Medical Coverage Policy | Blood Product Molecular Antigen Typing

EFFECTIVE DATE: 02|01|2025
POLICY LAST REVIEWED: 03|19|2025

OVERVIEW

For patients who require a blood product transfusion, an important step taken prior to the transfusion of any blood product is compatibility testing between the recipient's serum and the blood product being transfused. In addition to the ABO and Rh system there are 34 other recognized blood group antigen systems by the International Society of Blood Transfusion. Identifying the blood product antigens to which the transfusion recipient will have an immune reaction is a critical component of this compatibility testing, though for most patients identification of ABO and Rh compatibility is sufficient.

The following test(s) is addressed in this policy:

- BLOODchip® ID CORE XT™ (Grifols Diagnostic Solutions, Inc.) CPT code 0084U
- Precise Type ® HEA test (Immucor, Inc.) CPT code 0001U

MEDICAL CRITERIA

Medicare Advantage Plans and Commercial Products

This policy provides coverage for molecular phenotyping of blood product antigens as part of the pretransfusion evaluation for patients who may require or are expected to require a blood product transfusion(s) (Red Blood Cells [RBCs], Platelets or Leukocytes) when at least one of the following criteria is met:

- Long term, frequent transfusions anticipated to prevent the development of alloantibodies (e.g., sickle cell anemia, thalassemia, chronic transfusion dependent hematologic disorders or other reasons); OR
- 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); OR
- Suspected antibody against an antigen for which typing sera is not available; OR
- Laboratory discrepancies on serologic typing (e.g., rare Rh D antigen variants)

PRIOR AUTHORIZATION

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products.

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products
The following test may be considered medically necessary when the medical criteria above are met:

- BLOODchip® ID CORE XT™
- Precise Type ® HEA test

The following test may be considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products when the medical criteria above are not met:

- BLOODchip® ID CORE XT™
- Precise Type ® HEA test

Commercial Products
Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L**. §27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory benefits/coverage.

BACKGROUND

For patients who require a blood product transfusion, an important step taken prior to the transfusion of any blood product is compatibility testing between the recipient's serum and the blood product being transfused. In addition to the ABO and Rh system there are 34 other recognized blood group antigen systems by the International Society of Blood Transfusion. Identifying the blood product antigens to which the transfusion recipient will have an immune reaction is a critical component of this compatibility testing, though for most patients identification of ABO and Rh compatibility is sufficient. However, for patients who have alloantibodies or patients who have a predisposition to develop alloimmunization (e.g., patients with sickle cell disease and others who are chronically transfused), compatibility testing of additional systems may be needed. Hemagglutination has traditionally been the most common serologic method of determining a blood product phenotype. In this technique, the patient's RBCs are tested with antisera specific for the antigens of interest. However, this method has limitations. It requires direct agglutination typing sera for the antigen, and hemagglutination testing results are not meaningful if a patient has a positive direct antiglobulin test (DAT). In addition, serologic phenotyping is likely to be erroneous in the transfused patient who may have persistent donor blood products in circulation, such as patients getting chronic frequent transfusions, and it has been suggested that chronically transfused patients or patients who have had a massive transfusion should not receive phenotyping using serological methods, or that if serological methods are used, they should be confirmed with molecular techniques.

Because molecular genotyping is not subject to the limitations of conventional serologic testing, the transfusion community has recognized molecular typing as a potential tool to aid in the determination of immune compatibility between donated blood products and the transfusion recipient in a number of circumstances where conventional methods may not be adequate, such as in patients who have a positive direct antigen test, in patients who have been recently transfused or those who are chronically transfused, in patients where a distinction between autoantibodies and alloantibodies is needed, or in situations where the presence of a weakly reactive anti-body is suspected.

Prior to broad clinical availability of molecular genotyping in the United States, a number of studies demonstrated both the feasibility of this technique and the incremental information it could provide over serologic typing in limited clinical contexts.

As early as 1999, a study from Germany in patients receiving chronic transfusions demonstrated disparate molecular Rh phenotyping in 7 of 27 patients compared to serologic typing. Soon afterwards, Reid et al demonstrated that Deoxyribonucleic acid (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 highlighted the practical utility of molecular testing over serologic testing for chronically transfused patients.

It has long been recognized that immunohematologic compatibility is critical to a successful blood product transfusion. It has also long been recognized that serologic methods of determining compatibility, while useful in many cases have limitations for particular groups of patients. Molecular methods for blood product antigen determination are not subject to the same limitations, and Food and Drug Administration (FDA)-approved tests using molecular methods have been developed and validated to detect particular alleles within particular blood group systems. As such, FDA-approved tests are reasonable and necessary for blood product antigen typing in patients for whom a transfusion is needed when conventional serologic testing methods are inadequate or at a high risk of producing unreliable or misleading results.

The evidence reviewed here did not seek to identify laboratory-developed tests intended to be used for the same purpose. However, since FDA-approved tests to detect all clinically significant alleles are not available at this time as the position statement from Association for the Advancement of Blood & Biotherapies (AABB), America's Blood Centers, and American Red Cross notes, laboratory developed tests (LDTs) remain important to allow for the identification of unusual alleles unlikely to be readily available on FDA-approved platforms. LDTs may be considered reasonable and necessary if peer-reviewed evidence demonstrates that a rigorous validation has been done to show that they accurately predict/identify the blood product antigens.

CODING

Medicare Advantage Plans and Commercial Products

The following CPT code(s) may be medically necessary for Medicare Advantage Plans and Commercial Products when medical criteria above are met:

This code can be used for BLOODchip® ID CORE XT™:

0084U Red blood cell antigen typing, DNA, genotyping of 10 blood groups with phenotype prediction of 37 red blood cell antigens

This code can be used for Precise Type ® HEA test:

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

RELATED POLICIES

Biomarker Testing Mandate
Proprietary Laboratory Analyses (PLA)

PUBLISHED

Provider Update, May 2025
Provider Update, April/December 2024
Provider Update, November 2023

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: Blood Product Molecular Antigen Typing (L38240)

2. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: MolDX: Blood Product Molecular Antigen Typing (A58308)
3. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: Blood Product Molecular Antigen Typing (L38331)
4. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: MolDX: Blood Product Molecular Antigen Typing (A57124)