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BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Fetal RhD Genotyping Using Maternal Plasma

Policy #: 554
Category: Laboratory

Latest Review Date: November 2014
Policy Grade:B

Background:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Description of Procedure or Service:

Rhesus (Rh) D-negative women who are exposed to RhD-positive red blood cells can develop anti-Rh antibodies, which can cross the placenta and cause fetal anemia. If undiagnosed and untreated, alloimmunization can cause significant perinatal morbidity and mortality. Determining the Rh status of the fetus may guide subsequent management of the pregnancy. The use of cell-free fetal DNA in maternal blood has been proposed as a noninvasive method to determine fetal RhD genotype.

Alloimmunization refers to the development of antibodies in a patient whose blood type is Rh-negative and who is exposed to Rh-positive red blood cells (RBCs). This most commonly occurs from fetal-placental hemorrhage and entry of fetal blood cells into maternal circulation. The management of an Rh-negative pregnant patient who is not alloimmunized and is carrying a known Rh-positive fetus, or if fetal Rh status is unknown involves administration of Rh immune globulin at standardized times during the pregnancy to prevent formation of anti-Rh antibodies. If the patient is already alloimmunized, monitoring the levels of anti-Rh antibody titers and for the development of fetal anemia is performed. Both noninvasive and invasive tests to determine fetal Rh status exist.

Policy:

Blue Advantage will treat **fetal RhD genotyping using maternal plasma** as a **non-covered benefit** and as **investigational.**

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Rh blood groups

The (Rhesus) Rh system includes more than 100 antigen varieties found on RBCs. RhD is the most common and the most immunogenic. When people have the RhD antigen on their RBCs, they are considered to be RhD-positive; if their RBCs lack the antigen, they are considered to be RhD-negative. The RhD-antigen is inherited in an autosomally dominant fashion, and a person may be heterozygous (Dd) (~60% of Rh-positive people) or homozygous (DD) (~40% of Rh-positive people). Homozygotes always pass the RhD antigen to their offspring, whereas heterozygotes have a 50% chance of passing the antigen to their offspring. A person who is RhD-negative does not have the Rh antigen. Although nomenclature refers to RhD-negative as dd, there is no small d antigen (i.e., they lack the *RHD* gene and the corresponding RhD antigen).

RhD-negative status varies among ethnic group and is 15% in whites, 5 to 8% in African Americans, 5% to 8%, and 1 to 2% in Asians and Native Americans, respectively.

In the white population, almost all RhD-negative individuals are homozygous for a deletion of the *RHD* gene. However, in the African-American population, only 18% of RhD-negative individuals are homozygous for an RHD deletion, and 66% of RhD-negative African Americans have an inactive RHDy. There are also numerous rare variants of the D antigen, which are recognized by weakness of expression of D and/or by absence of some of the epitopes of D. Some individuals with variant D antigens, if exposed to RhD-positive RBCs, can make antibodies to one or more epitopes of the D antigen.

RhD-negative women can have a fetus that is RhD-positive if the fetus inherits the RhD-positive antigen from the paternal father.

Causes of alloimmunization
By 30 days of gestation, the RhD antigen is expressed on the red blood cell (RBC) membrane, and alloimmunization can be caused when fetal Rh-positive RBCs enter maternal circulation, and the Rh-negative mother develops anti-D antibodies. Once anti-D antibodies are present in a pregnant woman's circulation, they can cross the placenta and cause destruction of fetal RBCs.

The production of anti-D antibodies in RhD-negative women is highly variable and significantly affected by several factors, including the volume of fetomaternal hemorrhage, the degree of maternal immune response, concurrent ABO incompatibility, and fetal homozygosity versus heterozygosity for the D antigen. Therefore, although ~10% of pregnancies are Rh-incompatible, <20% of Rh-incompatible pregnancies actually lead to maternal alloimmunization.

Small feto-maternal hemorrhages of RhD-positive fetal RBCs into the circulation of an RhD-negative woman occurs in nearly all pregnancies, and percentages of feto-maternal hemorrhage increase as the pregnancy progresses: 7% in the first trimester, 16% in the second trimester, and 29% in the third trimester, with the greatest risk of RhD alloimmunization occurring at birth (15 to 50%). Transplacental hemorrhage accounts for almost all cases of maternal RhD alloimmunization.

Fetomaternal hemorrhage can also be associated with miscarriage, pregnancy termination, ectopic pregnancy, invasive in-utero procedures (e.g., amniocentesis), in utero fetal death, maternal abdominal trauma, antepartum maternal hemorrhage, and external cephalic version. Other causes of alloimmunization include inadvertent transfusion of RhD-positive blood and RhD-mismatched allogeneic hematopoietic stem-cell transplantation.

Consequences of alloimmunization
IgG antibody–mediated hemolysis of fetal RBCs, known as hemolytic disease of the fetus and newborn, varies in severity and can have a variety of manifestations. The anemia can range from mild to severe with associated hyperbilirubinemia and jaundice. In severe cases, hemolysis may lead to extramedullary hematopoiesis and reticuloendothelial clearance of fetal RBCs, which may result in hepatosplenomegaly, decreased liver function, hypoproteinemia, ascites, and anasarca. When accompanied by high-output cardiac failure and pericardial effusion, this

condition is known as hydrops fetalis, which without intervention, is often fatal. Intensive neonatal care, including emergent exchange transfusion, is required.

Cases of hemolysis in the newborn that do not result in fetal hydrops can still lead to kernicterus, a neurologic condition observed in infants with severe hyperbilirubinemia due to the deposition of unconjugated bilirubin in the brain. Symptoms that manifest several days after delivery can include poor feeding, inactivity, loss of the Moro reflex, bulging fontanelle, and seizures. The 10% of infants who survive may develop spastic choreoathetosis, deafness, and/or mental retardation.

The result of disease from alloimmunization, hemolytic disease of the fetus or newborn, was once a major contributor to perinatal morbidity and mortality. However, with the widespread adoption of antenatal and postpartum use of Rh immune globulin in developed countries, the result has been a major decrease in frequency of this disease. In developing countries without prophylaxis programs, stillbirth occurs in 14% of affected pregnancies, and 50% of pregnancy survivors either die in the neonatal period or develop cerebral injury.

Prevention of alloimmunization
There are four currently in use Rh immune globulin products available in the U.S., all of which undergo micropore filtration to eliminate viral transmission. To date, no reported cases of viral infection related to Rh immune globulin administration have been reported in the U.S. Theoretically, the Creutzfeldt-Jakob disease (CJD) agent could be transmitted by use of Rh immune globulin. Local adverse reactions may occur, including redness, swelling, and mild pain at the site of injection, and hypersensitivity reactions have been reported.

The American College of Obstetricians and Gynecologists (ACOG) and the American Association of Blood Banks (AABB) recommend the first dose of Rh_o(D) immune globulin (e.g., RhoGAM®) be given at 28 weeks' gestation, (or earlier if there's been an invasive event), followed by a postpartum dose given within 72 hours of delivery.

Diagnosis of alloimmunization
The diagnosis of alloimmunization is based on detection of anti-RhD antibodies in the maternal serum.

The most common test for determining antibodies in serum is the indirect Coombs test. Maternal serum is incubated with known RhD-positive RBCs. Any anti-RhD antibody present in the maternal serum will adhere to the RBCs. The RBCs are then washed and suspended in Coombs serum, which is antihuman globulin. RBCs coated with maternal anti-RhD will agglutinate, which is referred to as a positive indirect Coombs test. The indirect Coombs titer is the value used to direct management of pregnant alloimmunized women.

Management of alloimmunization during pregnancy
A patient's first alloimmunized pregnancy involves minimal fetal or neonatal disease. Subsequent pregnancies are associated with more severe degrees of fetal anemia. Treatment of an alloimmunized pregnancy requires monitoring of maternal anti-D antibody titers and serial ultrasound assessment of middle cerebral artery peak systolic velocity of the fetus.

If severe fetal anemia is present near term, delivery is performed. If severe anemia is detected remote from term, intrauterine fetal blood transfusions may be performed.

Determining fetal RhD status
ACOG recommends that all pregnant women should be tested at the time of their first prenatal visit for ABO blood group typing and Rh-D type and be screened for the presence of anti-RBC antibodies. These laboratory tests should be repeated for each subsequent pregnancy. The AABB also recommends that antibody screening be repeated before administration of anti-D immune globulin at 28 weeks' gestation, postpartum, and at the time of any event during pregnancy.

If the mother is determined to be Rh-negative, the paternal Rh status should also be determined at the initial management of a pregnancy. If paternity is certain and the father is Rh-negative, the fetus will be Rh-negative, and further assessment and intervention are unnecessary. If the father is RhD-positive, he can be either homozygous or heterozygous for the D allele. If he is homozygous for the D allele (i.e., D/D), then the fetus is RhD-positive. If the paternal genotype is heterozygous for Rh status or is unknown, determination of the Rh-status of the fetus is the next step.

Invasive and noninvasive testing methods to determine the Rh status of a fetus are available.

Invasive procedures use polymerase chain reaction (PCR) assays to assess the fetal cellular elements in amniotic fluid by amniocentesis or by chorionic villus sampling (CVS). Although CVS can be performed earlier in a pregnancy, amniocentesis is the preferred method because CVS is associated with disruption of the villi and the potential for larger fetomaternal hemorrhage and worsening alloimmunization if the fetus if RhD-positive. The sensitivity and specificity of fetal RHD typing by PCR are reported as 98.7% and 100%, respectively, with positive and negative predictive values of 100% and 96.9%, respectively.

Noninvasive testing involves molecular analysis of cell-free fetal DNA (cffDNA) in the maternal plasma or serum. In 1998, Lo et al. showed that about 3% of cell-free DNA in the plasma of first trimester pregnant women is of fetal origin, with this percentage rising to 6% in the third trimester. Fetal DNA cannot be separated from maternal DNA, but if the pregnant woman is RhD-negative, the presence of specific exons of the *RHD* gene, which are not normally present in the circulation of an RhD-negative patient, predicts an RhD-positive fetus. ccfDNA has been proposed as a noninvasive alternative to obtaining fetal tissue by invasive methods, which are associated with a risk of miscarriage.

The large quantity of maternal DNA compared to fetal DNA in the maternal circulation complicates the inclusion of satisfactory internal controls to test for successful amplification of fetal DNA. Therefore, reactions to detect Y chromosome-linked gene(s) can be included in the test, which will be positive when the fetus is a male. When Y chromosome-linked genes are not detected, tests for polymorphisms may be performed to determine whether the result is derived from fetal but not maternal DNA.

cffDNA testing to determine the fetal *RHD* genotype is standard of practice in many European countries.

Literature Rationale
This policy was created in 2013, with the most recent update using MEDLINE database through September 26, 2014. Assessment of this diagnostic technology focuses on three parameters: 1) technical performance; 2) diagnostic performance (sensitivity, specificity, and positive and negative predictive values) in appropriate populations of patients; and 3) demonstration that the diagnostic information can be used to improve patient outcomes (clinical utility).

No studies were identified that provide direct evidence of the analytic validity of RHD genotyping. The commercially available test uses next-generation sequencing. Neither the routine quality control procedures used for the test, nor the analytic performance metrics have been published.

Diagnostic Performance
In 2014, Zhu et al published a meta-analysis of studies on the diagnostic accuracy of noninvasive fetal RHD genotyping using cell-free fetal DNA. The investigators identified 37 studies conducted in RhD-negative pregnant women that were published by the end of 2013. The studies included a total of 11,129 samples, and 352 inconclusive samples were excluded. When all data were pooled, the sensitivity of fetal RhD genotyping was 99% and the specificity was 98%. Diagnostic accuracy was higher in samples collected in the first trimester (99.0%) than those collected in the second (98.3%) or third (96.4%) trimesters.

Also in 2014, Chitty et al published a prospective study from the U.K. that was not included in the Zhu meta-analysis. Samples from 2288 Rh-negative women who initiated prenatal care before 24 weeks' gestation were analyzed using RhD genotyping. Overall, the sensitivity of the test was 99.34% and the specificity was 94.91%. The likelihood of correctly detecting RhD status in the fetus increased with gestational age, with high levels of accuracy after 11 weeks. For example, for samples taken before 11 completed weeks of gestation, the sensitivity was 96.85% and the specificity was 94.40%, and at 14 to 17 weeks' gestation, sensitivity was 99.67% and specificity was 95.34%. The finding in the Chitty study of increased accuracy as pregnancies advanced differs from that of the Zhu meta-analysis, which found highest diagnostic accuracy in the first trimester.

Two key studies reporting the clinical validity of fetal RHD genotyping with the Sequenom assay, which is commercially available in the U.S., are detailed next, and findings are summarized in the Table.

Sequenom SensiGene Clinical Validation Studies

Author	Accuracy for RhD Status Determination (%)	False Negative Rate RhD Determination (%)
Moise 2012	98.1-99.1, depending on trimester during which it was performed	.45

Bombard 2011		
Cohort 1	97.1	1.9
Cohort 2	99.5	0

In 2012, Moise and colleagues analyzed samples from 120 patients who were enrolled prospectively between May 2009 and July 2010 from multiple centers. All patients were Rh-negative pregnant patients with no evidence of alloimmunization. Race/ethnicity was Caucasian/white (72.5%), African-American/black (12.5%), Hispanic/Latino (12.5%), Asian (0.8%), and other (1.7%). The samples were analyzed using the SensiGENE RHD test using MALDI-TOF mass spectrometry to detect control and fetal-specific DNA signals. The determination of fetal sex was: three Y-chromosome markers=male fetus, two markers=inconclusive, and one or no markers=female fetus. The algorithm for *RHD* determination was: pseudogene present=inconclusive, three *RHD* markers present=*RHD*-positive fetus, two markers present=inconclusive, one or no markers= *RHD*-negative fetus. If the results were *RHD*-positive and male, the fetus was determined to be *RHD*-positive and male, and if *RHD*-negative and male results were noted, the fetus was determined to be *RHD*-negative and male. If the results were *RHD* -positive and female, the fetus was determined to be *RHD*-positive and female. If an *RHD*-negative and female result was noted, reflex testing was performed with a panel of 92 single-nucleotide polymorphisms (SNPs). If a minimum of six informative paternal alleles (uniquely and unambiguously fetal in nature) were detected, the result was an *RHD*-negative, female fetus. If less than six alleles were detected, the sample was reported as inconclusive. Cord blood was obtained at delivery and RhD typing was determined using standard serologic methods, and phenotype assessment of the newborns was used to assign gender. The pregnant patients underwent planned venipunctures during three time periods in gestation: $11–13^{6/7}$, $16–19^{6/7}$, and $28–29^{6/7}$ weeks. At the second blood draw, two patients were not evaluated because they did not return during the prescribed gestational age window; and at the time of the third trimester blood draw, seven patients did not have a sample obtained.

Median gestational age of the first, second and third trimester samplings was 12.4 (range, 10.6–13.9) weeks, 17.6 (16–20.9) weeks and 28.7 (27.9–33.9) weeks, respectively. There were three samples in the first trimester and two samples in the second trimester insufficient in the quantity of samples to perform the DNA assay (1.4% of the total samples). Twenty-two samples (6.3% of the total samples; 2.5% of the patients) were deemed inconclusive. In 23% of these inclusive cases, there was an *RHD*-negative, female result, but there were an insufficient number of paternal SNPs detected to confirm the presence of fetal DNA. In the remaining 77% of the inconclusive results (4.8% of the total samples), the *RHD* psi (y)-pseudogene was detected, and the sample was deemed inconclusive. Erroneous results were observed for six of the samples (1.7%), and included discrepancies in four *RHD* typings (1.1%) and two fetal sex determinations (0.6%) following data un-blinding. Three cases of RhD typing were false positives (ccffDNA was *RHD*-positive but neonatal serology RhD-negative) and one case was a false negative (ccffDNA:*RHD*-negative but neonatal serology RhD-positive). Accuracy for determination of the RHD status of the fetus was 99.1%, 99.1%, and 98.1%, respectively for each of the three consecutive trimesters of pregnancy, and accuracy of fetal sex determination was 99.1%, 99.1%, and 100%, respectively.

In 2011, Bombard and colleagues analyzed the performance of the SensiGene Fetal RHD test in two cohorts. Cohort one used as a reference point the clinical RhD serotype obtained from cord blood at delivery. Samples from cohort two were originally genotyped at the Sequenom Center in Grand Rapids, Michigan and results were used for clinical validation of genotyping performed at the Sequenom Center in San Diego, California.

In cohort one, *RHD* genotyping was performed on 236 maternal plasma samples from singleton, non-sensitized pregnancies with documented fetal RhD serology. The samples were obtained at 11 to 13 weeks' gestation. Ethnic origin of the pregnant women was Caucasian 77.1%, African 19.1%, mixed race 3.4% and South Asian (0.4%). Neonatal RhD phenotype, determined by serology at the time of birth, was positive in 69.1% of samples and negative in 30.9% of samples. In two (0.9%) of the 236 samples, there the results were classified as invalid. In the 234 (99.1%) samples with sufficient DNA extraction, the result was conclusive in 207 samples (88.5%); inconclusive in 16 samples (6.8%); and psi (+)/RHD variant in 11 samples (4.7%). In the 207 samples with a conclusive result, the neonatal RhD phenotype was positive in 142 samples (68.6%) and negative in 65 samples (31.4%). The RHD Genotyping test correctly predicted the neonatal RhD phenotype in 201 of 207 samples for an accuracy of 97.1% (95% confidence interval [CI], 93.5 to 98.8). In the 142 samples with RhD-positive fetuses, the test predicted that the fetus was positive in 138 and in four that it was negative, for a sensitivity of prediction of RhD positivity of 97.2% (95% CI, 93.0 to 98.9). In 63 of the 65 samples with RhD-negative fetuses, the RHD Genotyping test predicted that the fetus was negative and, in the remaining two, that it was positive, for a specificity for the prediction of RhD positivity of 96.9% (95% CI, 89.5 to 99.1). The test predicted that the fetus was RhD-positive in 140 samples, of which, in 138 of these the prediction was correct, for a positive predictive value of 98.6% (95% CI, 94.9 to 99.6). The test predicted that the fetus was RhD-negative in 67 samples, of which, in 63 of these the prediction was correct, for a negative predictive value for RhD-positive fetuses of 94.0% (95% CI, 85.6 to 97.6).

Cohort two consisted of 205 samples from 6 to 30 weeks' gestation. Testing was for the presence of *RHD* exon sequences 4, 5, 7, the psi-pseudogene, and three Y-chromosome sequences (SRY, DBY and TTTY2), using MALDI-TOF MS-(the RHD Genotyping laboratory developed test). The laboratory performing the assays for both cohorts was blinded to the sex and fetal RhD genotype. In cohort two, the test correctly classified 198 of 199 patients, for a test accuracy of 99.5%, with a sensitivity and specificity for prediction of RHD genotype of 100.0% and 98.3%, respectively.

Clinical utility
The possible clinical utility of cffDNA RHD genotyping includes the following scenarios:

In the Rh-negative, non-alloimmunized pregnant patient:
- Avoidance of unnecessary anti-D immune globulin if the fetus is Rh-negative.
- Avoidance of invasive procedure to obtain fetal tissue when the paternity is unknown or the father is heterozygous for the D antigen.

In the Rh-negative, alloimmunized pregnant patient:

- Avoidance of invasive procedure to obtain fetal tissue if Rh-negative pregnant woman is alloimmunized to determine fetal Rh status.
- Avoidance of serial antibody testing in the mother and middle cerebral artery surveillance of the fetus if the fetus is determined to be Rh-negative.

No published data are identified showing that this type of testing leads to improved health outcomes. This type of testing could lead to the avoidance of the use of anti-D immune globulin (e.g., RhoGAM) in Rh-negative mothers with Rh-negative fetuses. However, the false negative rate of the test, which is low, is not zero, and a certain percentage of Rh-negative women will develop alloimmunization to Rh-positive fetuses. Other issues that still need to be defined include the optimal timing of testing during the pregnancy.

Summary
Rhesus (Rh) D-negative women who are exposed to RhD-positive red blood cells can develop anti-Rh antibodies, which can cross the placenta and cause fetal anemia. If undiagnosed and untreated, alloimmunization can cause significant perinatal morbidity and mortality. Determining the Rh status of the fetus may guide subsequent management of the pregnancy. The use of cell-free fetal DNA in maternal blood has been proposed as a noninvasive method to determine fetal RhD genotype.

The technical performance of genotyping for fetal RhD status is unknown, as no studies were identified that provide direct evidence of the analytic validity of RHD genotyping.

The diagnostic performance of fetal RhD genotyping is high, in that the test has shown a high degree of accuracy in correctly predicting fetal RhD status. However, in performing the test, there still are a certain percentage of false negatives, and the test will not identify all Rh-positive fetuses, potentially leading to alloimmunization of the Rh-negative mothers in these cases.

The clinical utility of fetal RhD genotyping is unknown, and it is uncertain whether it will lead to improved health outcomes. Therefore, fetal RHD genotyping using maternal plasma is considered investigational.

Practice Guidelines and Position Statements
Neither ACOG nor the AABB have issued specific practice guidelines or recommendations on the use of fetal RHD genotyping.

ACOG states that detection of fetal D by molecular analysis of maternal plasma or serum can be assessed in the second trimester with greater than 99% accuracy but that it should be noted that this is not a widely used clinical tool.

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force recommendations addressing fetal RHD genotyping were identified.

Key Words:
RHD genotyping, Rh genetic testing, SensiGene, Fetal, RHD

Approved by Governing Bodies:
Sequenom offers SensiGene™ Fetal RHD Genotyping test, performed by proprietary SEQureDx™ technology. The assay targets exons 4, 5, and 7 of the *RHD* gene located on chromosome 1, psi (y) pseudogene in exon 4, and assay controls which are three targets on the Y chromosome (SRY, TTTY, DBY).

The company claims that the uses of its test include:
- Clarify fetal RHD status without testing the father
    - Avoiding the cost of paternity testing and paternal genotyping
- Clarify fetal RHD status when maternal anti-D titers are unclear
- Identify the RHD (-) fetus in mothers who are opposed to immunization(s) and vaccines
- RhD (-) sensitized patients
    - Avoid invasive testing by CVS or genetic amniocentesis

No U.S. Food and Drug Administration (FDA)-cleared genotyping tests were found. Thus, genotyping is offered as a laboratory-developed test. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). The laboratory offering the service must be licensed by CLIA for high-complexity testing.

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Current Coding:
CPT Codes:

81403	Molecular pathology procedure, Level 4 (e.g., 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) including—*RHD (Rh blood group, D antigen)* (e.g., hemolytic disease of the fetus and newborn, Rh maternal/fetal compatibility), deletion analysis (e.g., exons 4, 5 and 7, pseudogene), performed on cell free fetal DNA in maternal blood
81479	Unlisted molecular pathology procedure

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Policy History:

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