Local Coverage Determination (LCD):
MolDX: Molecular RBC Phenotyping (L36074)

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Contractor Information

<table>
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<tr>
<th>Contractor Name</th>
<th>Contract Type</th>
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LCD Information

Document Information

- LCD ID: L36074
  - Original Effective Date: For services performed on or after 10/01/2015
  - Original ICD-9 LCD ID: N/A
  - LCD Title: MolDX: Molecular RBC Phenotyping
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  - Retirement Date: N/A
  - Notice Period Start Date: 05/07/2015
  - Notice Period End Date: 06/21/2015

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CMS National Coverage Policy Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that “are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim.

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS Internet Online ManualPub. 100-02 (Medicare Benefit Policy Manual), Chapter 15, Section 80, “Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests”

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) “Reporting ICD Diagnosis and Procedure Codes”

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This policy provides limited-coverage for molecular phenotyping of erythrocyte antigens performed on the HEA BeadChip™ (Immucor, Warren, NJ), a single nucleotide polymorphisms (SNP)-based microarray test. This high-throughput molecular assay received FDA PMA approval in May, 2014 and is the only IVD- approved molecular test to characterize human red blood cell (RBC) antigens.

Many clinically significant antigens are encoded by alleles defined by SNPs. This assay identifies 35 antigens and 3 phenotypic variants across 11 blood groups (Rh, Kell, Duffy, Kidd, MNS, Lutheran, Dombrock, Landsteiner-Wiener, Diego, Colton and Scianna). Genomic DNA targets isolated from whole blood are amplified and fluorescent signals are interpreted by online software as specific alleles and probable antigen phenotype. This test does not evaluate patient antibody status.

For more than ten years, RBC genotyping has been applied mainly to mass screen donors in blood centers. American Rare Donor Program, a consortium of the American Red Cross and American Association of Blood Banks (AABB) accredited immunohematology reference laboratories have used molecular genotype information for several years to identify antigen negative blood units from donor for patients with antibodies. Blood centers also use molecular technology to genotype donors for certain antigens (eg, Dombrock) that are hard to ascertain because of antisera unavailability or weak potency.

Hemagglutination is the most common serologic method of determining a RBC phenotype. In this technique, the patient’s RBCs are tested with antisera specific for the antigens of interest. However, hemagglutination testing cannot be used if a patient has a positive direct antiglobuin test (DAT), or if direct agglutination typing sera is not available for the antigen. In addition, serologic phenotyping is invalid in the transfused patient who may have persistent donor RBCs in circulation. Because molecular genotyping is not subject to the limitations of serologic testing, it has become a useful tool in large hospital transfusion services.

As early as 1999, Legler et al demonstrated disparate molecular Rh phenotyping in 7 of 27 patients compared to serologic typing. Soon afterwards, Reid and others demonstrated that DNA from blood samples could be used to genotype patients who had recently been transfused. Castilho et al confirmed the unreliability of serologic testing when they showed that 6 of 40 molecular genotypes differed from serologic phenotypes in multiply transfused sickle cell anemia (SCA) patients, and in 9 of 10 alloimmunized thalassemic patients. A number of investigators have replicated these findings, most notably Bakanay et al when they demonstrated genotypic and phenotypic discrepancies in 19 or 37 multi-transfused patients in multiple alleles. The discrepancies aided in the selection of
antigen-matched blood products and improved RBC survival, ultimately improving patient care. A recent case report by Wagner emphasizes the usefulness of molecular testing over serologic testing in chronically transfused patients.

In a prospective observational study, Klapper et al. used the HEA BeadChip™ to provide extended human erythrocyte antigen (xHEA) phenotyped donor units and recipient patient samples. XHEA-typed units were assigned to pending transfusion requests using a web-based inventory management system to simulate blood order processing at four hospital transfusion services. The fraction of requests filled (FF) in 3 of 4 sites was > 95% when matching for ABO, D and known alloantibodies, with a FF of > 90% when additional matching for C, c, E, e, and K antigens. The most challenging requests came from the fourth site where the FF was 62 and 51% respectively, even with a limited donor pool.

In a prospective observational study by Da Costa et al, 21 of 35 sickle cell anemia (SCA) patients had discrepancies or mismatches, mainly in the Rh, Duffy, Jk and MNS blood groups, between the genotype profile and the serologically-matched blood unit for multiple antigens. These authors report that their genotype-matching program resulted in elevated hemoglobin levels, increased time between transfusions and prevented the development of new alloantibodies.

Two recently published papers have shown the feasibility of routinely applying molecular blood banking techniques in a hospital transfusion service. Routine RBC testing has been implemented in a large tertiary care hospital in Los Angeles, CA to maximize efficient use of blood units. Patients with warm or cold reacting autoantibodies, patients with SCA and patients with antibodies that could not be identified were molecularly genotyped and received molecularly matched blood from the hospital’s genotyped donor inventory.

At a large hospital in Cleveland, OH, pre-transfusion molecular typing is performed on chronically transfused patients, patients with autoantibodies, multiple antibodies, when no antigen specific antibody is available for testing and to solve laboratory discrepancies. They authors note that the major benefit of molecular typing is its application for patients who cannot be typed by serology due to an unsuitable sample. Valid results can be obtained even when they have been transfused within a few days of testing or have been massively transfused. Samples selected for molecular testing were based on an algorithm.

Medicare will cover pretransfusion molecular testing using the HEA BeadChip™ assay for the following categories of patients:

- Long term, frequent transfusions anticipated to prevent the development of alloantibodies (e.g. sickle cell anemia, thalassemia or other reason);

- Autoantibodies or other serologic reactivity that impedes the exclusion of clinically significant alloantibodies (e.g. autoimmune hemolytic anemia, warm autoantibodies, patient recently transfused with a positive DAT, high-titer low avidity antibodies, other reactivity of no apparent cause);

- Suspected antibody against an antigen for which typing sera is not available; and

- Laboratory discrepancies on serologic typing (e.g. rare Rh D antigen variants)

Medicare does not expect molecular testing to be performed on patients undergoing surgical procedures such as bypass or other cardiac procedures, hip or knee replacements or revisions, or patients with alloantibodies identifiable by serologic testing that are not expected to require long term, frequent transfusions.

The medical necessity for molecular RBC phenotyping must be documented in the patient’s medical record.

Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.
Revenue Codes:

 Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

CPT/HCPCS Codes

**Group 1 Paragraph:** N/A

**Group 1 Codes:**

MOLECULAR PATHOLOGY PROCEDURE, LEVEL 4 (EG, ANALYSIS OF SINGLE EXON BY DNA SEQUENCE ANALYSIS, ANALYSIS OF >10 AMPICONS USING MULTIPLEX PCR IN 2 OR MORE INDEPENDENT REACTIONS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 2-5 EXONS)

ICD-10 Codes that Support Medical Necessity

**Group 1 Paragraph:** N/A

**Group 1 Codes:**

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<td>Vitamin B12 deficiency anemia due to intrinsic factor deficiency</td>
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<td>D53.9</td>
<td>Nutritional anemia, unspecified</td>
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<td>D55.0</td>
<td>Anemia due to glucose-6-phosphate dehydrogenase [G6PD] deficiency</td>
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<td>Anemia due to other disorders of glutathione metabolism</td>
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<td>D55.3</td>
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<td>D55.8</td>
<td>Other anemias due to enzyme disorders</td>
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### General Information

**Associated Information**

**Documentation Requirements**

The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the J11 MAC upon request.

**Sources of Information and Basis for Decision**

**References**


10. Reid ME, Rios M, Powell VA, et al. DNA from blood samples can be used to genotype patients who have recently received a transfusion. Transfusion 2000;40:48-53.


Please note: Most Revision History entries effective on or before 01/24/2013 display with a Revision History Number of "R1" at the bottom of this table. However, there may be LCDs where these entries will display as a separate and distinct row.

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<td>Per CMS Internet-Only Manual, Pub 100-08, Medicare Program Integrity Manual, Chapter 13, §13.1.3 LCDs consist of only &quot;reasonable and necessary&quot; information. All bill type and revenue codes have been removed.</td>
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**Associated Documents**

Attachments N/A

Related Local Coverage Documents N/A

Related National Coverage Documents N/A

Public Version(s) Updated on 06/03/2015 with effective dates 10/01/2015 - N/A Updated on 06/02/2015 with effective dates 10/01/2015 - N/A Updated on 05/13/2015 with effective dates 10/01/2015 - N/A Updated on 05/06/2015 with effective dates 10/01/2015 - N/A

**Keywords**

N/A Read the [LCD Disclaimer](#) Back to Top

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