EmblemHealth

# Carrier Screening for Parents or Prospective Parents

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## Definitions

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| Carrier screening | Used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. The testing is offered to individuals who have a family history of a genetic disorder and to people in certain ethnic groups with an increased risk of specific genetic conditions |
| Gene mutation | A change from the normal gene sequence of which underlies a detrimental clinical presentation associated with disease |
| First-degree relative | Parents, siblings, and children |
| Second-degree relative | Grandparents, aunts, uncles, half-siblings, nieces, nephews and grandchildren. |
| Third-degree relative | Great-grandparents, great-aunts, great-uncles, grand-niece, grand-nephew, first cousin, great-grandchildren |
| Hereditary (aka germline) gene mutations | Mutations inherited from a parent and present throughout an individual's life in virtually every cell in the body. When an egg and a sperm (germ) cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells |
| X-linked disorder | Disease caused by a gene mutation located on the X-sex. X-linked disorders are expressed in all males with the defective gene but only females with mutated genes on both X chromosomes express the disease |
| Autosomal dominant | A gene mutation located on a numbered or non-sex chromosome which expresses a disease condition when present as part of a heterozygotic gene pair |
| Autosomal recessive | A gene mutation located on a numbered or non-sex chromosome which expresses a disease condition only when present in homozygous pairs. Carriers are not at risk of developing the disease |

## Related Guidelines

Assisted Reproductive Technologies
Genetic Counseling and Testing
Genetic Testing for Cystic Fibrosis
Noninvasive Prenatal Testing (NIPT) for Fetal Aneuploidy
Nuchal Translucency Screening for Down Syndrome
Preimplantation Genetic Diagnosis Testing (within Assisted Reproductive Technologies)

## Guideline

Carrier screening for parents or prospective parents is considered medically necessary. Pre/post-test genetic counseling is strongly recommended:

**A.** Preconceptional or prenatal genetic testing is considered medically necessary when any of the following criteria based on family history is met:

1. Parents or prospective parents have a previously affected child with the genetic disease
2. One or both parents or prospective parents have 1st or 2nd degree relative who is affected or they have a first degree relative with an affected child
3. One parent or prospective parent is at high risk for a genetic disorder with a late onset presentation or is a known carrier for an autosomal recessive condition
4. One or both prospective parents have an autosomal dominant disorder
5. Prospective parents have a history of unexplained stillbirth or repeated 1st trimester miscarriages (≥ 3)

**B.** Specific genetic testing is considered medically necessary when any of the above criteria are met and all of the following criteria are met:

1. The genetic disorder has been established in the scientific literature to be reliably associated with the disease and is associated high morbidity in the homozygous or compound heterozygous state
2. Alternate biochemical or other clinical tests are not available, provide an indeterminate result or are less effective than genetic testing

**C.** The following test-specific policies are considered medically necessary:

1. Ashkenazi Jewish genetic disorders (JGDs) — to determine carrier status (i.e., Ashkenazi panel for Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia Type C, Gaucher disease, glycogen storage disease [GSD] Type 1a, mucolipidosis Type IV [MLIV], Niemann-Pick disease Type A, Tay-Sachs disease [TSD])
2. Cystic fibrosis (CF) — to determine carrier status for up to 23 CFTR gene mutations
3. Fragile X syndrome (no restrictions)
4. Hemoglobinopathies — to determine carrier status if any of the following is present:
    a. Mother is planning a pregnancy or currently pregnant and at least one parent is in an at-risk population (African, Southeast Asian and/or Mediterranean ancestry)
    b. Mother has a family history of hemoglobinopathy
5. The other partner is a known carrier or affected with a hemoglobinopathy (e.g., Sickle cell disease)
6. Spinal muscular atrophy (no restrictions)

## Limitations/Exclusions

**A.** Coverage is limited to once per lifetime, as repeat screening is not considered medically necessary.

**B.** Coverage for CF testing is limited to analysis of the 23 the most common CFTR gene mutations.

**C.** If one parent/prospective parent screens negative for a disease associated with an autosomal recessive disorder then testing the other parent is not considered medically necessary

**D.** Coverage is contingent on the following:

1. Test targets analysis to the number of genes associated with medically necessary indications listed above (applicable to "D" below)
2. Test result must impact medical management of a current pregnancy and/or the reproductive choices of the (if request is for conditions other than those listed above)
3. Test must has proven validity in the medical community for the identification of a specific genetically linked inheritable disease

**E.** Next generation sequencing (i.e., rapid sequencing of large numbers of DNA segments, up to and including entire genomes) is not considered medically necessary. Expanded panels (e.g., nonstandard universal-type genetic tests) typically screen for diseases present with increased frequency in specific populations; however, they also screen for diseases outside the carrier risk (diminishing the clinical utility of the test) and thus presenting considerable ethical and genetic counseling challenges.

**F.** Home testing (e.g., direct-to-consumer; aka home-testing kits) or self-referral testing (e.g., genetic tests ordered by members via telephone or Internet) is not considered medically necessary, as there is no evidence of efficacy.

## Revision History

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| Sept. 14, 2018 | Added to Limitations/Exclusions that if one parent screens negative for an autosomal recessive disorder then testing the other parent is not medically necessary. |
| Apr. 13, 2018 | Removed SMA restrictions. |
| Oct. 13, 2017 | Removed Fragile X restrictions. |
| Jan.1, 2016 | Added hemoglobinopathy and SMA criteria for clarification. |

## Applicable Procedure Codes

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| 81200 | ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X) |
| 81205 | BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X) |
| 81209 | BLM (Bloom syndrome, RecQ helicase-like) (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant |
| 81220 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines) |
| 81221 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants |
| 81222 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants |
| 81223 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence |
| 81224 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility) |

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| 81242 | FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T) |
| 81243 | FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles |
| 81244 | FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and methylation status) |
| 81250 | G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X) |
| 81251 | GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A) |
| 81255 | HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S) |
| 81257 | HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring) |
| 81260 | IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P) |
| 81290 | MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb) |
| 81330 | SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330) |
| 81400 | Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis) |
| 81401 | Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) LINC00518 (long intergenic non-protein coding RNA 518) (eg, melanoma), expression analysis PRAME (preferentially expressed antigen in melanoma) (eg, melanoma), expression analysis |
| 81402 | Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD]) |
| 81403 | Molecular pathology procedure, Level 4 (eg, 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) |
| 81404 | Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis) |
| 81405 | Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) CPOX (coproporphyrinogen oxidase) (eg, hereditary coproporphyria), full gene sequence CTRC (chymotrypsin C) (eg, hereditary pancreatitis), full gene sequence PKLR (pyruvate kinase, liver and RBC) (eg, pyruvate kinase deficiency), full gene sequence |
| 81406 | Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) ANOS1 (anosmin-1) (eg, Kallmann syndrome 1), full gene sequence HMBS (hydroxymethylbilane synthase) (eg, acute intermittent porphyria), full gene sequence PPOX (protoporphyrinogen oxidase) (eg, variegate porphyria), full gene sequence |
| 81407 | Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform) |
| 81408 | Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis) |
| 81412 | Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, AND SMPD1 |

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| 81479 | Unlisted molecular pathology procedure |
| 81507 | Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy |
| 81599 | Unlisted multianalyte assay with algorithmic analysis |

## Applicable ICD-10 Diagnosis Codes

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| D56.0 | Alpha thalassemia |
| D56.4 | Hereditary persistence of fetal hemoglobin [HPFH] |
| D56.5 | Hemoglobin E-beta thalassemia |
| D56.8 | Other thalassemias |
| D57.00 | Hb-SS disease with crisis, unspecified |
| D57.01 | Hb-SS disease with acute chest syndrome |
| D57.02 | Hb-SS disease with splenic sequestration |
| D57.1 | Sickle-cell disease without crisis |
| D57.20 | Sickle-cell/Hb-C disease without crisis |
| D57.211 | Sickle-cell/Hb-C disease with acute chest syndrome |
| D57.212 | Sickle-cell/Hb-C disease with splenic sequestration |
| D57.219 | Sickle-cell/Hb-C disease with crisis, unspecified |
| D57.3 | Sickle-cell trait |
| D57.40 | Sickle-cell thalassemia without crisis |
| D57.411 | Sickle-cell thalassemia with acute chest syndrome |
| D57.412 | Sickle-cell thalassemia with splenic sequestration |
| D57.419 | Sickle-cell thalassemia with crisis, unspecified |
| D57.80 | Other sickle-cell disorders without crisis |
| D57.811 | Other sickle-cell disorders with acute chest syndrome |
| D57.812 | Other sickle-cell disorders with splenic sequestration |
| D57.819 | Other sickle-cell disorders with crisis, unspecified |
| D58.2 | Other hemoglobinopathies |
| D61.09 | Other constitutional aplastic anemia |
| D82.1 | Di George's syndrome |
| E23.6 | Other disorders of pituitary gland |
| E28.8 | Other ovarian dysfunction |
| E74.00 | Glycogen storage disease, unspecified |
| E74.01 | von Gierke disease |

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| E74.02 | Pompe disease |
| E74.03 | Cori disease |
| E74.04 | McArdle disease |
| E74.09 | Other glycogen storage disease |
| E74.4 | Disorders of pyruvate metabolism and gluconeogenesis |
| E75.00 | GM2 gangliosidosis, unspecified |
| E75.01 | Sandhoff disease |
| E75.02 | Tay-Sachs disease |
| E75.09 | Other GM2 gangliosidosis |
| E75.10 | Unspecified gangliosidosis |
| E75.11 | Mucolipidosis IV |
| E75.19 | Other gangliosidosis |
| E75.21 | Fabry (-Anderson) disease |
| E75.22 | Gaucher disease |
| E75.23 | Krabbe disease |
| E75.240 | Niemann-Pick disease type A |
| E75.241 | Niemann-Pick disease type B |
| E75.242 | Niemann-Pick disease type C |
| E75.243 | Niemann-Pick disease type D |
| E75.248 | Other Niemann-Pick disease |
| E75.249 | Niemann-Pick disease, unspecified |
| E75.25 | Metachromatic leukodystrophy |
| E75.29 | Other sphingolipidosis |
| E75.3 | Sphingolipidosis, unspecified |
| E75.4 | Neuronal ceroid lipofuscinosis |
| E77.0 | Defects in post-translational modification of lysosomal enzymes |
| E77.1 | Defects in glycoprotein degradation |
| E77.8 | Other disorders of glycoprotein metabolism |
| E77.9 | Disorder of glycoprotein metabolism, unspecified |
| E84.0 | Cystic fibrosis with pulmonary manifestations |
| E84.11 | Meconium ileus in cystic fibrosis |
| E84.19 | Cystic fibrosis with other intestinal manifestations |
| E84.9 | Cystic fibrosis, unspecified |
| G11.0 | Congenital nonprogressive ataxia |
| G11.1 | Early-onset cerebellar ataxia |
| G11.2 | Late-onset cerebellar ataxia |
| G12.1 | Other inherited spinal muscular atrophy |
| G12.8 | Other spinal muscular atrophies and related syndromes |

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| G12.9 | Spinal muscular atrophy, unspecified |
| G90.1 | Familial dysautonomia [Riley-Day] |
| N96 | Recurrent pregnancy loss |
| O09.291 | Supervision of pregnancy with other poor reproductive or obstetric history, first trimester |
| O09.292 | Supervision of pregnancy with other poor reproductive or obstetric history, second trimester |
| O09.293 | Supervision of pregnancy with other poor reproductive or obstetric history, third trimester |
| O09.299 | Supervision of pregnancy with other poor reproductive or obstetric history, unspecified trimester |
| Q90.0 | Trisomy 21, nonmosaicism (meiotic nondisjunction) |
| Q90.1 | Trisomy 21, mosaicism (mitotic nondisjunction) |
| Q90.2 | Trisomy 21, translocation |
| Q90.9 | Down syndrome, unspecified |
| Q91.0 | Trisomy 18, nonmosaicism (meiotic nondisjunction) |
| Q91.1 | Trisomy 18, mosaicism (mitotic nondisjunction) |
| Q91.2 | Trisomy 18, translocation |
| Q91.3 | Trisomy 18, unspecified |
| Q91.4 | Trisomy 13, nonmosaicism (meiotic nondisjunction) |
| Q91.5 | Trisomy 13, mosaicism (mitotic nondisjunction) |
| Q91.6 | Trisomy 13, translocation |
| Q91.7 | Trisomy 13, unspecified |
| Q92.0 | Whole chromosome trisomy, nonmosaicism (meiotic nondisjunction) |
| Q92.1 | Whole chromosome trisomy, mosaicism (mitotic nondisjunction) |
| Q92.2 | Partial trisomy |
| Q92.7 | Triploidy and polyploidy |
| Q92.8 | Other specified trisomies and partial trisomies of autosomes |
| Q92.9 | Trisomy and partial trisomy of autosomes, unspecified |
| Q95.0 | Balanced translocation and insertion in normal individual |
| Q95.2 | Balanced autosomal rearrangement in abnormal individual |
| Q95.3 | Balanced sex/autosomal rearrangement in abnormal individual |
| Q96.0 | Karyotype 45, X |
| Q96.1 | Karyotype 46, X iso (Xq) |
| Q96.2 | Karyotype 46, X with abnormal sex chromosome, except iso (Xq) |
| Q96.3 | Mosaicism, 45, X/46, XX or XY |
| Q96.4 | Mosaicism, 45, X/other cell line(s) with abnormal sex chromosome |
| Q97.0 | Karyotype 47, XXX |
| Q97.1 | Female with more than three X chromosomes |
| Q97.2 | Mosaicism, lines with various numbers of X chromosomes |
| Q97.3 | Female with 46, XY karyotype |
| Q97.8 | Other specified sex chromosome abnormalities, female phenotype |

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| Q97.9 | Sex chromosome abnormality, female phenotype, unspecified |
| Q98.0 | Klinefelter syndrome karyotype 47, XXY |
| Q98.1 | Klinefelter syndrome, male with more than two X chromosomes |
| Q98.3 | Other male with 46, XX karyotype |
| Q98.4 | Klinefelter syndrome, unspecified |
| Q98.5 | Karyotype 47, XYY |
| Q98.6 | Male with structurally abnormal sex chromosome |
| Q98.7 | Male with sex chromosome mosaicism |
| Q98.8 | Other specified sex chromosome abnormalities, male phenotype |
| Q98.9 | Sex chromosome abnormality, male phenotype, unspecified |
| Q99.0 | Chimera 46, XX/46, XY |
| Q99.1 | 46, XX true hermaphrodite |
| Q99.2 | Fragile X chromosome |
| Q99.8 | Other specified chromosome abnormalities |
| Q99.9 | Chromosomal abnormality, unspecified |
| Z14.1 | Cystic fibrosis carrier |
| Z14.8 | Genetic carrier of other disease |
| Z15.89 | Genetic susceptibility to other disease |
| 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 |
| Z31.441 | Encounter for testing of male partner of patient with recurrent pregnancy loss |
| Z31.5 | Encounter for procreative genetic counseling |
| Z36.0 | Encounter for antenatal screening for chromosomal anomalies |
| Z36.1 | Encounter for antenatal screening for raised alphafetoprotein level |
| Z36.2 | Encounter for other antenatal screening follow-up |
| Z36.3 | Encounter for antenatal screening for malformations |
| Z36.4 | Encounter for antenatal screening for fetal growth retardation |
| Z36.5 | Encounter for antenatal screening for isoimmunization |
| Z36.81 | Encounter for antenatal screening for hydrops fetalis |
| Z36.82 | Encounter for antenatal screening for nuchal translucency |
| Z36.83 | Encounter for fetal screening for congenital cardiac abnormalities |
| Z36.84 | Encounter for antenatal screening for fetal lung maturity |
| Z36.85 | Encounter for antenatal screening for Streptococcus B |
| Z36.86 | Encounter for antenatal screening for cervical length |
| Z36.87 | Encounter for antenatal screening for uncertain dates |
| Z36.88 | Encounter for antenatal screening for fetal macrosomia |
| Z36.89 | Encounter for other specified antenatal screening |

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| Z36.8A | Encounter for antenatal screening for other genetic defects |
| Z84.81 | Family history of carrier of genetic disease |

## References

American College of Medical Genetics. Carrier screening in individuals of Ashkenazi Jewish descent. January 2008. reaffirmed 2013. https://www.acmg.net/docs/Published_Carrier_Screening_PG.pdf. Accessed September 17, 2019.

American College of Medical Genetics. Carrier screening for spinal muscular atrophy. November 2008, reaffirmed 2013. https://www.acmg.net/docs/SMA_GIM_2008.pdf. Accessed September 17, 2019.

Human Genome Research Institute. Talking Glossary of Genetic Terms. 2015. http://www.genome.gov/glossary/. Accessed September 17, 2019.

American College of Obstetricians and Gynecologists. Committee Opinion Number Number 691. Carrier Sreening for Genetic Conditions. March 2017. Replaces No 318, 432, 442, 469, 486. https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-for-Genetic-Conditions. Accessed September 17, 2019.

GeneReviews® Terms and Definitions. http://www.ncbi.nlm.nih.gov/books/NBK5191/#IX-C. 2018. Accessed September 17, 2019.

Genetics Home Reference Guide to Understanding Genetic Conditions. April 2018. http://ghr.nlm.nih.gov/handbook/testing/uses. Accessed September 19, 2018.

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