



If a conflict arises between a Clinical Payment and Coding Policy (“CPCP”) and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. “Plan documents” include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. BCBSNM may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act (“HIPAA”) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (“UB”) Editor, American Medical Association (“AMA”), Current Procedural Terminology (“CPT®”), CPT® Assistant, Healthcare Common Procedure Coding System (“HCPCS”), ICD-10 CM and PCS, National Drug Codes (“NDC”), Diagnosis Related Group (“DRG”) guidelines, Centers for Medicare and Medicaid Services (“CMS”) National Correct Coding Initiative (“NCCI”) Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

## Diagnostic Testing of Iron Homeostasis and Metabolism

**Policy Number: CPCPLAB008**

**Version 1.0**

**Enterprise Medical Policy Committee Approval Date: 1/25/2022**

**Plan Effective Date: May 1, 2022**

### Description

BCBSNM has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

### Reimbursement Information:

1. Measurement of serum ferritin levels **may be reimbursable** in any of the following situations:
  - a. In the evaluation of an individual with abnormal hemoglobin and/or hematocrit levels.
  - b. In the evaluation and monitoring of iron overload disorders.
  - c. In individuals with symptoms of hemochromatosis (See Note 1).

- d. In individuals with first-degree relatives with confirmed hereditary hemochromatosis (HH)
  - e. In the evaluation of individuals with liver disease.
  - f. In the evaluation and monitoring of patients with chronic kidney disease who are being considered for, or are receiving treatment for, anemia at a frequency of every 1 to 3 months.
  - g. In the evaluation of hemophagocytic lymphohistiocytosis (HLH) and Still's Disease.
  - h. For individuals on iron therapy, at a frequency of every 1 to 3 months.
  - i. In males with secondary hypogonadism.
2. Serum transferrin saturation (using serum iron and serum iron binding capacity measurements) **may be reimbursable** in the following:
    - a. For the evaluation of iron overload in individuals with symptoms of hemochromatosis (See Note 1).
    - b. For the evaluation of iron overload in individuals with first-degree relatives with confirmed hereditary hemochromatosis (HH).
    - c. For the evaluation of iron deficiency anemia.
  3. The use of ferritin or transferrin measurement, including transferrin saturation, as a screening test in asymptomatic patients **is not reimbursable**.
  4. Serum hepcidin testing, including immunoassays, **is not reimbursable**.
  5. The use of GlycA testing to measure or monitor transferrin or other glycosylated proteins **is not reimbursable**.

Please note that carbohydrate-deficient transferrin is out of the scope for this policy.

**NOTE 1:** Symptoms of hemochromatosis, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health include the following (NIDDK, 2014):

- Joint pain
- Fatigue
- Unexplained weight loss
- Abnormal bronze or gray skin color
- Abdominal pain
- Loss of sex drive

## Procedure Codes

Code
82728, 83540, 83550, 84466, 84999, 0024U, 0251U

## References:

Abioye, A. I., Aboud, S., Premji, Z., Etheredge, A. J., Gunaratna, N. S., Sudfeld, C. R., . . . Fawzi, W. (2019). Hemoglobin and hepcidin have good validity and utility for diagnosing iron deficiency anemia among pregnant women. *Eur J Clin Nutr.* doi:10.1038/s41430-019-0512-z

Ahmad, S., Moriconi, F., Naz, N., Sultan, S., Sheikh, N., Ramadori, G., & Malik, I. A. (2013). Ferritin L and Ferritin H are differentially located within hepatic and extra hepatic organs under physiological and acute phase conditions. *Int J Clin Exp Pathol*, 6(4), 622-629. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/?term=Ferritin+L+and+Ferritin+H+are+differentially+located+within+hepatic+and+extra+hepatic+organs+under+physiological+and+acute+phase+conditions>  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3606851/>

Alfrey, C. P. (1978). Serum ferritin assay. *CRC Crit Rev Clin Lab Sci*, 9(3), 179-208. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/401369>

Anderson, C. P., Shen, M., Eisenstein, R. S., & Leibold, E. A. (2012). Mammalian iron metabolism and its control by iron regulatory proteins. *Biochim Biophys Acta*, 1823(9), 1468-1483. doi:10.1016/j.bbamcr.2012.05.010

Arber, C. E., Li, A., Houlden, H., & Wray, S. (2016). Review: Insights into molecular mechanisms of disease in neurodegeneration with brain iron accumulation: unifying theories. *Neuropathol Appl Neurobiol*, 42(3), 220-241. doi:10.1111/nan.12242

Arosio, P., & Levi, S. (2010). Cytosolic and mitochondrial ferritins in the regulation of cellular iron homeostasis and oxidative damage. *Biochim Biophys Acta*, 1800(8), 783-792. doi:10.1016/j.bbagen.2010.02.005

ASCO, & ASH. (2019). Management of cancer-associated anemia with erythropoiesis-stimulating agents: ASCO/ASH clinical practice guideline update. Retrieved from <https://ashpublications.org/bloodadvances/article/3/8/1197/260121/Management-of-cancer-associated-anemia-with>

Auerbach, M., Staffa, S. J., & Brugnara, C. (2021). Using Reticulocyte Hemoglobin Equivalent as a Marker for Iron Deficiency and Responsiveness to Iron Therapy. *Mayo Clin Proc*, 96(6), 1510-1519. doi:10.1016/j.mayocp.2020.10.042

Bell, S., Rigas, A. S., Magnusson, M. K., Ferkingstad, E., Allara, E., Bjornsdottir, G., . . . Stefansson, K. (2021). A genome-wide meta-analysis yields 46 new loci associating with biomarkers of iron homeostasis. *Commun Biol*, 4(1), 156. doi:10.1038/s42003-020-01575-z

Bhasin, S., Brito, J. P., Cunningham, G. R., Hayes, F. J., Hodis, H. N., Matsumoto, A. M., . . . Yialamas, M. A. (2018). Testosterone Therapy in Men With Hypogonadism: An Endocrine Society\* Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, 103(5), 1715-1744. doi:10.1210/jc.2018-00229

Bohlius, J., Bohlke, K., Castelli, R., Djulbegovic, B., Lustberg, M. B., Martino, M., . . . Lazo-Langner, A. (2019). Management of Cancer-Associated Anemia With Erythropoiesis-Stimulating Agents: ASCO/ASH Clinical Practice Guideline Update. *Journal of Clinical Oncology*, 37(15), 1336-1351. doi:10.1200/jco.18.02142

Brandtner, A., Tymoszuk, P., Nairz, M., Lehner, G. F., Fritsche, G., Vales, A., . . . Pfeifhofer-Obermair, C. (2020). Linkage of alterations in systemic iron homeostasis to patients' outcome in sepsis: a prospective study. *J Intensive Care*, 8, 76. doi:10.1186/s40560-020-00495-8

Bresgen, N., & Eckl, P. M. (2015). Oxidative stress and the homeodynamics of iron metabolism.

Biomolecules, 5(2), 808-847. doi:10.3390/biom5020808

Byrne, S. L., Krishnamurthy, D., & Wessling-Resnick, M. (2013). Pharmacology of iron transport. *Annu Rev Pharmacol Toxicol*, 53, 17-36. doi:10.1146/annurev-pharmtox-010611-134648

Cabantchik, Z. I. (2014). Labile iron in cells and body fluids: physiology, pathology, and pharmacology. *Front Pharmacol*, 5, 45. doi:10.3389/fphar.2014.00045

Camaschella, C. (2015). Iron-Deficiency Anemia. *N Engl J Med*, 373(5), 485-486. doi:10.1056/NEJMc1507104

Camaschella, C. (2020). Regulation of iron balance. Uptodate.com. Retrieved from <https://www.uptodate.com/contents/regulation-of-iron-balance>

Campanella, A., Rovelli, E., Santambrogio, P., Cozzi, A., Taroni, F., & Levi, S. (2009). Mitochondrial ferritin limits oxidative damage regulating mitochondrial iron availability: hypothesis for a protective role in Friedreich ataxia. *Hum Mol Genet*, 18(1), 1-11. doi:10.1093/hmg/ddn308

Chen, M., Liu, J., & Wright, B. (2019). A sensitive and cost-effective HPLC/MS/MS (MRM) method for the clinical measurement of serum hepcidin. *Rapid Commun Mass Spectrom*. doi:10.1002/rcm.8644

Cohen, L. A., Gutierrez, L., Weiss, A., Leichtmann-Bardoogo, Y., Zhang, D. L., Crooks, D. R., . . . Meyron-Holtz, E. G. (2010). Serum ferritin is derived primarily from macrophages through a nonclassical secretory pathway. *Blood*, 116(9), 1574-1584. doi:10.1182/blood-2009-11-253815

Costa Matos, L., Batista, P., Monteiro, N., Ribeiro, J., Cipriano, M. A., Henriques, P., . . . Carvalho, A. (2013). Iron stores assessment in alcoholic liver disease. *Scand J Gastroenterol*, 48(6), 712-718. doi:10.3109/00365521.2013.781217

da Silva, W. R., Silveira, L., Jr., & Fernandes, A. B. (2019). Diagnosing sickle cell disease and iron deficiency anemia in human blood by Raman spectroscopy. *Lasers Med Sci*. doi:10.1007/s10103-019-02887-1

Dahlfors, G., Stal, P., Hansson, E. C., Barany, P., Sisowath, C., Onelov, L., . . . Beshara, S. (2015). Validation of a competitive ELISA assay for the quantification of human serum hepcidin. *Scand J Clin Lab Invest*, 75(8), 652-658.

DeLoughery, T. G. (2017). Iron Deficiency Anemia. *Med Clin North Am*, 101(2), 319-332. doi:10.1016/j.mcna.2016.09.004

Dignass, A., Farrag, K., & Stein, J. (2018). Limitations of Serum Ferritin in Diagnosing Iron Deficiency in Inflammatory Conditions. *Int J Chronic Dis*, 2018, 9394060. doi:10.1155/2018/9394060

Dignass, A., Gasche, C., Bettenworth, D., Birgegård, G., Danese, S., Gisbert, J. P., . . . Colitis, O. (2015). European Consensus on the Diagnosis and Management of Iron Deficiency and Anaemia in Inflammatory Bowel Diseases. *Journal of Crohn's and Colitis*, 9(3), 211-222. doi:10.1093/ecco-jcc/jju009

- Emmenegger, U., Frey, U., Reimers, A., Fux, C., Semela, D., Cottagnoud, P., . . . Neftel, K. A. (2001). Hyperferritinemia as indicator for intravenous immunoglobulin treatment in reactive macrophage activation syndromes. *Am J Hematol*, 68(1), 4-10. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/11559930>
- Enko, D., Wagner, H., Kriegshauser, G., Kimbacher, C., Stolba, R., & Halwachs-Baumann, G. (2015). Assessment of human iron status: A cross-sectional study comparing the clinical utility of different laboratory biomarkers and definitions of iron deficiency in daily practice. *Clin Biochem*, 48(13-14), 891-896. doi:10.1016/j.clinbiochem.2015.05.008
- Evensen, K. J., Swaak, T. J., & Nossent, J. C. (2007). Increased ferritin response in adult Still's disease: specificity and relationship to outcome. *Scand J Rheumatol*, 36(2), 107-110. doi:10.1080/03009740600958504
- Finazzi, D., & Arosio, P. (2014). Biology of ferritin in mammals: an update on iron storage, oxidative damage and neurodegeneration. *Arch Toxicol*, 88(10), 1787-1802. doi:10.1007/s00204-014-1329-0
- Finch, C. A., Bellotti, V., Stray, S., Lipschitz, D. A., Cook, J. D., Pippard, M. J., & Huebers, H. A. (1986). Plasma ferritin determination as a diagnostic tool. *West J Med*, 145(5), 657-663. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/3541387>
- Fleming, R. E., & Ponka, P. (2012). Iron overload in human disease. *N Engl J Med*, 366(4), 348-359. doi:10.1056/NEJMra1004967
- Ganz, T. (2013). Systemic iron homeostasis. *Physiol Rev*, 93(4), 1721-1741. doi:10.1152/physrev.00008.2013
- Ganz, T., & Nemeth, E. (2009). Iron sequestration and anemia of inflammation. *Semin Hematol*, 46(4), 387-393. doi:10.1053/j.seminhematol.2009.06.001
- Garcia-Casal, M. N., Pasricha, S. R., Martinez, R. X., Lopez-Perez, L., & Peña-Rosas, J. P. (2021). Serum or plasma ferritin concentration as an index of iron deficiency and overload. *Cochrane Database Syst Rev*, 5(5), Cd011817. doi:10.1002/14651858.CD011817.pub2
- Gerday, E., Brereton, J. B., Bahr, T. M., Elmont, J. O., Fullmer, S., Middleton, B. A., . . . Christensen, R. D. (2020). Urinary ferritin; a potential noninvasive way to screen NICU patients for iron deficiency. *J Perinatol*. doi:10.1038/s41372-020-0746-6
- Gozzelino, R., & Arosio, P. (2016). Iron Homeostasis in Health and Disease. *Int J Mol Sci*, 17(1). doi:10.3390/ijms17010130
- Hayflick, S. J., Kurian, M. A., & Hogarth, P. (2018). Neurodegeneration with brain iron accumulation. *Handb Clin Neurol*, 147, 293-305. doi:10.1016/b978-0-444-63233-3.00019-1
- Hentze, M. W., Muckenthaler, M. U., & Andrews, N. C. (2004). Balancing acts: molecular control of mammalian iron metabolism. *Cell*, 117(3), 285-297. doi:10.1016/S0092-8674(04)00343-5
- Hentze, M. W., Muckenthaler, M. U., Galy, B., & Camaschella, C. (2010). Two to tango: regulation of Mammalian iron metabolism. *Cell*, 142(1), 24-38. doi:10.1016/j.cell.2010.06.028

- Hogarth, P., Kurian, M. A., Gregory, A., Csanyi, B., Zagustin, T., Kmiec, T., . . . Hayflick, S. J. (2017). Consensus clinical management guideline for pantothenate kinase-associated neurodegeneration (PKAN). *Mol Genet Metab*, 120(3), 278-287. doi:10.1016/j.ymgme.2016.11.004
- Hou, W., Xie, Y., Song, X., Sun, X., Lotze, M. T., Zeh, H. J., 3rd, . . . Tang, D. (2016). Autophagy promotes ferroptosis by degradation of ferritin. *Autophagy*, 12(8), 1425-1428. doi:10.1080/15548627.2016.1187366
- Ismail, N. A., Habib, S. A., Talaat, A. A., Mostafa, N. O., & Elghoroury, E. A. (2019). The Relation between Serum Hcpidin, Ferritin, Hcpidin: Ferritin Ratio, Hydroxyurea and Splenectomy in Children with beta-Thalassemia. *Open Access Maced J Med Sci*, 7(15), 2434-2439. doi:10.3889/oamjms.2019.636
- Jacobs, A., Miller, F., Worwood, M., Beamish, M. R., & Wardrop, C. A. (1972). Ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *Br Med J*, 4(5834), 206-208. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/5082548>
- Jones, K. S., Meadows, S. R., Chamberlain, K., Parkington, D. A., Collins, D., Page, P., & Koulman, A. (2021). Delayed Processing of Chilled Whole Blood for 24 Hours Does Not Affect the Concentration of the Majority of Micronutrient Status Biomarkers. *J Nutr*. doi:10.1093/jn/nxab267
- Karlsson, T. (2017). Evaluation of a competitive hepcidin ELISA assay in the differential diagnosis of iron deficiency anaemia with concurrent inflammation and anaemia of inflammation in elderly patients. *J Inflamm (Lond)*, 14, 21. doi:10.1186/s12950-017-0166-3
- Kassebaum, N. J., Jasrasaria, R., Naghavi, M., Wulf, S. K., Johns, N., Lozano, R., . . . Murray, C. J. (2014). A systematic analysis of global anemia burden from 1990 to 2010. *Blood*, 123(5), 615-624. doi:10.1182/blood-2013-06-508325
- KDIGO. (2012). KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Int Suppl*, 2(4), 279-335. Retrieved from [http://www.kdigo.org/clinical\\_practice\\_guidelines/pdf/KDIGO-Anemia%20GL.pdf](http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO-Anemia%20GL.pdf)
- Kell, D. B., & Pretorius, E. (2014). Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. *Metallomics*, 6(4), 748-773. doi:10.1039/c3mt00347g
- Keogh, M. J., Morris, C. M., & Chinnery, P. F. (2013). Neuroferritinopathy. *Int Rev Neurobiol*, 110, 91-123. doi:10.1016/b978-0-12-410502-7.00006-5
- Kliger, A. S., Foley, R. N., Goldfarb, D. S., Goldstein, S. L., Johansen, K., Singh, A., & Szczech, L. (2013). KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. *American Journal of Kidney Diseases*, 62(5), 849-859. doi:10.1053/j.ajkd.2013.06.008
- Knovich, M. A., Storey, J. A., Coffman, L. G., Torti, S. V., & Torti, F. M. (2009). Ferritin for the clinician. *Blood Rev*, 23(3), 95-104. doi:10.1016/j.blre.2008.08.001
- Knutson, M. D. (2017). Iron transport proteins: Gateways of cellular and systemic iron homeostasis. *J Biol Chem*, 292(31), 12735-12743. doi:10.1074/jbc.R117.786632

- Ko, C. W., Siddique, S. M., Patel, A., Harris, A., Sultan, S., Altayar, O., & Falck-Ytter, Y. (2020). AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia. *Gastroenterology*, 159(3), 1085-1094. doi:10.1053/j.gastro.2020.06.046
- Koperdanova, M., & Cullis, J. O. (2015). Interpreting raised serum ferritin levels. *BMJ*, 351, h3692. doi:10.1136/bmj.h3692
- Kroot, J. J., Tjalsma, H., Fleming, R. E., & Swinkels, D. W. (2011). Hepcidin in human iron disorders: diagnostic implications. *Clin Chem*, 57(12), 1650-1669. doi:10.1373/clinchem.2009.140053
- Kruszewski, M. (2003). Labile iron pool: the main determinant of cellular response to oxidative stress. *Mutat Res*, 531(1-2), 81-92. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/14637247>
- Kumar, N., Rizek, P., & Jog, M. (2016). Neuroferritinopathy: Pathophysiology, Presentation, Differential Diagnoses and Management. *Tremor Other Hyperkinet Mov (N Y)*, 6, 355. doi:10.7916/d8kk9bhf
- Kuwata, T., Okada, Y., Yamamoto, T., Sato, D., Fujiwara, K., Fukumura, T., & Ikeguchi, M. (2019). Structure, Function, Folding, and Aggregation of a Neuroferritinopathy-Related Ferritin Variant. *Biochemistry*, 58(18), 2318-2325. doi:10.1021/acs.biochem.8b01068
- Kwiatek-Majkusiak, J., Geremek, M., Kozirowski, D., Tomasiuk, R., Szlufik, S., & Friedman, A. (2020). Serum levels of hepcidin and interleukin 6 in Parkinson's disease. *Acta Neurobiol Exp (Wars)*, 80(3), 297-304.
- Kwo, P. Y., Cohen, S. M., & Lim, J. K. (2017). ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. *Am J Gastroenterol*, 112(1), 18-35. doi:10.1038/ajg.2016.517
- La, A., Nguyen, T., Tran, K., Sauble, E., Tu, D., Gonzalez, A., . . . Linder, M. C. (2018). Mobilization of iron from ferritin: new steps and details. *Metallomics*, 10(1), 154-168. doi:10.1039/c7mt00284j
- Lanier, J. B., Park, J. J., & Callahan, R. C. (2018). Anemia in Older Adults. *Am Fam Physician*, 98(7), 437-442. Retrieved from <https://www.aafp.org/afp/2018/1001/p437.html>
- Lehn, A., Boyle, R., Brown, H., Airey, C., & Mellick, G. (2012). Neuroferritinopathy. *Parkinsonism & Related Disorders*. Retrieved from <https://www.sciencedirect.com/science/article/abs/pii/S1353802012002593>
- Lewkowicz, A. K., & Tuuli, M. G. (2019). Iron-deficiency anaemia in pregnancy: the role of hepcidin. *Lancet Glob Health*, 7(11), e1476-e1477. doi:10.1016/s2214-109x(19)30414-0
- Liu, X., & Theil, E. C. (2005). Ferritins: dynamic management of biological iron and oxygen chemistry. *Acc Chem Res*, 38(3), 167-175. doi:10.1021/ar0302336
- Lv, Q., Niu, H., Yue, L., Liu, J., Yang, L., Liu, C., . . . Wang, H. (2020). Abnormal Ferroptosis in Myelodysplastic Syndrome. *Front Oncol*, 10, 1656. doi:10.3389/fonc.2020.01656



- Madore, F., White, C. T., Foley, R. N., Barrett, B. J., Moist, L. M., Klarenbach, S. W., . . . Manns, B. J. (2008). Clinical practice guidelines for assessment and management of iron deficiency. *Kidney Int Suppl*(110), S7-s11. doi:10.1038/ki.2008.269
- Mancias, J. D., Wang, X., Gygi, S. P., Harper, J. W., & Kimmelman, A. C. (2014). Quantitative proteomics identifies NCOA4 as the cargo receptor mediating ferritinophagy. *Nature*, 509(7498), 105-109. doi:10.1038/nature13148
- Marell, P. S., Blohowiak, S. E., Evans, M. D., Georgieff, M. K., Kling, P. J., & Tran, P. V. (2019). Cord Blood-Derived Exosomal CNTN2 and BDNF: Potential Molecular Markers for Brain Health of Neonates at Risk for Iron Deficiency. *Nutrients*, 11(10). doi:10.3390/nu11102478
- McLaren, C. E., Barton, J. C., Adams, P. C., Harris, E. L., Acton, R. T., Press, N., . . . Iron Overload Study Research, I. (2003). Hemochromatosis and Iron Overload Screening (HEIRS) study design for an evaluation of 100,000 primary care-based adults. *Am J Med Sci*, 325(2), 53-62. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/12589228>
- McNally, J. R., Mehlenbacher, M. R., Luscieti, S., Smith, G. L., Reutovich, A. A., Maura, P., . . . Bou-Abdallah, F. (2019). Mutant L-chain ferritins that cause neuroferritinopathy alter ferritin functionality and iron permeability. *Metallomics*, 11(10), 1635-1647. doi:10.1039/c9mt00154a
- Mei, Z., Addo, O. Y., Jefferds, M. E., Sharma, A. J., Flores-Ayala, R. C., & Brittenham, G. M. (2021). Physiologically based serum ferritin thresholds for iron deficiency in children and non-pregnant women: a US National Health and Nutrition Examination Surveys (NHANES) serial cross-sectional study. *Lancet Haematol*, 8(8), e572-e582. doi:10.1016/s2352-3026(21)00168-x
- Miller, J. L. (2013). Iron deficiency anemia: a common and curable disease. *Cold Spring Harb Perspect Med*, 3(7). doi:10.1101/cshperspect.a011866
- Munoz, M., Acheson, A. G., Auerbach, M., Besser, M., Habler, O., Kehlet, H., . . . Klein, A. A. (2017). International consensus statement on the peri-operative management of anaemia and iron deficiency. *Anaesthesia*, 72(2), 233-247. doi:10.1111/anae.13773
- Munoz, M., Gomez-Ramirez, S., Besser, M., Pavia, J., Gomollon, F., Liunbruno, G. M., . . . Auerbach, M. (2017). Current misconceptions in diagnosis and management of iron deficiency. *Blood Transfus*, 15(5), 422-437. doi:10.2450/2017.0113-17
- Nalado, A. M., Olorunfemi, G., Dix-Peek, T., Dickens, C., Khambule, L., Snyman, T., . . . Naicker, S. (2020). Hepcidin and GDF-15 are potential biomarkers of iron deficiency anaemia in chronic kidney disease patients in South Africa. *BMC Nephrol*, 21(1), 415. doi:10.1186/s12882-020-02046-7
- NIDDK. (2014, March 2014). Hemochromatosis. Retrieved from <https://www.niddk.nih.gov/health-information/liver-disease/hemochromatosis>
- Otvos, J. D., Shalaurova, I., Wolak-Dinsmore, J., Connelly, M. A., Mackey, R. H., Stein, J. H., & Tracy, R. P. (2015). GlycA: A Composite Nuclear Magnetic Resonance Biomarker of Systemic Inflammation. *Clin Chem*, 61(5), 714-723. doi:10.1373/clinchem.2014.232918
- Ozdemir, N. (2015). Iron deficiency anemia from diagnosis to treatment in children. *Turk Pediatri Ars*, 50(1), 11-19. doi:10.5152/tpa.2015.2337



- Paul, B. T., Manz, D. H., Torti, F. M., & Torti, S. V. (2017). Mitochondria and Iron: current questions. *Expert Rev Hematol*, 10(1), 65-79. doi:10.1080/17474086.2016.1268047
- Peng, Y. Y., & Uprichard, J. (2017). Ferritin and iron studies in anaemia and chronic disease. *Ann Clin Biochem*, 54(1), 43-48. doi:10.1177/0004563216675185
- Phillips, R., Wood, H., Weaving, G., & Chevassut, T. (2021). Changes in full blood count parameters with age and sex: results of a survey of almost 900 000 patient samples from primary care. *Br J Haematol*, 192(4), e102-e105. doi:10.1111/bjh.17290
- Pietrangelo, A. (2015). Genetics, Genetic Testing, and Management of Hemochromatosis: 15 Years Since Heparin. *Gastroenterology*, 149(5), 1240-1251. doi:10.1053/j.gastro.2015.06.045
- Ritchie, S. C., Wurtz, P., Nath, A. P., Abraham, G., Havulinna, A. S., Fearnley, L. G., . . . Inouye, M. (2015). The Biomarker GlycA Is Associated with Chronic Inflammation and Predicts Long-Term Risk of Severe Infection. *Cell Syst*, 1(4), 293-301. doi:10.1016/j.cels.2015.09.007
- Roetto, A., Mezzanotte, M., & Pellegrino, R. M. (2018). The Functional Versatility of Transferrin Receptor 2 and Its Therapeutic Value. *Pharmaceuticals (Basel)*, 11(4). doi:10.3390/ph11040115
- Saeed, H., Woods, R. R., Lester, J., Herzig, R., Gul, Z., & Monohan, G. (2015). Evaluating the optimal serum ferritin level to identify hemophagocytic lymphohistiocytosis in the critical care setting. *Int J Hematol*, 102(2), 195-199. doi:10.1007/s12185-015-1813-1
- Salgia, R. J., & Brown, K. (2015). Diagnosis and management of hereditary hemochromatosis. *Clin Liver Dis*, 19(1), 187-198. doi:10.1016/j.cld.2014.09.011
- Sankaran, V. G., & Weiss, M. J. (2015). Anemia: progress in molecular mechanisms and therapies. *Nat Med*, 21(3), 221-230. doi:10.1038/nm.3814
- Santambrogio, P., Cozzi, A., Levi, S., & Arosio, P. (1987). Human serum ferritin G-peptide is recognized by anti-L ferritin subunit antibodies and concanavalin-A. *Br J Haematol*, 65(2), 235-237. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/3828232>
- Santos, P. C., Krieger, J. E., & Pereira, A. C. (2012). Molecular diagnostic and pathogenesis of hereditary hemochromatosis. *Int J Mol Sci*, 13(2), 1497-1511. doi:10.3390/ijms13021497
- Sekigawa, I., Suzuki, J., Nawata, M., Ikeda, K., Koike, M., Iida, N., . . . Oshimi, K. (2001). Hemophagocytosis in autoimmune disease. *Clin Exp Rheumatol*, 19(3), 333-338. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/11407091>
- Suchdev, P. S., Williams, A. M., Mei, Z., Flores-Ayala, R., Pasricha, S. R., Rogers, L. M., & Namaste, S. M. (2017). Assessment of iron status in settings of inflammation: challenges and potential approaches. *Am J Clin Nutr*, 106(Suppl 6), 1626s-1633s. doi:10.3945/ajcn.117.155937
- Ueda, N., & Takasawa, K. (2018). Impact of Inflammation on Ferritin, Heparin and the Management of Iron Deficiency Anemia in Chronic Kidney Disease. *Nutrients*, 10(9). doi:10.3390/nu10091173

USPSTF. (2015a). Iron Deficiency Anemia in Pregnant Women: Screening and Supplementation. Retrieved from <https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/iron-deficiency-anemia-in-pregnant-women-screening-and-supplementation?ds=1&s=anemia>

USPSTF. (2015b). Iron Deficiency Anemia in Young Children: Screening. Retrieved from <https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/iron-deficiency-anemia-in-young-children-screening?ds=1&s=anemia>

van Bokhoven, M. A., van Deursen, C. T., & Swinkels, D. W. (2011). Diagnosis and management of hereditary haemochromatosis. *BMJ*, 342, c7251. doi:10.1136/bmj.c7251

Vujić, M. (2014). Molecular basis of HFE-hemochromatosis. *Front Pharmacol*, 5. doi:10.3389/fphar.2014.00042

Wang, W., Knovich, M. A., Coffman, L. G., Torti, F. M., & Torti, S. V. (2010). Serum ferritin: Past, present and future. *Biochim Biophys Acta*, 1800(8), 760-769. doi:10.1016/j.bbagen.2010.03.011

WHO. (2020). WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations.

Wiegersma, A. M., Dalman, C., Lee, B. K., Karlsson, H., & Gardner, R. M. (2019). Association of Prenatal Maternal Anemia With Neurodevelopmental Disorders. *JAMA Psychiatry*, 76(12), 1-12. doi:10.1001/jamapsychiatry.2019.2309

Wood, J. C. (2014). Guidelines for quantifying iron overload. *Hematology Am Soc Hematol Educ Program*, 2014(1), 210-215. doi:10.1182/asheducation-2014.1.210

Xie, Y., Hou, W., Song, X., Yu, Y., Huang, J., Sun, X., . . . Tang, D. (2016). Ferroptosis: process and function. *Cell Death Differ*, 23(3), 369-379. doi:10.1038/cdd.2015.158

Yuniati, T., Judistiani, R. T. D., Natalia, Y. A., Irianti, S., Madjid, T. H., Ghozali, M., . . . Setiabudiawan, B. (2019). First trimester maternal vitamin D, ferritin, hemoglobin level and their associations with neonatal birthweight: Result from cohort study on vitamin D status and its impact during pregnancy and childhood in Indonesia. *J Neonatal Perinatal Med*. doi:10.3233/npm-180043

Zandman-Goddard, G., & Shoenfeld, Y. (2007). Ferritin in autoimmune diseases. *Autoimmun Rev*, 6(7), 457-463. doi:10.1016/j.autrev.2007.01.016

Zanella, A., Gridelli, L., Berzuini, A., Colotti, M. T., Mozzi, F., Milani, S., & Sirchia, G. (1989). Sensitivity and predictive value of serum ferritin and free erythrocyte protoporphyrin for iron deficiency. *J Lab Clin Med*, 113(1), 73-78. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/2909654>

Zhang, D. L., Ghosh, M. C., & Rouault, T. A. (2014). The physiological functions of iron regulatory proteins in iron homeostasis - an update. *Front Pharmacol*, 5. doi:10.3389/fphar.2014.00124

## Policy Update History:

5/1/2022	New policy
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