

# MEDICAL POLICY

<b>POLICY TITLE</b>	<b>CARRIER SCREENING FOR GENETIC DISEASES</b>
<b>POLICY NUMBER</b>	<b>2.258</b>

<b>CLINICAL BENEFIT</b>	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
<b>Effective Date:</b>	<b>RETIRED 7/1/2026</b>

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## I. POLICY

### Targeted Risk Based Carrier Screening

Targeted carrier screening for X-linked or autosomal recessive genetic diseases is considered **medically necessary** for individuals who are pregnant or considering pregnancy and are at increased risk of having offspring with an X-linked or autosomal recessive disease when one of the following criteria is met:

- One or both individuals have a first- or second-degree relative who is affected; **or**
- One individual is known to be a carrier; **or**
- One or both individuals are members of a population known to have a carrier rate that exceeds a threshold considered appropriate for testing for a particular condition.

**AND** all of the following criteria are met:

- The natural history of the disease is well understood and there is a reasonable likelihood that the disease is one with high morbidity in the homozygous or compound heterozygous state.
- Alternative biochemical or other clinical tests to definitively diagnose carrier status are not available, or, if available, provide an indeterminate result or are individually less efficacious than genetic testing.
- The genetic test has adequate clinical validity to guide clinical decision making and residual risk is understood (see Policy Guidelines section).
- An association of the marker with the disorder has been established.
- If targeted testing is performed by a panel, the panel meets the minimum number of recommended gene variants but does not exceed the maximum, as determined by professional clinical guidelines (See policy guidelines) Non targeted panels can be used instead of targeted testing when the criteria for non-targeted carrier screening are met (see Policy Guidelines)

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- Previous carrier screening or individual gene testing for the gene variant(s) of interest has not been performed (see Policy Guidelines)

All targeted screening not meeting any of the above criteria is considered **investigational**. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

First-degree relatives include a biological parent, brother, sister, or child; second-degree relatives include a biologic grandparent, aunt, uncle, niece, nephew, grandchildren, and half-sibling.

### Non-Targeted Carrier Screening

Non-targeted carrier screening panels for autosomal recessive and X-linked genetic disorders may be considered **medically necessary** as an alternative to testing for individual genes (e.g. SMN1 gene and CFTR gene) for individuals who are pregnant or are considering pregnancy at any risk level when all of the following criteria are met:

- The natural history of each disease is well understood and there is reasonable likelihood that the disease is one with high morbidity or early mortality in the homozygous or compound homozygous state (see Policy Guidelines);
- Alternative biochemical or other clinical tests to definitively diagnose carrier status are not available, or, if available, provide an indeterminate result or are individually less efficacious than genetic testing;
- The genetic test has adequate clinical validity to guide clinical decision-making and residual risk is understood;
- An association of the markers with the disorders has been established;
- If testing is performed by a panel, the panel meets the minimum number of recommended gene variants but does not exceed the maximum, as determined by professional clinical guidelines (see Policy Guidelines);
- Previous screening has not been performed (see Policy Guidelines)

Non-targeted carrier screening panels are considered **investigational** in all other situations when above criteria are not met. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure. (see Policy Guidelines).

#### ***Cross-References:***

**MP 2.257 Genetic Testing for Duchene Muscular Dystrophy**

**MP 2.276 Genetic Testing for Pathogenic FMR1 Variants (Including Fragile X Syndrome)**

**MP 2.320 Genetic Testing for Alpha Thalassemia**

**MP 2.362 Genetic Testing for Fanconi Anemia**

### POLICY GUIDELINES

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Non-targeted carrier screening applies to persons of any risk, including average risk.

Targeted carrier screening is also called risk-based testing or ethnic-based testing.

The American College of Obstetrics and Gynecology lists these 22 conditions as reasonable to include in a carrier screening panel:  $\alpha$ -thalassemia,  $\beta$ -thalassemia, Bloom syndrome, Canavan disease, CF, familial dysautonomia, familial hyperinsulinism, Fanconi anemia C, fragile X syndrome, galactosemia, Gaucher disease, glycogen storage disease type 1A, Joubert syndrome, medium-chain acyl-CoA dehydrogenase deficiency, maple syrup urine disease types 1A and 1B, mucopolidosis IV, Niemann-Pick disease type A, phenylketonuria, sickle cell anemia, Smith-Lemli-Opitz syndrome, spinal muscular atrophy, and Tay-Sachs disease.

### **ACOG Committee Opinion Number 691, Reaffirmed 2023: General Recommendations:**

- Information about genetic carrier screening should be provided to every pregnant woman. After counseling, a patient may decline any or all screening.
- Carrier screening and counseling ideally should be performed before pregnancy.
- 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. Concurrent screening of the patient and her partner is suggested if there are time constraints for decisions about prenatal diagnostic evaluation.
- If both partners are found to be carriers of a genetic condition, genetic counseling should be offered. Prenatal diagnosis and advanced reproductive technologies to decrease the risk of an affected offspring should be discussed.
- 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. The patient should be encouraged to inform his or her relatives of the risk and the availability of carrier screening. The obstetrician–gynecologist or other health care provider should not disclose this information without permission from the patient.
- It is important to obtain the family history of the patient and, if possible, her partner as a screening tool for inherited risk. The family history should include the ethnic background of family members as well as any known consanguinity. Individuals with a positive family history of a genetic condition should be offered carrier screening for the specific condition and may benefit from genetic counseling.
- Carrier screening for a particular condition generally should be performed only once in a person's lifetime, and the results should be documented in the patient's health record. Because of the rapid evolution of genetic testing, additional mutations may be included in newer screening panels. The decision to rescreen a patient should be undertaken only with the guidance of a genetics professional who can best assess the incremental benefit of repeat testing for additional mutations.
- Prenatal carrier screening does not replace newborn screening, nor does newborn screening replace the potential value of prenatal carrier screening.
- If a patient requests carrier screening for a particular condition for which testing is readily available and which reasonably would be considered in another screening strategy, the

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requested test should be offered to her (regardless of ethnicity and family history) after counseling on the risks, benefits, and limitations of screening.

- The cost of carrier screening for an individual condition may be higher than the cost of testing through commercially available expanded carrier screening panels. When selecting a carrier screening approach, the cost of each option to the patient and the health care system should be considered.

### **ACOG Committee Opinion Number 690, Reaffirmed 2023: Recommendations**

- Ethnic-specific, pan-ethnic, 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.
- If a patient requests a screening strategy other than the one used by the obstetrician–gynecologist or other health care provider, the requested test should be made available to her after counseling on its limitations, benefits, and alternatives.
- 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. 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, or women with a personal history of ovarian insufficiency. Additional screening also may be indicated based on family history or specific ethnicity.
- Couples with consanguinity should be offered genetic counseling to discuss the increased risk of recessive conditions being expressed in their offspring and the limitations and benefits of carrier screening.
- Carrier screening will not identify all individuals who are at risk of the screened conditions. Patients should be counseled regarding residual risk with any test result.
- Prenatal carrier screening does not replace newborn screening, nor does newborn screening diminish the potential benefit of prenatal carrier screening.
- If a woman is found to be a carrier for a specific condition, her reproductive partner should be offered screening to provide accurate genetic counseling for the couple with regard to the risk of having an affected child. Additional genetic counseling should be provided to discuss the specific condition, residual risk, and options for prenatal testing.
- If a carrier couple (i.e., carriers for the same condition) is identified before pregnancy, genetic counseling is encouraged so that reproductive options (e.g., donor gametes, preimplantation genetic diagnosis, prenatal diagnosis) can be discussed.
- Individuals with a family history of a genetic disorder may benefit from the identification of the specific familial mutation or mutations rather than carrier screening. Knowledge of the specific familial mutation may allow for more specific and rapid prenatal diagnosis.
- Given the multitude of conditions that can be included in expanded carrier screening panels, the disorders selected for inclusion should meet several of the following

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consensus-determined criteria: have a carrier frequency of 1 in 100 or greater, have a well-defined phenotype, have a detrimental effect on quality of life, cause cognitive or physical impairment, require surgical or medical intervention, or have an onset early in life. Additionally, screened conditions should be able to be diagnosed prenatally and may afford opportunities for antenatal intervention to improve perinatal outcomes, changes to delivery management to optimize newborn and infant outcomes, and education of the parents about special care needs after birth.

- Carrier screening panels should not include conditions primarily associated with a disease of adult onset.

### American College of Genetics and Genomics

The updated ACMG guideline now recommends a multi-tier approach to carrier screening for autosomal recessive and X-linked conditions, incorporating recommendations from the ACOG Committee Opinion 691 to enhance communication and precision while advancing equity in carrier screening (see Table PG1). The consensus group recognized no accepted standard in defining the severity of various conditions; and, based off previously published work, use the following definitions: (1) profound: shortened lifespan during infancy or childhood, intellectual disability; (2) severe: death in early adulthood, impaired mobility or a [disabling] malformation involving an internal organ; (3) moderate: neurosensory impairment, immune deficiency or cancer, mental illness, dysmorphic features; and (4) mild: not meeting one of those described.

The ACMG consensus group recommends offering Tier 3 carrier screening (see Table PG1) to all pregnant patients and those planning a pregnancy. This corresponds to disorders with a carrier frequency of  $\geq 1$  in 200 and includes X-linked disorders. Specific gene recommendations include 97 autosomal recessive genes and 16 X-linked genes all of which are associated with disorders of moderate, severe or profound severity. Non-targeted carrier screening panels that test for genes beyond Tier 3 provide diminishingly small results, and pleiotropy, locus heterogeneity, variant interpretation, and poor genotype-phenotype correlation may disproportionately impact the ability to provide accurate prognostic information.

Moving from the Tier 2 ( $\geq 1/100$ ) carrier frequency to that of Tier 3 ( $\geq 1/200$ ) translates to an annual increase of identifying 2,400 additional U.S. couples, assuming there are ~4 million births annually. Additionally, male partners of pregnant women and those planning a pregnancy may be offered Tier 3 carrier screening for autosomal recessive conditions when carrier screening is performed simultaneously with their female partner. Tier 4 screening may be offered when a pregnancy stems from a known or possible consanguineous relationship (second cousins or closer) or when family or personal medical history warrants. The ACMG does not recommend offering Tier 1 and/or Tier 2 screening, because these do not provide equitable evaluation of all racial/ethnic groups, or the routine offering of Tier 4 panels.

For complete information from the ACMG, their position statement can be found here: <https://www.gimjournal.org/action/showPdf?pii=S1098-3600%2821%2905120-0>.

### Testing Strategy

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Non-targeted carrier screening applies to persons of any risk including average risk. It is appropriate for these panels to include the *CFTR* and *SMN1* genes (See M2017). Non-targeted carrier screening panels should include the minimum number of genes but not exceed the maximum number of genes recommended by professional guidelines from the American College of Obstetricians and Gynecologists (ACOG; 2-22 conditions) or the American College of Medical Genetics and Genomics (ACMG; 113 genes).

After testing the proband, targeted testing on the reproductive partner is preferred. Testing only applies to genes meeting criteria outlined above. If a lab does a more extensive test, then testing for other findings in the reproductive partner would not meet criteria. In general, carrier screening can be done once per lifetime. However, if only targeted or limited testing was done previously, then a more general non-targeted panel could be performed, particularly in cases where there is a new reproductive partner. In this case it is likely that genes could be re-tested.

**Table PG1. American College of Medical Genetics and Genomics Tiered Approach to Carrier Screening<sup>a</sup>**

<b>Tier</b>	<b>Screening Recommendations</b>
1	Cystic fibrosis + spinal muscular atrophy + risk-based screening
2	≥1/100 carrier frequency + Tier 1
3	≥1/200 carrier frequency + Tier 2 (includes X-linked conditions)
4	<1/200 carrier frequency + Tier 3 (genes and conditions will vary by laboratory)

ACMG: American College of Medical Genetics and Genomics

<sup>a</sup> Adapted from Gregg AR et al (2021; PMID 34285390).

X-linked genes considered appropriate for carrier screening in Tier 3 include: *ABCD1*, *AFF2*, *ARX*, *DMD*, *F8*, *F9*, *FMR1*, *GLA*, *L1CAM*, *MID1*, *NR0B1*, *OTC*, *PLP1*, *RPGR*, *RS1*, and *SLC6A8*. Refer to Tables 1 through 5 in the ACMG position statement for additional details regarding appropriate autosomal recessive conditions and their associated carrier frequencies. Additional details are available in the Supplemental Information section.

### 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. Carrier screening with appropriate genetic counseling is performed in adults.

### Genetics Nomenclature Update

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Human Genome Variation Society (HGVS) 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 PG2). HGVS nomenclature is recommended by HGVS, the Human Variome Project, and the Human Genome Organization (HUGO).

The American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP) standards and guidelines for interpretation of sequence variants represent expert opinion from ACMG, AMP, and 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 PG3 shows the recommended standard terminology- “pathogenic,” “likely pathogenic,” “uncertain significance,” “likely benign,” and “benign”—to describe variants identified that cause Mendelian disorders.

**Table PG2. Nomenclature to Report on Variants Found in DNA**

<b>Previous</b>	<b>Updated</b>	<b>Definition</b>
<b>Mutation</b>	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 PG3. ACMG-AMP Standards and Guidelines for Variant Classification**

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

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

## II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

**FEP PPO** - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

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### III. DESCRIPTION/BACKGROUND

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Carrier screening is performed to identify individuals at risk of having offspring with inherited recessive single-gene disorders. Carriers are usually not at risk of developing the disease but can pass pathogenic variants to their offspring. Carrier testing may be performed in the prenatal or preconception periods.

There are more than 1300 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 childhood.

#### Targeted Carrier Screening

Carrier screening tests asymptomatic individuals to identify those who are heterozygous for serious or lethal single-gene disorders. The purpose of screening is to determine the risk of conceiving an affected child and “to optimize pregnancy outcomes based on ... personal preferences and values”. Risk-based carrier screening is performed in individuals having an increased risk based on population carrier prevalence, or personal or family history. Conditions selected for screening can be based on ethnicities at high risk or may be pan-ethnic. An example of effective ethnicity-based screening involves Tay-Sachs disease, with a 90% reduction in the disease following the introduction of carrier screening in the 1970s in the United States and Canada. An example of pan-ethnic screening involves cystic fibrosis, when the American College of Obstetricians and Gynecologists (ACOG) noted that ethnic intermarriage was increasing in the US and recommended pan-ethnic cystic fibrosis carrier screening in 2005.

#### Non-targeted Carrier Screening

Non-targeted carrier screening involves screening individuals or couples for disorders in many genes (up to 100s) by next generation sequencing (NGS). Non-targeted carrier screening 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 patient is not at increased risk of being a carrier. Arguments for non-targeted screening panels include the potential to assess ethnicity, identify more potential conditions, efficiency, and cost. Uncertain are the possible downsides of screening individuals at low-risk, including potential for incorrect variant ascertainment and the consequences of screening for rare single-gene disorders in which the likely phenotype may be uncertain (e.g., due to variable expressivity and uncertain penetrance). The conditions included in non-targeted panels are not standardized and the panels may include many conditions not routinely evaluated and for which there are no existing professional guidelines.

#### 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 Clinical Laboratory Improvement Amendments for high-complexity testing. To

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date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

A number of commercially available genetic tests exist for carrier screening. They range from testing for individual diseases, to small panels designed to address testing based on ethnicity as recommended by practice guidelines (American College of Obstetricians and Gynecologists, American College of Medical Genetics and Genomics), to large, expanded panels that test for numerous diseases.

### IV. RATIONALE

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#### Summary of Evidence

For individuals who are asymptomatic but at risk for having offspring with an inherited recessive genetic disorder who receive targeted risk-based carrier screening, the evidence includes studies supporting clinical validity and clinical utility. Relevant outcomes are test validity and changes in reproductive decision making. Results of carrier testing can be used to inform reproductive decisions such as preimplantation genetic diagnosis, in vitro fertilization, not having a child, invasive prenatal testing, adoption, or pregnancy termination. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are either at increased risk or population risk for having offspring with an inherited recessive genetic disorder who receive non-targeted carrier screening panels the evidence includes studies supporting clinical validity and clinical utility. Relevant outcomes are test validity and changes in reproductive decision making. Several studies have made it clear that ECS offered to all patients is a clinically superior approach for effective identification of at-risk couples compared to past ethnicity-based paradigms. Many of the genes in carrier screening panels do not meet the ACOG consensus-driven criteria of at least 1% carrier rate for all ethnic groups. However, non-targeted testing can address the discrepancies between self-reported ethnicity and genetic ancestry in an ethnically mixed population. As panels become larger the likelihood of being identified as a carrier of a rare genetic disorder increases, leading to an at-risk couple rate of nearly 2% for having an offspring with a recessive or X-linked disorder. Many, though notably not all, of these rare genetic disorders are associated with severe or profound symptoms including shortened lifespan and intellectual or physical disability. With adequate genetic counseling non-targeted carrier screening panels can inform reproductive choices, and observational studies have shown that a majority of couples would consider intervention that depends on the severity of the condition. Therefore, non-targeted carrier screening for severe recessive and X-linked genetic disorders can have a significant clinical impact. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

### V. DEFINITIONS

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N/A

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### VI. DISCLAIMER

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Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

### VII. CODING INFORMATION

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**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

**Carrier screening that does NOT meet criteria are considered Investigational; therefore, not covered:**

Procedure Codes							
0400U	81479						

**Covered when Medically Necessary:**

Procedures Codes							
81161	81171	81172	81200	81205	81209	81220	81221
81222	81223	81224	81242	81243	81244	81250	81251
81255	81257	81260	81290	81329	81330	81361	81362
81364	81412	81443	81479	0449U			

ICD-10-CM Diagnosis Codes	Description
Z13.71	Encounter for nonprocreative screening for genetic disease carrier status
Z31.430	Encounter of female for testing for genetic disease carrier status for procreative management
Z31.438	Encounter for other genetic testing of female for procreative management
Z31.440	Encounter of male for testing for genetic disease carrier status for procreative management

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ICD-10-CM Diagnosis Codes	Description
Z31.448	Encounter for other genetic testing of male for procreative management
Z31.7	Encounter for procreative management and counseling for gestational carrier
Z33.3	Pregnant state, gestational carrier
Z36.0	Encounter for antenatal screening for chromosomal anomalies
Z84.81	Family history of carrier of genetic disease

### VIII. REFERENCES

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### IX. POLICY HISTORY

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<b>MP 2.258</b>	<b>11/17/2020 Minor Review.</b> <ul style="list-style-type: none"> <li>Added “Pan-ethnic panels for autosomal recessive and X-linked genetic disorders that meet the criteria listed above may be considered medically necessary as an alternative to testing of individual genes (e.g., SMN1 gene and CFTR gene) for members who are pregnant or are considering pregnancy” to match BCBSA policy.</li> <li>Removed “Genetic counseling and testing associated with pregnancy management may be considered medically necessary for evaluation of previous unexplained stillbirth or repeated (two or more) miscarriages occurring prior to fetal viability (less than 24 weeks’ gestation)” as no longer appears on BCBSA policy and is addressed in another policy.</li> <li>Removed Policy Guidelines 1 (If there is no family history, risk-based predilection for a disease, carrier screen is not recommended when the carrier rate is less than 1% in the general population) and 2 (The American College of Medical Genetics and Genomics (ACMG) has recommended testing for specific variants, which will result in a carrier detection rate of 95% or higher for most disorders) to align with BCBSA <ul style="list-style-type: none"> <li>Policy Guideline 3 condensed/updated</li> <li>Background and Rationale updated. References added</li> </ul> </li> </ul>
	<b>10/21/2021 Consensus Review.</b> Policy statement unchanged. FEP language updated.
	<b>09/14/2022 Administrative Update.</b> Added new codes 0335U & 0336U as Covered Conditionally
	<b>12/07/2022 Minor Review.</b> Updates from BCBSA; policy now references targeted and non-targeted carrier screening. No longer refers to “pan-ethnic” or “expanded screening carrier panels” due to language updates by ACMG and ACOG. Updates to policy guidelines and background. New references. Codes 0335U and 0336U taken off, these are not screening tests.
	<b>05/26/2023 Administrative Update.</b> Added cross reference M2017, updated policy guidelines. Removed codes 81220-81224
	<b>10/31/2023. Minor Review.</b> Included definitions of targeted and non-targeted into policy statement. Moved non-targeted testing first in policy statement. Removed “panels” from non-targeted testing statement. Updated cross

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<p>references. Updated policy guidelines, background, rationale, and codes. Code 0400U INV, added 81250, 81361, 81362, 81364 as MN. 81220-81224 also placed back onto policy.</p> <p><b>03/15/2024 Administrative Update.</b> New code 0449U effective 04/01/2024.</p> <p><b>11/20/2024 Minor Review.</b> Reformatted for targeted based testing to be first. Removed definitions of targeted and non-targeted testing in policy stance and are now in policy guidelines. No coding changes.</p> <p><b>07/03/2025 Consensus review.</b> No change to policy statement.</p> <p><b>10/17/2025 Administrative Update.</b> Removed Benefit Variations Section and updated Disclaimer.</p> <p><b>03/17/2026 Retirement Review.</b></p>
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