-to-Head Summary: KDIGO 2012 vs. 2026

Domain	KDIGO 2012	KDIGO 2026
Iron deficiency terminology	Absolute / Functional iron deficiency	Systemic iron deficiency / Iron-restricted erythropoiesis

Domain	KDIGO 2012	KDIGO 2026
Diagnostic workup	Iron and EPO focused	Multi-cause: nutritional, inflammatory, endocrine, hemorrhagic, marrow-related
IV iron strategy (HD)	Reactive (treat when deficient)	**Proactive** (~400 mg/month unless ceiling met) — PIVOTAL-based
IV iron ceiling (HD)	Ferritin > 500 ng/mL → withhold	**Ferritin > 700 ng/mL OR TSAT ≥ 40%** → withhold
Iron without anemia	Not addressed	**Consider** if ferritin < 30 + TSAT < 20% + symptoms
IV iron test dose	Recommended	❌ Not recommended
Hypophosphatemia monitoring	Not flagged	⚠ Monitor with ferric carboxymaltose and related agents
ESA initiation (dialysis)	Individualize (no threshold)	Hb ≤ 9–10 g/dL
ESA Hb upper target	≤ 11.5 g/dL [1C]	≤ 11.5 g/dL [**1D** — grade strengthened]
ESA hyporesponsiveness	Investigate and treat	Formally defined; CV risk marker; structured algorithm
HIF-PHIs	Not addressed (unavailable)	**Second-line** agent class; full contraindication list
Transfusion decision	Numeric Hb-based	**Symptom-driven**; Hb cutoffs as guides only
Alloimmunization	Mentioned	Explicitly central rationale for restrictive strategy in transplant candidates
Monitoring schedule	Periodic (unstructured)	Structured: annually (G3), biannually (G4), every 3 months (G5/G5D)