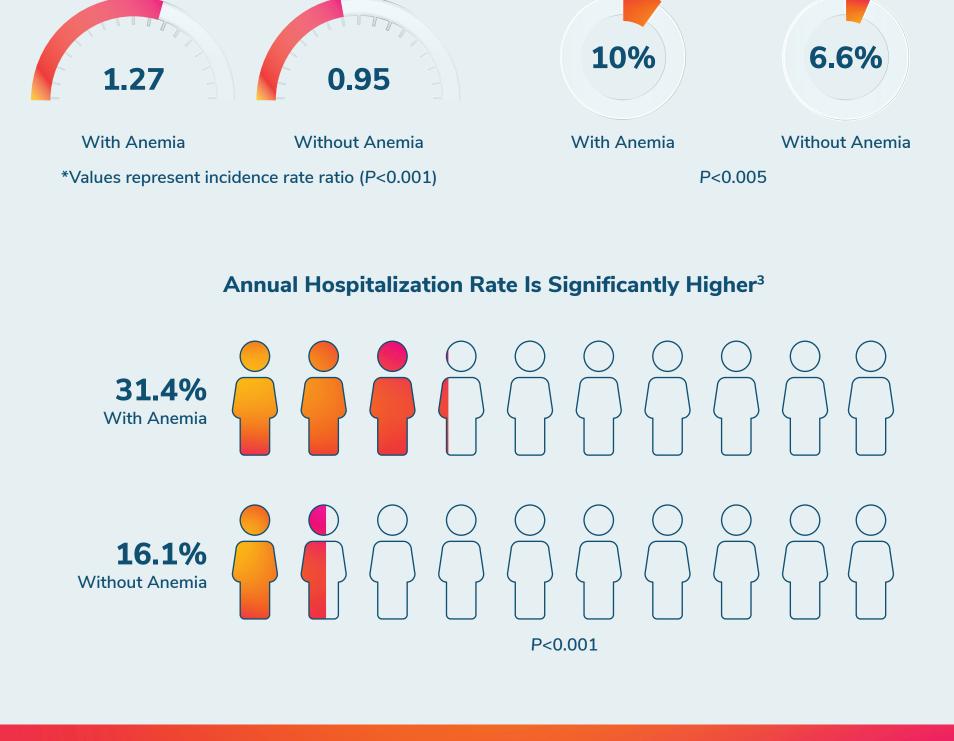
Burden of Anemia Due to Chronic Kidney Disease

Prevalence of Anemia Due to CKD **Increases With Disease Progression**¹ 4.8 Million **Anemia Prevalence Increases Patients With CKD Have Anemia** With CKD Progression 50.3% 53.4% **15.4%** 12.2% 17.4% 6.3% CKD General Stage 1 Stage 2 Stage 3 **Population** Stage 4 Stage 5

Patients With Anemia and CKD (Stages 3-4) Mean Number of CV-Related Mortality Rate Is Higher³ Comorbidities Is Higher^{2,*}

Higher Clinical Burden is Demonstrated in



Fatigue Is More Common⁴ **Activity Impairment Increases** With Disease Progression⁴

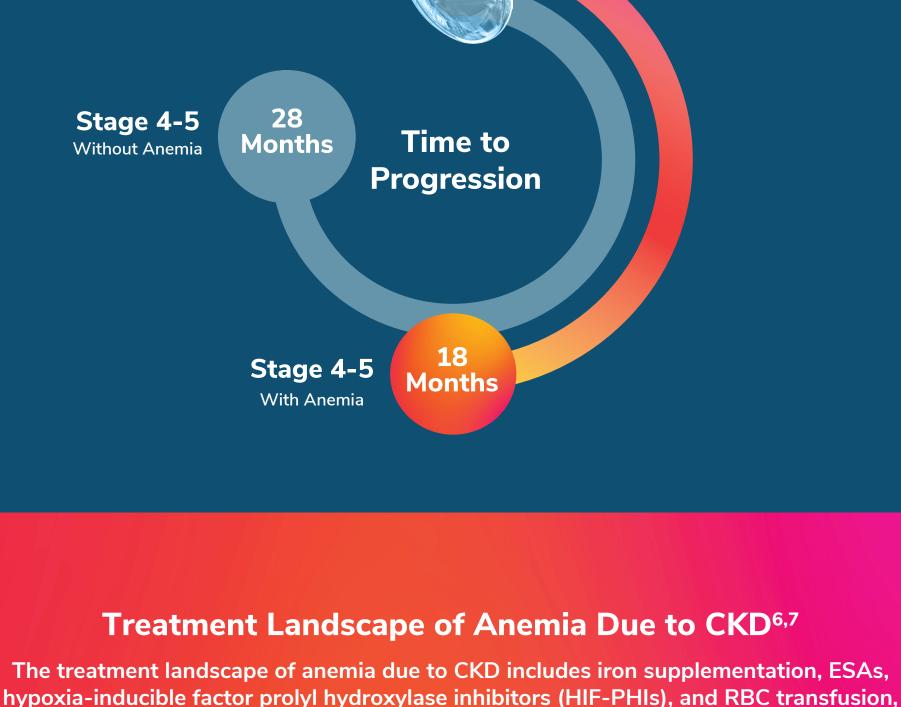
Reduced Quality of Life Is Associated With

Anemia in Patients With CKD (Stages 3-5D)



Stage 3

Anemia Is Correlated With Accelerated CKD Progression³



regulatory and clinical practice guidance outlined below.

which all improve clinical measures by balancing potential benefits with risks.

ESAs have remained a mainstay for 30 years by increasing Hb levels and decreasing the need for RBC transfusions. HIF-PHIs are the latest addition to the treatment

landscape as oral treatments which stimulate endogenous erythropoietin production.

Both ESAs and HIF-PHIs are recommended to be used to maintain Hb levels within 10

to 11 g/dL and have a warning of increased risk of death and cardiovascular events.

This is based on findings from randomized clinical trials that led to changes in

Clinical Evidence Regulations Guidelines

1989

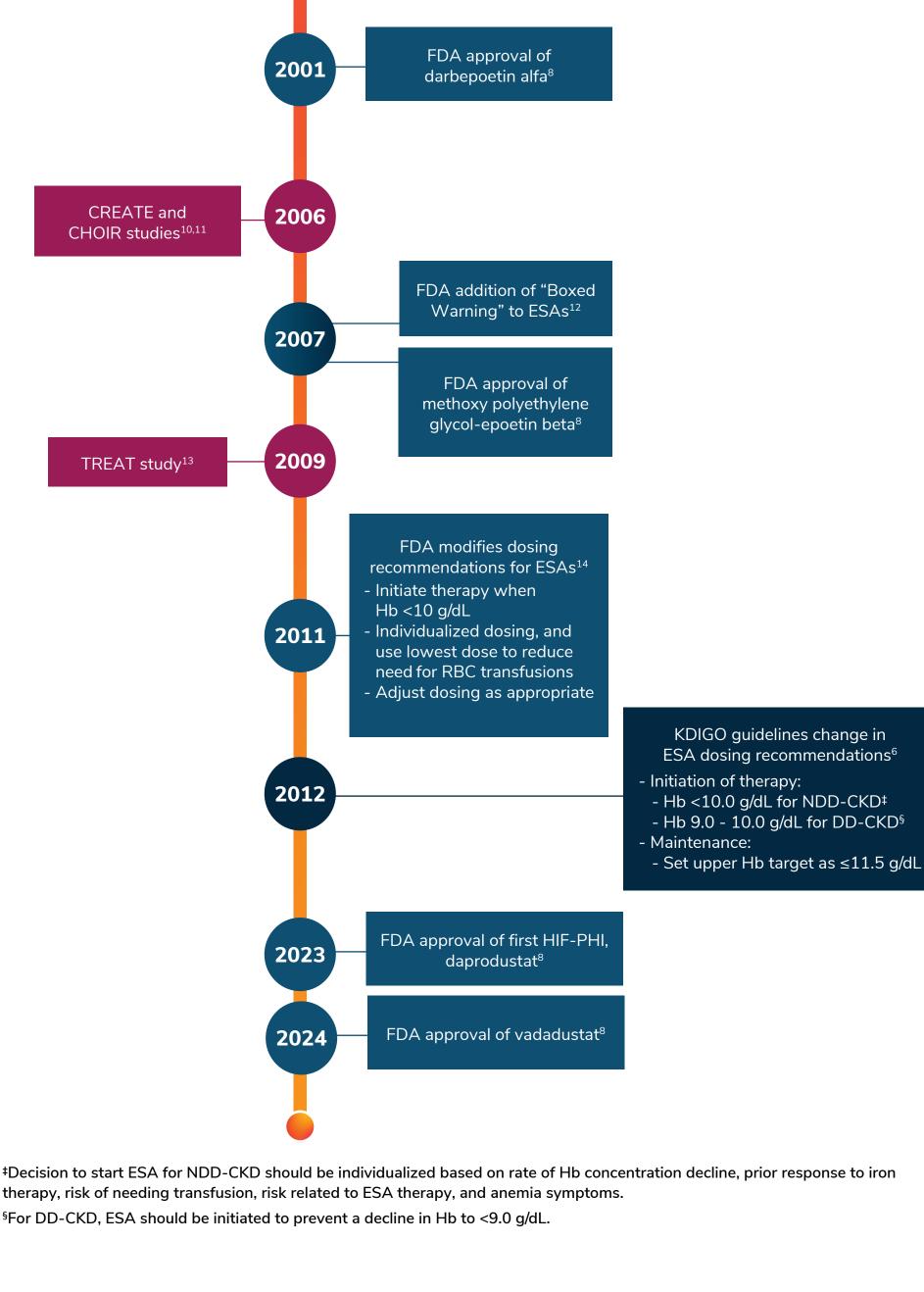
1998

Normal

Hematocrit Trial⁹

FDA approval for first ESA,

epoetin alfa⁸



Mean Hemoglobin Levels in ESA-Treated Hemodialysis Patients¹⁵

FDA ESA Dose

Recommendation¹⁴

20,000

2007:

FDA Boxed Warning¹²



Abbreviations List: CKD, chronic kidney disease; CV, cardiovascular; DD, dialysis-dependent; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; FDA, Food and Drug Administration; Hb, hemoglobin; KDIGO, Kidney Disease Improving Global Outcomes; NDD, non-dialysis-dependent; pts, patients; RBC, red blood cell; USRDS, United States Renal Data System

References: 1. Stauffer ME, Fan T. PLoS One. 2014;9:e84943.; 2. Covic A, et al. Adv Ther. 2017;34:1662-1672.; 3. Portolés J, et al. BMC Nephrol. 2013;14:2.; 4. Eriksson D, et al. BMC Nephrol. 2016;17:97.; 5. Odden MC, et al. J Am Soc Nephrol. 2004;15(11):2908-2915.; 6. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int Suppl. 2012;2:279-335.; 7. Haase VH. Kidney Int Suppl (2011). 2021 Apr;11(1):8-25.; 8. US Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed April 11, 2024.; 9. Besarab A, et al. N Engl J Med. 1998;339:584-590.; 10. Drüeke TB, et al. N Engl J Med. 2006;355:2071-2084.; 11. Singh AK, et al. N Engl J Med. 2006;16;355:2085-2098.; 12. Fishbane S, Nissenson AR. Kidney Int. 2007;72(7):806-813.; 13. Pfeffer MA, et al. N Engl J Med. 2009;361:2019-2032.; 14. US Food and Drug Administration. FDA Drug Safety Communication: Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents (ESAs) in chronic kidney disease. https://www.fda.gov/drugs/drugsafety-and-availability/fda-drug-safety-communication-modified-dosing-recommendations-improve-safe-use-erythropoiesis. Accessed April 11, 2024.; 15. United States Renal Data System. 2018 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States. Volume 2: End-Stage Renal Disease in the United States. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases; 2018: chap 2.



14

Last Updated 04/24 MED-DS-US-0012