



# Challenging the Status Quo in Hereditary Hemorrhagic Telangiectasia:



## A Comprehensive Review of IV Iron Best Practices at the Hematology-Primary Care Interface



### **Bibliography & Suggested Reading**

- Abdulrehman J, Tang GH, Auerbach M, et al. The safety and efficacy of ferumoxytol in the treatment of iron deficiency: a systematic review and meta-analysis. *Transfusion*. 2019;59(12):3646-3656.
- Adkinson NF, Strauss WE, Macdougall IC, et al. Comparative safety of intravenous ferumoxytol versus ferric carboxymaltose in iron deficiency anemia: A randomized trial. *Am J Hematol*. 2018;93(5):683-690.
- Anand IS, Gupta P. Anemia and Iron Deficiency in Heart Failure: Current Concepts and Emerging Therapies. *Circulation*. 2018;138(1):80-98.
- Auerbach M, Gafter-Gvili A, Macdougall IC. Intravenous iron: a framework for changing the management of iron deficiency. *Lancet Haematol*. 2020;7(4):e342-e350.
- Auerbach M, Henry D, DeLoughery TG. Intravenous ferric derisomaltose for the treatment of iron deficiency anemia. *Am J Hematol*. 2021;96(6):727-734.
- Auerbach M, Wolf M. Intravenous Iron Associated Hypophosphatemia: Much More Than a Laboratory Curiosity. *Am J Hematol*. 2025;100(5):752-754.
- Avni T, Bieber A, Grossman A, et al. The safety of intravenous iron preparations: systematic review and meta-analysis. *Mayo Clin Proc*. 2015;90:12-23.



Birgegård G, Henry D, Glaspy J, et al. A randomized noninferiority trial of intravenous iron isomaltoside versus oral iron sulfate in patients with nonmyeloid malignancies and anemia receiving chemotherapy: the PROFOUND trial. *Pharmacotherapy*. 2016;36(4):402–414.

Callejas-Moraga EL, Casado E, Gomez-Nuñez M, et al. Severe osteomalacia with multiple insufficiency fractures secondary to intravenous iron therapy in a patient with Rendu-Osler-Weber syndrome. *Bone Rep*. 2020;13:100712.

Camaschella C, Nai A, Silvestri L. Iron metabolism and iron disorders revisited in the hepcidin era. *Haematologica*. 2020;105(2):260–272.

CDC website. Facts about hereditary hemorrhagic telangiectasia (HHT). April 28, 2023. Available at: <https://www.cdc.gov/ncbddd/hht/index.html>. Accessed June 2025.

CureHHT website. HHT medical summary. Available at: <https://curehht.org/understanding-hht/what-is-hht/medical-summary/>. Accessed June 2025.

CureHHT website. Knowing signs and symptoms of HHT leads to a faster diagnosis. Available at: <https://curehht.org/understanding-hht/what-is-hht/signs-and-symptoms/>. Accessed June 2025.

DeLoughery TG. Iron Deficiency Anemia. *Med Clin North Am*. 2017;101(2):319-332.

DeLoughery TG. Safety of Oral and Intravenous Iron. *Acta Haematol*. 2019;142(1):8-12.

Droege F, Thangavelu K, Stuck BA, et al. Life expectancy and comorbidities in patients with hereditary hemorrhagic telangiectasia. *Vasc Med*. 2018;23(4):377-383.

Drugs@FDA: FDA-Approved Drug Products. Ferric derisomaltose. August 1, 2024. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/208171s003lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208171s003lbl.pdf). Accessed June 2025.

Drugs@FDA: FDA-Approved Drug Products. Ferumoxytol. June 16, 2022. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2022/022180s025lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/022180s025lbl.pdf). Accessed June 2025.

Drugs@FDA: FDA-Approved Drug Products. Iron dextran. August 1, 2024. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/017441s181lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/017441s181lbl.pdf). Accessed June 2025.

Drugs@FDA: FDA-Approved Drug Products. Iron sucrose. August 1, 2024. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/021135s038lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021135s038lbl.pdf). Accessed June 2025.

Drugs@FDA: FDA-Approved Drug Products. Sodium ferric gluconate. February 28, 2012. Accessed June 2025.



Drugs@FDA: FDA-Approved Drugs. Ferric carboxymaltose. January 3, 2025. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2023/203565s020lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/203565s020lbl.pdf). Accessed June 2025.

Faughnan ME, Mager JJ, Hetts SW, et al. Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia. *Ann Intern Med.* 2020;173(12):989-1001.

Felsenfeld AJ, Levine BS. Approach to treatment of hypophosphatemia. *Am J Kidney Dis.* 2012;60(4):655-661.

Ferry AM, Wright AE, Baillargeon G, Kuo YF, Chaaban MR. Epidemiology and Trends of Hereditary Hemorrhagic Telangiectasia in the United States. *Am J Rhinol Allergy.* 2020;34(2):230-237.

Finnamore H, Le Couteur J, Hickson M, et al. Hemorrhage-adjusted iron requirements, hematinics and hepcidin define hereditary hemorrhagic telangiectasia as a model of hemorrhagic iron deficiency. *PLoS One.* 2013;8(10):e76516.

Ganzoni AM. Eisen-Dextran intravenös: therapeutische und experimentelle Möglichkeiten [Intravenous iron-dextran: therapeutic and experimental possibilities]. *Schweiz Med Wochenschr.* 1970;100(7):301-303.

Garg N, Khunger M, Gupta A, et al. Optimal management of hereditary hemorrhagic telangiectasia. *J Blood Med.* 2014;5:191-206.

Girelli D, Nemeth E, Swinkels DW. Hepcidin in the diagnosis of iron disorders. *Blood.* 2016;127(23):2809-2813.

Glaspy JA, Wolf M, Strauss WE. Intravenous Iron-Induced Hypophosphatemia: An Emerging Syndrome. *Adv Ther.* 2021;38(7):3531-3549.

International HHT Guidelines website. Anemia and anticoagulation. Available at: <https://www.hhtguidelines.org/anemia>. Accessed June 2025.

Jackson SB, Villano NP, Benhammou JN, Lewis M, Pisegna JR, Padua D. Gastrointestinal Manifestations of Hereditary Hemorrhagic Telangiectasia (HHT): A Systematic Review of the Literature. *Dig Dis Sci.* 2017;62(10):2623-2630.

Kalantar-Zadeh K, Ganz T et al. Parenteral iron therapy and phosphorus homeostasis: A review. *Am J Hematol.* 2021;96(5):606-616.

Kasthuri RS, Chaturvedi S, Thomas S, et al. Development and performance of a hereditary hemorrhagic telangiectasia-specific quality-of-life instrument. *Blood Adv.* 2022;6(14):4301-4309.

Kasthuri RS, Montifar M, Nelson J, et al. Prevalence and predictors of anemia in hereditary hemorrhagic telangiectasia. *Am J Hematol.* Published online June 22, 2017.



- Koch TA, Myers J, Goodnough LT. Intravenous Iron Therapy in Patients with Iron Deficiency Anemia: Dosing Considerations. *Anemia*. 2015;2015:763576.
- Kritharis A, Al-Samkari H, Kuter DJ. Hereditary hemorrhagic telangiectasia: diagnosis and management from the hematologist's perspective. *Haematologica*. 2018;103(9):1433-1443.
- Leung AKC, Leong KF, Barankin B. Hereditary Hemorrhagic Telangiectasia. *J Pediatr*. 2019;210:232.
- Lopez A, Cacoub P, Macdougall IC, et al. Iron deficiency anaemia. *Lancet*. 2016;387(10021):907-16.
- Magagnoli J, Knopf K, Hrushesky WJ, et al. Ferric Carboxymaltose (FCM)-Associated Hypophosphatemia (HPP): A Systematic Review. *Am J Hematol*. 2025;100(5):840-846.
- Makharadze T, Boccia R, Krupa A, et al. Efficacy and safety of ferric carboxymaltose infusion in reducing anemia in patients receiving chemotherapy for nonmyeloid malignancies: a randomized, placebo-controlled study (IRON-CLAD). *Am J Hematol*. 2021;96(12):1639–1646.
- Martens KL, Wolf M. Incidence, mechanism, and consequences of IV iron-induced hypophosphatemia. *Hematology Am Soc Hematol Educ Program*. 2023;2023(1):636-639.
- McDonagh T, Macdougall IC. Iron therapy for the treatment of iron deficiency in chronic heart failure: intravenous or oral? *Eur J Heart Fail*. 2015;17(3):248–262.
- McDonald J, Wooderchak-Donahue W, VanSant Webb C, Whitehead K, Stevenson DA, Bayrak-Toydemir P. Hereditary hemorrhagic telangiectasia: genetics and molecular diagnostics in a new era. *Front Genet*. 2015;6:1.
- Mehta AR, Wolf M, Zoller H. Differential Effects of Ferric Derisomaltose and Ferric Carboxymaltose on Fatigue in Patients with Iron Deficiency Anemia and Inflammatory Bowel Disease. *Blood*. 2022;140(Supplement 1):2469–2470.
- Nikravesh N, Borchard G, Hofmann H, et al. Factors influencing safety and efficacy of intravenous iron-carbohydrate nanomedicines: from production to clinical practice. *Nanomedicine*. 2020;26:102178.
- Ola R, Hessels J, Hammill A, et al. Executive summary of the 14th HHT international scientific conference. *Angiogenesis*. 2023;26(Suppl 1):27-37.
- Peyrin-Biroulet L, Williet N, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. *Am J Clin Nutr*. 2015;102(6):1585-1594.
- Schaefer B, Glodny B, Zoller H. Blood and Bone Loser. *Gastroenterology*. 2017;152(6):e5-e6.
- Schaefer B, Tobiasch M, Viveiros A, et al. Hypophosphatemia after treatment of iron deficiency with intravenous ferric carboxymaltose or iron isomaltoside-a systematic review and meta-analysis. *Br J Clin Pharmacol*. 2021;87(5):2256-2273.



Schaefer B, Tobiasch M, Wagner S, et al. Hypophosphatemia after intravenous iron therapy: Comprehensive review of clinical findings and recommendations for management. *Bone*. 2022;154:116202.

Shovlin CL, Awan I, Cahilog Z, Abdulla FN, Guttmacher AE. Reported cardiac phenotypes in hereditary hemorrhagic telangiectasia emphasize burdens from arrhythmias, anemia and its treatments, but suggest reduced rates of myocardial infarction. *Int J Cardiol*. 2016;215:179-185.

Shovlin CL, Guttmacher AE, Buscarini E, et al. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Am J Med Genet*. 2000;91(1):66-67.

Strubbe M, David K, Peene B, et al. No longer to be ignored: Hypophosphatemia following intravenous iron administration. *Rev Endocr Metab Disord*. 2025;26(1):125-135.

Trevise LA, Lopes Vieira Pinto MP, Hasselmann G, et al. Multifocal Abscesses, Necrotizing Fasciitis, Iron Deficiency Anemia, and Hypophosphatemia Induced by Ferric Carboxymaltose Infusions: Report of a Case of Hereditary Hemorrhagic Telangiectasia. *Cureus*. 2023;15(8):e44020.

U.S. National Library of Medicine. ClinicalTrials.gov. Available at: <https://classic.clinicaltrials.gov/>. Accessed June 2025.

Vasquez-Rios G, Chapel A, Philip I, Martin KJ, Merando A. Life-threatening hypophosphatemia following intravenous iron infusion. *Nefrologia (Engl Ed)*. 2021;41(4):467-470.

Viteri-Noël A, González-García A, Patier JL, et al. Hereditary Hemorrhagic Telangiectasia: Genetics, Pathophysiology, Diagnosis, and Management. *J Clin Med*. 2022;11(17):5245.

Wang C, Graham DJ, Kane RC, et al. Comparative risk of anaphylactic reactions associated with intravenous iron products. *JAMA*. 2015;314:2062-2068

Wolf M, Chertow GM, Macdougall IC, et al. Randomized trial of intravenous iron-induced hypophosphatemia. *JCI Insight*. 2018;3(23):124486.

Wolf M, Koch TA, Bregman DB. Effects of iron deficiency anemia and its treatment on fibroblast growth factor 23 and phosphate homeostasis in women. *J Bone Miner Res*. 2013;28(8):1793-1803.

Wolf M, Rubin J, Achebe M, et al. Effects of iron isomaltoside vs ferric carboxymaltose on hypophosphatemia in iron-deficiency anemia: two randomized clinical trials. *JAMA*. 2020;323(5):432-443.

Zarrabeitia R, Fariñas-Álvarez C, Santibáñez M, et al. Quality of life in patients with hereditary hemorrhagic telangiectasia (HHT). *Health Qual Life Outcomes*. 2017;15(1):19.

Zhang E, Virk ZM, Rodriguez-Lopez J, Al-Samkari H. Hereditary hemorrhagic telangiectasia may be the most morbid inherited bleeding disorder of women. *Blood Adv*. Published online April 9, 2024.



Zoller H, Pammer LM, Schaefer B, et al. Incidence of fractures after intravenous iron: a retrospective analysis comparing ferric carboxymaltose and ferric derisomaltose. 2023 ASH Annual Meeting; San Diego, CA. December 11, 2023. Poster 3838.

Zoller H, Wolf M, Blumenstein I, et al. Hypophosphatemia following ferric derisomaltose and ferric carboxymaltose in patients with iron deficiency anaemia due to inflammatory bowel disease (PHOSPHARE-IBD): a randomised clinical trial. *Gut*. 2023;72(4):644-653.