Genetic testing: prenatal diagnosis (via amniocentesis, CVS, or PUBS) and pregnancy loss

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

Administrative Process

Prior authorization is required for genetic testing for exome sequencing and Noonan spectrum disorders/RASopathies for prenatal diagnosis.

Prior authorization is not required for all other tests addressed on this policy.

Note: This policy does not address the use of conventional chromosome analysis, CMA, and FISH for preimplantation genetic testing or the evaluation of suspected chromosome abnormalities in the postnatal period.

Policy Reference Table

If available, codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes
Chromosomal Microarray Analysis (CMA) for Prenatal Diagnosis	Reveal SNP Microarray - Prenatal (Integrated Genetics)	81228, 81229, 81265, 88235	O26.2, O28, Q00-Q99, Z14.8
	Prenatal Whole Genome Chromosomal Microarray (GeneDx)		
	IriSight CNV Analysis (Variantyx)	0469U	
Conventional Karyotype Analysis for Prenatal Diagnosis	Chromosome Analysis, Chorionic Villus Sample (Quest Diagnostics)	88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291	O26.2, O28, Q00-Q99, Z14.8
	Chromosome Analysis, Amniotic Fluid (Quest Diagnostics)		
Chromosomal Microarray Analysis (CMA) for Pregnancy Loss	SNP Microarray-Products of Conception (POC)/Tissue (Reveal) (Labcorp)	81228, 81229, 81265, 88235	O03, Z37
	Chromosomal Microarray, POC, ClariSure Oligo-SNP (Quest Diagnostics)		
Conventional Karyotype Analysis for Pregnancy Loss	Chromosome Analysis, POC, Tissue (Bioreference Labs)	88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291	O03, Z37
	Chromosome Analysis, Products of Conception (POC) (ARUP Laboratories)		
Prenatal Diagnosis for Noonan Spectrum Disorders/RASopathies	Prenatal Noonan Spectrum Disorders Panel (GeneDx)	81404, 81405, 81406, 81407, 81479, 81442, 81265, 88235	O28.3, O35.8XX0
	Prenatal Noonan Syndrome (Integrated Genetics)		
Prenatal Diagnosis for Skeletal Dysplasias	Prenatal Skeletal Dysplasia Panel (GeneDx)	81404, 81405, 81408, 81479, 81265, 88235	O35.8XX0, O28.3
	Skeletal Dysplasia Core NGS Panel (Connective Tissue Gene Tests)		
Prenatal Diagnosis via Exome Sequencing	XomeDx Prenatal-Comprehensive (GeneDx)	81415, 81416, 81265, 88235	O35.8XX0, O28.3

	Prenatal Exome Sequencing (Greenwood Genetic Center - Molecular Diagnostic Laboratory)		
Prenatal Diagnosis via Genome Sequencing	Prenatal Whole Genome Sequencing	81425, 81426, 81427, 88235, 81265	O35.8XX0, O28.3
	IriSight Prenatal Analysis (Variantyx)	0335U, 0336U	

Coverage

Chromosomal Microarray Analysis (CMA) for Prenatal Diagnosis

1. Chromosome microarray analysis for prenatal diagnosis via amniocentesis, CVS, or PUBS may be considered **medically necessary** when:
   - A. The member has received counseling regarding the benefits and limitations of prenatal screening and diagnostic testing (including chromosome microarray via amniocentesis, CVS or PUBS) for fetal chromosome abnormalities.
2. Chromosome microarray analysis for prenatal diagnosis via amniocentesis, CVS, or PUBS is considered **investigational** for all other indications.

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Conventional Karyotype Analysis for Prenatal Diagnosis

1. Conventional karyotype analysis for prenatal diagnosis via amniocentesis, CVS, or PUBS may be considered **medically necessary** when:
   - A. The member has received counseling regarding the benefits and limitations of prenatal screening and diagnostic testing (including karyotyping via amniocentesis, CVS or PUBS) for fetal chromosome abnormalities.
2. Conventional karyotype analysis for prenatal diagnosis via amniocentesis, CVS, or PUBS is considered **investigational** for all other indications.

Note: Current guidelines recommend that chromosome microarray analysis (CMA) be performed as the primary test for patients undergoing prenatal diagnosis when the fetus has one or more major structural abnormalities identified by ultrasound examination.

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Chromosomal Microarray Analysis (CMA) for Pregnancy Loss

1. Chromosomal microarray analysis on products of conception (POC) may be considered **medically necessary** as an alternative to conventional karyotype analysis when:
   - A. The member meets one of the following:
     - i. The member has history of recurrent pregnancy loss, **or**
     - ii. The member has a pregnancy loss at or greater than 20 weeks of gestation (i.e., IUFD or stillbirth), **and**
   - B. The member has received counseling regarding the benefits and limitations of chromosome microarray analysis on products of conception.
2. Chromosome microarray analysis on products of conception (POC) is considered **investigational** for all other indications.

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Conventional Karyotype Analysis for Pregnancy Loss

1. Conventional karyotype analysis on products of conception (POC) may be considered **medically necessary** when:
   - A. The member has a history recurrent pregnancy loss.
2. Conventional karyotype analysis on products of conception (POC) is considered **investigational** for all other indications.

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Prenatal Diagnosis for Noonan Spectrum Disorders/RASopathies

1. Prenatal diagnosis for Noonan spectrum disorders/RASopathies, via amniocentesis, CVS, or PUBS, using a Noonan syndrome panel may be considered **medically necessary** when:
   - A. The member's current pregnancy has had a normal karyotype and/or microarray, **and**
   - B. The member meets one of the following:
     - i. The member's current pregnancy has an ultrasound finding of increased nuchal translucency or cystic hygroma of at least 5.0 mm in the first trimester, **or**
     - ii. The member's current pregnancy has both of the following:
       - a) An increased nuchal translucency of at least 3.0mm, **and**
       - b) One of the following ultrasound findings:
         - (a) Distended jugular lymph sacs (JLS), **or**
         - (b) Hydrops fetalis, **or**

(c) Polyhydramnios, **or**
(d) Pleural effusion, **or**
(e) Cardiac defects (e.g., pulmonary valve stenosis, atrioventricular septal defect, coarctation of the aorta, hypertrophic cardiomyopathy, atrial septal defect, etc.).

2. Prenatal diagnosis for Noonan spectrum disorders/RASopathies, via amniocentesis, CVS, or PUBS, using a Noonan syndrome panel is considered **investigational** for all other indications.

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Prenatal Diagnosis for Skeletal Dysplasias

1. Prenatal diagnosis for skeletal dysplasias, via amniocentesis, CVS, or PUBS, using a skeletal dysplasia panel may be considered **medically necessary** when:
   A. The member's current pregnancy has any of the following ultrasound findings:
      i. Long bones less than 5th percentile, **or**
      ii. Poor mineralization of the calvarium, **or**
      iii. Fractures of long bones (particularly femora), **or**
      iv. Bent/bowed bones, **or**
      v. Poor mineralization of the vertebrae, **or**
      vi. Absent/hypoplastic scapula, **or**
      vii. Equinovarus, **and**
   B. The panel being ordered includes, at a minimum, the following genes: *COL1A1, COL1A2, COL2A1, FGFR3*.
2. Prenatal diagnosis for skeletal dysplasias, via amniocentesis, CVS, or PUBS, using a skeletal dysplasia panel is considered **investigational** for all other indications.

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Prenatal Diagnosis via Exome Sequencing

1. Prenatal diagnosis, via amniocentesis, CVS, or PUBS, using exome sequencing may be considered **medically necessary** when:
   A. The member's current pregnancy has had a karyotype and/or microarray performed and the results were negative/normal, **and**
   B. Alternate etiologies have been considered and ruled out when possible (examples: environmental exposure, injury, infection, maternal condition), **and**
   C. The member's current pregnancy has either of the following:
      i. Non-immune hydrops fetalis, **or**
      ii. Two or more major malformations on ultrasound, which are affecting different organ systems
2. Prenatal diagnosis, via amniocentesis, CVS, or PUBS, using exome sequencing is considered **investigational** for all other indications.

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Prenatal Diagnosis via Genome Sequencing

1. Prenatal diagnosis, via amniocentesis, CVS, or PUBS, using genome sequencing is considered **investigational**.

Definitions

1. **Major malformations** are structural defects that have a significant effect on function or appearance. They may be lethal or associated with possible survival with severe or moderate immediate or long-term morbidity. Examples by organ system include:
   - Genitourinary: renal agenesis (unilateral or bilateral), hypoplastic/cystic kidney
   - Cardiovascular: complex heart malformations (such as pulmonary valve stenosis, tetralogy of fallot, transposition of the great arteries, coarctation of the aorta, hypoplastic left heart syndrome
   - Musculoskeletal: osteochondrodysplasia/osteogenesis imperfecta, clubfoot, craniosynostosis, fetal growth restriction/intrauterine growth restriction (IUGR)
   - Central nervous system: anencephaly, hydrocephalus, myelomeningocele
   - Body wall: omphalocele/gastroschisis
   - Respiratory: cystic adenomatoid lung malformation
2. **Amniocentesis** is a procedure in which a sample of amniotic fluid is removed from the uterus for prenatal diagnostic testing.
3. **Chorionic Villi Sampling (CVS)** is a procedure where a sample of chorionic villi is removed from the placenta for prenatal diagnostic testing.
4. **Percutaneous Umbilical Cord Blood Sampling (PUBS)** is a procedure where a sample of fetal blood is extracted from the vein in the umbilical cord.

5. **Recurrent pregnancy loss (RPL)** is defined as having two or more failed clinical pregnancies, including a current loss if applicable

Products

This information is for most, but not all, HealthPartners plans. Please read your plan documents to see if your plan has limits or will not cover some items. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage. These coverage criteria do not apply to Medicare Products. For more information regarding Medicare coverage criteria or for a copy of a Medicare coverage policy, contact Member Services at 952-883-7272 or 1-877-778-8384.

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References

1. Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril. 2012;98(5):1103-1111. doi:10.1016/j.fertnstert.2012.06.048
2. Committee on Genetics and the Society for Maternal-Fetal Medicine. Committee Opinion No.682: Microarrays and Next-Generation Sequencing Technology: The Use of Advanced Genetic Diagnostic Tools in Obstetrics and Gynecology. Obstet Gynecol. 2016;128(6):e262-e268. Reaffirmed 2020 and 2023. doi:10.1097/AOG.0000000000001817
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal–Fetal Medicine. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. Obstet Gynecol. 2016 (Reaffirmed 2020) 127(5):e108-e122. doi:10.1097/AOG.0000000000001405
4. Krakow D, Lachman RS, Rimoin DL. Guidelines for the prenatal diagnosis of fetal skeletal dysplasias. Genet Med. 2009;11(2):127-133. doi:10.1097/GIM.0b013e3181971ccb
5. Monaghan KG, Leach NT, Pekarek D, Prasad P, Rose NC; ACMG Professional Practice and Guidelines Committee. The use of fetal exome sequencing in prenatal diagnosis: a points to consider document of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020;22(4):675-680. doi:10.1038/s41436-019-0731-7
6. Stuurman KE, Joosten M, van der Burgt I, et al. Prenatal ultrasound findings of rasopathies in a cohort of 424 fetuses: update on genetic testing in the NGS era. J Med Genet. 2019;56(10):654-661. doi:10.1136/jmedgenet-2018-105746
7. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstet Gynecol. 2020;136(4):e48-e69. doi:10.1097/AOG.0000000000004084
8. Roberts AE. Noonan Syndrome. 2001 Nov 15 [Updated 2022 Feb 17]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1124/
9. Papas RS, Kutteh WH. Genetic testing for aneuploidy in patients who have had multiple miscarriages: a review of current literature. Appl Clin Genet. 2021;14:321-329.
10. Zhou J, Yang Z, Sun J, et al. Whole Genome Sequencing in the Evaluation of Fetal Structural Anomalies: A Parallel Test with Chromosomal Microarray Plus Whole Exome Sequencing. *Genes*. 2021; 12(3):376. https://doi.org/10.3390/genes12030376
11. Scocchia, A., Kangas-Kontio, T., Irving, M. et al. Diagnostic utility of next-generation sequencing-based panel testing in 543 patients with suspected skeletal dysplasia. Orphanet J Rare Dis 16, 412 (2021). https://doi.org/10.1186/s13023-021-02025-7
12. Al-Kouatly HB, Shivashankar K, Mossayebi MH, et al. Diagnostic yield from prenatal exome sequencing for non-immune hydrops fetalis: A systematic review and meta-analysis. Clin Genet. 2023;103(5):503-512. doi:10.1111/cge.14309