



## FEP Medical Policy Manual

### FEP 2.04.128 Genetic Testing for Fanconi Anemia

**Annual Effective Policy Date: April 1, 2026**

**Original Policy Date: March 2019**

**Related Policies:**

2.04.107 - Carrier Screening for Genetic Diseases  
2.04.116 - Invasive Prenatal (Fetal) Diagnostic Testing

## Genetic Testing for Fanconi Anemia

### Description

#### Description

Fanconi anemia (FA) is an inherited disorder characterized by congenital abnormalities, bone marrow failure, and predisposition to hematologic malignancies. The disease is associated with early mortality and a high degree of morbidity for affected individuals. The potential utility of genetic testing is in confirming the diagnosis in cases that are inconclusive after standard workup, in testing asymptomatic individuals for future risk of disease, in carrier testing for individuals at increased risk for the variant, and in the prenatal testing of a fetus that has a high-risk for the disorder.

#### OBJECTIVE

The objective of this evidence review is to determine whether genetic testing for Fanconi anemia improves the net health outcome compared with standard clinical workup or no genetic testing in individuals who are symptomatic for Fanconi anemia, or have a close relative with a confirmed diagnosis. Carrier, preimplantation, and in utero testing for Fanconi anemia are addressed in evidence reviews 2.04.107, 2.04.116, and 4.02.05.

## POLICY STATEMENT

Genetic testing for the diagnosis of Fanconi anemia may be considered **medically necessary** when the following criteria are met:

- Clinical signs and symptoms of Fanconi anemia are present; AND
- A definitive diagnosis of Fanconi anemia cannot be made after standard workup, ie, nondiagnostic results on chromosome breakage analysis.

Genetic testing for the diagnosis of Fanconi anemia is considered **investigational** when the above criteria are not met.

Genetic testing of asymptomatic individuals to determine future risk of disease may be considered **medically necessary** when there is a first-degree relative with a documented diagnosis of Fanconi anemia (see Policy Guidelines).

Genetic testing for Fanconi anemia is considered **investigational** in all other situations.

## POLICY GUIDELINES

Genetic testing for Fanconi anemia is a complex process that involves multiple steps and a number of different potential approaches. Most testing procedures described in the literature involve a combination of polymerase chain reaction, direct sequencing, and next-generation sequencing to identify a full complement of variants associated with Fanconi anemia.

However, in clinical care, a more directed approach can be taken. In many cases, testing complementation groups will have been performed prior to genetic testing, and this will direct genetic testing to 1 of the 15 known genes associated with Fanconi anemia. Direct sequencing and/or deletion/duplication analysis of these few genes may be the most accurate and efficient approach in many cases.

In the absence of complementation testing, the greatest yield will be in testing for the *FANCA* gene, followed by the *FANCC* and *FANCG* genes. If a patient with Fanconi anemia is negative for variants in these genes, then testing for many low-frequency variants may be necessary. Next-generation sequencing offers considerable advantages in testing multiple genes simultaneously for patients in this situation.

First-degree relatives include parents, siblings, and offspring. Fanconi anemia can be transmitted by autosomal recessive, autosomal dominant, or X-linked inheritance. Testing the father of an individual with X-linked Fanconi anemia would not be indicated.

Carrier, preimplantation, and in utero testing for Fanconi anemia are addressed in evidence reviews 2.04.107 and 2.04.116.

Plans may need to alter local coverage medical policy to conform to state law regarding coverage of biomarker testing.

## Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the HUman Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology-"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"-to describe variants identified that cause Mendelian disorders.

**Table PG1. Nomenclature to Report on Variants Found in DNA**

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence

Familial variant

Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

**Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification**

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology.

## Genetic Counseling

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual's family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

## BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

## FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

## RATIONALE

### Summary of Evidence

For individuals who have signs and/or symptoms of Fanconi anemia (FA) who receive genetic testing for FA, the evidence includes small cohort studies and case series. Relevant outcomes are test validity, other test performance measures, change in disease status, and morbid events. Due to the rarity of clinical FA, there is limited published evidence to determine whether genetic testing for FA improves outcomes. The available evidence demonstrates that most patients with a clinical diagnosis of FA have identified pathogenic variants. This supports the use of genetic testing for the diagnosis when standard testing, including chromosomal breakage analysis, is inconclusive. Therefore, when signs and/or symptoms of FA are present, but the diagnosis cannot be made by standard testing, genetic testing will improve the ability to make a definitive diagnosis and direct care. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals who have a close relative with the diagnosis of FA who receive genetic testing for FA to determine future risk of the disease, the evidence consists of small cohort studies and case series. Relevant outcomes are test validity, other test performance measures, and changes in reproductive decision making. Genetic testing has clinical utility if there is a close relative with FA primarily first-degree relatives. This will primarily apply to young siblings of an affected individual and may help to direct early monitoring and treatment of bone marrow failure that may prevent or delay progression. Treatment of bone marrow failure with hematopoietic cell transplantation is considered more likely to be successful if initiated earlier in the course of the disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

## SUPPLEMENTAL INFORMATION

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

#### American College of Obstetricians and Gynecologists

In 2017, the American College of Obstetricians and Gynecologists updated the committee Opinion on carrier screening for genetic diseases in individuals of Eastern European and Jewish descent.<sup>15</sup> The opinion made the following 7 recommendations:

1. The family history of individuals considering pregnancy, or who are already pregnant, should determine whether either member of the couple is of Eastern European (Ashkenazi) Jewish ancestry or has a relative with one or more of the genetic conditions listed in Table 1.
2. Carrier screening for Tay-Sachs disease, Canavan disease, cystic fibrosis, and familial dysautonomia should be offered to Ashkenazi Jewish individuals before conception or during early pregnancy so that a couple has an opportunity to consider prenatal diagnostic testing options. If the woman is already pregnant, it may be necessary to screen both partners simultaneously so that the results are obtained in a timely fashion to ensure that prenatal diagnostic testing is an option.
3. Individuals of Ashkenazi Jewish descent may inquire about the availability of carrier screening for other disorders. Carrier screening is available for mucopolidosis IV, Niemann-Pick disease type A, Fanconi anemia group C, Bloom syndrome, and Gaucher disease. Patient education materials can be made available so that interested patients can make an informed decision about having additional screening tests. Some patients may benefit from genetic counseling.
4. "When only one partner is of Ashkenazi Jewish descent, that individual should be screened first. If it is determined that this individual is a carrier, the other partner should be offered screening. However, the couple should be informed that the carrier frequency and the detection rate in non-Jewish individuals are unknown for most of these disorders, except for Tay-Sachs disease and cystic fibrosis. Therefore, it is difficult to accurately predict the couple's risk of having a child with the disorder."
5. Individuals with a positive family history of one of these disorders should be offered carrier screening for the specific disorder and may benefit from genetic counseling.
6. When both partners are carriers of one of these disorders, they should be referred for genetic counseling and offered a prenatal diagnosis. Carrier couples should be informed of the disease manifestations, the range of severity, and available treatment options. Prenatal diagnosis by DNA-based testing can be performed on cells obtained by chorionic villus sampling and amniocentesis.

- When an individual is found to be a carrier, his or her relatives are at risk for carrying the same mutation. The patient should be encouraged to inform his or her relatives of the risk and the availability of carrier screening. The provider does not need to contact these relatives because there is no provider-patient relationship with the relatives, and confidentiality must be maintained.

The committee reaffirmed these recommendations in 2025.

## Fanconi Anemia Research Fund

In 2020, the Fanconi Anemia Research Fund issued updated guidelines on diagnosis and management of the disease.<sup>16</sup> The chapter on diagnosis was updated after 2020, but the exact date of update is not available.

The guideline states that the chromosome breakage test is the gold standard for diagnosing Fanconi anemia. If chromosome breakage testing is unavailable, genetic testing can be performed instead. If chromosome breakage testing is positive, Fanconi anemia panel testing (using next generation sequencing and copy number analysis to identify large deletions, duplications, and insertions) should be performed, followed by whole exome sequencing if panel testing is negative. The goal of genetic testing is to identify the specific pathogenic variant, which "enables accurate diagnosis, which may improve clinical care for individuals with anticipated genotype-phenotype associations and for relatives who are heterozygous carriers of pathogenic variants that confer an increased risk for malignancy."

## U.S. Preventive Services Task Force Recommendations

No **U.S. Preventive Services Task Force** recommendations for genetic testing for Fanconi anemia have been identified.

## Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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**POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:**

Date	Action	Description
March 2019	New policy	Policy created with literature review through October 16, 2018. Genetic testing is medically necessary for the diagnosis of Fanconi anemia
March 2020	Replace policy	Policy updated with literature review through October 14, 2019. Policy statements unchanged.
March 2021	Replace policy	Policy updated with literature review through October 14, 2020; no references added. Policy statements unchanged.
March 2022	Replace policy	Policy updated with literature review through September 20, 2021; no references added. Policy statements unchanged.
March 2023	Replace policy	Policy updated with literature review through September 20, 2022; not medically necessary language changed to investigational; intent unchanged.
March 2024	Replace policy	Policy updated with literature review through November 16, 2023; Fanconi Anemia Research Fund guideline updated. Policy statements unchanged.
June 2025	Replace policy	Policy updated with literature review through October 14, 2024; no references added. Policy statements unchanged.
March 2026	Replace policy	Policy updated with literature review through November 3, 2025; no references added. Policy statements unchanged.

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