

Centers for Medicare & Medicaid Services

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Local Coverage Determination (LCD): MolDX: Molecular RBC Phenotyping (L36167)

- Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Noridian Healthcare Solutions, LLC	A and B MAC	01111 - MAC A	J - E	California - Entire State
Noridian Healthcare Solutions, LLC	A and B MAC	01112 - MAC B	J - E	California - Northern
Noridian Healthcare Solutions, LLC	A and B MAC	01182 - MAC B	J - E	California - Southern
Noridian Healthcare Solutions, LLC	A and B MAC	01211 - MAC A	J - E	American Samoa Guam Hawaii Northern Mariana Islands
Noridian Healthcare Solutions, LLC	A and B MAC	01212 - MAC B	J - E	American Samoa Guam Hawaii Northern Mariana Islands
Noridian Healthcare Solutions, LLC	A and B MAC	01311 - MAC A	J - E	Nevada
Noridian Healthcare Solutions, LLC	A and B MAC	01312 - MAC B	J - E	Nevada
Noridian Healthcare Solutions, LLC	A and B MAC	01911 - MAC A	J - E	American Samoa California - Entire State Guam Hawaii Nevada Northern Mariana Islands

- LCD Information

Document Information

LCD ID

L36167

LCD Title

MolDX: Molecular RBC Phenotyping

Proposed LCD in Comment Period

N/A

Source Proposed LCD

N/A

Original Effective Date

For services performed on or after
04/01/2016

Revision Effective Date

For services performed on or after
02/01/2017

Revision Ending Date

N/A

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Retirement Date

N/A

Notice Period Start Date

02/11/2016

Notice Period End Date

03/31/2016

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 Manual Pub. 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 antiglobulin 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. The 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.

Two recent research studies have demonstrated that treatment with daratumumab, a CD38 monoclonal antibody, can bind to CD38 expressed on the surface of red blood cells (RBCs) and interferes with serologic testing, thereby preventing cross-match. False-positive reactions may persist for 2 to 6 months after infusion.

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, patients about to receive or on daratumumab therapy, 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.

Summary of Evidence

N/A

**Analysis of Evidence
(Rationale for Determination)**

N/A

- 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.

013x	Hospital Outpatient
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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.

N/A

CPT/HCPCS Codes

Group 1 Paragraph:

N/A

Group 1 Codes:

81403	MOLECULAR PATHOLOGY PROCEDURE, LEVEL 4 (EG, ANALYSIS OF SINGLE EXON BY DNA SEQUENCE ANALYSIS, ANALYSIS OF >10 AMPLICONS USING MULTIPLEX PCR IN 2 OR MORE INDEPENDENT REACTIONS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 2-5 EXONS)
0001U	RED BLOOD CELL ANTIGEN TYPING, DNA, HUMAN ERYTHROCYTE ANTIGEN GENE ANALYSIS OF 35 ANTIGENS FROM 11 BLOOD GROUPS, UTILIZING WHOLE BLOOD, COMMON RBC ALLELES REPORTED

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODES	DESCRIPTION
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse
D51.0	Vitamin B12 deficiency anemia due to intrinsic factor deficiency
D53.9	Nutritional anemia, unspecified
D55.0	Anemia due to glucose-6-phosphate dehydrogenase [G6PD] deficiency
D55.1	Anemia due to other disorders of glutathione metabolism

D55.2	Anemia due to disorders of glycolytic enzymes
D55.3	Anemia due to disorders of nucleotide metabolism
D55.8	Other anemias due to enzyme disorders
D55.9	Anemia due to enzyme disorder, unspecified
D56.0	Alpha thalassemia
D56.1	Beta thalassemia
D56.2	Delta-beta thalassemia
D56.3	Thalassemia minor
D56.5	Hemoglobin E-beta thalassemia
D56.8	Other thalassemias
D56.9	Thalassemia, unspecified
D57.00	Hb-SS disease with crisis, unspecified
D57.01	Hb-SS disease with acute chest syndrome
D57.02	Hb-SS disease with splenic sequestration
D57.1	Sickle-cell disease without crisis
D57.20	Sickle-cell/Hb-C disease without crisis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.219	Sickle-cell/Hb-C disease with crisis, unspecified
D57.3	Sickle-cell trait
D57.40	Sickle-cell thalassemia without crisis
D57.411	Sickle-cell thalassemia with acute chest syndrome
D57.412	Sickle-cell thalassemia with splenic sequestration
D57.419	Sickle-cell thalassemia with crisis, unspecified
D57.80	Other sickle-cell disorders without crisis
D57.811	Other sickle-cell disorders with acute chest syndrome
D57.812	Other sickle-cell disorders with splenic sequestration
D57.819	Other sickle-cell disorders with crisis, unspecified
D58.0	Hereditary spherocytosis
D58.1	Hereditary elliptocytosis
D58.9	Hereditary hemolytic anemia, unspecified
D59.0	Drug-induced autoimmune hemolytic anemia
D59.1	Other autoimmune hemolytic anemias
D59.9	Acquired hemolytic anemia, unspecified

D60.0	Chronic acquired pure red cell aplasia
D60.1	Transient acquired pure red cell aplasia
D60.8	Other acquired pure red cell aplasias
D60.9	Acquired pure red cell aplasia, unspecified
D61.01	Constitutional (pure) red blood cell aplasia
D61.09	Other constitutional aplastic anemia
D61.1	Drug-induced aplastic anemia
D61.2	Aplastic anemia due to other external agents
D61.3	Idiopathic aplastic anemia
D61.89	Other specified aplastic anemias and other bone marrow failure syndromes
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D63.8	Anemia in other chronic diseases classified elsewhere
D64.0	Hereditary sideroblastic anemia
D64.1	Secondary sideroblastic anemia due to disease
D64.2	Secondary sideroblastic anemia due to drugs and toxins
D64.3	Other sideroblastic anemias
D64.4	Congenital dyserythropoietic anemia
D64.89	Other specified anemias

ICD-10 Codes that DO NOT Support Medical Necessity

N/A

ICD-10 Additional Information

– 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 MAC upon request.

This final LCD, effective 04/01/2016, combines JEA DL36135 into the JEB LCD so that both JEA and JEB contract numbers will have the same final MCD LCD number.

Sources of Information

References

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Bibliography

N/A

- Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
02/01/2017	R2	Added HCPCS code 0001U to CPT/HCPCS Group 1, effective February 1, 2017. 11/08/2017: At this time 21st	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction

Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.

04/01/2016

R1

Added statement RBC phenotyping of MM patients eligible for daratumumab therapy (anti CD-38) because it interferes with serologic testing and included coverage for Medicare eligible patients "prior to and following treatment with anti-CD-38 therapy for MM.

- Creation of Uniform LCDs With Other MAC Jurisdiction
- Revisions Due To ICD-10-CM Code Changes

Added ICD-10 codes: C90.00, C90.01 and C90.02 and three (#'s 1, 5 and 12) additional sources of information under References.

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– Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A54865 - Response to Comments: MolDX: Molecular RBC Phenotyping LCD(s)

DL36135 - (MCD Archive Site)

DL36167 - (MCD Archive Site)

Related National Coverage Documents

N/A

Public Version(s)

Updated on 11/09/2017 with effective dates 02/01/2017 - N/A

Updated on 05/18/2016 with effective dates 04/01/2016 - 01/31/2017

Updated on 01/29/2016 with effective dates 04/01/2016 - N/A

– Keywords

- Molecular RBC Phenotyping
- 81403
- genotyping

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