

Dean Health Plan Coverage Policy

Policy Name: Genetic Testing: Prenatal Diagnosis (Via Amniocentesis, CVS, Or PUBS) and Pregnancy Loss MP9576

Effective Date: January 01, 2025

Important Information – Please Read Before Using This Policy

These services may or may not be covered by Dean Health Plan. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Dean Health Plan Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this medical policy see Provider Communications for additional information.

<https://deancare.com/Providers/Provider-communications>

Dean Health Plan medical policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

OVERVIEW

Prenatal diagnostic testing may be used to identify genetic conditions in fetuses at an increased risk based on prenatal screening or for women who choose to undergo diagnostic testing due to other risk factors, such as abnormal ultrasound findings, previous pregnancy with aneuploidy, etc. Prenatal diagnostic testing for genetic disorders is performed on fetal cells derived from amniotic fluid, and/or [percutaneous umbilical blood sampling \(PUBS\)](#) (cordocentesis) or from placental cells via [chorionic villus sampling \(CVS\)](#). Genetic testing techniques include conventional chromosome analysis, chromosome fluorescence in situ hybridization (FISH), chromosomal microarray analysis (CMA), targeted or Sanger sequencing, and next-generation sequencing (NGS). Exome and genome sequencing are also emerging as new prenatal diagnostic tools.

Genetic testing may also be used in an attempt to determine the cause of isolated or [recurrent pregnancy loss](#), including miscarriages, intrauterine fetal demise (IUFD), and stillbirth. The evaluation of both recurrent and isolated miscarriages and IUFD or stillbirth may involve genetic testing of the products of conception (POC) and/or testing of fetal/placental cells from amniotic fluid, CVS, or PUBS if available. Such testing of POC has typically been carried out through cell culture and karyotyping of cells in metaphase. However, the analysis of fetal or placental tissue has been inhibited by the following limitations: the need for fresh tissue, the potential for cell culture failure, and the potential for maternal cell contamination. Potential benefits of identifying a genetic abnormality in a miscarriage or IUFD include reducing emotional distress for families, eliminating the need for additional testing to assess for causes of pregnancy loss, and assisting in reproductive decision making for future pregnancies.

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The decision to elect a prenatal diagnostic test and/or genetic testing following pregnancy loss should be made jointly by the mother and/or parents and the treating clinician. Genetic counseling, including facilitation of decision making, is strongly recommended.

In most cases, prenatal genetic testing for single gene disorders using molecular genetic testing requires knowledge of the familial genetic variant which has been identified in a family member (e.g., biological mother, biological father, and/or sibling).

POLICY REFERENCE TABLE

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

Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
Chromosomal Microarray Analysis (CMA) for Prenatal Diagnosis	Reveal SNP Microarray - Prenatal (Integrated Genetics)	81228, 81229, 81265, 88235	O26.2, O28, Q00-Q99, Z14.8	3, 7
	Prenatal Whole Genome Chromosomal Microarray (Ge986neDx)	0469U		
	IriSight CNV Analysis (Variantyx)			
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	7
	Chromosome Analysis, Amniotic Fluid (Quest Diagnostics)			
Chromosomal Microarray Analysis	SNP Microarray-Products of Conception (POC)/Tissue (Reveal) (Labcorp)	81228, 81229, 81265, 88235	O03, Z37	1, 2, 9

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Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
(CMA) for Pregnancy Loss	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	1
	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	6, 7, 8
	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	4, 11
	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	5, 12
	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	2, 10
	IriSight Prenatal Analysis (Variantyx)	0335U, 0336U		

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OTHER RELATED POLICIES

This policy document provides coverage criteria for prenatal or pregnancy loss diagnostic testing, and does not address the use of conventional chromosome analysis, CMA, or FISH for preimplantation genetic testing or the evaluation of suspected chromosome abnormalities in the postnatal period. Please refer to:

- **Genetic Testing: Prenatal Cell-free DNA Testing** for coverage criteria related to prenatal cell-free DNA screening tests.
- **Genetic Testing: Prenatal and Preconception Carrier Screening** for coverage criteria related to carrier screening for genetic disorders.
- **Genetic Testing: Preimplantation Genetic Testing** for coverage criteria related to genetic testing of embryos prior to in vitro fertilization.
- **Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability and Developmental Delay** for coverage criteria related to suspected chromosome abnormalities in the postnatal period.
- **Genetic Testing: General Approach to Genetic and Molecular Testing** for coverage criteria related to prenatal diagnostic or pregnancy loss genetic testing that is not specifically discussed in this or other non-general policies, including known familial variant testing.

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COVERAGE CRITERIA

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*

CHROMOSOMAL MICROARRAY ANALYSIS (CMA) FOR PRENATAL DIAGNOSIS

- I. Chromosome microarray analysis (81228, 81229, 81265, 88235, 0469U) 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.
- II. Chromosome microarray analysis (81228, 81229, 81265, 88235, 0469U) 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

- I. Conventional karyotype analysis (88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291) for prenatal diagnosis via [amniocentesis, CVS, or PUBS](#) may be considered **medically necessary** when:

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- 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.
- II. Conventional karyotype analysis (88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291) 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 (see [Background and Rationale](#) for more information).

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CHROMOSOMAL MICROARRAY ANALYSIS (CMA) FOR PREGNANCY LOSS

- I. Chromosomal microarray analysis (81228, 81229, 81265, 88235) 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:
 - 1. The member has a history of [recurrent pregnancy loss](#), **OR**
 - 2. 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.
- II. Chromosome microarray analysis (81228, 81229, 81265, 88235) on products of conception (POC) is considered **investigational** for all other indications.

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CONVENTIONAL KARYOTYPE ANALYSIS FOR PREGNANCY LOSS

- I. Conventional karyotype analysis (88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291) on products of conception (POC) may be considered **medically necessary** when:
 - A. The member has a history of [recurrent pregnancy loss](#).
- II. Conventional karyotype analysis (88235, 88261, 88262, 88263, 88264, 88267, 88269, 88280, 88291) on products of conception (POC) is considered **investigational** for all other indications.

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PRENATAL DIAGNOSIS FOR NOONAN SPECTRUM DISORDERS/RASOPATHIES

- I. Prenatal diagnosis for Noonan spectrum disorders/RASopathies, via amniocentesis, CVS, or PUBS, using a Noonan syndrome panel (81404, 81405, 81406, 81407, 81479, 81442, 81265, 88235) may be considered **medically necessary** when:
 - A. The member's current pregnancy has had a normal karyotype and/or microarray, **AND**

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B. The member meets one of the following:

1. 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**
2. 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:
 - (1) Distended jugular lymph sacs (JLS), **OR**
 - (2) Hydrops fetalis, **OR**
 - (3) Polyhydramnios, **OR**
 - (4) Pleural effusion, **OR**
 - (5) Cardiac defects (e.g., pulmonary valve stenosis, atrioventricular septal defect, coarctation of the aorta, hypertrophic cardiomyopathy, atrial septal defect, etc.).

- II. Prenatal diagnosis for Noonan spectrum disorders/RASopathies, via [amniocentesis, CVS, or PUBS](#), using a Noonan syndrome panel (81404, 81405, 81406, 81407, 81479, 81442, 81265, 88235) is considered **investigational** for all other indications.

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PRENATAL DIAGNOSIS FOR SKELETAL DYSPLASIAS

- I. Prenatal diagnosis for skeletal dysplasias, via [amniocentesis, CVS, or PUBS](#), using a skeletal dysplasia panel (81404, 81405, 81408, 81479, 81265, 88235) may be considered **medically necessary** when:

A. The member's current pregnancy has any of the following ultrasound findings:

1. Long bones less than 5th percentile, **OR**
2. Poor mineralization of the calvarium, **OR**
3. Fractures of long bones (particularly femora), **OR**
4. Bent/bowed bones, **OR**
5. Poor mineralization of the vertebrae, **OR**
6. Absent/hypoplastic scapula, **OR**
7. Equinovarus, **AND**

B. The panel being ordered includes, at a minimum, the following genes: *COL1A1*, *COL1A2*, *COL2A1*, *FGFR3*.

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- II. Prenatal diagnosis for skeletal dysplasias, via [amniocentesis, CVS, or PUBS](#), using a skeletal dysplasia panel (81404, 81405, 81408, 81479, 81265, 88235) is considered **investigational** for all other indications.

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PRENATAL DIAGNOSIS VIA EXOME SEQUENCING

- I. Prenatal diagnosis, via [amniocentesis, CVS, or PUBS](#), using exome sequencing (81415, 81416, 81265, 88235) 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:
 - 1. Non-immune hydrops fetalis, **OR**
 - 2. Two or more [major malformations](#) on ultrasound, which are affecting different organ systems.
- II. Prenatal diagnosis, via [amniocentesis, CVS, or PUBS](#), using exome sequencing (81415, 81416, 81265, 88235) is considered **investigational** for all other indications.

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PRENATAL DIAGNOSIS VIA GENOME SEQUENCING

- I. Prenatal diagnosis, via [amniocentesis, CVS, or PUBS](#), using genome sequencing (81425, 81426, 81427, 88235, 81265, 0335U, 0336U) is considered **investigational**.

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

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

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- 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

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BACKGROUND AND RATIONALE

Chromosomal Microarray Analysis (CMA) for Prenatal Diagnosis

American College of Obstetricians and Gynecologists (ACOG)

An ACOG practice bulletin (#162, 2016, reaffirmed 2020) states the following:

- Chromosomal aberrations that are smaller than the resolution of conventional karyotype also can result in phenotypic anomalies; these copy number variants can be detected in the fetus using chromosomal microarray analysis. When structural abnormalities are detected by prenatal ultrasound examination, chromosomal microarray will identify clinically significant chromosomal abnormalities in approximately 6% of the fetuses that have a normal karyotype. For this reason, chromosomal microarray analysis should be recommended as the primary test (replacing conventional karyotype) for patients undergoing prenatal diagnosis for the indication of a fetal structural abnormality detected by ultrasound examination. (p. e109)
- Chromosomal microarray analysis has been found to detect a pathogenic (or likely pathogenic) copy number variant in approximately 1.7% of patients with a normal ultrasound examination and a normal karyotype, and it is recommended that chromosomal microarray analysis be made available to any patient choosing to undergo invasive diagnostic testing. (p. e.110)

ACOG practice bulletin #226 (2020) states the following regarding counseling patients: "Each patient should be counseled in each pregnancy about options for testing for fetal chromosomal abnormalities. It is important that obstetric care professionals be prepared to discuss not only the risk of fetal chromosomal abnormalities but also the relative benefits and limitations of the available screening and diagnostic tests." (p. 859)

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Conventional Karyotype Analysis for Prenatal Diagnosis

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM)

The ACOG and SMFM practice bulletin (#226, 2020) states the following:

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"Prenatal genetic screening (serum screening with or without nuchal translucency [NT] ultrasound or cell-free DNA screening) and diagnostic testing (chorionic villus sampling [CVS] or amniocentesis) options should be discussed and offered to all pregnant women regardless of maternal age or risk of chromosomal abnormality." (p. 862)

"Each patient should be counseled in each pregnancy about options for testing for fetal chromosomal abnormalities. It is important that obstetric care professionals be prepared to discuss not only the risk of fetal chromosomal abnormalities but also the relative benefits and limitations of the available screening and diagnostic tests." (p. 859)

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Chromosomal Microarray Analysis (CMA) for Pregnancy Loss

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM)

The ACOG and SMFM practice bulletin (#682) supports the following evaluation for pregnancy loss in their 2016 statement (reaffirmed 2020 and 2023):

"Chromosomal microarray analysis of fetal tissue (i.e., amniotic fluid, placenta, or products of conception) is recommended in the evaluation of intrauterine fetal death or stillbirth when further cytogenetic analysis is desired because of the test's increased likelihood of obtaining results and improved detection of causative abnormalities." (p. e263)

American Society for Reproductive Medicine (ASRM)

The American Society for Reproductive Medicine (2012) issued an opinion on the evaluation and treatment of recurrent pregnancy loss. The statement drew multiple conclusions, one of which states: "Evaluation of recurrent pregnancy loss can proceed after 2 consecutive clinical pregnancy losses." (p. 1108)

Papas and Kutteh (2021)

A review published in the *Application of Clinical Genetics* in 2021 by Papas and Kutteh recommends that genetic testing on products of conception should be performed after the second and subsequent pregnancy loss. Chromosome microarray is the preferred testing method. (p. 321)

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Conventional Karyotype Analysis for Pregnancy Loss

American Society for Reproductive Medicine (ASRM)

According to the ASRM's 2012 statement, recurrent pregnancy loss (RPL) is defined as a distinct disorder defined by two or more failed clinical pregnancies. Evaluation of RPL can proceed after two consecutive clinical pregnancy losses, which may include karyotypic analysis of products of conception (p. 1103 and 1108) For the purposes of this committee, the ASRM defines clinical pregnancy as "...documented by ultrasonography or histopathological examination." (p. 1103)

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Prenatal Diagnosis for Noonan Spectrum Disorders/RASopathies

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Stuurman KE, Joosten M, van der Burgt I, et al, 2019

This cohort study of ultrasound findings of 424 fetuses in the Netherlands concluded with the recommendation for “testing of fetuses with solely an increased NT after chromosomal abnormalities have been excluded when the NT is greater than or equal to 5.0 mm. We also recommend testing when the NT is greater than or equal to 3.5 mm and at least one of the following anomalies is present: distended jugular lymph sacs (JLS), hydrops fetalis, polyhydramnios, pleural effusion and cardiac defects.” (p. 660)

“In general, an NGS panel of known rasopathy genes should be used when a rasopathy is suspected. Although we did not find pathogenic variants in every gene in the panel, in all genes, a prenatal phenotype has been documented in literature. Therefore, a smaller panel is not advisable. However, in countries where an extensive panel is not available, testing for only *PTPN11* gene would catch at least 50% of the fetuses with a rasopathy.” (p. 661)

American College of Obstetricians and Gynecologists

The ACOG and SMFM practice bulletin (#226, 2020) defines an enlarged nuchal translucency (NT) as 3.0 mm or more or above the 99th percentile for the crown–rump length”. (p. e53)

GeneReviews: Noonan Syndrome

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online. The clinical summary for Noonan Syndrome gives the following prenatal features (Roberts, 2022):

- Polyhydramnios
- Lymphatic dysplasia including increased distended jugular lymphatic sacs, nuchal translucency, cystic hygroma, pleural effusion, and ascites
- Relative macrocephaly
- Cardiac and renal anomalies

The author points out that 3%-15% of chromosomally normal fetuses with increased nuchal translucency have *PTPN11*-associated Noonan syndrome.

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Prenatal Diagnosis for Skeletal Dysplasias

Krakow et al 2009

A guideline for prenatal diagnosis of fetal skeletal dysplasias (Krakow, Lachman, Rimoin, 2009) recommends the follow criteria:

- Fetuses with long bone measurements at or less than the 5th centile or greater than 3 SD below the mean should be evaluated in a center with expertise in the recognition of skeletal dysplasias. (p. 5)
- In addition, close attention should be paid to the shape and mineralization pattern of the fetal calvarium and fetal skeleton (poor or ectopic mineralization). Determining the elements of the skeleton that are abnormal, coupled with the findings of mineralization and shape of the bones can aid in diagnosis. (p. 3)

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The guideline also lists several other common abnormal ultrasound findings in Table 2, including fractures of long bones (primarily femora), poor mineralization of the vertebrae, bent/bowed legs, and absent/hypoplastic scapula, as additional ultrasound findings that would prompt evaluation. (p. 10)

Scocchia, et al.

A 2021 study of the clinical utility of multigene panel testing for an unselected population of individuals with suspected skeletal dysplasia demonstrated a high diagnostic yield in prenatal cases. (p. 1)

A molecular diagnosis was established in 42% of patients (228/543). Diagnostic variants were identified in 71 genes, with variation in nearly half of these genes contributing to a molecular diagnosis for a single patient in this cohort. Overall, the most common genes in which molecular diagnoses were identified included: *COL2A1* associated with type II collagenopathies; *FGFR3* associated with achondroplasia, thanatophoric dysplasia, hypochondroplasia, and other conditions such as FGFR-related craniosynostoses; and *COL1A1* or *COL1A2*, associated with osteogenesis imperfecta. Together, these four genes accounted for over one third of all molecular diagnoses across the cohort. (p. 2-3)

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Prenatal Diagnosis via Exome Sequencing

American College of Medical Genetics and Genomics (ACMG)

ACMG issued a statement on the use of fetal exome sequencing in prenatal diagnosis (2020) that included the following points to consider:

- “Exome sequencing may be considered for a fetus with ultrasound anomalies when standard CMA and karyotype analysis have failed to yield a definitive diagnosis. If a specific diagnosis is suspected, molecular testing for the suggested disorder (with single-gene test or gene panel) should be the initial test. At the present time, there are no data supporting the clinical use for ES for other reproductive indications, such as the identification of sonographic markers suggestive of aneuploidy or a history of recurrent unexplained pregnancy loss.” (p. 676)
- “Pretest counseling is ideally provided by a genetics professional during which the types of variants that may be returned in a laboratory report for all tested family members would be reviewed.” (p. 676)
- “With the use of prenatal ES, the turnaround time has to be rapid to maintain all aspects of reproductive choice. A rapid turnaround time has been demonstrated in the postnatal setting for critical genetic diagnoses in a pediatric and neonatal setting. Laboratories offering prenatal ES should have clearly defined turnaround times for this time-sensitive test.” (p. 677)
- “Post-test counseling is recommended, regardless of the test result. It should be provided by individuals with relevant expertise, preferably a genetics professional.” (p. 678)
- The statement also indicates that the detection rate of fetal anomalies is proportional to the severity of phenotype, with a range of 6% for fetuses with a single anomaly to 35% of fetuses with more than two anomalies. (p. 676)

Al-Kouatly, et al 2022

“We performed a systematic literature review and meta-analysis focusing specifically on ES in cases of NIHF to determine the contribution of monogenic etiologies.” (p.504)

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“In our meta-analysis, greater than one-third (37%) of cases of NIHF with negative clinical workup for anemia, infections, and chromosomal disorders have a monogenic disorder detectable by ES providing clarification of etiological category (e.g., syndromic, neuromuscular, metabolic, etc.) and inheritance pattern (e.g., autosomal dominant de novo, autosomal dominant inherited, autosomal recessive, or X-linked).” (p. 507)

“ES should be considered in the diagnostic workup of NIHF with and without associated ultrasound findings regardless of history of recurrence or consanguinity.” (p. 503-504)

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Prenatal Diagnosis Via Genome Sequencing

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM)

ACOG and SMFM (2016, reaffirmed in 2020 and 2023) issued a committee opinion No. 682, which included the following conclusions and recommendations for the use of chromosomal microarray testing and next-generation sequencing in prenatal diagnosis. *Note that while whole exome sequencing is addressed in this opinion, whole genome sequencing is not yet recommended:*

“Whole-exome sequencing also is a broad molecular diagnostic approach to identify the etiology for fetal abnormalities, and whole-exome sequencing of fetal DNA obtained by amniocentesis, chorionic villi, or umbilical cord blood is being offered on a research basis in some laboratories and for specific clinical indications in other laboratories. However, the routine use of whole-genome or whole-exome sequencing for prenatal diagnosis is not recommended outside of the context of clinical trials until sufficient peer-reviewed data and validation studies are published.” (p. 4)

Zhou J, et al. 2021

An article by Zhou, et al prospectively evaluated the clinical utility of whole genome sequencing (WGS) compared with standard chromosome microarray (CMA) in fetuses with structural anomalies. WGS was found to have a diagnostic rate of 19.8%, and was able to provide additional clinical information, such as a balanced translocation. “The article concludes by saying that “with a rapid TAT, good diagnostic yield, and less DNA required, WGS could be an alternative test in lieu of two separate analyses as it has an equivalent diagnostic yield to that of CMA plus WES and provides comprehensive detection of various genomic variants in fetuses with structural or growth anomalies. However, more prospective studies with larger cohorts and further evaluation are warranted to demonstrate the value of WGS in prenatal diagnosis.” (p. 12)

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

Dean Health Plan Coverage Policy

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