Clinical Policy: Ferriscan R2-MRI

Reference Number: PA.CP.MP.53
Effective Date: 10/18
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Coding Implications
Revision Log

Description
FerriScan® R2-MRI is a magnetic resonance imaging (MRI)-based solution for measuring liver iron concentration (LIC) in patients with iron overload.

Policy/Criteria
I. It is the policy of PA Health & Wellness® that the FerriScan® R2-MRI is **medically necessary** for the measurement of liver iron concentration in suspected cases of iron overload due to the following conditions:
- **A.** Hereditary hemochromatosis;
- **B.** Iron-loading anemias with or without multiple transfusions:
  1. Thalassemia major or thalassemia intermedia;
  2. Sideroblastic anemia;
  3. Chronic hemolytic anemias (e.g., sickle cell disease);
  4. Inherited or acquired aplastic anemia;
  5. Myelodysplastic syndromes;
  6. Hematopoietic stem cell transplantation;
- **C.** Dietary iron overload;
- **D.** Iron overload in liver diseases:
  1. Hepatitis C or B;
  2. Alcohol-induced liver disease;
  3. Porphyria cutanea tarda;
  4. Fatty liver disease;
  5. Gestational alloimmune liver disease;
  6. Suspicion of rare genetic variants affecting iron absorption or distribution[4];
- **E.** Neonatal iron overload;
- **F.** Aceruloplasminemia;
- **G.** Repeated hemin infusions for acute porphyrias;
- **H.** Hemodialysis for end stage renal failure.

Background
Iron overload is a potentially life-threatening problem that is commonly overlooked due to nonspecific symptoms that tend to develop slowly over time. Excess iron does not only affect the liver, but can also accumulate in, and damage other organs like the heart, skin and endocrine organs, as well as joints. Clinical issues resulting from excess iron include tissue damage, inflammation, and fibrosis. Left untreated, iron overload can result in organ toxicity, end-organ damage and dysfunction due to oxidative stress resulting in excess oxygen radicals and injury from tissue peroxidation. Once identified, iron overload is treated with therapeutic phlebotomy and chelation therapy as well as exchange transfusion in sickle cell disease.[4,5]

Disorders associated with hepatic iron deposition include[4,5]:
- Hereditary hemochromatosis;

- Syndromes of ineffective erythropoiesis such as beta thalassemia, sideroblastic anemia and other inherited anemias;
- Chronic liver disease;
- Gestational alloimmune liver disease
- Alcoholic liver disease;
- Hepatitis;
- Nonalcoholic fatty liver disease;
- Cirrhosis;
- Wilson disease;
- Porphyria cutanea tarda;
- Hematopoietic stem cell transplantation,
- Myelodysplastic syndrome,
- Dialysis;
- Blood transfusions for sickle cell disease.

FerriScan® is a non-invasive technology based on magnetic resonance imaging (MRI). It has a high sensitivity and specificity for the measurement of liver iron concentration (LIC) over the entire range encountered in clinical practice. It can be set up on most 1.5 Tesla MRI scanners, which are the most common type of clinical scanner, and it was announced by Resonance Health in 2022 that FerriScan is now available on 3 Tesla MRI machines.[16] FerriScan works by making a map of the LIC and calculating the mean LIC. The results are unaffected by the presence of fibrosis or cirrhosis. Image data is acquired on an MRI scanner and is electronically transmitted to a data analysis center. All data is analyzed to ensure correct acquisition, and the LIC results are transmitted back to the originating MRI center.

Measurements have been shown to have a high degree of sensitivity and specificity for LIC measured by biopsy. Ferriscan has become increasingly accurate in the determination of hepatic and cardiac iron deposition and is replacing direct tissue biopsy in the assessment of iron overload.[4] FerriScan images give information on liver iron distribution. The mean LIC value given in the FerriScan report is then used to guide chelation therapy.

The operational principle of the R2-MRI Analysis System is based on fitting signal decay curves to the image signal intensities (e.g., of the liver) at the different echo times for the magnetic resonance data set on a voxel-by-voxel (3-D pixel) basis to determine transverse relaxation rate (R2) images. These may be further transformed by a defined calibration to provide a quantitative measure of liver iron concentrations.

Although magnetic resonance evaluation for hepatic iron concentration is improved compared with older programs, this type of imaging will not detect cellular liver damage due to iron overload.

The American College of Radiology's 2020 Practice Parameter for the performance of MRI of the liver states that indications for MRI of the liver include, but are not limited to, evaluation and noninvasive quantification of iron, fat, and fibrosis in chronic liver disease, such as hemochromatosis, hemosiderosis, nonalcoholic steatohepatitis (NASH), and hepatitis in adults and pediatric patients. Additionally, multiple studies have confirmed the clinical utility of R2-

MRI in the measurement of LIC for iron-overloading conditions such as thalassemia and sickle cell anemia.[9] A study of R2-MRI results vs. simulated liver biopsy results found R2-MRI to be superior to liver biopsy for serial LIC observations.[10] Furthermore, a review of the current state of liver iron quantification by MRI states that R2-MRI provides validated measurement of LIC and has advantages over liver biopsy, in that it is non-invasive.[11]

The R2-MRI Analysis System (Inner Vision Biometrics PTY LTD) received 510(k) clearance (K043271) from the United Stated Food and Drug Administration (FDA)on January 21, 2005. In January 2013, the FDA authorized the FerriScan R2-MRI to be marketed as an imaging companion diagnostic device for the safe and effective use of Exjade in patients with non-transfusion-dependent thalassemia.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2022, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
76498	Unlisted MRI procedure

Reviews, Revisions, and Approvals	Revision Date	Approval Date
References reviewed and updated. Codes reviewed and updated.	10/18	10/18
Changed "thalassemia major and thalassemia intermedia" to "thalassemia major or thalassemia intermedia." Changed "hepatitis C and B" to "hepatitis C or B"	01/19	02/19
Replaced codes D61.89 and D61.9 with expanded range of D61.01-D61.9. Replaced "member" with "member/enrollee/enrollee" in all instances. References reviewed and updated. Reviewed by specialist.	12/2020	1/18/2021
References reviewed and updated. Reviewed by specialist.	10/2021	
Annual review. Added "Hemodialysis for end stage renal failure" as an indication. Changed "review date" in the header to "date of last revision" and "date" in the revision log header to "revision date." Updated background with no clinical significance or impact on criteria. ICD-10 codes removed from policy. References reviewed and updated. Reviewed by specialist.	02/22/2023	
Annual Review. Added criterion I.B.6. Hematopoietic stem cell transplantation as an iron-loading anemia indication. Added criterion I.G.6., "Suspicion of rare genetic variants affecting iron absorption or distribution." Updated background with no clinical significance or	10/2023	

Reviews, Revisions, and Approvals	Revision Date	Approval Date
impact to criteria. Reviewed and updated references. Reviewed and updated CPT code description. Reviewed by external specialist		

References

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