BlueCross BlueShield Nebraska

GENETIC TESTING: PRENATAL AND PRECONCEPTION CARRIER SCREENING (REQUIRES PREAUTHORIZATION)

V.31

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DESCRIPTION

There are more than 1,300 inherited recessive disorders (autosomal or X-linked) that affect 30 out of every 10,000 children. Some diseases have limited impact on either length or quality of life, while others are uniformly fatal in infancy or childhood. By definition, autosomal recessive disorders arise when both parents pass on disease-causing copies of genes to a child. X-linked recessive conditions arise when a disease-causing version of a gene is on the X-chromosome and is passed to a male child who only has one copy of the X-chromosome.

Carrier screening is performed to identify individuals at risk of having offspring with inherited recessive or X-linked single-gene disorders. Carriers are typically asymptomatic but can pass disease-causing variants to their offspring. The majority of professional societies recommend carrier screening prior to pregnancy. Risk-based carrier screening is performed in individuals who have an increased risk to be a carrier based on population carrier frequency, ethnicity, and/or family history.

Expanded carrier screening (ECS) involves screening individuals or couples for disorders in many genes simultaneously (up to 100s) by next-generation sequencing. ECS panels may screen for diseases that are present with increased frequency in specific populations, but also include a wide range of diseases for which the individual seeking testing is not at increased risk for positive carrier status. The conditions included on ECS panels are not standardized and the panels may include conditions that are not well understood and for which there are no existing professional guidelines.

condition(s) screened. The residual risk is the chance that the individual is still a carrier based on a normal/negative carrier screen. The residual risk will vary depending on which test is performed, how many mutations are included for each condition, the patient's ethnicity, etc.

It is important to recognize that family history, ethnicity, and race are self-reported, and may not be completely accurate, particularly in multi-ethnic and multi-racial societies.

When one member of a couple is at high risk of being a carrier for a certain condition due to ancestry (e.g., Ashkenazi Jewish, French-Canadian, Cajun, etc.) or has a family history of a condition, the high-risk partner should be offered screening. If the high-risk partner is found to be a carrier, the other partner should then be offered screening.

Genetic counseling is strongly recommended for patients considering expanded carrier screening.

Dates

Original Effective
09-01-2016
Last Review
08-07-2024
Next Review
08-11-2025

REFERENCE TABLE

The tests, associated laboratories, CPT codes, and ICD codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Platform for a comprehensive list of registered tests.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	

	GeneSeq Plus (Labcorp)	81336, 81405,81408, 81479		
	QHerit Expanded Carrier Screen (Quest Diagnostics)	81243, 81443		
	Horizon 27 (27 disease Pan-ethnic Standard Panel) (Natera)	81243, 81257, 81329, 81443		
	Genesys Carrier Panel (Genesys Diagnostics)	0400U		
Basic Carrier Screening Panels (Cystic Fibrosis, Spinal Muscular Atrophy, Fragile X, Hemoglobinopathies, not more than 14 genes)	Inheritest Core Panel (Labcorp)	81220, 81222, 81223, 81243, 81257, 81329, 81336, 81361	O09, Z13, Z31, Z34, Z36, Z84	
	Inheritest 14-gene Panel (Labcorp)			
	Prenatal Carrier Panel (CFvantage, Fragile X, SMA) (Quest Diagnostics)			
	Foresight Fundamental Panel (Myriad Genetics)			
	UNITY Carrier Screen (BillionToOne)	0449U		
Cystic Fibrosis Carrier Screening				
CFTR Targeted Variant Analysis	CFTR One Known Familial Variant in a Nuclear Gene (GeneDx)	81221	O09, Z13, Z31, Z36, Z83.49	
CFTR Sequencing, Deletion/Duplication Analysis, or Mutation Panel	Cystic Fibrosis Complete Rare Variant Analysis, Entire Gene Sequence (Quest Diagnostics)	81223		
	Cystic Fibrosis Gene Deletion or Duplication (Quest Diagnostics)	81222		
	CFvantage Cystic Fibrosis Expanded Screen (Quest Diagnostics)	81220		
CFTR Intron 9 PolyT and TG Analysis (previously called Intron 8 polyT/TG Analysis)	*CFTR* Intron 8 Poly-T Analysis (Quest Diagnostics)	81224		
Spinal Muscular Atrophy Carrier Screening				

	(Labcorp)			
SMN1 Sequencing and/or Deletion/ Duplication and *SMN2* Deletion/Duplication Analysis	Spinal Muscular Atrophy Carrier Test (Natera)	81329, 81336, 81401, 81405		
	Genomic Unity SMN1/2 Analysis (Variantyx Inc)	0236U		
Fragile X Syndrome Carrier Screening				
FMR1 Repeat Analysis for Carrier Screening	FMR1 CGG Repeat Analysis (GeneDx)	81243, 81244	O09, Z13, Z31, Z34, Z36, Z84	
	Fragile X Syndrome, Carrier (Labcorp)			
Hemoglobinopathy Carrier Screening				
HBA1, *HBA2*, or *HBB* Targeted Variant Analysis	Alpha-Globin Common Mutation Analysis (Quest Diagnostics)	81257, 81258	O09, Z13, Z31, Z34, Z36, Z84	
	HBA1 One Known Familial Variant in a Nuclear Gene (GeneDx) *HBA2* One Known Familial Variant in a Nuclear Gene (GeneDx)			
	HBB One Known Familial Variant in a Nuclear Gene (GeneDx)	81361, 81362		
HBA1, *HBA2*, or *HBB* Sequencing and/or Deletion/Duplication Analysis	Alpha-Globin Gene Sequencing and Deletion/Duplication (Quest Diagnostics)	81259, 81269, 81363, 81364		
	HBA1 Deletion/Duplication (GeneDx) HBA2 Deletion/Duplication (GeneDx)			
	Beta Globin Gene Dosage Analysis (Quest Diagnostics)			
	Beta-Globin Complete (Quest Diagnostics)			
Ashkenazi Jewish Carrier Panel Testing				
Ashkenazi Jewish Carrier Panel Testing	Ashkenazi Jewish Panel (11 Tests) (Quest Diagnostics)	81412	O09, Z13, Z31, Z34, Z36, Z84	
Duchenne and Becker Muscular Dystrophy Carrier Screening				

and/or Deletion/Duplication Analysis	Sequencing (GeneDx)			
	Duchenne/Becker MD (DMD) Del/Dup (GeneDx)			
	Genomic Unity DMD Gene Analysis (Variantyx)	0218U		

RELATED POLICIES

This policy document provides coverage criteria for prenatal and preconception carrier screening. Please refer to:

- ***V.30 Genetic Testing: Prenatal Diagnosis (via amniocentesis, CVS, or PUBS) and Pregnancy Loss*** for coverage related to prenatal and pregnancy loss diagnostic genetic testing intended to diagnose genetic conditions following amniocentesis, chorionic villus sampling, or pregnancy loss.
- ***V.17 Genetic Testing: Noninvasive Prenatal Screening (NIPS)*** for coverage criteria related to prenatal cell-free DNA screening tests.
- ***V.75 Genetic Testing: Preimplantation Genetic Testing*** for coverage criteria related to genetic testing of embryos prior to in vitro fertilization.
- ***V.62 Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability and Developmental Delay*** for coverage criteria related to suspected multisystem genetic conditions in the postnatal period.
- ***V.35 Genetic Testing: Hereditary Hearing Loss*** for coverage related to diagnostic genetic testing for hereditary hearing loss.
- ***V.63 Genetic Testing: Hematologic Conditions (non-cancerous)*** for coverage related to diagnostic genetic testing for alpha-thalassemia and other hemoglobinopathies.
- ***V.68 Genetic Testing: Metabolic, Endocrine, and Mitochondrial Disorders*** for coverage related to diagnostic genetic testing for mitochondrial and other disorders.

non-general policies, including known familial variant testing not otherwise addressed in this policy.

POLICY

EXPANDED CARRIER SCREENING PANELS

I. Expanded carrier screening panels (0400U, 81243, 81257, 81329, 81336, 81405, 81408, 81479, 81443*) may be considered **medically necessary** when:

A. The member is considering pregnancy or is currently pregnant**, **AND**

B. The panel includes CFTR and SMN1, **AND**

II. Expanded carrier screening panels (0400U,81243, 81257, 81336, 81405, 81408, 81479 81443) are considered **investigational** for all other indications.

*Fragile X (81243) and spinal muscular atrophy (SMA) (81329) carrier screening may be billed along with 81443 if performed separately from the remainder of the panel per CPT Code Book Guidelines. If 81243 is billed along with 81443, the patient should still meet the specific Fragile X syndrome criteria.

**ACMG recommends follow up screening for the partner of the member that is pregnant or considering pregnancy via analysis of the same gene that has the pathogenic or LP variant as identified in the member. Therefore, expanded carrier screening panels are not recommended to be completed by both reproductive partners in tandem.

BASIC CARRIER SCREENING PANELS (Cystic fibrosis, Spinal Muscular Atrophy, Fragile X, Hemoglobinopathies, not more than 14 genes)

I. Basic carrier screening panels (*CRTR, SMN1/2, FMR1, HBB/HBA1/HBA2,* but not more than 14 genes) (81222, 81223, 81243, 81257, 81336, 81361, 0449U) may be considered scientifically validated when:

A. The member is considering pregnancy or is currently pregnant* AND

B. The panel includes the genes CFTR and SMN1

II. Basic carrier screening panels (*CRTR, SMN1/2, FMR1, HBB/HBA1/HBA2,* but not more than 14 genes) (81222, 81223,

ACMG recommends follow up screening for the partner of the member that is pregnant or considering pregnancy via analysis of the same gene that has the pathogenic or LP variant as identified in the member. Therefore, expanded carrier screening panels are not recommended to be completed by both reproductive partners in tandem.

CYSTIC FIBROSIS CARRIER SCREENING

Note: CPT 81220 CFTR (cystic fibrosis transmembrane conductance regulator) Cystic fibrosis gene analysis (carrier testing) does not require preauthorization or medical review and is a covered benefit.

***CFTR* Targeted Variant Analysis**

I. Cystic fibrosis carrier screening via *CFTR* targeted mutation analysis for a known familial mutation (81221) may be considered **medically necessary** when:

A. The member and/or the member's reproductive partner is considering pregnancy or is currently pregnant, **AND**

B. The member has a close relative with a known pathogenic or likely pathogenic variant in *CFTR,* **AND**

II. Cystic fibrosis carrier screening via CFTR targeted mutation analysis for known familial mutation (81221) is considered **investigational** for all other indications.

***CFTR* Sequencing, Deletion/Duplication Analysis, or Mutation Panel**

I. Cystic fibrosis carrier screening via *CFTR* sequencing (81223), deletion/duplication analysis (81222) or a mutation panel using at a minimum the ACMG-23 variant panel, may be considered **medically necessary** when:

A. The member and/or the member's reproductive partner is considering pregnancy or is currently pregnant, **OR**

B. The member's reproductive partner is a known carrier for cystic fibrosis.

II. Cystic fibrosis carrier screening via *CFTR* sequencing (81233), deletion/duplication analysis (81222), or a mutation panel using at minimum the ACMG-23 variant panel, is considered **investigational** for all other indications.

I. Analysis of the *CFTR* intron 9 polyT and TG regions (81224) for cystic fibrosis carrier screening may be considered **medically necessary** when:

A. The member and/or the member's reproductive partner is considering pregnancy or is currently pregnant, **AND**

B. The member is known to have an R117H variant in the CFTR gene**.**

II. Analysis of the *CFTR* intron 9 polyT and TG regions (81224) for cystic fibrosis carrier screening is considered **investigational** for all other indications.

Note: Refer to *Genetic Testing for Multisystem Inherited Disorders, Intellectual Disability and Developmental Delay* for coverage criteria for genetic testing to establish a diagnosis of cystic fibrosis.

SPINAL MUSCULAR ATROPHY CARRIER SCREENING

Note: CPT 81329 SMN1 (survival of motor neuron 1) Spinal muscular atrophy gene analysis dosage/deletion analysis including SMN2 does not require preauthorization or medical review and is a covered benefit.

SMN1 Targeted Variant Analysis

I. Spinal muscular atrophy (SMA) carrier screening via *SMN1* targeted variant analysis (81337, 81403) may be considered **medically necessary** when:

A. The member and/or the member's reproductive partner is considering pregnancy or is currently pregnant, **AND**

B. The member has a close relative with a known pathogenic or likely pathogenic variant in *SMN1.*

II. Spinal muscular atrophy (SMA) carrier screening via *SMN1* targeted variant analysis (81337, 81403) is considered **investigational** when the above criteria for all other indications.

SMN1 Sequencing and/or Deletion/Duplication Analysis and SMN2 Deletion/Duplication Analysis

I. Spinal muscular atrophy (SMA) carrier screening via *SMN1* sequencing and/or deletion/duplication analysis (81329, 81336, 81401, 81405, 0236U) is considered **medically necessary** when:

B. The member's reproductive partner is a known carrier for spinal muscular atrophy.

II. Spinal muscular atrophy (SMA) carrier screening via *SMN1* sequencing and/or deletion/duplication analysis (81329, 81336, 81401, 81405, 0236U) is considered **investigational** for all other indications.

Note: Refer to *Genetic Testing for Epilepsy, Neuromuscular, and Neurodegenerative Disorders* for coverage criteria for genetic testing to establish a diagnosis of spinal muscular atrophy (SMA).

FRAGILE X SYNDROME CARRIER SCREENING

FMR1 Repeat Analysis for Carrier Screening

I. Fragile X carrier screening via *FMR1* CGG-trinucleotide repeat analysis (81243, 81244) may be considered **medically necessary** when:

A. The member has been diagnosed with premature ovarian insufficiency or elevated follicle-stimulating hormone level before age 40 years, **OR**

B. The member is considered a pregnancy or is currently pregnant, **AND**

1. The member has one of the following:

a. Close relative with Fragile X syndrome (i.e., close relative has >200 CGG repeats in the *FMR1* gene), **OR**

b. Close relative who is a known carrier for Fragile X syndrome (i.e., close relative has between 55-200 CGG repeats in the *FMR1* gene), **OR**

c. Close relative with unexplained intellectual disability, developmental delay, or autism spectrum disorder, **OR**

d. Close relative diagnosed with premature ovarian insufficiency or elevated follicle-stimulating hormone level before age 40 years.

II. Fragile X carrier screening via *FMR1* CGG-trinucleotide repeat analysis (81243, 81244) is considered **investigational** for all other indications.

additional carrier screen panel code (81443), the patient should still meet the above Fragile X syndrome criteria.

HEMOGLOBINOPATHY CARRIER SCREENING

HBA1, HBA2, or HBB Targeted Variant Analysis

I. Hemoglobinopathy carrier screening via *HBA1*, *HBA2* (81257, 81258), or *HBB* (81361, 81362) targeted variant analysis may be considered m**edically necessary** when:

A. The member or the member's reproductive partner is considering pregnancy or is currently pregnant **AND**

B. The member has a close relative with a known pathogenic or likely pathogenic variant in HBA1, HBA2, or HBB II. Hemoglobinopathy carrier screening via *HBA1*, *HBA2* (81257, 81258), or *HBB* (81361, 81362) targeted variant analysis is considered **investigational** for all other indications.

Note: If a member's reproductive partner is known to be a carrier of a hemoglobinopathy, via genetic testing results and/or hematologic screening results, the more appropriate test for the member is likely *HBA1*, *HBA2*, or *HBB* Sequencing and/or Deletion/Duplication Analysis.

HBA1, HBA2, or HBB Sequencing and/or Deletion/Duplication Analysis

I. Hemoglobinopathy carrier screening via *HBA1*, *HBA2* (81259, 81269), or *HBB* (81363, 81364) sequencing and/or deletion/duplication analysis may be considered **medically necessary** when:

A. The member or the member's reproductive partner is considering pregnancy or is currently pregnant.

II. Hemoglobinopathy carrier screening via *HBA1*, *HBA2* (81259, 81269), or *HBB* (81363, 81364) sequencing and/or duplication analysis is considered **investigational** for all other indications, including fetal hemoglobin testing via circulating fetal DNA. .

NOTE: Refer to *Genetic Testing for Hematologic Disorders (non-cancerous)* for coverage criteria for genetic testing to establish a diagnosis of a hemoglobinopathy.

ASHKENAZI JEWISH CARRIER PANEL TESTING

A. The member or the member's reproductive partner is considering pregnancy or is currently pregnant, **AND**

B. The member is of Ashkenazi Jewish ancestry, **AND**

C. The panel includes, at a minimum, screening for carrier status for genetic conditions associated with the following genes, as recommended by the American College of Obstetricians and Gynecologists (ACOG):

1. Tay Sachs disease *(HEXA)*
2. Canavan disease *(ASPA)*
3. Cystic fibrosis *(CFTR)*
4. Familial dysautonomia *(ELP1)*
5. Bloom syndrome *(BLM)*
6. Fanconi anemia *(FANCC)*
7. Niemann-Pick disease: Type A *(SMPD1)*
8. Gaucher disease: Type 1 *(GBA)*
9. Mucolipidosis IV *(MCOLN1)*
10. Glycogen storage disease: Type 1 *(G6PC1)*
11. Joubert Syndrome *(TMEM216)*
12. Maple syrup urine disease *(BCKDHB)*
13. Usher syndrome types 1F and III *(PCDH15* and *CLRN1)*

II. Ashkenazi Jewish carrier panel testing (81412) is considered **investigational** for all other indications.

Note: If only one partner is of Ashkenazi Jewish ancestry, then testing of that partner is considered medically necessary. Testing of the other partner is considered medically necessary only if the result of testing of the Ashkenazi Jewish partner is positive.

DUCHENNE AND BECKER MUSCULAR DYSTROPHY CARRIER SCREENING

DMD Targeted Variant Analysis

A. The member is considering pregnancy or is currently pregnant, **AND**

B. The member has a close relative with a known pathogenic or likely pathogenic variant in *DMD,* **AND**

II. Duchenne and Becker muscular dystrophy carrier screening via *DMD* targeted variant analysis (81479) is considered **investigational** for all other indications.

DMD Sequencing and/or Deletion/Duplication Analysis

I. Duchenne and Becker muscular dystrophy carrier screening via *DMD* sequencing and/or deletion/duplication analysis (81161, 81408, 0218U) may be considered **medically necessary** when:

A. The member is considering pregnancy or is currently pregnant, **AND**

B. The member has a first- or second-degree relative diagnosed with Duchenne or Becker muscular dystrophy.

II. Duchenne and Becker muscular dystrophy carrier screening via *DMD* sequencing and/or deletion/duplication analysis (81161, 81408, 0218U) is considered **investigational** for all other indications.

Note: Refer to *Genetic Testing for Epilepsy, Neuromuscular, and Neurodegenerative Disorders* for coverage criteria for genetic testing to establish a diagnosis of Duchenne or Becker muscular dystrophy.

NOTES AND DEFINITIONS

1. **Close relatives** include first, second, and third degree relatives on the same side of the family:
    a. **First-degree relatives** are parents, siblings, and children
    b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
    c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins.

BACKGROUND

The American College of Obstetricians and Gynecologists (ACOG) published practice bulletin No. 690 (2017, reaffirmed 2023) regarding “Carrier Screening in the Age of Genomic Medicine”, which made the following recommendations: “Ethnic-specific, panethnic, and expanded carrier screening are acceptable strategies for pre pregnancy and prenatal carrier screening. Each obstetrician–gynecologist or other health care provider or practice should establish a standard approach that is consistently offered to and discussed with each patient, ideally before pregnancy. After counseling, a patient may decline any or all carrier screening.” (p. e35)

It was also recommended that: “All patients who are considering pregnancy or are already pregnant, regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies.” (p. e35)

American College of Medical Genetics and Genomics (ACMG):

ACMG published a practice resource (2021) regarding screening for autosomal recessive and X-linked conditions during pregnancy and preconception, which includes the following recommendations:

-The phrase “expanded carrier screening” be replaced by “carrier screening”.
-Adopting a more precise tiered system based on carrier frequency (p. 1796)
- Tier 1: CF + SMA + Risk Based Screening
- Tier 2: 1/100 carrier frequency or higher (includes Tier 1)
- Tier 3: 1/200 carrier frequency or higher (includes Tier 2) includes X-linked conditions
- Tier 4: 1/200 carrier frequency or higher (includes Tier 3) genes/condition will vary by lab

-All pregnant patients and those planning a pregnancy should be offered Tier 3 carrier screening for autosomal recessive and X-linked conditions. (p. 1797)
-Tier 4 screening should be considered (p. 1797):
- When a pregnancy stems from a known or possible consanguineous relationship (second cousins or closer)
- When a family or personal medical history warrants.

-Reproductive partners of pregnant patients and those planning a pregnancy may be offered Tier 3 carrier screening

partner with analysis of the same gene that has the pathogenic or LP variant as that identified in the partner. (p. 1804)

ACMG does not recommend:

-Offering Tier 1 and/or Tier 2 screening without Tier 3, because these do not provide equitable evaluation of all racial/ethnic groups.
-Routine offering of Tier 4 panels. (p. 1797)

Basic Carrier Screening Panels (Cystic Fibrosis, Spinal Muscular Atrophy, Fragile X, Hemoglobinopathies, not more than 14 genes)

American College of Obstetricians and Gynecologists (ACOG)

ACOG published practice bulletin No. 691 (March 2017, reaffirmed 2023), which includes the following recommendations related to carrier screening (p. 2)*:*

-Screening for spinal muscular atrophy should be offered to all women who are considering pregnancy or are currently pregnant.
-Cystic fibrosis carrier screening should be offered to all women who are considering pregnancy or are currently pregnant.

ACOG published practice bulletin No. 690 (March 2017, reaffirmed 2023), which includes the following recommendations related to carrier screening (p. e35):

All patients who are considering pregnancy or are already pregnant, regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies.

***CFTR* Targeted Variant Analysis**

ACOG published practice bulletin No. 691 (March 2017, reaffirmed 2023) and the following recommendations related to carrier screening:

Cystic fibrosis carrier screening should be offered to all women who are considering pregnancy or are currently pregnant. When both partners are unaffected, but one or both has a family history of cystic fibrosis, genetic counseling and medical record review should be performed to determine if *CFTR* mutation analysis in the affected family member is available. Carrier screening should be offered for both partners, with

CFTR Sequencing, Deletion/Duplication Analysis, or Mutation Panel

American College of Medical Genetics and Genomics (ACMG)

In their 2023 position statement for *CFTR* variant testing, the American College of Medical Genetics and Genomics (ACMG) recommends a minimum number of 100 variants tested in the *CFTR* gene if carrier testing is pursued: “The new *CFTR* variant set [n=100; see p. 6] represents an updated minimum recommended variant set for CF [cystic fibrosis] carrier screening, and this new set now supersedes the previous set of 23 *CFTR* variants recommended by the ACMG.” (p. 7)

In their 2020 technical standard for *CFTR*, the ACMG recommends that laboratories performing initial *CFTR* variant testing on an individual can use either targeted or comprehensive methods to evaluate the gene. If pathogenic or likely pathogenic *CFTR* variants have been confirmed in *both* biological parents, or an affected full sibling, only targeted methods should be used. (p. 7)

CFTR Intron 9 PolyT and TG Analysis (previously called Intron 8 polyT/TG Analysis)

American College of Medical Genetics and Genomics (ACMG)

In their 2020 technical standard for *CFTR* variant testing, the American College of Medical Genetics and Genomics (ACMG) recommends that, for all prenatal, postnatal, and adult diagnostic testing indications for *CFTR*, the R117H status as well as the results from at least the associated polyT tract be reported. For all adult carrier screening indications for *CFTR*, polyT status should be reported when the R117H variant is detected; laboratories may also want to consider reporting the results from the associated polyT tract in the partner of an individual who had a pathogenic or likely pathogenic variant detected during screening. (p. 12)

SMN1 Targeted Variant Analysis

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists (ACOG) published practice bulletin No. 691 (2017, reaffirmed 2023) regarding “Carrier Screening for Genetic Conditions”, which made the following recommendations (p. 1):

When an individual is found to be a carrier for a genetic condition, the individual’s relatives are at risk of carrying the same mutation. Individuals

SMN1 Sequencing and/or Deletion/Duplication and _SMN2_ Deletion/Duplication Analysis

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists (ACOG) published practice bulletin No. 691 (March 2017, reaffirmed 2023) and the following recommendations (p. 2:

> -Screening for spinal muscular atrophy should be offered to all women who are considering pregnancy or are currently pregnant.
>
> -In patients with a family history of spinal muscular atrophy, molecular testing reports of the affected individual and carrier testing of the related parent should be reviewed, if possible, before testing. If the reports are not available, *SMN1* deletion testing should be recommended for the low-risk partner.

American College of Medical Genetics and Genomics (ACMG)

The American College of Medical Genetics and Genomics recommended the following on carrier screening for spinal muscular atrophy (Gregg et al 2021): “Tier 1 screening adopts an ethnic and population neutral approach when screening for cystic fibrosis and spinal muscular atrophy.” (p. 1796)

FMR1 Repeat Analysis for Carrier Screening

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists (ACOG) published practice bulletin No. 691 (2017, reaffirmed in 2023) regarding “Carrier Screening for Genetic Conditions”, which made the following recommendations (p. 2):

> -Fragile X premutation carrier screening is recommended for women with a family history of fragile X-related disorders or intellectual disability suggestive of fragile X syndrome and who are considering pregnancy or are currently pregnant.
> -If a woman has unexplained ovarian insufficiency or failure or an elevated follicle-stimulating hormone level before age 40 years, fragile X carrier screening is recommended to determine whether she has an *FMR1* premutation.
> -All identified individuals with intermediate results and carriers of a fragile X premutation or full mutation should be provided follow-up genetic counseling to discuss the risk to their offspring of inheriting an

-Prenatal diagnostic testing for fragile X syndrome should be offered to known carriers of the fragile X premutation or full mutation.

American College of Medical Genetics and Genomics (ACMG)

ACMG published practice guidelines for carrier screening for Fragile X syndrome (2005), which recommended that Fragile X syndrome carrier testing should be offered to individuals with the following (p. 586):

-Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed mental retardation.

-Women who are experiencing reproductive or fertility problems associated with elevated follicle stimulating hormone (FSH) levels, especially if they have (a) a family history of premature ovarian failure, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.

American College of Obstetricians and Gynecologists (ACOG)

ACOG published practice bulletin No. 605 (July 2014, reaffirmed 2021), which states the following:

“If a woman has a personal or family history of ovarian failure or an elevated follicle-stimulating hormone (FSH) level before age 40 years without a known cause, fragile X premutation carrier testing should be offered”. (p. 194)

***HBA1, HBA2*, or *HBB* Targeted Variant Analysis**

American College of Obstetricians and Gynecologists (ACOG)

ACOG published practice bulletin No. 691 (2017, reaffirmed 2023) and following recommendations related to carrier screening (p. 1):

If an individual is found to be a carrier for a specific condition, the individual’s reproductive partner should be offered testing in order to receive informed genetic counseling about potential reproductive outcomes. Additionally, when an individual is found to be a carrier of a genetic condition, the individual’s relatives are at risk of carrying the same mutation. The patient should be encouraged to inform his or her relatives of the risk and the availability of carrier screening.

***HBA1, HBA2*, or *HBB* Sequencing and/or Deletion/Duplication Analysis**

recommends offering universal hemoglobinopathy testing to individuals who are considering pregnancy or who are currently pregnant (at the initial prenatal visit). The testing may be performed using either hemoglobin electrophoresis or molecular testing, such as expanded carrier screening.

Ashkenazi Jewish Carrier Panel Testing

American College of Obstetricians and Gynecologists (ACOG) ACOG published practice bulletin No. 691 (2017, reaffirmed 2023), which provided carrier screening guidelines in individuals of Eastern and Central European Jewish descent (i.e., Ashkenazi Jewish). Specifically, they made the following recommendations:

> -Cystic fibrosis, Canavan disease, familial dysautonomia, and Tay-Sachs disease carrier screening should be offered to all Ashkenazi Jewish individuals who are pregnant or considering pregnancy
> -Consider carrier screening for Fanconi anemia (Group C), Niemann-Pick (Type A), Bloom syndrome, mucolipidosis IV, glycogen storage disease type I, Joubert syndrome, maple syrup urine disease, Usher syndrome, and Gaucher disease. (p. 11-13)
> -When only one partner is of Ashkenazi Jewish descent, that individual should be offered screening 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. (p. 3)

***DMD* Targeted Variant Analysis**

GeneReviews: Dystrophinopathies

GeneReviews is an expert-authored review of current literature on a genetic disease and goes through a rigorous editing and peer review process before being published online.

Per GeneReviews, it is appropriate to evaluate at-risk female family members (i.e., the sisters or maternal female relatives of an affected male and first-degree relatives of a known or possible heterozygous female) in order to identify as early as possible heterozygous females who would benefit from cardiac surveillance. Evaluations can include molecular genetic testing if the *DMD* pathogenic variant in the family is known.

***DMD* Sequencing and/or Deletion/Duplication Analysis**

dystrophinopathies (2020), which included the following in regard to carrier testing in females:

"When the familial pathogenic variant is unknown and an affected male is not available to be tested, female relatives at risk of being carriers should be offered the full cohort of level 1 and 2 genetic testing (i.e., CNV analysis and sequencing) since these two approaches are cost effective and offer ~99% sensitivity." (p. 1147)

RECOMMENDED MEDICAL RECORDS

- History and Physical Report
- Office Notes
- Genetic counseling report

Quick Code Search

Use this feature to find out if a procedure and diagnosis code pair will be approved, denied or held for review. Simply put in the procedure code, then the diagnosis code, then click "Add Code Pair". If the codes are listed in this policy, we will help you by showing a dropdown to help you.

Procedure

Please type a procedure code

Enter at least the first 3 characters of the code

Diagnosis

Please type a diagnosis code

Enter at least the first 3 characters of the code

Add

CODES

+ **CPT-PLA**

+ **CPT4**

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REVISIONS

08-06-2024
Added 81361 to Basic Carrier Screening Panel section.

03-26-2024
Added new 04/01/2023 PLA code 0449U

09-27-2023
Changed "may be considered medically necessary" to "may be considered scientifically validated"

Added: "investigational when the above criteria is not met and for all other indications"

07-01-2023
Updated background and references

06-02-2023
Added new code for 07/01/2023: 0400U

07-01-2022
Updated Practice Guidelines

12-23-2021
Updated references, background and rationale and minor changes in policy.

08-17-2021
Effective 09/01/2021: Add criteria for Hemogolobinopathy, updated criteria for general carrier screening,

06-08-2021
Removed preimplantation criteria and created a new policy V.75

03-26-2021
Updated policy name to GENETIC TESTING FOR PRENATAL, PREIMPLANTATION, AND PRECONCEPTION CARRIER SCREENING, previously titled CARRIER TESTING FOR GENETIC DISEASES
Removed codes not applicable to this policy

03-01-2021
Removed 81242 as this is addressed in V.62 - GENETIC TESTING FOR MULTISYSTEM INHERITED DISORDERS, INTELLECTUAL DISABILITY, AND

Added criteria for expanded carrier screening panels.

04-30-2020
Removed 81329. 81329 is medically necessary from 1/1/2019 to current.

04-03-2020
Removed CPT 81220

07-10-2019
Added 81220 81329 to this policy, these codes are also in specifica genetic carrrier testing policies

09-22-2016
Removing CPT 81220 81221 81222 81223 81224 as this testing is in policy V.15