

# Pre-conceptional, Prenatal, Preimplantation Genetic Testing

## Table of Content

[Purpose](#)  
[Description & Definitions](#)  
[Criteria](#)  
[Coding](#)  
[Document History](#)  
[References](#)  
[Special Notes](#)  
[Keywords](#)

[Effective Date](#) 8/2011  
[Next Review Date](#) 03/15/2024  
[Coverage Policy](#) Medical 34D  
[Version](#) 1

**Member-specific benefits take precedence over medical policy and benefits may vary across plans. Refer to the individual's benefit plan for details \*.**

## Purpose:

This policy addresses genetic testing for pre-conception, prenatal and pre-implantation.

## Description & Definitions:

**Prenatal diagnosis or prenatal screening** is testing for diseases or conditions in a fetus or embryo before it is born.

**Preconceptual diagnosis** for pregnancy planning and care in the form of genetic testing for members of reproductive age may be initiated.

**Preimplantation genetic diagnosis** (PGD or PIGD) (also known as embryo screening) refers to procedures that are performed on embryos prior to implantation, sometimes even on oocytes prior to fertilization.

**Inheritest Carrier Screen:** The Inheritest Carrier Screen offers a broad genetic screening option, providing genetic information regarding greater than 90 autosomal recessive inherited diseases found throughout the pan-ethnic US population, all in one simple test.

**Cell-free fetal DNA-based prenatal screening for fetal aneuploidies**, including but not limited to Trisomy 13 (Patau Syndrome), Trisomy 18 (Edwards Syndrome) and Trisomy 21 (Down syndrome) uses sequence analysis of cell-free fetal DNA in maternal plasma.

**Autosomal recessive:** A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a nonsex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene

**X-linked recessive inheritance** - hereditary pattern in which a recessive gene on the X chromosome results in the manifestation of characteristics in male offspring and a carrier state in female offspring.

## Criteria:

**Preconceptional carrier status genetic testing** for pregnancy planning for members of reproductive age OR **preimplantation genetic testing**, OR **prenatal genetic testing** to determine carrier status of a fetus, are medically necessary for **1 or more** of the following if criteria are met:

- **Ashkenazi Jewish** genetic panel testing may be indicated when **ALL** of the following are present:

- Individual to be tested is of Ashkenazi Jewish ancestry and of reproductive age.
- Panel testing is being ordered to assess for mutations associated with **3 or more** of the following diseases:
  - Bloom syndrome
  - Canavan disease
  - Cystic fibrosis
  - Dihydrolipoamide dehydrogenase deficiency
  - Familial dysautonomia (Riley-Day syndrome)
  - Familial hyperinsulinism
  - Fanconi anemia group C
  - Gaucher disease
  - Glycogen storage disease type 1A
  - Joubert syndrome 2
  - Maple syrup urine disease
  - Mucopolysaccharidosis IV
  - Nemaline myopathy
  - Niemann-Pick disease type A
  - Spinal muscle atrophy
  - Tay-Sachs disease
  - Usher syndrome type 1F
  - Usher syndrome type 3
- **Bloom syndrome** (BLM Gene) for **1 or more** of the following:
  - Preimplantation or prenatal genetic diagnosis when disease-causing mutation in BLM gene has been identified in both parents
  - Carrier testing for individual of Ashkenazi Jewish ancestry who is of reproductive age
  - Patient with family history of Bloom syndrome
  - Reproductive partner of BLM gene mutation carrier
  - Need to establish disease-causing mutation in patient with confirmed diagnosis
- **Canavan disease** (ASPA Gene) with **1 or more** of the following indications:
  - Preimplantation genetic diagnosis or Prenatal diagnosis, when disease-causing mutation in ASPA gene has been identified in both parents
  - Preconceptional or prenatal carrier testing when reproductive partner is an ASPA gene mutation carrier
  - Preconceptional, prenatal, or preimplantation testing if a member is of Ashkenazi Jewish ancestry and of reproductive age
  - The member has a family history of Canavan disease in first or second degree relative
  - Preconceptional or prenatal testing for a member with levels of urinary N-acetyl aspartic acid that are equivocal or indeterminate
- **Cystic Fibrosis** is medically necessary for **1 or more** of the following:
  - The Plan covers requests for common mutations with included in CPT codes 81221 (single mutation) or 81220 (common variants) endorsed by the American College of Medical Genetics (ACMG) for Cystic Fibrosis testing of members in **1 or more** of the following groups:
    - Couples seeking prenatal care;
    - Couples who are planning a pregnancy.
  - Extended CFTR mutation panels (Code 81222 and 81224) are approved for patients meeting **ANY** of the following 3 criteria (but not full sequencing, see exclusions):
    - Individuals with reproductive partners with cystic fibrosis or congenital absence of the vas deferens and no identified mutation with standard gene sequencing
    - Individuals with a family history of cystic fibrosis with no identified mutation on basic/standard gene sequencing,
    - Individuals with elevated or indeterminate sweat chloride levels where from zero to up to 2 mutations have been identified by basic/standard gene sequencing.
- **Duchene Muscular Dystrophy** for the **1 or more** of the following indications:
  - Preimplantation genetic diagnosis, when the DMD gene mutation in has been identified in mother
  - Prenatal diagnosis in fetus with 46, XY karyotype, when DMD gene mutation in has been identified in carrier mother or if linkage has been established suggesting mother is carrier

- Carrier testing for asymptomatic female with family history of Duchenne muscular dystrophy, Becker muscular dystrophy, or DMD-associated dilated cardiomyopathy
- Member with confirmed diagnosis of muscular dystrophy with need establish disease-causing mutation
- **Familial Dysautonomia (Riley-Day syndrome)** for **1 or more** of the following indication:
  - Preimplantation or prenatal genetic diagnosis when the IKBKAP gene mutation in has been identified in both parents
  - The member is of Ashkenazi Jewish ancestry and of reproductive age
  - The member has a family history (in a 1st or 2nd degree relative) of familial dysautonomia
  - The member is a reproductive partner of an individual that has been confirmed to be a IKBKAP gene mutation carrier
- **Familial Hemophagocytic Lymphohistiocytosis:** Covered if requested by name without criteria (there is no specific code)
- **Familial Mediterranean Fever (FMF)** for **1 or more** of the following:
  - Carrier testing for MEFV gene may be indicated when one of the following are present: Member is from an ethnic group at increased risk (eg, Armenian, Turkish, Arab, North African Jewish) and of reproductive age.
  - Prior to gamete donation if gamete recipient is known carrier
  - Reproductive partner of MEFV gene mutation carrier
- **Fanconi anemia group (FANC Gene)** for **1 or more** of the following indication:
  - Preimplantation or prenatal genetic test when the disease causing mutation has been found in both parents
  - Carrier testing for individual of Ashkenazi Jewish ancestry who is of reproductive age
  - The member has a family history of Fanconi anemia, and prior identification of disease-causing mutations in a first or second degree relative
  - Reproductive partner of FANC gene mutation carrier
  - Identification of disease-causing mutation in patient with confirmed diagnosis
  - Equivocal or indeterminate cytogenetic testing for chromosomal breakage or rearrangement in presence of DNA interstrand cross-linking agent (eg, diepoxybutane or mitomycin C);
  - Prior to gamete donation if gamete recipient is carrier;
- **Gaucher's disease** for **1 or more** of the following indication:
  - Preimplantation or prenatal genetic diagnosis for families in which disease-causing mutations have been identified in both parents or in previously affected child,
  - Carrier testing for individual of Ashkenazi Jewish ancestry
  - Carrier testing for preconception testing of partner of known carrier or affected individual
- **Glycogen storage disease (Maple syrup urine disease)** for **1 or more** of the following indication:
  - Preimplantation or prenatal genetic diagnosis when the G6PC or SLC37A4 gene mutation in has been identified in both parents.
  - The member is of Ashkenazi Jewish ancestry and of reproductive age
  - The member has a family history of glycogen storage disease type I
  - The member is a reproductive partner of an individual that has been confirmed to be a G6PC or SLC37A4 gene mutation carrier
- **Huntington's Disease** for 1 or more of the following indication:
  - Preimplantation or prenatal genetic diagnosis when the HTT gene disease-causing has been confirmed in one parent
  - Preimplantation or prenatal diagnostic testing for couples in at-risk family who do not wish to undergo presymptomatic mutation testing themselves
- **Karyotyping codes** along with 88230 and 88289 codes are covered without criteria or preauthorization.
- **Marfan Syndrome** for **1 or more** of the following indications:
  - The use of Marfan syndrome gene testing in patients fulfilling the Ghent diagnostic criteria for the purpose of obtaining information for reproductive decision making or facilitating the diagnosis of Marfan syndrome in at-risk relatives;
  - The prenatal diagnosis or preimplantation genetic testing for Marfan syndrome in the offspring of patients with known disease-causing
- **Mucopolipidosis Type IV (MCOLN1)** for **1 or more** of the following indications

- Preimplantation or Prenatal diagnosis genetic diagnosis, when disease-causing mutation in MCOLN1 gene has been identified in both parents
- Carrier testing for an individual of Ashkenazi Jewish ancestry
- The member has a family history of mucopolidosis IV in first or second degree relative
- Reproductive partner of MCOLN1 gene mutation carrier
- Need to establish disease-causing mutation in patient with confirmed diagnosis
- **Myotonic Dystrophy, DMPK and CNBP gene testing for 1 or more** of the following indications:
  - Prenatal diagnosis when CNBP expansion has been identified in affected parent
  - Preimplantation, prenatal, or preconceptional genetic testing when a CNBP mutation has been identified in an affected first-degree relative
- **Nieman Pick Disease for 1 or more** of the following indication:
  - Preimplantation or Prenatal genetic diagnosis, when disease-causing mutations, SMPD1 NPC1 or NPC2 gene have been identified in both parents or in a couple with previously affected child
  - Carrier testing for individual of Ashkenazi Jewish ancestry who is of reproductive age
  - Carrier testing for individual with family history of Niemann-Pick disease type A or type B
  - Establishment of disease-causing mutation in patient with confirmed diagnosis of Niemann-Pick disease type A or type B
- **Nonsyndromic Deafness:** Genes GJB2, GJB6, POU3F4, PRPS1, and SMPX. See Milliman guideline A-0823 Deafness and Hearing Loss, Nonsyndromic - Gene and Gene Panel Testing for criteria.
- **Neurofibromatosis Type1 and 2 (NF1/ NF2) gene testing** may be indicated for **1 or more** of the following Indications:
  - Preimplantation genetic diagnosis when NF1 or NF2 gene mutation has been identified in parent
  - Prenatal testing, when parent has NF1 or NF2 gene mutation, or linkage is established in family.
  - Carrier testing, when there is a first-degree relative with either NF1 or NF2.
- **Paraganglioma-Pheochromocytoma Syndromes, Hereditary - SDHB, SDHC, SDHD, and TMEM127** Genes: See Milliman guideline Paraganglioma-Pheochromocytoma (Hereditary) - Gene Testing and Gene Panel A-0798 for criteria.
- **Retinoblastoma RB1 gene testing** may be indicated for **1 or more** of the following indication:
  - Preimplantation or prenatal genetic diagnosis for families RB1 mutation has been identified in either parent.
  - The member has a first degree relative with a known RB1 mutation
  - Prenatal diagnosis for pregnancies at increased risk when disease-causing allele of affected family member has been identified or linkage has been established in family
- **Spinal Muscular Atrophy (SMA) testing** of the SMN1 and SM2 genes is approved for carrier screening in prospective parents who wish to reproduce
- **Tay-Sach's disease (HEXA gene)** is approved for **1 or more** of the following:
  - Carrier testing for **1 or more** of the following:
    - Individual of Ashkenazi Jewish ancestry and of reproductive age
    - Individual with deficiency of beta-hexosaminidase A enzyme activity on carrier screening assay
    - Individual with family history of Tay-Sachs disease and of reproductive age, when both disease-causing mutations in HEXA gene have been identified in affected relative
    - Prior to gamete donation if gamete recipient is carrier
  - Confirmation of diagnosis of Tay-Sachs disease in symptomatic patient with inconclusive leukocyte or serum activity of beta-hexosaminidase A
  - Establishment of disease-causing mutation in patient with confirmed diagnosis of Tay-Sachs disease
  - Preimplantation genetic diagnosis when disease-causing mutation in HEXA gene has been identified in both parents
  - Prenatal diagnosis when disease-causing mutation in HEXA gene has been identified in both parents
- **Wiskott-Aldrich syndrome (WAS) gene mutation testing 1 or more** of the following:
  - Individual is male with **All** of the following:
    - Initial testing points to a WAS related disorder (Wiskott Aldrich Syndrome, X linked thromblytopenia, X-linked congenital neutropenia)

- Individual is female with **All** of the following:
  - There is a known family history of WAS gene mutation (testing is to identify female carriers)
- Testing is prenatal with **All** of the following indications:
  - Fetus is male. Testing is being done with chorionic villi sampling or cultured amniocytes
  - There is known risk of WAS gene mutation (positive family history of WAS gene mutation and/or of known positive carrier females)
- **Preconceptional carrier status genetic testing** for pregnancy planning for members of reproductive age or prenatal genetic testing to determine **carrier status** of a fetus for **other** inherited disorders when **ALL** of the following criteria are met:
  - **Family history** genetic testing are considered **medically necessary** when **1 or more** of the following criteria is met:
    - An affected child is identified with either an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance;
    - One or both parents or prospective parent(s) have another first or a second degree relative who is affected, or the first degree relative has an affected child, with either an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance;
    - The parent or prospective parent is at high risk for a genetic disorder with a late onset presentation;
    - The parents or prospective parents are members of an ethnic group with a high risk of a specific genetic disorder with an autosomal recessive pattern of inheritance and testing is performed to determine carrier status and to guide subsequent reproductive decisions.
  - **Specific genetic testing** is considered medically necessary when **ALL** of the following criteria are met:
    - Testing is accompanied by genetic counseling.
    - Testing is for **1 or more** of the following:
      - A biochemical or other test is identified and the results are indeterminate
      - The genetic disorder cannot be identified through biochemical or other testing
  - **Approved Disorders** for targeted disease processes, Testing is for **1 or more** of the following:
    - 22q11.2 deletion syndromes (Velocardiofacial / DiGeorge syndrome, Catch22, Familial third and fourth pharyngeal pouch syndrome, Hypoplasia of thymus and parathyroid, Pharyngeal pouch syndrome, Sedlackova syndrome, Third and fourth pharyngeal pouch syndrome, Thymic aplasia syndrome, and Velofacial hypoplasia)
    - Adrenoleukodystrophy DNA Sequencing (ABCD1 gene) 8/23/16
    - Alpha Thalassemia, Beta Thalassemia and Sickle Cell
    - Autosomal recessive or autosomal dominant centronuclear myopathy (DNM2 and/or BIN1)
    - Congenital muscular dystrophy
    - Deficiency, Familial hyperinsulinism,
    - Dihydrolipoamide dehydrogenase
    - Ellis-van Creveld syndrome EVC/EVC2 gene
    - Emery-Dreifuss muscular dystrophy (EDMD1, 2, and 3) (FGFR2, Facioscapulohumeral muscular dystrophy (FSHMD1A)FGFR3)
    - Familial HEMOPHAGOCYTIC,
    - Familial hyperinsulinism
    - Familial Myotonic Dystrophy, (FMD)
    - Facioscapulohumeral Muscular Dystrophy (FSHD)
    - Hemophilia A or B
    - Hereditary sensory and autonomic neuropathies
    - Inheritest Universal screening
    - Leopard syndrome
    - Limb girdle muscular dystrophy (LGMD1, LGMD2) (FKRP (Fukutin related protein))
    - Lissencephaly
    - LYMPHOHISTIOCYTOSIS (FHL),
    - Mucopolysaccharidosis (MPS)
    - NemaLine myopathy,
    - Noonan syndrome

- Pontocerebellar Hypoplasia (TSEN54, EXOSC8)
  - Primary Ciliary Dyskinesia (PCD)
  - type 1C (MDC1C) (FKRP (Fukutin related protein))
  - Ullrich Muscular Dystrophy COL6A2
  - Usher syndrome type 1F or Usher syndrome type 3,
  - von Willebrand factor
  - Walker-Warburg syndrome (POMGNT1)
  - X-linked centronuclear myopathy (MTM1)
  - X-linked Lymphoproliferative Syndromes for transplant patients
- **Prenatal diagnosis testing** is covered for **1 or more** of the following:
  - Echogenic bowel is detected on ultrasound examination of fetus during pregnancy
  - VLDLR Associated Cerebellar Hypoplasia.
  - Disease-causing mutation in RYR1 (Malignant Hyperthermia) gene has been identified in one parent
- **Cell-free fetal DNA-based prenatal screening for common fetal aneuploidies:** Covered without precertification. (i.e., Trisomy 13 (Patau Syndrome), Trisomy 18 (Edwards Syndrome), and Trisomy 21 (Down syndrome)) (e.g., MaterniT21, Informaseq, Verifi)
- **Comparative Genomic Hybridization Microarray testing or Single Nucleotide Polymorphism (SNP) Chromosomal Microarray Analysis** for the evaluation of a fetus for **1 or more** of the following:
  - Evaluating abnormal fetal anatomic findings detected on fetal ultrasound or fetal magnetic resonance imaging which are characteristic of a genetic abnormality;
  - Women undergoing invasive prenatal diagnostic testing (i.e. amniocentesis, chorionic villus sampling or fetal tissue sampling).
  - Evaluation of recurrent pregnancy loss, after the second consecutive loss
  - Evaluation of intrauterine fetal demise (IUID) or stillbirth after 20 weeks of gestational age
  - Evaluation of a pregnancy loss with one or more major structural anomalies
- **Preimplantation genetic diagnosis** when **1 or more** of the following:
  - used to determine the sex of an embryo only when there is a documented history of an X-linked disorder, such that deselection of an affected embryo can be made on the basis of sex alone.
  - used to evaluate human leukocyte antigen (HLA) status alone is in families with a child with a bone marrow disorder requiring a stem cell transplant, and in whom there is no other source of a compatible bone marrow donor other than an HLA matched sibling.
  - used as a technique to improve the implantation rate of in vitro fertilization (IVF) procedures in otherwise infertile couples, when **1 or more** of the following below are met:
    - Three prior failed attempts at IVF;
    - One of the partners is known to harbor a balanced translocation
  - used to deselect embryos with genetic mutations in partners who meet any criteria in **All** of the following:
    - Must meet at **1 or more** of the following:
      - Both partners are known carriers of the same autosomal recessive disorder;
      - One partner is a known carrier of an autosomal recessive disorder, and the couple has previously produced offspring affected by that disorder;
      - One partner is a known carrier of a single gene autosomal dominant disorder;
      - One partner is a known carrier of a single X-linked disorder;
    - Must meet **ALL** of the following:
      - A specific mutation, or set of mutations, has been identified, that specifically identifies the genetic disorder with a high degree of reliability;
      - The genetic disorder is associated with severe disability or has a lethal natural history
      - Testing is accompanied by genetic counseling.

Pre-conception, prenatal and pre-implantation genetic testing is considered **not medically necessary** for any use other than those indicated in clinical criteria, to include but not limited to:

- Ambry's Cystic Fibrosis 508 First and reflex testing if negative to Cystic Fibrosis Full Gene Sequencing Analysis or Cystic Fibrosis Amplified genetic testing
- Any other test not listed above as covered is considered among those that are not medically necessary.
- APOE 4 or other Genetic Testing for Alzheimer's Disease (S3852)

- CFTR Full Gene Sequencing (81223)
- Comparative genomic hybridization microarray testing and single nucleotide polymorphism (SNP) chromosomal microarray analysis are unproven and not medically necessary for preimplantation genetic diagnosis or screening in embryos.
- EPG5 Gene-VICI Syndrome testing
- EpiSign Complete
- Exome Sequence Analysis (CPT 81415, 81416, 81417)
- FGFR3 mutation Achondroplasia (Dwarfism)
- Genetic disease carrier panel testing for multiple heritable disorders in the general population is considered not medically necessary if the genetic testing includes genes not recommended for routine preconceptional or prenatal screening by the American College of Medical Genetics and the American College of Obstetricians and Gynecologists (e.g. HerediT, Inheritest, NxGen MDx Super Panel/Universal Panels)
- Genetic testing related to seizure disorders
- Genome Sequence Analysis (CPT 81425, 81426, 81427)
- GPR56 gene for polymicrogyria
- Hereditary Retinal Disorders Genetic Panel Lab Test
- Holoprosencephaly, schizencephaly & craniosynostosis genetic testing including, but not limited to genes SHH, ZIC2, SIX3, and TGIF1
- Human leukocyte antigen (HLA) typing of an embryo to identify a future suitable stem cell, tissue or organ transplantation donor
- Hyperimmunoglobulin D syndrome (HIDS)
- JAG1 and/or NOTCH2 testing for Alagille Syndrome
- KCNC2 or KCNC3
- Mevalonate kinase deficiency (MKD)
- MTHFR
- MYH8 Gene(Trismus-pseudocamptodactyly syndrome)
- Repeat/Duplicative genetic testing
- Routine requests for cell-free prenatal genetic testing beyond fetal trisomies 21, 18, and 13 are considered not medically necessary (e.g., microdeletion testing, MaterniT21 Plus, InformaSeq with Y analysis, InformaSeq with XY analysis).
- Signature Precision Panel™ | Prenatal
- SPRED1 (sprout-related, EVH1 domain containing 1) (eg, Legius syndrome)
- Tumor necrosis factor receptor-1 associated periodic syndrome (TRAPS) genetic testing
- Uniparental Disomy
- Whole Exome Sequencing (WES)
- Whole Genome Sequencing (WGS)
- Y Chromosome Microdeletion Analysis

## Coding:

### Medically necessary with criteria:

| Coding | Description   |
|--------|---|
| 81130  | SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)         |
| 81161  | DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed   |
| 81187  | CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles |
| 81200  | ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)   |
| 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   |
| 81224 | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)   |
| 81228 | Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis   |
| 81229 | Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis                      |
| 81234 | DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles   |
| 81239 | DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)  |
| 81242 | FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)  |
| 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)  |
| 81252 | GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence   |
| 81253 | GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants  |
| 81254 | GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])  |
| 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, Constant Spring) |
| 81258 | HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant   |
| 81259 | HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence   |
| 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)   |
| 81261 | HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)  |
| 81269 | HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants  |
| 81271 | HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles   |



|       |   |
|-------|---|
| 81272 | HTT (huntingtin) (eg, Huntington disease) gene analysis; characterization of alleles (eg, expanded size)  |
| 81290 | MCOLN1 (mucopolipin 1) (eg, Mucopolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)  |
| 81329 | SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed  |
| 81336 | SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence  |
| 81337 | SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)  |
| 81362 | HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)  |
| 81363 | HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)  |
| 81364 | HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence   |
| 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)  |
| 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)  |
| 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)  |
| 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 |
| 81430 | Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1  |
| 81431 | Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes  |

|       |   |
|-------|---|
| 81443 | Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucopolidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH) |
| 81479 | Unlisted molecular pathology procedure  |
| 83080 | b-Hexosaminidase, each assay  |
| 84999 | Unlisted chemistry procedure  |
| 88230 | Tissue culture for non-neoplastic disorders; lymphocyte   |
| 89290 | Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos  |
| 89291 | Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos   |
| S3841 | Genetic testing for retinoblastoma  |
| S3844 | DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness   |
| S3845 | Genetic testing for alpha-thalassemia   |
| S3846 | Genetic testing for hemoglobin E beta-thalassemia   |
| S3849 | Genetic testing for Niemann-Pick disease  |
| S3850 | Genetic testing for sickle cell anemia  |
| S3853 | Genetic testing for myotonic muscular dystrophy   |

**Considered Not Medically Necessary:**

| Coding | Description  |
|--------|--|
| 81223  | CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence   |
| 81241  | F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant  |
| 81331  | SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis  |
| 81415  | Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis  |
| 81416  | Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)   |
| 81417  | Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)  |
| 81425  | Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis   |
| 81426  | Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)   |
| 81427  | Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)  |
| 81434  | Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A |

|       |   |
|-------|---|
| 0318U | Pediatrics (congenital epigenetic disorders), whole genome methylation analysis by microarray for 50 or more genes, blood |
| S3842 | Genetic testing for Von Hippel-Lindau disease   |
| S3852 | DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease  |

Procedure Codes listed do not confirm coverage. Not all codes may be present.

## Document History:

### Revised Dates:

- 2022: July
- 2022: March
- 2021: April
- 2020: June
- 2020: January
- 2019: December
- 2019: October
- 2018: March
- 2016: August
- 2016: June
- 2016: May
- 2016: April
- 2016: March
- 2016: February
- 2012: March
- 2016: January
- 2015: December
- 2015: November
- 2015: October
- 2015: September
- 2015: August
- 2015: July
- 2015: June
- 2015: March
- 2015: February
- 2015: January
- 2014: November
- 2014: October
- 2014: September
- 2014: August
- 2014: July
- 2014: June
- 2014: May
- 2014: March
- 2014: January
- 2013: December
- 2013: October
- 2013: July
- 2013: April
- 2013: February
- 2012: November
- 2012: October
- 2012: July

### Reviewed Dates:

- 2021: February
- 2020: December
- 2019: October
- 2017: April
- 2016: April
- 2015: November
- 2014: January
- 2011: July

### Effective Date:

- August 2011

## References:

Specialty Association Guidelines; Government Regulations; Winifred S. Hayes, Inc; UpToDate; Literature Review; Specialty Advisors; National Coverage Determination (NCD); Local Coverage Determination (LCD).

(2020). Retrieved May 28, 2020, from Hayes, Inc.:

<https://evidence.hayesinc.com/search?q=%257B%2522phrase%2522:%2522retinal%2520disorders%2520genetic%2520panel%2522,%2522style%2522:%2522ALL%2522,%2522size%2522:10,%2522page%2522:1,%2522bundle%2522:%257B%2522path%2522:%2522%2522,%2522title%2522:%2522%2522%>

(2020). Retrieved May 29, 2020, from Centers for Medicare and Medicaid Services: [https://www.cms.gov/medicare-coverage-database/search/search-](https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&Keyword=Genetic+testing&KeywordLookU)

[results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&Keyword=Genetic+testing&KeywordLookU](https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&Keyword=Genetic+testing&KeywordLookU)

(2020). Retrieved May 29, 2020, from National Comprehensive Cancer Network: <https://cse.google.com/cse?cx=007894372670309631110:vocdaeamxuy&ie=UTF-8&q=hereditary%20retinal%20disorders&safe=high>

(2020, Feb 05). Retrieved May 28, 2020, from MCG: <https://careweb.careguidelines.com/ed24/index.html>

(2020). Retrieved May 29, 2020, from DynaMed: <https://www.dynamed.com/results?q=retinal+disorder+genetic+testing&lang=en>

(2020). Retrieved Jun 01, 2020, from Department of Medical Assistance Services: <http://www.dmas.virginia.gov/#/index>

AAO Quality of Care Secretariat, Hoskins Center for Quality Eye Care. (2016, Jun). Retrieved May 29, 2020, from American Academy of Ophthalmology: <https://www.aao.org/clinical-statement/recommendations-on-clinical-assessment-of-patients>

Clinical Guidelines: Genetic Testing. (2020). Retrieved May 29, 2020, from AIM Specialty Health: <https://aimspecialtyhealth.com/resources/clinical-guidelines/genetic-testing/>

Garg, S. (2019, Nov 08). Retinitis pigmentosa: Clinical presentation and diagnosis. Retrieved May 29, 2020, from UpToDate: [https://www.uptodate.com/contents/retinitis-pigmentosa-clinical-presentation-and-diagnosis?search=hereditary%20retinal%20dystrophy&source=search\\_result&selectedTitle=1~23&usage\\_type=default&display\\_rank=1#H420617337](https://www.uptodate.com/contents/retinitis-pigmentosa-clinical-presentation-and-diagnosis?search=hereditary%20retinal%20dystrophy&source=search_result&selectedTitle=1~23&usage_type=default&display_rank=1#H420617337)

Lenassi, E., Clayton-Smith, J., Douzgou, S., Ramsden, S., Ingram, S., Hall, G., . . . Sergouniotis, P. (2020, Apr). Clinical Utility of Genetic Testing in 201 Preschool Children with Inherited Eye Disorders. Retrieved May 29, 2020, from PubMed: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7118019/>

Recommendations for Genetic Testing of Inherited Eye Diseases 2014. (2014, Jun). Retrieved May 29, 2020, from American Academy of Ophthalmology: <https://www.aao.org/clinical-statement/recommendations-genetic-testing-of-inherited-eye-d>

Retinal Dystrophy Xpanded Panel. (2020). Retrieved May 27, 2020, from GeneDx: <https://www.genedx.com/test-catalog/available-tests/retinal-dystrophy-xpanded-panel/>

Regulations of Genetic Tests. (2019, Nov 20). Retrieved Jun 01, 2020, from National Human Genome Research Institute: <https://www.genome.gov/about-genomics/policy-issues/Regulation-of-Genetic-Tests>

(2019). Retrieved Dec 30, 2019, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&Keyword=Uniparental+Disomy&KeyWordLo>

(2019, Feb 11). Retrieved Dec 31, 2019, from MCG: <https://careweb.careguidelines.com/ed23/index.html>

(2019). Retrieved Dec 30, 2019, from National Comprehensive Cancer Network: <https://cse.google.com/cse?cx=007894372670309631110:vocdaeamxuy&ie=UTF-8&q=uniparental%20disomy&safe=high>

Beygo, J., Buitine, K., Ramsden, S., Ellis, R., Clayton-Smith, J., & Kanber, D. (2019, Jun 24). Update of the EMQN/ACGS best practice guidelines for molecular analysis of Prader-Willi and Angelman syndromes. Retrieved Dec 31, 2019, from European Journal of Human Genetics: <https://www.nature.com/articles/s41431-019-0435-0>

Butler, M. G., Miller, J. L., & Forster, J. L. (2019, Jun 24). Pradar-Willi Syndrome - Clinical Genetics, Diagnosis and Treatment Approaches: An Update. Retrieved Dec 31, 2019, from <http://www.eurekaselect.com/173540/article>. Doi: 10.2174/1573396315666190716120925

Clinical Guidelines Genetic Testing. (2019). Retrieved Dec 30, 2019, from AIM Specialty Health: <https://aimspecialtyhealth.com/resources/clinical-guidelines/genetic-testing/>

Epidemiology and genetics of Prader-Willi syndrome. (2019, Dec 03). Retrieved Dec 30, 2019, from UpToDate: [https://www.uptodate.com/contents/epidemiology-and-genetics-of-prader-willi-syndrome?search=uniparental%20disomy&source=search\\_result&selectedTitle=2~40&usage\\_type=default&display\\_rank=2](https://www.uptodate.com/contents/epidemiology-and-genetics-of-prader-willi-syndrome?search=uniparental%20disomy&source=search_result&selectedTitle=2~40&usage_type=default&display_rank=2)

Prader-Willi Syndrome. (2018, Nov 30). Retrieved Dec 30, 2019, from DynaMed: <https://www.dynamed.com/condition/prader-willi-syndrome-27>

Uniparental Disomy (UPD) for Chromosomes 6, 7, 11, 14, or 15. (2012, Nov 13). Retrieved Dec 30, 2019, from Hayes, Inc.: <https://evidence.hayesinc.com/report/gte.unicompartmental>

Carrier Screening for Genetic Conditions, Number 691. (2017, March). Retrieved October 8, 2019, from American College of Obstetricians and Gynecologists: <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-for-Genetic-Conditions>

Clinical Appropriateness Guidelines: Genetic Testing for Reproductive Carrier Screening and Prenatal Diagnosis. (2019, September 9). Retrieved Oct 8, 2019, from AIM Specialty Health: [https://aimspecialtyhealth.com/wp-content/uploads/2019/07/ReproductiveCarrierScreeningandPrenatalDiagnosis\\_Sep\\_2019.pdf](https://aimspecialtyhealth.com/wp-content/uploads/2019/07/ReproductiveCarrierScreeningandPrenatalDiagnosis_Sep_2019.pdf)

HEXA Gene Analysis Coding and Billing Guidelines. (2019, Jan 01). Retrieved Oct 8, 2019, from Centers for Medicare and Medicaid Services: <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=53598&ver=14&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&Keyword=HEX>X

HGNC Data for HEXA. (2019). Retrieved October 8, 2019, from HUGO Gene Nomenclature Committee: [https://www.genenames.org/data/gene-symbol-report#!/hgnc\\_id/HGNC:4878](https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:4878)

Late-onset Tay–Sachs disease, Volume 17, Issue 5. (2017, October 17). doi:10.1136/practneurol-2017-001665

NCCN Guidelines. (2019). Retrieved Oct 8, 2019, from National Comprehensive Cancer Network: [https://www.nccn.org/professionals/physician\\_gls/default.aspx](https://www.nccn.org/professionals/physician_gls/default.aspx)

Preconception and Prenatal Carrier Screening for Genetic Disease More Common in the Ashkenazi Jewish Population and Others With A Family History Of These Disorders. (2019, Aug 1). Retrieved Oct 8, 2019, from UpToDate: [https://www.uptodate.com/contents/preconception-and-prenatal-carrier-screening-for-genetic-disease-more-common-in-the-ashkenazi-jewish-population-and-others-with-a-family-history-of-these-disorders?search=tay%20sachs&source=search\\_result&selectedTitle=1~2](https://www.uptodate.com/contents/preconception-and-prenatal-carrier-screening-for-genetic-disease-more-common-in-the-ashkenazi-jewish-population-and-others-with-a-family-history-of-these-disorders?search=tay%20sachs&source=search_result&selectedTitle=1~2)

Prenatal Diagnosis of Tay-Sachs Disease, MIMB, volume 1885. (2018, December 1). doi:10.1007/978-1-4939-8889-1\_16

Tay - Sachs Disease (TSD) Testing in Individuals of Non–Ashkenazi Jewish Origin. (2014, December 12). Retrieved Oct 8, 2019, from Hayes, Inc.: <https://evidence.hayesinc.com/report/gte.taysachs2351>

Tay-Sachs Disease. (2018, November 30). Retrieved Oct 8, 2019, from DynaMed Plus: <https://www.dynamed.com/condition/tay-sachs-disease#GUID-403E22E0-1B95-4631-A687-EFD512585AFD>

Tay - Sachs disease and Variants - HEXA Gene, ACG: A-0614 (AC). (2019, Feb 11). Retrieved Oct 8, 2019, from MCG: <https://careweb.careguidelines.com/ed23/index.html>

ACOG Practice Bulletin No. 88, December 2007. Invasive prenatal testing for aneuploidy. *Obstetrics and Gynecology* 2007; 110(6):1459-67. DOI: 10.1097/01.AOG.0000291570.63450.44.

ACOG Practice Bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstetrics and Gynecology* 2007; 109(1):217-27.

Tabor A, Alfirovic Z. Update on Procedure-Related Risks for Prenatal Diagnosis Techniques. *Fetal Diagnosis and Therapy* 2009; 27(1):1-7. DOI: 10.1159/000271995.

Odibo AO, Gray DL, Dicke JM, Stamilio DM, Macones GA, Crane JP. Revisiting the fetal loss rate after second-trimester genetic amniocentesis: a single center's 16-year experience. *Obstetrics and Gynecology* 2008; 111(3):589-95. DOI: 10.1097/AOG.0b013e318162eb53.

Ekoukou D, Khuong-Josses MA, Ghibaudo N, Mechali D, Rotten D. Amniocentesis in pregnant HIV-infected patients. Absence of mother-to-child viral transmission in a series of selected patients. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2008; 140(2):212-7. DOI: 10.1016/j.ejogrb.2008.04.004.

Breathnach FM, et al. First- and second-trimester screening: detection of aneuploidies other than Down syndrome. *Obstetrics and Gynecology* 2007; 110(3):651-7. DOI: 10.1097/01.AOG.0000278570.76392.a6.

Bornstein E, Lenchner E, Donnerfeld A, Barnhard Y, Seubert D, Divon MY. Advanced maternal age as a sole indication for genetic amniocentesis; risk-benefit analysis based on a large database reflecting the current common practice. *Journal of Perinatal Medicine* 2008; 37(2):99-102. DOI: 10.1515/JPM.2009.032.

Bornstein E, Lenchner E, Donnerfeld A, Barnhard Y, Seubert D, Divon MY. Advanced maternal age as a sole indication for genetic amniocentesis; risk-benefit analysis based on a large database reflecting the current common practice. *Journal of Perinatal Medicine* 2008; 37(2):99-102. DOI: 10.1515/JPM.2009.032.

Intracytoplasmic sperm injection (ICSI) in 2006: evidence and evolution. *Human Reproduction Update* 2007;13(6):515-26. DOI: 10.1093/humupd/dmm024.

Bethune M. Literature review and suggested protocol for managing ultrasound soft markers for Down syndrome: thickened nuchal fold, echogenic bowel, shortened femur, shortened humerus, pyelectasis and absent or hypoplastic nasal bone. *Australasian Radiology* 2007;51(3):218-25. DOI: 10.1111/j.1440-1673.2007.01713.x.

Breathnach FM, Fleming A, Malone FD. The second trimester genetic sonogram. *American Journal of Medical Genetics. Part C. Seminars in medical genetics* 2007; 145(1):62-72. DOI: 10.1002/ajmg.c.30116.

Aagaard-Tillery KM, et al. Role of second-trimester genetic sonography after Down syndrome screening. *Obstetrics and Gynecology* 2009; 114(6):1189-96. DOI: 10.1097/AOG.0b013e3181c15064

Breathnach FM, Malone FD. Screening for aneuploidy in first and second trimesters: is there an optimal paradigm? *Current Opinion in Obstetrics and Gynecology* 2007;19(2):176-82. DOI: 10.1097/GCO.0b013e3280895e00.

Rosen T, D'Alton ME, Platt LD, Wapner R. First-trimester ultrasound assessment of the nasal bone to screen for aneuploidy. *Obstetrics and Gynecology* 2007; 110(2 Pt 1):399-404. DOI: 10.1097/01.AOG.0000275281.19344.66.

Bethune M. Management options for echogenic intracardiac focus and choroid plexus cysts: a review including Australian Association of Obstetrical and Gynaecological Ultrasonologists consensus statement. *Australasian Radiology* 2007; 51(4):324-9. DOI: 10.1111/j.1440-1673.2007.01716.x

Bianco K, Caughey AB, Shaffer BL, Davis R, Norton ME. History of miscarriage and increased incidence of fetal aneuploidy in subsequent pregnancy. *Obstetrics and Gynecology* 2006; 107(5):1098-102. DOI: 10.1097/01.AOG.0000215560.86673.22.

ACOG Practice Bulletin No. 97: Fetal lung maturity. *Obstetrics and Gynecology* 2008; 112(3):717-26. DOI: 10.1097/AOG.0b013e318188d1c2.

Premature rupture of membranes. *ACOG Practice Bulletin Number 80*:. *Obstetrics and Gynecology* 2007; 109(4):1007-19. DOI: 10.1097/01.AOG.0000263888.69178.1f.

Porreco RP, Heyborne KD, Shapiro H. Amniocentesis in the management of preterm premature rupture of the membranes: a retrospective cohort analysis. *Journal of Maternal-Fetal & Neonatal Medicine* 2008;21(8):573-9. DOI: 10.1080/14767050802178011

Gelb BD, Tartaglia M. Noonan Syndrome with Multiple Lentiginos. 2007 Nov 30 [Updated 2015 May 14]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1383/>

Snape KM, Ruddy D, Zenker M, Wuyts W, Whiteford M, Johnson D, Lam W, Trembath RC (2009). "The spectra of clinical phenotypes in aplasia cutis congenita and terminal transverse limb defects.". *Am J Med Genet A* 149 (8): 1860–1881. doi:10.1002/ajmg.a.32708

### Special Notes: \*

Medical policies can be highly technical and complex and are provided here for informational purposes. These medical policies are intended for use by health care professionals. The medical policies do not constitute medical advice or medical care. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Sentara Health Plan members should discuss the information in the medical policies with their treating health care professionals. Medical technology is constantly evolving, and these medical policies are subject to change without notice, although Sentara Health Plan will notify providers as required in advance of changes that could have a negative impact on benefits.

Services mean both medical and behavioral health (mental health) services and supplies unless We specifically tell You otherwise. We do not cover any services that are not listed in the Covered Services section unless required to be covered under state or federal laws and regulations. We do not cover any services that are not Medically Necessary. We sometimes give examples of specific services that are not covered but that does not mean that other similar services are covered. Some services are covered only if We authorize them. When We say You or Your We mean You and any of Your family members covered under the Plan. Call Member Services if You have questions.

**Medical Director approval is required for Extended Mutation Panels.**

### Keywords:

22q11.2 deletion syndrome, Adrenoleukodystrophy DNA Sequencing, Alpha Thalassemia, Beta Thalassemia and Sickle Cell, Analysis, Ashkenazi Jewish, Autosomal recessive or autosomal dominant centronuclear myopathy, Bloom syndrome, Canavan disease, Cell-free fetal DNA-based, chromosomal microarray analysis, Congenital muscular dystrophy, Cystic Fibrosis, Deficiency, Familial hyperinsulinism, Dihydrolipoamide dehydrogenase, disease carrier, Disease-causing mutation, Duchene Muscular Dystrophy, Duplicative, Echogenic bowel, Ellis-van Creveld syndrome, Emery-Dreifuss muscular dystrophy, Facioscapulohumeral muscular dystrophy, Familial Dysautonomia, Familial HEMOPHAGOCYTIC, Familial Hemophagocytic Lymphohistiocytosis, Familial hyperinsulinism, Familial Mediterranean Fever, Familial Myotonic Dystrophy, Fanconi anemia group, Fascioscapulohumeral Muscular Dystrophy, Gaucher's disease, Gene Sequencing, Genetic testing, Glycogen storage disease, Hemophilia A or B, Hereditary sensory and autonomic neuropathies, Huntington's Disease, Hybridization, Inheritest Universal screening, Leopard syndrome, Limb girdle muscular dystrophy, Lissencephaly, LYMPHOHISTIOCYTOSIS, Maple syrup urine disease, Marfan Syndrome, MTHFR, Mucopolysaccharidosis Type IV, Mucopolysaccharidosis, Myotonic Dystrophy, Nemaline myopathy, Nieman Pick Disease, Nonsyndromic Deafness, Noonan syndrome, Paraganglioma-Pheochromocytoma Syndromes, Pontocerebellar Hypoplasia, Pre-conception, pre-implantation, Prenatal, Primary Ciliary Dyskinesia, Repeat, Retinoblastoma, Riley-Day syndrome, single nucleotide polymorphism (SNP), Spinal Muscular Atrophy, Syndrome testing, Tay-Sach's disease, Ullrich Muscular Dystrophy COL6A2, Usher syndrome, VLDLR Associated Cerebellar Hypoplasia, von Willebrand factor, Walker-Warburg syndrome, Whole Exome Sequencing (WES), Wiskott-Aldrich syndrome, X-linked centronuclear myopathy, X-linked Lymphoproliferative Syndromes